ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 1
January 1980
Pages 1–78

Reaction Paths on Multidimensional Energy Hypersurfaces[**]

By Klaus Müller[*]

Theoretical investigation of a chemical reaction requires detailed knowledge of the potential energy of the molecular system. As a first step in such a study, minimum-energy reaction paths have to be mapped on a generally multidimensional molecular potential surface. Even at this stage problems are encountered that have only recently been solved satisfactorily. The difficulties involved and various ways to handle them are discussed in connection with a two-parametric model potential. Three chemical reactions examined illustrate the usefulness of such theoretical investigations as well as their current limitations.

1. Introduction

A chemical reaction is conveniently discussed in terms of a reaction energy profile covering aspects of mechanism, structure, and energy[1]. Figure 1 shows such a profile for the simplest case, the one-step transformation of a reactant to a product. According to *Eyring* and *Polanyi*[2], we imagine the molecular system to go from the energy minimum of the reactant state *via* a transition state (a saddle point corresponding to an energy maximum along the reaction path) to the energy minimum of the product state. The reaction coordinate includes all the structural changes that characterize the chemical transformation. Figure 1 is a one-dimensional representation of an inherently multidimensional problem. In most cases, therefore, the reaction coordinate is extremely complex and can hardly be given in analytical terms. As regards the energy, we are primarily concerned with the free enthalpy, which, however, is related to the potential energy of the molecular system by a sequence of well-defined logical steps[3]. A more or less satisfactory potential energy can be obtained by means of theoretical models, *e.g.*, quantum-chemical computational procedures. In principal, there are no restrictions on a theoretical study. The potential energy of a molecular system can be evaluated at any point along the reaction path. By contrast, the experimental situation is less

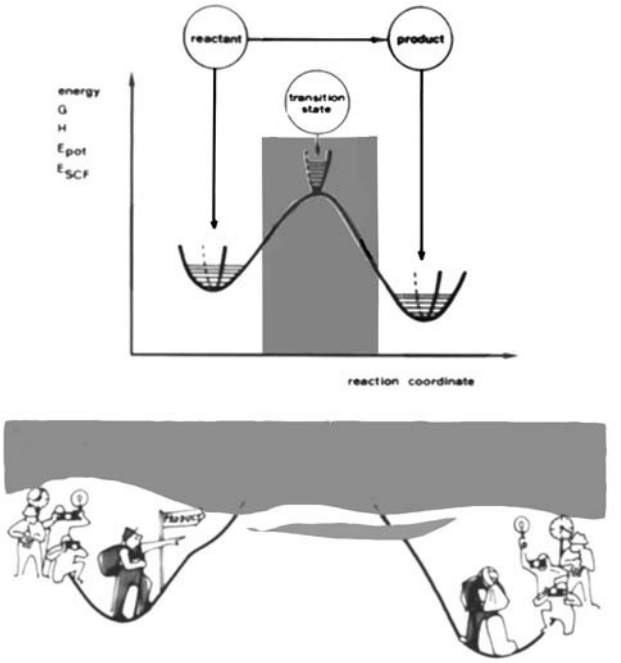


Fig. 1. Reaction energy profile for a one-step chemical transformation.

[*] Priv.-Doz. Dr. K. Müller
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
Universitätstrasse 16, CH-8092 Zürich (Switzerland)

[**] Based on an inaugural lecture at ETH Zürich, June 14, 1979.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0101-0001 $ 02.50/0*

straightforward. The transition state as well as the region around it are generally not amenable to direct experimental observation. Instead, we have to resort to recording the properties and behavior of the molecular system in its initial and final states and to measuring the progress of transformation from reactant to product in order to guess probable events in the gray area of a chemical reaction (cf. Figure 1).

Nevertheless, various techniques are nowadays available that provide experimental access to this gray area. Some of them are summarized in Figure 2. First of all, there are classical kinetic experiments, such as the determination of activation parameters[4], the measurement of kinetic isotope effects[5], and extensive structure reactivity correlations[6]. All of these, individually or combined, can provide insight into the nature of a transition state. More recently, a variety of mass spectrometric and ion cyclotron resonance (ICR) spectroscopic methods[7,8] have become available, by which detailed kinetic studies can be performed in the gas phase, thus giving information about more or less isolated molecular systems. Such experiments often produce valuable starting points for theoretical investigations. Of particular interest are collision experiments with crossed molecular beams[7,9-11], consisting of neutral and/or charged particles, and their combination with chemiluminescence studies[12]. In connection with suitable model calculations, they may provide information about the behavior of the molecular system in the transition state region. However, the reliable interpretation of such experiments is still limited to rather small molecular systems containing not more than about two to five atoms. Hence, these techniques continue to be part of chemical physics rather than of physical chemistry. Furthermore, there are spectroscopic methods, especially infrared and microwave spectroscopy[13,14], by which information about potential energy profiles can be obtained for hindered intramolecular motions. Finally, we direct attention to the structure correlation method, developed by *Bürgi* and *Dunitz*[15,16] some years ago and since applied successfully[17-22], by which insights into the qualitative course of a reaction path may be gained by correlating crystal structure data of carefully chosen molecular systems. With this short summary we wish to emphasize that theory has no exclusive rights in dealing with the gray area of a chemical reaction; rather, it serves as an important auxiliary tool in promoting experimental access to this region.

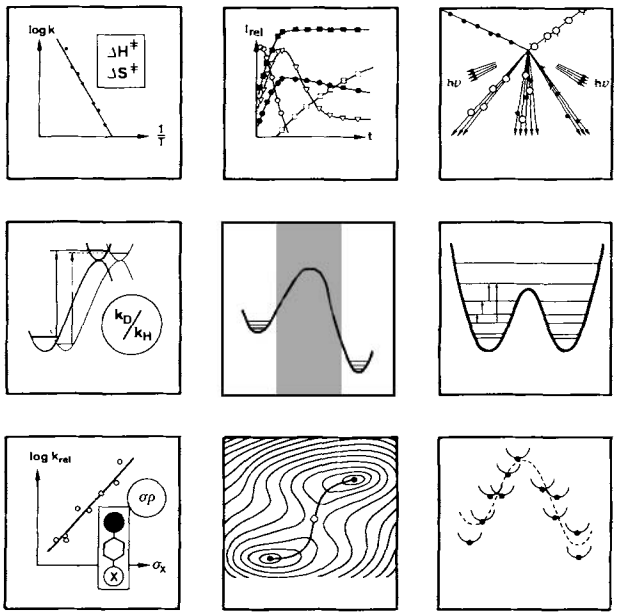


Fig. 2. Experimental methods for the investigation of the molecular behavior near the transition state of a reaction. From top to bottom and columnwise from left to right: Kinetic methods for the determination of activation parameters, kinetic isotope effects, linear "free energy relationships"; MS and ICR methods; region of the transition state (symbolic); potential energy surface; molecular beam and chemiluminescence methods; IR and microwave spectroscopy; correlation method with X-ray structure data.

As an illustration for the combined use of theoretical, spectroscopic, and crystallographic information, we discuss the inversion-rotation motion of the amino group in enam-

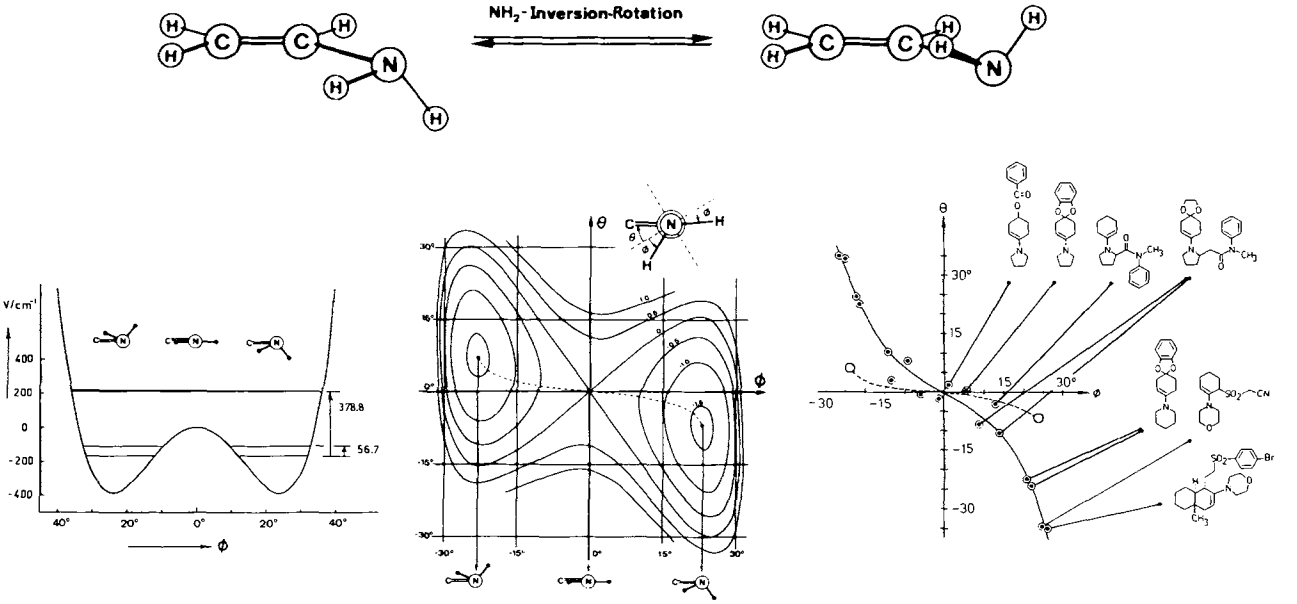


Fig. 3. The inversion-rotation motion of the amino group in enamines as an example for the combined use of theoretical and experimental methods for the elucidation of preferred reaction paths. Middle: Calculated double-minimum potential for a coupled inversion-rotation motion in vinylamine [23]. Left: Energy profile for the fully relaxed inversion-rotation motion of the NH_2 group in vinylamine [26] based on microwave spectroscopic data. Right: Preferred inversion-rotation path of the amino group as derived by correlation of X-ray structural data of crystalline enamine derivatives [21].

ines (Figure 3). The theoretical treatment of this process in the unsubstituted vinylamine[23] produced a double-minimum potential with a planar transition state. The position of the two energy minima, lying clearly off the axes of pure NH_2 inversion and rotation, respectively, indicates a pronounced coupling between inversion and rotation of the amino group. These results, as well as further refinements by means of complete and partial structure optimizations, established the basis for an application of the recently proposed method of flexible models for intramolecular motion[24]. With this method a quantitative interpretation of the microwave spectroscopic data of vinylamine[25] was achieved, providing an energy profile for the fully relaxed inversion-rotation motion of the amino group[26]. In an independent effort by *Eschenmoser et al.* and *Dunitz et al.*[21], a number of crystalline enamine derivatives were synthesized and examined by X-ray diffraction. For each enamine derivative, the amount of pyramidality at the nitrogen atom as well as the degree of torsion around the CN single bond were determined from the structural data. Correlation of these parameters in an inversion-rotation diagram produced a set of points that can be taken to represent valley points on a common potential surface describing the intramolecular motion of the amino group in a generalized aliphatic enamine. The so-derived reaction path provides a particularly clear documentation of the coupling between inversion and rotation of the amino group, being of the same type as that evidenced for unsubstituted vinylamine by theoretical and spectroscopic means.

2. Calculation of Reaction Paths

The theoretical treatment of a chemical reaction requires detailed knowledge of the potential energy of a molecular system in terms of all internal degrees of freedom. This prerequisite is independent of whether a static description of the reaction is pursued, *e.g.*, by localizing a minimum-energy reaction path (thick curve in Fig. 4), or whether a dynamic treatment of reactivity is attempted, *e.g.*, by computing numerous classical trajectories (thin curve in Fig. 4), along which the molecular system oscillates back and forth over the reaction valley. However, the call for detailed knowledge of the molecular energy function is faced with two problems. The first arises from the fact that, in general, the potential energy of a molecular system is a function of a large number of parameters and thus does not lend itself to a graphic representation. A two-parameter energy function can be visualized as a three-dimensional relief or mapped by a two-dimensional contour diagram. Accordingly, a multiparametric energy function can be taken as an energy hypersurface in multidimensional space; nevertheless it evades visualization. This does not seem to be a severe problem at first. After all, computers may be run without imagination. However, an intuitive insight into the shape of such a potential surface is often of considerable help (see *e.g.* Section 2.2). For the sake of clarity, our discussions will be based on a two-parameter model potential, whose contour diagram is shown in Figure 4; it contains three energy minima and two saddle points. The results that are obtained here are easily transferred to multidimensional energy hypersurfaces. The second problem arises from the fact that the molecular energy function is usually not analytically available but has to be defined numerically point by point. This, too, does not look like a severe hindrance; in principle, a grid of points could be spanned in the domain of a reaction path. With sufficient resolution this would come close to a knowledge of the analytical form of the energy function. However, such a procedure is

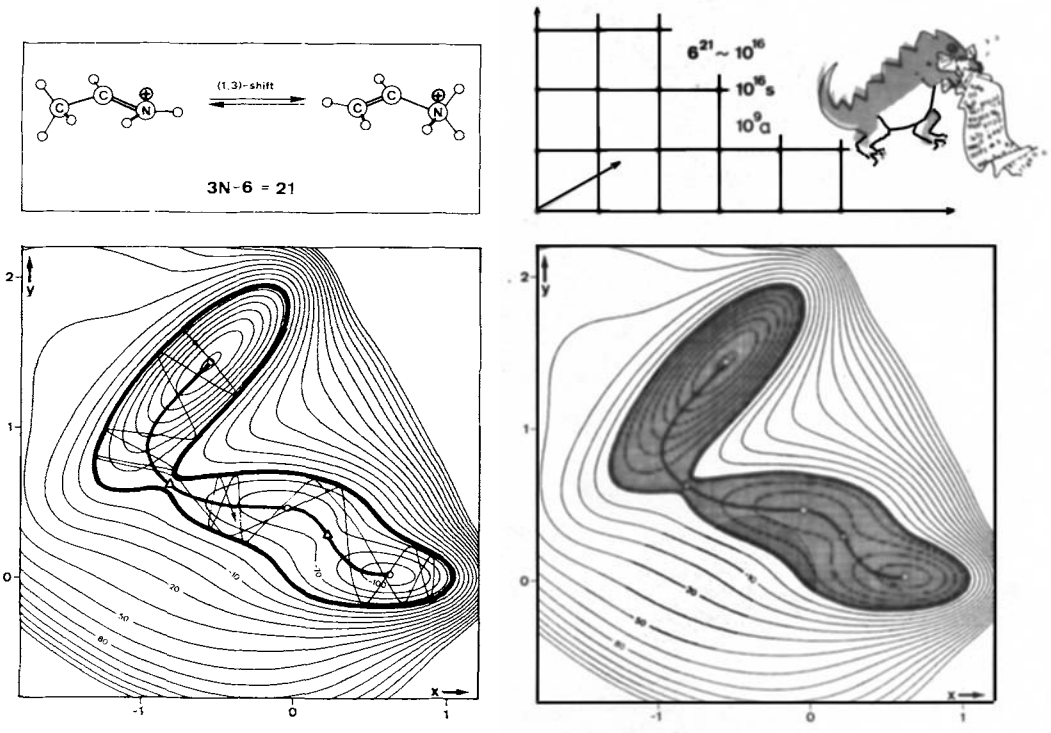


Fig. 4. Two-parametric model potential with three minima (circles) and two saddle points (△) [45]. Left: The minimum-energy reaction path (thick line) shows the course of the reaction valley. The dynamics of a reactive system with specified initial conditions may be described, for example, by means of a classical trajectory (schematically shown by a thin line). Right: An exhaustive examination of the reaction region on a multidimensional potential surface by scanning a grid of points is impracticable for lack of time.

ill-advised. Consider, for example, the case of a hydrogen shift in protonated vinylamine (Figure 4). This molecular system consists of only nine atoms, but has 21 internal degrees of freedom. Let us suppose, as a first step, we want to span a coarse grid with only six points for each degree of freedom. As can be seen from Figure 4, such a grid would not provide sufficient resolution in the case of the two-parameter model potential. Yet, for 21 degrees of freedom, $6^{21} \sim 10^{16}$ points would have to be evaluated. Even if each energy calculation took only one second—still a visionary situation!—our preliminary study would require 10^{16} seconds or roughly 10^9 years. Had we started with the dinosaurs, we would still be calculating. Thus, the bullheaded approach, spanning a grid of points, is out of the question. A theoretical investigation of a chemical reaction therefore concentrates, first of all, on the minimum-energy reaction path in order to locate the reaction valley on the multidimensional potential surface. For this purpose we need special numerical techniques that determine such reaction paths more or less directly, *i.e.*, circumvent the above mentioned "dinosaur-like" problem.

2.1. The Minimum-energy Reaction Path

According to work by *Fukui*[27-29], *Morokuma*[30], and *Basilevsky*[31], a minimum-energy reaction path is nowadays identified as that orthogonal trajectory which connects two energy minima *via* a common saddle point; it is composed of the two steepest-descent paths that emerge from a saddle point in both directions along the principal axis of negative curvature and enter the two adjacent energy minima, each along the principal axis of least curvature. From a physical point of view, it may be considered as a relaxation path, albeit imaginary, along which the molecular system glides from a high-energy saddle point down to either of the two minima, with continuous dissipation of energy, but almost infinitely slow motion (Fig. 5). Strictly speaking, this interpretation holds only if the potential surface is defined in terms of mass-weighted Cartesian coordinates, as commonly used in normal coordinate analyses of molecular vibrations.

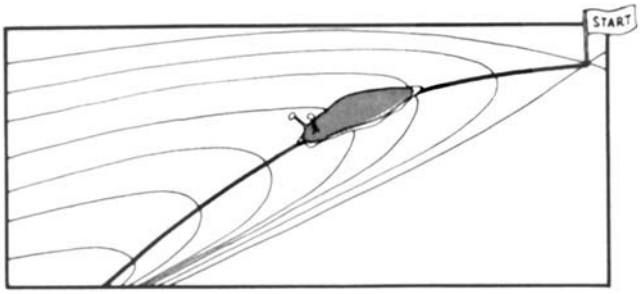


Fig. 5. The minimum-energy reaction path corresponds to an imaginary relaxation path of steepest descent, along which the molecular system glides with almost infinitely slow motion from a saddle point to an adjacent minimum.

2.2. Methods for the Calculation of the Minimum-energy Reaction Path

If the energy function is not analytically available but has to be evaluated point by point, the localization of such reaction paths is beset with difficulties. For a proper assessment of the problems involved it is appropriate to review the most important currently available methods for the calculation of reaction paths. This will be done with reference to the two-parameter model potential.

The traditional and by far most frequently used method consists in choosing a suitable structural parameter as a reaction coordinate[32-34], along which the reaction is driven. This choice is often quite difficult. For selected values of this parameter, the energy of the molecular system is minimized with respect to all remaining structural parameters. This procedure, which will be referred to as the reaction coordinate method, looks quite simple, to be sure, but it is full of pitfalls. Let us apply it to the two-parameter model potential, starting at the minimum A with x as the reaction coordinate (Fig. 6).

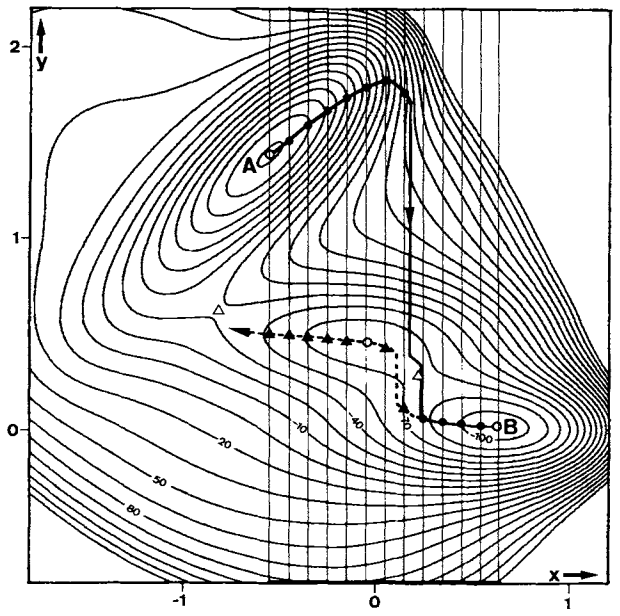


Fig. 6. Application of the reaction coordinate method to the two-parametric model potential.

We obtain a reaction path that starts out in a wrong direction, climbing up the valley wall, until it reaches a point from which it suddenly jumps into the true reaction valley, without ever having passed through the saddle point. After a short travel along the valley bottom, our path takes another discontinuous jump before getting to the destination point B. Using the same reaction coordinate, but this time going in the opposite direction, starting out from minimum B, a completely different reaction path is obtained. It is again discontinuous. Moreover, it does not reach the target minimum A for the limiting value of the x parameter. Instead, it remains in the middle of the energy surface. Such failures of the seemingly simple reaction coordinate method have often been documented and commented on in the more recent literature[33,35-39]: apart from the fact that this method does not provide true minimum-energy paths, it should not be used in cases of doubt.

Likewise, the proposal[39] of using an equipotential curve as a reaction coordinate, instead of an individual structural parameter, does not solve the problems satisfactorily (Fig. 7). This procedure, referred to as the reference coordinate method, first of all requires a suitable equipotential curve, *i.e.*, one

that passes through the regions of two minima as well as a saddle point between. Furthermore, a relatively expensive contour-following algorithm is needed. Advancing step by step along such an equipotential curve, while simultaneously minimizing the energy orthogonal to it, we generate a set of valley points which, in simple cases, trace approximately a minimum-energy reaction path. However, in more complicated cases this procedure may lead to nonsensical results, as shown by its application to the two-parameter model potential. Starting from the energy minimum A (Fig. 7) the series

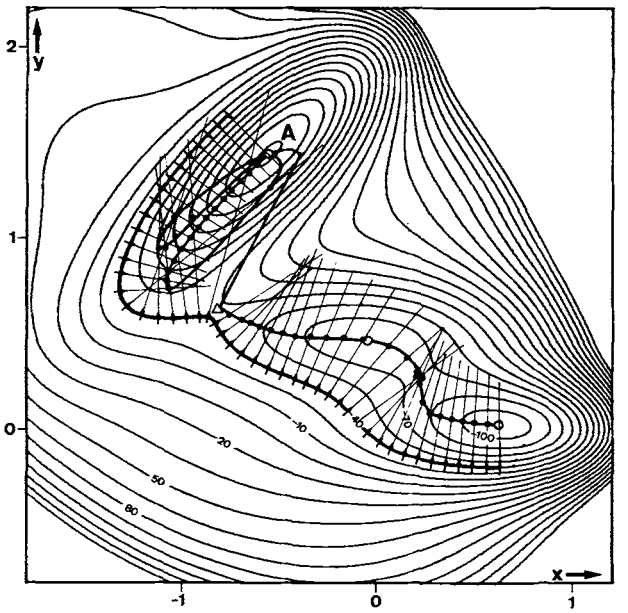


Fig. 7. Application of the reference coordinate method [39] to the two-parametric model potential.

of valley points describes a reaction path that at first heads for the saddle point, correctly following the valley bottom, but, stopping short of it, falls back into the start minimum, performs another unproductive loop, winds up on the valley wall, and jumps abruptly into the saddle point region. It is only from this point on that it leads to the target minimum more or less along the valley bottom.

A rigorous determination of minimum-energy reaction paths requires primarily the localization of saddle points and subsequently the calculation of gradient paths, *i.e.*, steepest-descent paths starting from the saddle points. In comparison to the localization of energy minima (or maxima), which can be effected by various standard function optimization procedures[40], the search for a saddle point is by far more difficult. During the past few years some methods have been developed for this purpose[35,38,41-44].

One group of methods is based on the fact that saddle points, like minima and maxima, belong to the so-called stationary points on an energy hypersurface, *i.e.*, points where the slope vanishes in all directions. Thus, the procedure consists in minimizing the absolute value of the energy gradient (gradient norm) in order to find a stationary point between the start and end minima. That indeed a saddle point has been found must be verified subsequently by calculating the principal axes of curvature at this point. These methods are quite powerful if the energy gradient is obtained directly (*i.e.*, not by taking finite differences), as can be done with several current quantum-chemical procedures. Nevertheless, gradient norm minimization methods have their drawbacks. A first problem lies in the uncertainty that convergence to a stationary point produces a saddle point. As an illustration consider Figure 8, which shows the gradient norm of the two-parameter model potential by means of a contour diagram. The five zero-minima of the gradient norm (full circles), corresponding to minima and saddle points on the energy surface (see Fig. 4), are easily seen. Starting from point 2 in Figure 8, minimization of the gradient norm leads to a zero-minimum that corresponds to a saddle point on the energy surface. On the other hand, starting from point 3, such a minimization converges only to an intermediate energy minimum.

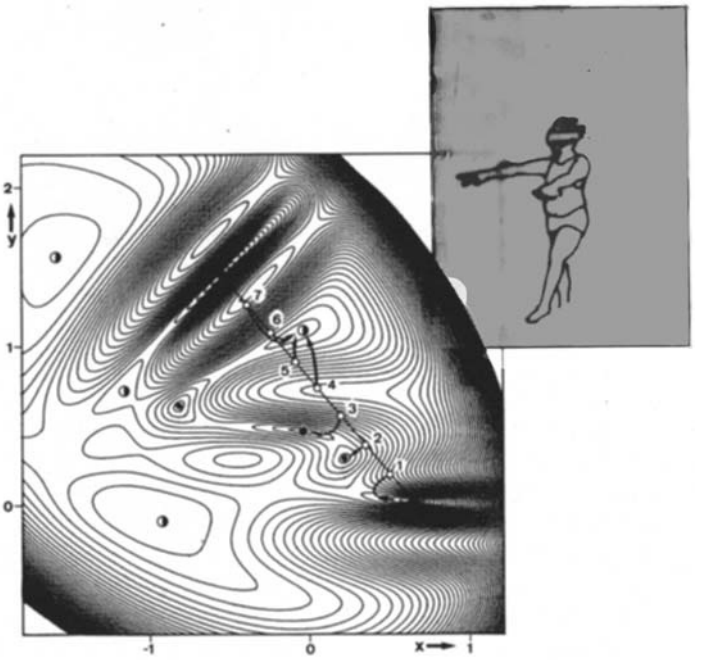


Fig. 8. Contour diagram of the gradient norm of the two-parametric model potential. Zero-minima and secondary minima are marked by filled and half-filled circles, respectively. The open circles 1—7 indicate possible starting points for a saddle point localization by means of gradient norm minimization.

To avoid this uncertainty, a modified procedure has been proposed[42], in which principal axes of curvature are repeatedly evaluated. With this additional, if costly, information convergence can be directed away from energy minima and maxima and guided into regions of possible saddle points. Of course, one has to pay for the assurance of proper convergence. A second problem arises from the fact that a gradient norm may contain not only zero-minima but also secondary minima. For example, the gradient norm of our two-parameter model potential exhibits a total of four secondary minima (half-filled circles) in addition to the five zero-minima. There happens to be a deep secondary minimum just where one might expect to find a saddle point, *i.e.*, in the linearly interpolated region between start and end minima. Wherever we start minimizing the gradient norm in this region, *e.g.* at points 4—7, we are likely to fall into this secondary minimum, which does not correspond to a stationary point on the energy surface but to a flat region on a long crest. Such secondary minima considerably impede the

search for saddle points. Thus, for a straightforward application of gradient norm minimization procedures, the approximate position of a saddle point should be known in advance. However, it is just in this respect that the already mentioned difficulties of visualizing features of multidimensional energy hypersurfaces become most serious. We find ourselves blindfolded, as it were, and chemical intuition is not always a safe guide (Fig. 8).

The so-called X-method[43] is an alternative way to locate saddle points. It is based on the mathematical property that a three-dimensional hyperbolic paraboloid (Fig. 9) contains two straight contour lines that intersect at the saddle point. Thus,

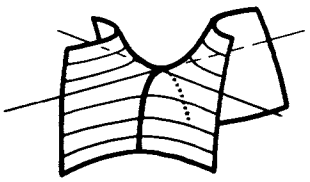


Fig. 9. The hyperbolic paraboloid with two straight contour lines through the saddle point.

for a two-parametric potential function, the procedure consists in a search for those points where an "X", *i. e.* two intersecting lines of constant energy, can be optimally fitted to the potentional surface. In the n-parametric case, an n-dimensional double cone of constant energy has to be embedded into the energy hypersurface, requiring $n+(n-1)+\frac{1}{2}n(n-1)$ parameters to specify its location, shape, and orientation. Hence, with increasing complexity of the energy function, the X-method soon becomes very expensive. To our knowledge, it has only been used once in connection with a 2-parameter potential.

Halgren and *Lipscomb*[38] proposed another procedure, the so-called synchronous transit method. Its basic search strategy may be clarified by considering a network consisting of linearly and quadratically interpolated transit paths between a start and an end minimum and surfaces of constant path coordinates (nonconcentric circles in the 2-dimensional case, as shown in Figure 10, or hyperspheres in the multidimensional case). The localization of a saddle point is effected by

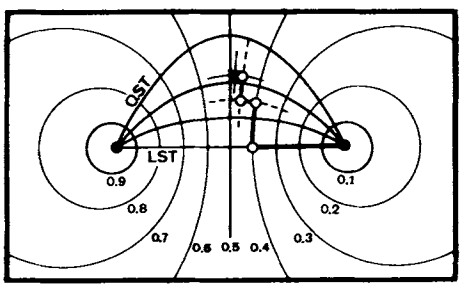


Fig. 10. The search strategy of the synchronous transit method [38] in the two-dimensional case: energy optimizations are performed alternately along linearly and quadratically interpolated transit paths (LST and QST) and along lines of constant path coordinates (nonconcentric circles).

alternately searching for energy maxima along transit paths and energy minima on surfaces of constant path coordinates until a point is reached which represents both an energy maximum along a transit path and an energy minimum on a surface of constant path coordinate. This simple strategy is not without problems, however, as can be shown by application to the two-parameter model potential (Fig. 11). Starting from minimum A, we would first get to maximum B on the

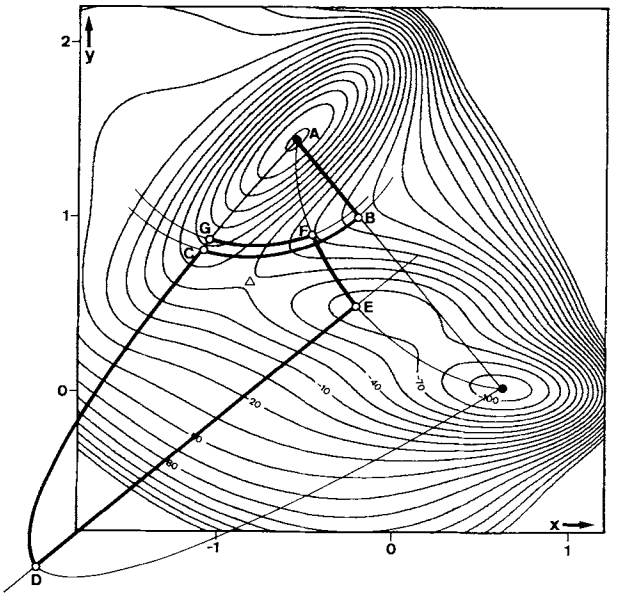


Fig. 11. Application of the synchronous transit method to the two-parametric model potential: failure of the simple search strategy.

linearly interpolated transit path. From there the line of constant path coordinate leads us to minimum C. On the quadratically interpolated transit path through C, we find maximum D. From there we get to E with constant path coordinate, to F on a quadratically interpolated transit path, and so on. Instead of converging into the saddle-point region in due time, this search strategy keeps us beating about the bush. Various additional strategies[44] have been developed to cope with such problems. One, for example, would consist in taking A and E as new starting points (Fig. 12), assuring prompt convergence to the saddle point. The synchronous transit

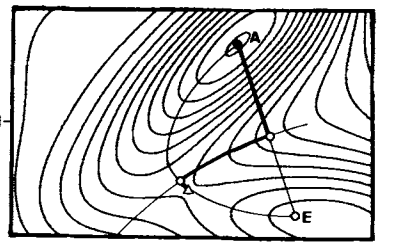


Fig. 12. Application of the synchronous transit method to the two-parametric model potential: successful localization of a saddle point by reapplication of the method to points A and E of Figure 11.

method thus seems to be a powerful tool, especially since no previous knowledge about the approximate position of a saddle point is required.

Recently, a new procedure[45] has been developed which is also characterized by a remarkably simple search strategy. It makes use of the fact that, given a high-energy point on the gradient path along the valley bottom, it is in principle always possible to generate a new point of lower energy, lying on the same gradient path, by minimizing the energy on a hypersphere (or circle in the 2-dimensional case) centered at the higher point. First of all, this helps us to gain a method

for the approximate calculation of minimum energy reaction paths. Provided the initial point is a saddle point, this procedure allows us to descend to an adjacent minimum step by step by generating one path point after another (Fig. 13). With a sufficiently small search radius a set of path points is

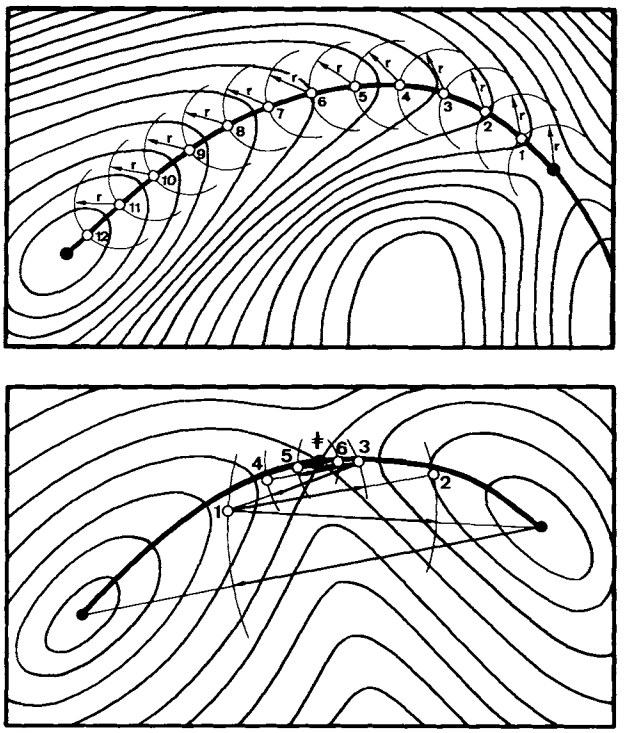


Fig. 13. Localization of valley points by energy minimizations on circles (two-dimensional case) or hyperspheres (multidimensional case) [45]. Top: Calculation of an approximate minimum-energy reaction path by generating a series of descending path points. Bottom: Localization of a saddle point by generating a series of ascending valley points.

obtained that represents a good approximation to the true gradient path. The strategy for the localization of a saddle point now consists in minimizing the energy on suitable hyperspheres between start and end minima so as to generate a series of valley points of increasing energy, which close in on a saddle point from opposite sides. At first sight, a strategy based on ascending valley points seems to be inconsistent with the underlying principle of generating descending path points. However, the crucial point, and one where the new procedure differs basically from the synchronous transit method, is that the search region on the hypersphere and the corresponding center are always on opposite sides of a saddle point. This generally ensures that hypersphere and hypersurface penetrate each other in a way suitable for the generation of descending path points. This strategy depends on a simple energy/distance analysis which, at each round, selects the highest of the growing set of valley points as center of a new hypersphere and directs the search region towards the more distant of the two neighboring points. The typical performance of this localization method may be illustrated by means of the two-parameter model potential (Fig. 14). Beginning with A and B as start and end minima and arbitrarily choosing A as center of the first hypersphere, the saddle point is successfully localized after a series of thirteen valley points. Those generated in the early stages, *i.e.*, with relatively large search radii, may deviate strongly from the minimum energy

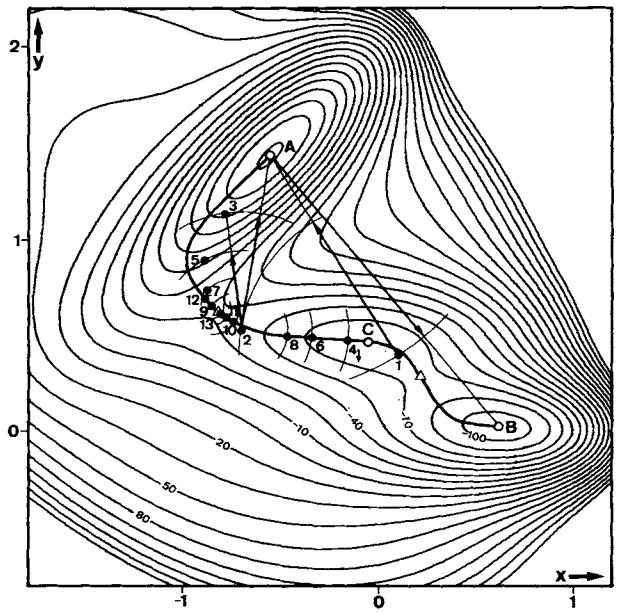


Fig. 14. Localization of a saddle point on the two-parametric model potential surface by means of ascending valley points.

reaction path, whereas those obtained at later stages, *i.e.*, with smaller search radii, represent better path points. Thus, the numerical effort produces not only the saddle point itself but also, as a bonus, a set of valley points which provides at least a rough guide to the course of the reaction path. In our example, the energy/distance analysis properly diagnoses the fourth valley point as one that lies within the region of an intermediate minimum. This is an important piece of information. It initiates the search for another saddle point, which is easily found by first locating the exact position of minimum C and then applying the saddle point localization procedure to the region between B and C. More accurate minimum-energy reaction paths can now be obtained using the technique of descending path points. This is shown in Figure 15 for the two-parameter model potential. The search radii have been

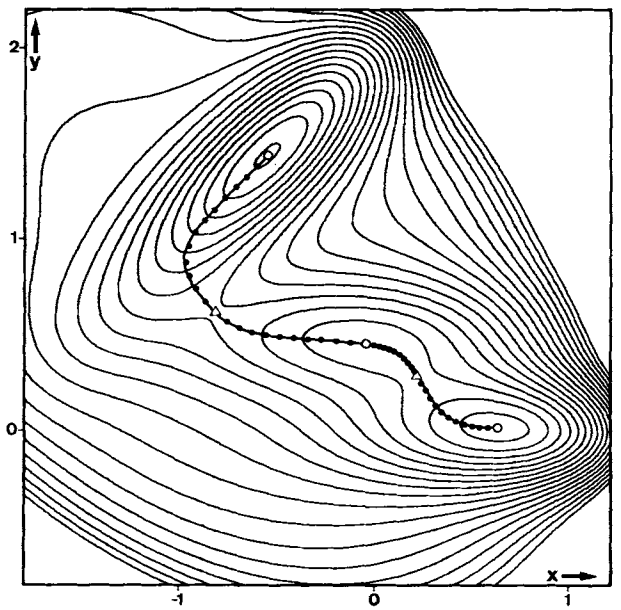


Fig. 15. Approximate minimum-energy reaction path for the two-parametric model potential by means of descending path points.

set to $^1/_{11}$ of corresponding distances between saddle points and adjacent minima, ensuring at least ten path points for each descent path.

To conclude, we mention yet another recently proposed method for the calculation of minimum-energy reaction paths[46]. It is of questionable value, but warrants a comment because it is based on the apparently plausible assumption that, along the valley bottom, one of the principal axes of curvature always lies parallel to the energy gradient. As can be shown mathematically[29], this assumption is generally not valid along a minimum energy reaction path, *i.e.*, the steepest-descent path from a saddle point. However, a procedure that rests on such an assumption may still produce useful reaction paths. Again, an application to the two-parameter model potential brings the problems to the fore (Fig. 16). In those regions where the minimum-energy path (marked by open circles) shows little curvature, *e.g.*, between points C and D, a reaction path (marked by a series of dots) is obtained which approximately follows the gradient path. However, it exhibits a distinct tendency to swing more than the gradient path whenever the valley is curved. In the region between D and A this property even causes it to climb up the valley wall—a result which is incompatible with the concept of a minimum-energy reaction path, whatever its definition.

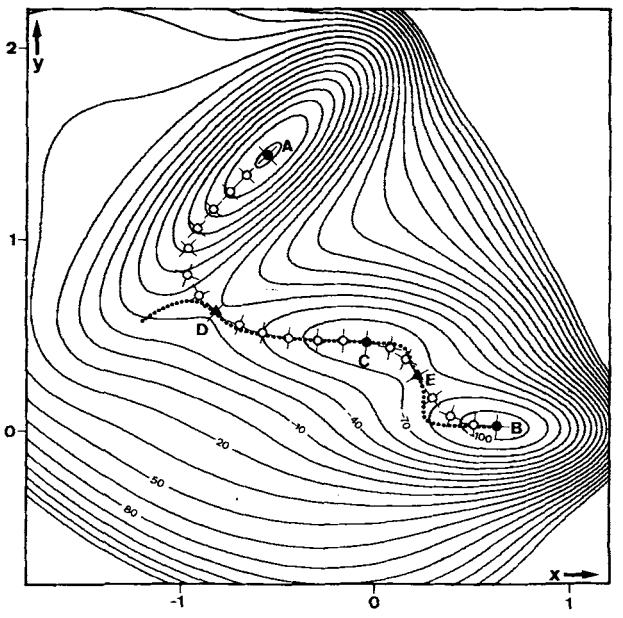


Fig. 16. Principal axes of curvature at points (circles) along the minimum-energy reaction path for the two-parametric model potential. Points at which one of the principal axes of curvature lies parallel to the energy gradient are marked by dots.

3. Examples

Having discussed fundamental difficulties in calculating reaction paths on multidimensional energy hypersurfaces, it is time to illustrate the localization of saddle points and of minimum-energy reaction paths by means of some chemically relevant examples. We shall concentrate mainly on the new methods based on ascending and descending valley points. The potential surfaces are defined within the framework of the nonempirical PRDDO SCF procedure[47].

3.1. Isomerization of Hydrogen Isocyanide to Hydrogen Cyanide

The first example concerns the transformation of hydrogen isocyanide into hydrogen cyanide. This reaction is of both chemical and theoretical interest[30,41,48]. In contrast to the long-known hydrogen cyanide, evidence for the existence of its isomer CNH came only during the sixties, when HCN or CH_3N_3 were photolyzed in an argon matrix at 4 K and 14 K[49]. It was not until 1975/76 that several independent research groups[50-52], using special laboratory techniques,

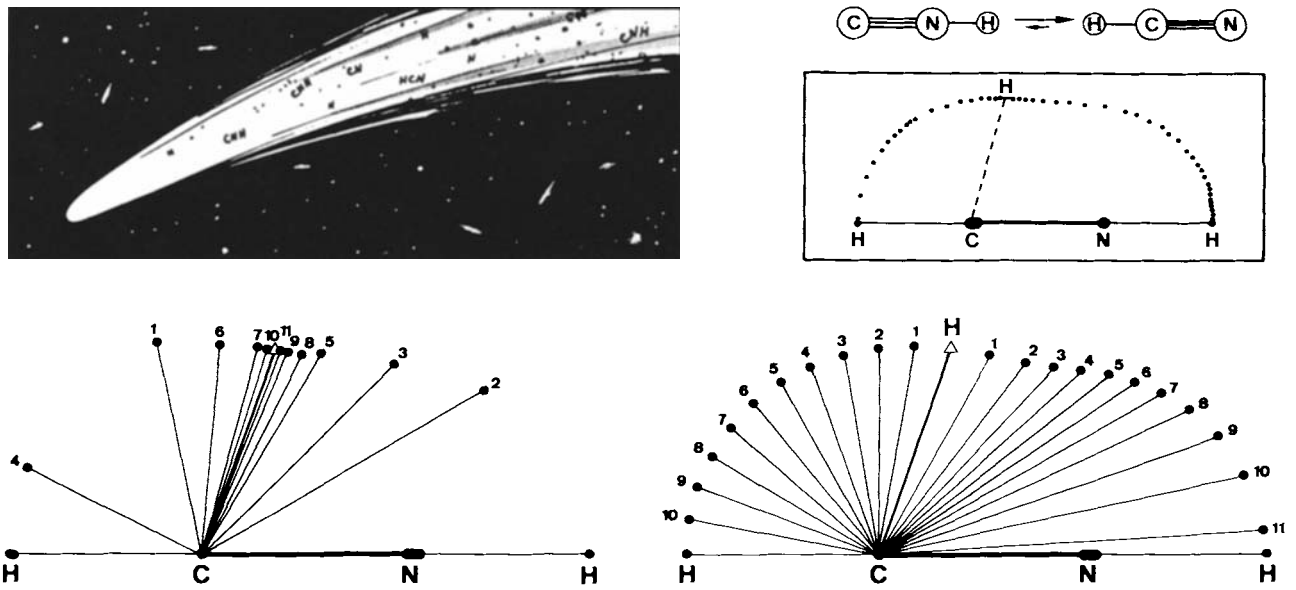


Fig. 17. In the laboratory hydrogen isocyanide CNH can be observed only under special conditions. Its existence in the interstellar space is spectroscopically well documented. The localization of the saddle point and the calculation of the minimum-energy reaction path for the transformation CNH⇄HCN using ascending and descending valley points [45] (bottom) and gradient procedures [30] (top) are shown by means of superimposed molecular structures.

managed to produce CNH in the gas phase in steady-state concentrations sufficient for a spectroscopic characterization of this labile species. Nevertheless, considerable amounts of both hydrogen cyanide and hydrogen isocyanide are present in the interstellar space. Thus, CNH has been detected spectroscopically in various galactic sources, in dark nebulae, and in comets[52-55] (Fig. 17).

The potential energy of this molecular system depends on three structural parameters. Such an energy function is already too complex to be plotted as a contour diagram and, as a hypersurface in 4-dimensional space, it cannot be visualized. Therefore, the results for the rearrangement CNH⇄HCN[45] are presented in Figure 17 by means of superimposed molecular structures, each corresponding to a point on the 4-dimensional potential surface. Apart from the start and end minima CNH and HCN, respectively, we note eleven ascending valley points which lead to the successful localization of the saddle point (lower part of Fig. 17). Clearly, this set of valley points alone provides a qualitatively correct representation of the minimum-energy reaction path. For comparison, the two gradient paths calculated more accurately by means of, respectively, ten and eleven descending path points are also shown in Figure 17. According to the theoretical model of this rearrangement, the hydrogen atom migrates on nearly circular paths around the nitrogen and carbon atoms, but in between, moves more or less parallel to the CN bond axis, thus exhibiting a marked tendency to keep optimum bonding distances as long as possible. Figure 17 also shows the results of an *ab initio* SCF study by *Morokuma et al.*[30], who first localized the saddle point by gradient norm minimization and subsequently calculated the minimum-energy reaction path by repeated gradient evaluations. The results obtained by means of ascending and descending valley points are in full harmony with those based on gradient procedures.

3.2. S_N2 Reaction of the Hydride Ion and Methane

As a second example we consider the S_N2 reaction involving hydride ion and methane. This reaction is prototypical of nucleophilic substitutions at a saturated carbon atom and has frequently been examined theoretically in recent years[56-62], *e.g.*, by *Morokuma et al.*[30] using gradient methods in connection with a standard *ab initio* SCF procedure. It served as a test case for the new methods based on ascending and descending valley points[45]. If we assume that the threefold symmetry of the molecular system is conserved throughout the reaction, the potential energy depends on four structural

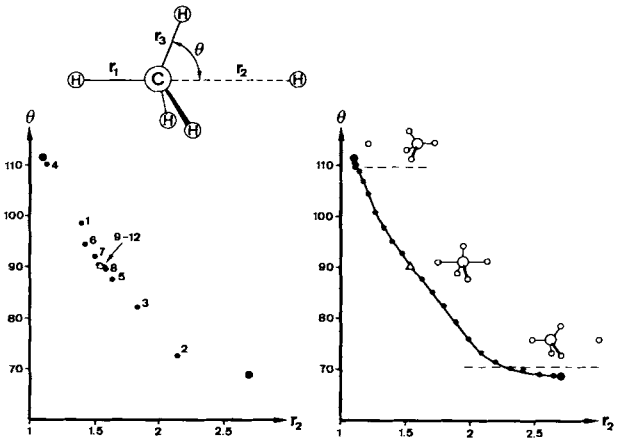


Fig. 18. The localization of the saddle point and the calculation of the minimum-energy reaction path for the S_N2 reaction involving $H^{\ominus}$ and CH_4 by means of ascending and descending valley points [45].

parameters (Fig. 18). To show the computational results we make use of a parametric representation, concentrating on the dependence of the angle, θ, of the CH_3 pyramid upon the distance, r_2, between the entering hydride ion and the central carbon atom. The symmetrically lying saddle point of trigonal bipyramidal structure, which can also be determined directly by partial geometry optimization, is correctly localized after a series of twelve ascending valley points. Again, these valley points provide a satisfactory picture of the minimum-energy reaction path. Indeed, little is gained by a more quantitative calculation of this path using eleven descending path points. This path suggests a slow but continuous opening of the CH_3 pyramid during the approach of the nucleophile $H^{\ominus}$, comparable perhaps to the smooth opening of an umbrella (Fig. 19). It is in good qualitative agreement with the gradient path obtained by *Morokuma et al.*[30]. Moreover, it is consistent with ideas about such a reaction path, as derived

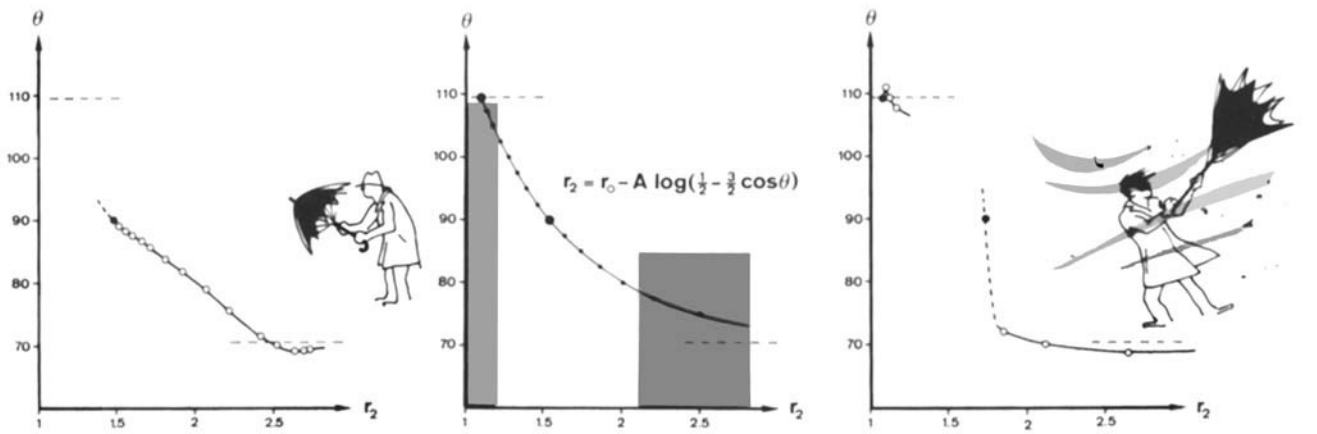


Fig. 19. Reaction paths for the S_N2 reaction involving $H^{\ominus}$ and CH_4. Left: Minimum-energy reaction path using gradient procedures in connection with a standard *ab initio* SCF model [30]. Middle: Idealized reaction path as derived by correlation of X-ray structural data of five-coordinated cadmium complexes [15, 17] and normalized to the molecular system $CH_5^{\ominus}$. Right: Reaction path obtained within the framework of an *ab initio* SCF model using the reaction coordinate method with r_2 as reaction coordinate [59].

by *Bürgi*[15] on the basis of X-ray structural data of five-coordinated cadmium complexes using the structure correlation method. On the other hand, it sharply contrasts with earlier results[59] obtained within the framework of an admittedly sound quantum-chemical procedure, but using the reaction coordinate method with the distance r_2 as reaction coordinate. This seems a natural choice for a substitution reaction, but the method produces a reaction path along which the CH_3 umbrella undergoes virtually no change for a long time and then, suddenly, at a critical value of r_2, shows one of those unfortunate discontinuitites (Fig. 19) for which, no doubt, the reaction coordinate method is to be blamed rather than the underlying quantum-chemical procedure.

3.3. The Computational Effort

Thus far, little attention has been given to an important aspect, the computational effort. In fact, it is not easy to give *valid comments on the costs of a particular method*, particularly since the computational effort depends not only on the localization procedure used but also on the complexity of the energy hypersurface, on the availability of suitable starting points for a saddle point localization, on the desired density of path points for the description of a gradient path, and, last but not least, on the numerical accuracy required for the calculation of molecular structures. Nevertheless, a few comments are in order to caution against an overoptimistic view of current possibilities in a theoretical treatment of chemically relevant problems.

For a number of quantum-chemical procedures, especially semiempirical methods, the energy gradient can be evaluated directly in connection with an energy calculation at only moderate additional expense[41]. Here, gradient procedures are the methods of choice for the localization of saddle points and minimum-energy reaction paths. A simultaneous calculation of the energy and the energy gradient is also feasible by standard *ab initio* SCF procedures. However, this is a much more expensive undertaking than the calculation of the energy alone[30,41]. Thus, it is also for economy that the use of gradient methods for the localization of a saddle point requires an *a priori* knowledge of its approximate position. In principle, there are two ways to get at this information. The first consists in localizing a saddle point within the framework of a less expensive semiempirical method as a starting point for the more expensive *ab initio* procedure. This technique runs the risk that different theoretical models may disagree in their predictions concerning the position of a saddle point. The second consists in narrowing down the saddle point region using a search strategy without gradients. Such a procedure will generally be more expensive, but it allows us to remain within one and the same theoretical model. For various quantum-chemical methods direct evaluation of the gradient is not feasible or is unduly expensive. In these cases, search strategies such as the synchronous transit method or the procedure based on ascending valley points may be of considerable value. Regardless of which localization method is applied, when used in connection with nonempirical calculations, the computational effort soon becomes prohibitive with increasing structural complexity of the molecular system.

The computational effort required by the new methods using ascending and descending valley points has been investigated by a series of systematically selected test cases[45]. The results are summarized in Figure 20. The number of energy

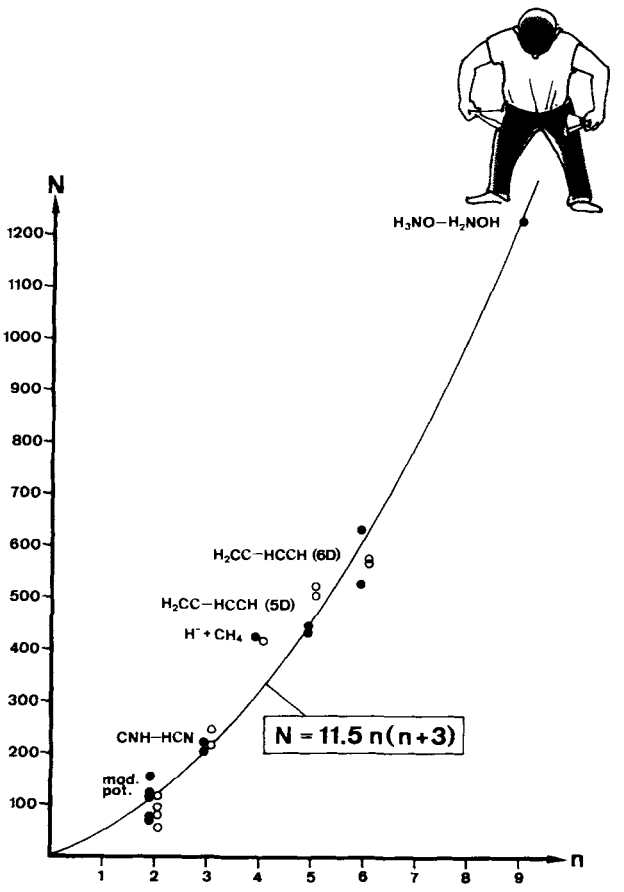


Fig. 20. The number (N) of energy evaluations required for the localization of a saddle point (filled circles, 0.005 A, 0.5°) and a minimum-energy reaction path (open circles, 0.002 A, 0.2°) by means of ascending and descending valley points, respectively, increases with growing dimensionality ($n+1$) of the potential surface (mod. pot. = 2-parameter model potential).

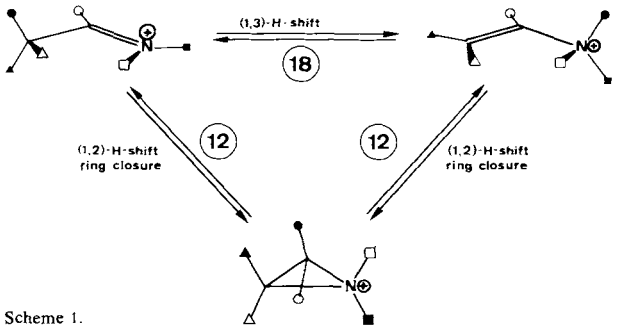
evaluations required for the localization of a saddle point as well as for the calculation of a gradient path increases more or less quadratically with the dimension of the energy hypersurface. Unfortunately, the proportionality factor is rather large. Of course, the computational effort could be reduced at the expense of numerical accuracy; but, as before, a more expeditious localization of a saddle point can be achieved only if its approximate location is known in advance. On the other hand, a definite advantage of the new method (and of the synchronous transit method) is that no prior information regarding the position or the nature of a saddle point is required for its localization; but we have to pay for this.

3.4. Transformation of Vinylammonium into Ethylideneammonium Ion

Finally, we return to the transformation of the vinylammonium ion into the ethylideneammonium ion, already mentioned in Figure 4. This reaction has been studied within the PRDDO SCF approximation in connection with theoretical[23] and experimental[63] work on enamines[64]. It is easily recognized by an experienced chemist as a [1,3] sigmatropic hydrogen or proton shift. Biased by current views

about such reactions[65-67], he is prepared to accept, in principle, two possible modes for the migrating proton, *viz.*, a suprafacial, thermally forbidden process (with a large activation energy) and an antarafacial, thermally allowed process (with a smaller activation energy). However, we recall that the molecular system $C_2H_6N^{\oplus}$ has 21 internal degrees of freedom. As a matter of fact, 18 different reaction paths are formally possible just for the one-step transformation because of permutational symmetries in the reactant and product systems (Scheme 1). In addition, two-step as well as multistep





Scheme 1.

processes have to be considered. For example, a [1,2] hydrogen shift with concomitant ring closure may lead from the ethylideneammonium to the aziridinium ion, which can then rearrange to the vinylammonium ion *via* ring opening and another [1,2] hydrogen shift. Again the permutational symmetry permits twelve different reaction paths for each of the two individual steps. Thus, a sigmatropic rearrangement that looks fairly innocuous at first sight turns out to be extremely complex. According to Figure 20, the rigorous localization of a saddle point on a 21-parameter energy hypersurface by means of ascending valley points is expected to require about 6000 energy calculations. With an average of 15 seconds per energy value[64], this amounts to roughly 90000 seconds or one full day of computer time. Such an undertaking is dangerous for budgetary reasons (Fig. 20), particularly if several saddle points are to be found on this hypersurface. The necessity for a structural simplification led to a number of preliminary studies which helped to differentiate between twelve essential and nine non-essential structural parameters, among them five bond distances to hydrogen atoms. Saddle points and minimum-energy reaction paths were then localized on the simplified 12-parameter potential surface by means of ascending and descending valley points, respectively. The results are summarized in the reaction scheme of Figure 21.

Given the energy minima of the vinylammonium, aziridinium, and ethylideneammonium ions as starting points, a total of seven saddle points were found, in addition to those for internal rotations of the methyl and the ammonium group, respectively; all associated minimum-energy reaction paths were calculated, and two high-energy intermediates were detected. Of the eighteen conceivable possibilities for a one-step transformation of the vinylammonium into the ethylideneammonium ion, only two have survived: a suprafacial and an antarafacial [1,3] sigmatropic hydrogen shift. The remaining reaction modes are linked with these by prior internal rotations of the CH_3 group in the ethylideneammonium ion or of the $NH_3^{\oplus}$ group in the vinylammonium ion. Both [1,3] sigmatropic shifts involve very high energy barriers. There are also two independent paths with considerably reduced barriers leading from the ethylideneammonium ion to the two enantiomeric β-aminoethyl cation intermediates, which are separated by a small conformational energy barrier of about 0.5 kcal/mol. In spite of repeated efforts, no saddle point has been found in the region between the aziridinium and the vinylammonium ion. Likewise, attempts to localize saddle points between the high-lying β-aminoethyl cation and the vinylammonium ion have been unsuccessful. Only one other reaction path has been detected, leading from one of the two intermediates up to the saddle point of the one-step suprafacial [1,3] hydrogen shift; the two saddle points are of roughly equal energy.

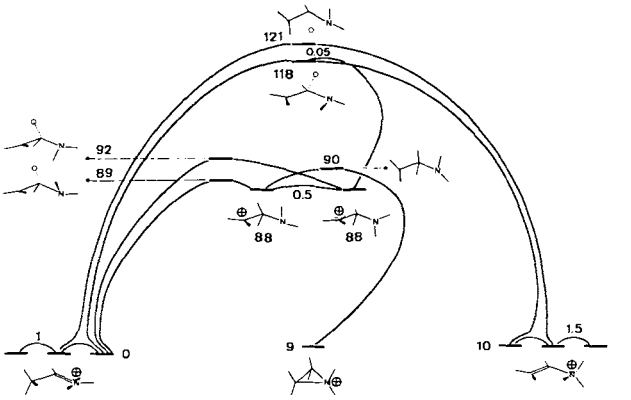


Fig. 21. Reaction scheme involving the vinylammonium, aziridinium, and ethylideneammonium ions, as obtained by localization of saddle points using ascending valley points on a simplified 12-parametric potential surface defined within the PRDDO SCF approximation [64].

In an independent mass spectrometric study, *Williams* and *Hvistendahl*[68] investigated the gas-phase chemistry of $C_2H_6N^{\oplus}$ ions. Based on the analysis of fragmentation products from different isotopically labeled ion precursors and the determination of appearance potentials for various ions, they proposed the approximate reaction scheme shown in Figure 22 (the relevant parts are specifically marked). Of course, the theoretical model can produce a much more detailed description than any currently available experimental technique. Nevertheless, the two reaction schemes agree remarkably well in all their essential features. The vinylammonium and the aziridinium ions are both found to be less

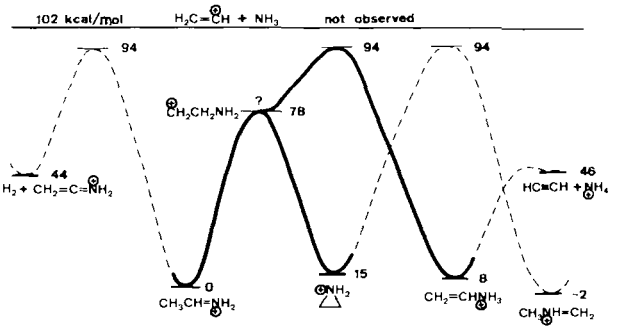


Fig. 22. Approximate reaction scheme for the gas-phase chemistry of $C_2H_6N^{\oplus}$ ions based on mass spectrometric evidence [68].

stable by about 10 kcal/mol[23] than the ethylideneammonium ion. A reaction path leads from the ethylideneammonium to the aziridinium ion, but there is no path with comparable energy barrier from the aziridinium to the vinylammonium ion. The latter can be reached only *via* a much higher barrier, possibly involving the β-aminoethyl cation as a transient intermediate, which has not yet been well characterized experimentally. The calculated energy barriers are consistently too high by about 10—20 kcal/mol. This systematic overestimation is due not so much to the reduction from 21 to 12 internal degrees of freedom but rather to shortcomings of the underlying quantum-chemical procedure, *viz.*, the neglect of electronic correlation effects.

Beyond the mere reaction scheme, the theoretical model provides for each reaction path a detailed description of the cooperation between individual degrees of freedom. This is shown in Figure 23 for the suprafacial [1,3] sigmatropic hydrogen shift. The minimum-energy reaction path is here approximated by sets of, respectively, twelve and thirteen descending path points and is displayed by means of superimposed molecular structures in four different projections. A naive consideration of this reaction might suggest that the hatched hydrogen atom migrates along a more or less straight line from the nitrogen atom (vinylammonium ion) to the terminal carbon atom (ethylideneammonium ion), with two more hydrogen atoms moving so as to planarize the amino group and to pyramidalize the methylene group. Not at all! The theoretical model offers a reaction path that is considerably more intricate. First of all, the $NH_3^{\oplus}$ group in the vinylammonium ion is rotated about the NC bond axis until the predestined hydrogen atom makes an HNCC torsion angle of approximately 90°. From this favorable starting position, the hydrogen atom glides parallel to the NC bond axis, keeping as close as possible to the bonding region. During this process the amino group remains pyramidal, with its conformation virtually unchanged so as to provide optimum partial bonding to the migrating proton. Before the hydrogen atom reaches the central carbon atom, the molecular system crosses the saddle point (atomic positions at the saddle point are marked with arrows in Figure 23). While the hydrogen atom passes over the central carbon atom, the methine proton is temporarily forced out of the CCN plane. The hydrogen atom then glides parallel to the CC bond axis towards the terminal carbon atom. It is only at this stage that the pyramidal amino group is gradually transformed into the planar imminium group and the methylene group starts to pyramidalize, always adjusting its conformation so as to provide optimum partial bonding to the incoming hydrogen atom. Finally, after completion of the intact ethylideneammonium structure, the CH_3 group is rotated about the CC bond axis until its equilibrium position is reached. The process described here is considerably more complicated than is generally assumed to be the case for a suprafacial [1,3] sigmatropic hydrogen shift[65-67]. However, with all its structural complexity it stands much closer to chemical intuition than, for example, a process in which a hydrogen atom is shifted along a more or less straight line over the molecule.

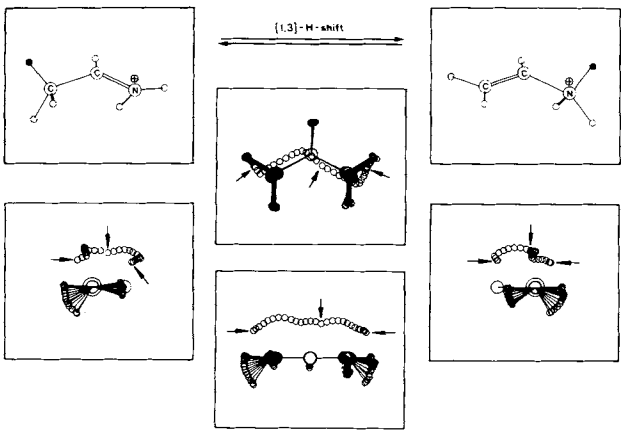


Fig. 23. Minimum-energy reaction path for the suprafacial [1,3] sigmatropic hydrogen shift in protonated vinylamine as shown by means of superimposed molecular structures in four different projections: top view onto the CCN plane (middle top), side view in the CCN plane (middle bottom), view along the CC bond axis (bottom left), view along the NC bond axis (bottom right). Start, end, and saddle point positions of the migrating hydrogen atom are indicated by arrows.

With this example, we emphasize the benefit to be gained from rigorous localization of saddle points as well as from the calculation of gradient paths on multidimensional energy hypersurfaces. With the advent of improved localization methods and more powerful quantum-chemical procedures, such studies will become more and more feasible in the future. A thorough examination of carefully chosen prototype reactions by means of appropriate theoretical models will provide valuable contributions to our understanding of chemical reactivity.

I am particularly grateful to my co-authors who are cited in the bibliography. Financial support by the Swiss National Science Foundation and by Hoffmann-La Roche & Co. (Basel) is gratefully acknowledged.

Received: September 28, 1979 [A 301 IE]
German version: Angew. Chem. *92*, 1 (1980)

[1] *A. A. Frost, R. G. Pearson:* Kinetics and Mechanism: A Study of Homogenous Chemical Reactions. 2nd Ed. Wiley, New York 1961.
[2] *H. Eyring, M. Polanyi,* Z. Phys. Chem. *B 12*, 279 (1931).
[3] *J. H. Knox:* Molecular Thermodynamics; An Introduction to Statistical Mechanics for Chemists. Wiley, New York 1978.
[4] *S. W. Benson:* Thermochemical Kinetics; Methods for the Estimation of Thermochemical Data and Rate Parameters. Wiley, New York 1976.
[5] *C. J. Collins, N. S. Bowman:* Isotope Effects in Chemical Reactions. Van Nostrand Reinhold, New York 1970.
[6] *N. B. Chapman, J. Shorter:* Advances in Linear Free Energy Relationships. Plenum Press, New York 1972.
[7] *J. L. Franklin:* Ion-Molecule Reactions. Vol. 1 and 2. Butterworths, London 1972.
[8] *T. A. Lehman, M. M. Bursey:* Ion Cyclotron Resonance Spectrometry. Wiley, New York 1976.
[9] *M. T. Bowers:* Gas Phase Ion Chemistry. Vol. 1. Academic Press, New York 1979.
[10] *W. H. Miller:* Dynamics of Molecular Collisions. Part A and B. Plenum Press, New York 1976.
[11] *J. C. Polanyi, J. L. Schreiber:* Physical Chemistry—An Advanced Treatise. Vol. VIA, Chap. 6. Academic Press, New York 1974.
[12] *J. P. Toennies:* Physical Chemistry—An Advanced Treatise. Vol. VIA, Chap. 5. Academic Press, New York 1974.
[13] *W. J. Orville-Thomas:* Internal Rotation in Molecules. Wiley, New York 1974.
[14] *D. G. Lister, J. N. McDonald, N. L. Owen:* Internal Rotation and Inversion. Academic Press, New York 1978.

[15] *H. B. Bürgi*, Inorg. Chem. *12*, 2321 (1973).
[16] *H. B. Bürgi, J. D. Dunitz, E. Shefter:* J. Am. Chem. Soc. *95*, 5065 (1973).
[17] *H. B. Bürgi*, Angew. Chem. *87*, 461 (1975); Angew. Chem. Int. Ed. Engl. *14*, 460 (1975).
[18] *R. E. Rosenfield, Jr., R. Parthasarathy, J. D. Dunitz*, J. Am. Chem. Soc. *99*, 4860 (1977).
[19] *R. E. Rosenfield, Jr., J. D. Dunitz*, Helv. Chim. Acta *61*, 2176 (1978).
[20] *W. B. Schweizer, G. Procter, M. Kaftory, J. D. Dunitz*, Helv. Chim. Acta *61*, 2783 (1978).
[21] *K. L. Brown, L. Damm, J. D. Dunitz, A. Eschenmoser, R. Hobi*, Helv. Chim. Acta *61*, 3108 (1978).
[22] *J. D. Dunitz:* X-Ray Analysis and the Structure of Organic Molecules. Chap. 7. Cornell University Press, Ithaca 1979.
[23] *K. Müller, L. D. Brown*, Helv. Chim. Acta *61*, 1407 (1978).
[24] *R. Meyer*, J. Mol. Spectrosc. *76*, 266 (1979).
[25] *F. J. Lovas, F. O. Clark, E. Tiemann*, J. Chem. Phys. *62*, 1925 (1975).
[26] *R. Meyer*, Helv. Chim. Acta *61*, 1418 (1978).
[27] *K. Fukui*, J. Phys. Chem. *74*, 4161 (1970).
[28] *K. Fukui, S. Kato, H. Fujimoto*, J. Am. Chem. Soc. *97*, 1 (1975).
[29] *A. Tachibana, K. Fukui*, Theor. Chim. Acta *49*, 321 (1978).
[30] *K. Ishida, K. Morokuma, A. Komornicki*, J. Chem. Phys. *66*, 2153 (1977).
[31] *M. V. Basilevsky*, Chem. Phys. *24*, 81 (1977).
[32] *P. Empedocles*, Int. J. Quantum Chem. *3S*, 47 (1969).
[33] *M. J. S. Dewar, S. Kirschner*, J. Am. Chem. Soc. *93*, 4290, 4291, 4292 (1971).
[34] *O. Ermer*, Struct. Bonding (Berlin) *27*, 161, 202 (1976).
[35] *J. W. McIver, Jr., A. Komornicki*, J. Am. Chem. Soc. *94*, 2625 (1972).
[36] *A. Komornicki, J. W. McIver, Jr.*, J. Am. Chem. Soc. *96*, 5798 (1974).
[37] *K. Jug*, Theor. Chim. Acta *42*, 303 (1976).
[38] *T. A. Halgren, W. N. Lipscomb*, Chem. Phys. Lett. *49*, 225 (1977).
[39] *R. F. Nalewajski, T. S. Carlton*, Acta Phys. Pol. *A 53*, 321 (1978).
[40] *L. C. W. Dixon:* Nonlinear Optimization. The English Universities Press, London 1972.
[41] *A. Komornicki, K. Ishida, K. Morokuma, R. Ditchfield, M. Conrad*, Chem. Phys. Lett. *45*, 595 (1977).
[42] *D. Poppinger*, Chem. Phys. Lett. *35*, 550 (1975).
[43] *P. G. Mezey, M. R. Peterson, I. G. Csizmadia*, Can. J. Chem. *55*, 2941 (1977); *M. R. Peterson, I. G. Csizmadia* in *I. G. Csizmadia:* Applications of MO Theory in Organic Chemistry. Progress in Theoretical Organic Chemistry, Vol. 2. Elsevier, Amsterdam 1977, p. 117.
[44] *T. A. Halgren*, private communication; see also ref. [4] in [38].
[45] *K. Müller, L. D. Brown*, Theor. Chim. Acta *53*, 75 (1979).
[46] *J. Pancíř*, Collect. Czech. Chem. Commun. *40*, 1112 (1975).
[47] *T. A. Halgren, W. N. Lipscomb*, J. Chem. Phys. *58*, 1569 (1973).
[48] *P. K. Pearson, H. F. Schaefer III, U. Wahlgren*, J. Chem. Phys. *62*, 350 (1975).
[49] *D. E. Milligan, M. E. Jacox*, J. Chem. Phys. *39*, 712 (1963); *47*, 278 (1967).
[50] *C. A. Arrington, E. A. Ogryzlo*, J. Chem. Phys. *63*, 3670 (1975).
[51] *G. L. Blackman, R. D. Brown, P. D. Godfrey, H. I. Gunn*, Nature *261*, 395 (1976).
[52] *R. J. Saykally, P. G. Szanto, T. G. Anderson, R. C. Woods*, Astrophys. J. *204*, L143 (1976).
[53] *L. E. Snyder, J. M. Hollis*, Astrophys. J. *204*, L139 (1976).
[54] *W. F. Huebner, D. Buhl, L. E. Snyder*, Astronom. J. *81*, 671 (1976).
[55] *R. D. Brown*, Nature *270*, 39 (1977).
[56] *W. Th. A. M. Van der Lugt, P. Ros*, Chem. Phys. Lett. *4*, 389 (1969).
[57] *J. J. C. Mulder, J. S. Wright*, Chem. Phys. Lett. *5*, 445 (1970).
[58] *C. D. Ritchie, G. A. Chappell*, J. Am. Chem. Soc. *92*, 1819 (1970).
[59] *A. Dedieu, A. Veillard*, J. Am. Chem. Soc. *94*, 6730 (1972).
[60] *P. Baybutt*, Mol. Phys. *29*, 389 (1975).
[61] *F. Keil, R. Ahlrichs*, J. Am. Chem. Soc. *98*, 4787 (1976).
[62] *C. Leforestier*, J. Chem. Phys. *68*, 4406 (1978).
[63] *K. Müller, F. Previdoli*, to be published.
[64] *K. Müller, L. D. Brown*, to be published.
[65] *R. B. Woodward, R. Hoffmann:* The Conservation of Orbital Symmetry. Verlag Chemie, Weinheim 1970; Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[66] *Ian Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, New York 1976.
[67] *N. D. Epiotis:* Theory of Organic Reactions. Reactivity and Structure—Concepts in Organic Chemistry, Vol. 5. Springer, Berlin 1978.
[68] *R. D. Bowen, D. H. Williams, G. Hvistendahl*, J. Am. Chem. Soc. *99*, 7509 (1977).

New analytical methods (17)

Chromatographic Resolution of Racemates

By Gottfried Blaschke[*]

A number of racemates can be resolved into optically pure enantiomers by chromatography on optically active adsorbents. Synthetic polymers with optically active amide, amino acid, and crown ether groups, natural products such as starch and cellulose, and also microcrystalline triacetylcellulose are suitable for this purpose. Racemates can also be resolved by gas chromatography on optically active stationary phases.

1. Introduction

Racemates are usually resolved by fractional recrystallization of diastereomeric salts. However, this conventional method is often laborious, involves high losses, is essentially restricted to carboxylic acids and amines, and does not always yield optically pure samples. One well-known textbook of stereochemistry makes the following comments[1a]: "Racemate separation still remains an art. This is why some of the resolutions described in the literature are difficult to reproduce, and also why a highly skilled experimentalist may get further, *i. e.* obtain higher optical purity or a better yield than a previous author!" Attempts have therefore been made to develop other methods for the resolution of racemic mixtures[1b]. Accordingly, racemic alcohols have been converted with optically active isocyanates into diastereomeric carbamates[2] and racemic amines with optically active lactones into diastereomeric amides [3] and then separated on alumina

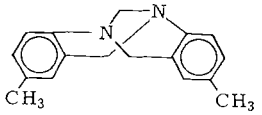
[*] Prof. Dr. G. Blaschke
Pharmazeutisches Institut der Universität
An der Immenburg 4, D-5300 Bonn 1 (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0101-0013 $ 02.50/0*

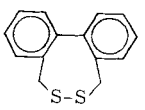
or on silica gel. However, these resolutions too require the presence of specific functional groups in the enantiomers, and are inconvenient because of the need to prepare and then to hydrolyze the diastereomers.

The present review is concerned with the direct chromatographic method, *i.e.* with the resolution of racemates on optically active adsorbents. Diastereomeric complexes are formed by reversible adsorption, and their different stabilities result in different rates of elution of the two enantiomers. A separation is thus possible.

Although many research groups have sought suitable optically active adsorbents for the chromatographic resolution of racemates since *Willstätter*[4], until recently the numerous attempts at separations, described in some 400 publications[5] and several reviews[6-8], have only been successful in exceptional cases. One known example is the resolution of Tröger's base *(1)* which, because of its sensitivity to acids, is otherwise not resolvable. In the chromatography of *(1)* on (+)-lactose hydrate as an optically active adsorbent, *Prelog* and *Wieland*[9] enriched the enantiomers in the initial and the final fraction and separated the excess of enantiomers by fractional crystallization. However, from 6 g of the racemate eluted with 18 liters of petroleum ether on 2.7 kg of adsorbent, they obtained only 150 mg of (+)- and (−)-*(1)*.



(1)



(2)

Similarly, *Lüttringhaus et al.*[10] resolved the cyclic disulfide *(2)* into the enantiomers by repeated chromatography on a 6.5 m-long column packed with partially acetylated cellulose, followed by fractional crystallization. Chromatographic enrichments of enantiomers have also been accomplished on starch[7], cellulose, and many synthetic adsorbents such as polymer-bound L-ephedrine or polymer-bound L-amino acids[11]. In 1970 *Losse et al.*[6] described the state of the chromatographic resolution of racemates as follows: "The survey shows that reliably reproducible separation effects can now be demonstrated on many asymmetric carriers and phases... Nonetheless, it may by expected that in the foreseeable future this separation principle, by further development of the carrier substances and the methodology, can be transformed into an economical preparative process". In the case of many racemates this expectation has since been fulfilled.

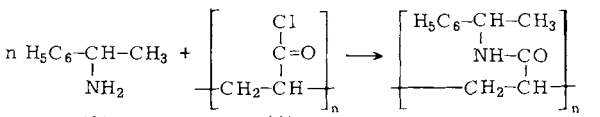
2. Polymerizates of Optically Active Acrylamides and Methacrylamides

2.1. Search for New Adsorbents with the Use of Doubly-Labeled Racemates

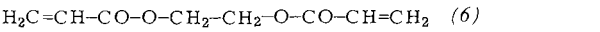
A systematic search for better adsorbents is made more difficult by the material and time expenditure on the preparation of large quantities of the column material and the performance and evaluation of the chromatographic experiments. Moreover, optically active impurities from the column material frequently simulate a separation.

Enantiomer-specifically doubly-labeled racemates[12] have proved very successful in the search for new adsorbents. As in the majority of earlier experiments, mandelic acid was at first used as a test racemate for efficiency of the column resolution, one enantiomer being labeled with ^3H and the other with ^{14}C. The weight or the concentration of one enantiomer is accordingly proportional to the ^3H and that of the other to the ^{14}C activity. The experiment is performed with about 1 mg of the racemate, requiring only about 5 g of adsorbent. Since neither the impurities from the solvent nor any optically active impurities interfere with the radioactivity measurements, double-labeling makes it possible to determine the resolving power of new adsorbents rapidly and reliably.

Synthetic chromatographic adsorbents had previously always been prepared by polymer-analogous reactions of optically active monomers with reactive polymers. The new adsorbents were also at first synthesized by reacting optically active amines, such as 1-phenylethylamine *(3)*, with cross-linked polyacrylic acid chloride *(4)* [cross-linking agent: ethylene diacrylate *(6)*][13].

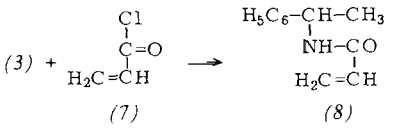


(3) *(4)* *(5)*

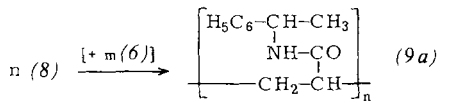


(6)

Adsorbents such as the polyamide *(5)* also do not separate racemic mandelic acid to a significant extent[13,14]. Only on some basic polyesters[13] could a low degree of enrichment be established in the initial and final fractions, as on cellulose and starch, and even this slight resolving action was restricted to carboxylic acids[13,14]. Chromatographic resolution of racemates on adsorbents prepared by polymer-analogous reactions is accordingly an exception rather than the rule.



(7) *(8)*



(9a)

The resolving power of polymeric adsorbents is extremely dependent on the method of synthesis. Thus, the polyamide *(9a)*, obtained by radical copolymerization of acrylamide *(8)* with the cross-linking agent ethylene diacrylate *(6)*, in contrast to the polymer-analogously prepared adsorbent *(5)* having the same composition, separates both racemic mandelic acid and racemic mandelamide[15]. *(8)* can be obtained in a high yield by the reaction of (*S*)-1-phenylethylamine *(3)* with acrylic acid chloride *(7)*. The resolving power of such polymers is strongly influenced by the polymerization conditions and emulsifier and by the concentration of solvent and cross-linking agent. Optimization was achieved by systematic variation of the polymerization parameters and testing the polymers by chromatography with doubly-labeled mandelic acid[15].

Radical suspension polymerization gives the adsorbents in practically quantitative yields as snow-white bead polymerizates that swell in benzene, toluene, or chloroform to give transparent gels and enable high flow velocities in the chromatographic column. Because of the cross-linking the adsorbents are insoluble and mechanically stable, can be dried and swelled again, and can be used for chromatography as often as desired without losing their resolving power.

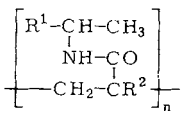
The resolution of mandelic acid and mandelamide on some of these polyamides is summarized in Table 1 (phenylethyl- and cyclohexylethylamine derivatives[16, 17]) and Table 2 (amino acid esters[18]). The efficiency of the resolution is expressed by the optical yield[14]. This was calculated from the optical purity p_i [Eq. (1)] and the mass m_i of each chromatographic fraction in accordance with Eq. (2).

$$p_i = \text{optical purity} = \frac{\text{specific rotation of the enantiomer mixture}}{\text{specific rotation of the pure enantiomer}} \times 100\,[\%] \quad (1)$$

$$\text{optical yield} = \frac{\sum (p_i m_i)}{\sum m_i}\,[\%] \quad (2)$$

If the entire eluate of a chromatographic experiment is collected in the form of a levorotatory fraction and a dextrorotatory fraction, the average of the optical purities of these two fractions is the optical yield. For this reason it is also described as the "average activation Ā"[19] or as the "percentage activation calculated over all chromatographic fractions"[20].

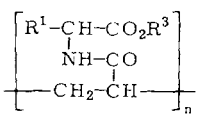
Table 1. Resolving power of polyacrylic and polymethacrylic amides of optically active phenylethyl- and cyclohexylethylamine derivatives of type *(9a)*—*(9f)* [16, 17], crosslinked with ethylene diacrylate *(6)* [Column length: 11—28 cm; solvent system: benzene/dioxane mixtures].



(9a)-*(9f)*

Polymer	R^1	R^2	Optical yield [%] Mandelic acid	Mandelamide
(9a)	C_6H_5	H	28	35
(9b)	C_6H_5	CH_3	8.0	81
(9c)	*c*-C_6H_{11}	H	12	35
(9d)	*c*-C_6H_{11}	CH_3	58	92
(9e)	1-Naphthyl	CH_3	0.0	97
(9f)	*p*-I C_6H_4	H	0.0	0.0

Table 2. Resolving power of polyacrylamides of optically active aminoacid esters of type *(9g)*—*(9m)* [18], cross-linked with ethylene diacrylate *(6)* [Column length: 17—34 cm; solvent system: benzene/dioxane mixtures].



(9g)-*(9m)*

Polymer	R^1	R^2	Optical yield [%] Mandelic acid	Mandelamide
(9g)	CH_3	C_2H_5	14	18
(9h)	*c*-$C_6H_{11}CH_2$	C_2H_5	31	59
(9i)	C_6H_5	C_2H_5	46	34
(9j)	$C_6H_5CH_2$	C_2H_5	51	96
(9k)	*p*-$HOC_6H_4CH_2$	C_2H_5	0	0
(9l)	*p*-$CH_3CO_2C_6H_4CH_2$	C_2H_5	21	42
(9m)	$C_6H_5CH_2$	*t*-C_4H_9	89	80

With a few exceptions, short columns of polymerizates *(9)* resolve both mandelic acid and mandelamide to a considerable extent (Fig. 1). Replacement of benzene, the toxic component of the solvent system, by toluene leads in all the cases tested to practically the same results[22].

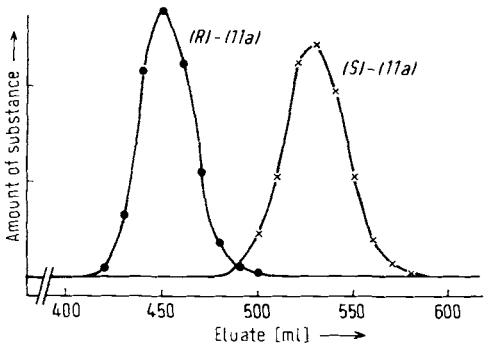


Fig. 1. Chromatographic resolution of 0.1 mg of doubly-labeled racemic mandelamide *(11a)* on 9.0 g of *(9j)* [column: 23 × 1.7 cm; solvent system: toluene/dioxane (95:5)]. The total amount of the substance applied to the column is recovered.

As can be seen from Tables 1 and 2, even small differences in the structure of the optically active group exert an effect on the outcome of the resolution. Moreover, substitution of the polymer chain changes the stereoselectivity of the adsorption. Whereas, for example, the polyacrylamide *(9a)* retains (*S*)-mandelic acid and (*R*)-mandelamide more strongly, on the polymethacrylamide *(9b)*, with otherwise similar structure and configuration, the other enantiomer is adsorbed in preference[16]. This observation as well as the complete absence of a resolving action of polyamides, such as *(5)*, prepared from reactive polymers excludes the interaction of *individual* optically active residues of the adsorbent with the enantiomers as the cause of the resolution. More likely, the resolution proceeds because of different fitting of the enantiomers into asymmetric cavities in the polymer chain. In the radical polymerization of the acrylamides and methacrylamides with bulky substituents it is supposed that ordered regions with a helix structure are produced. Within the helix is the polymer chain with the adsorptively active amide groups; the optically active substituents point outward. Asymmetric cavities are formed between them, and substances are attracted by hydrogen bonding. The different degrees of fit determine the average residence times of the enantiomers in the adsorbent's cavities.

As expected, when the configuration of the optically active residues on the adsorbent is changed, the configuration of the more strongly bound enantiomer also changes, the results being otherwise the same[15].

2.2. Preparative Resolution of Racemic Model Compounds

Table 3 gives a small selection of preparative resolution experiments on the polyacrylamides *(9a)*, *(9c)*, and *(9j)* and also on the polymethacrylamides *(9b)* and *(9d)*[17, 21]. *(9a, b)* can be readily prepared from (*S*)-1-phenylethylamine (*S*)-*(3)*, *(9c, d)* from (*S*)-1-cyclohexylethylamine and *(9j)* from (*S*)-phenylalanine. The standard solvent used in the chromatographic experiments was benzene. If the substance was eluted too slowly, the more polar benzene/dioxane mixtures were used, if too fast, the less polar benzene/cyclohexane

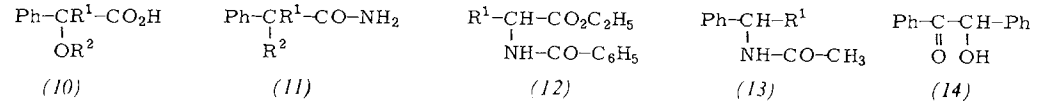
mixtures. Also in these preparative separations replacement of the benzene by toluene did not change the results. According to blank tests, the eluate of the cross-linked polyamides contained no residues; the experiments were thus evaluated by weighing the evaporation residues and measuring the rotation values. Since the resolving power of the columns remained unchanged after repeated use, the preparative resolutions were performed on the same column packings with 150—300 mg of the non-labeled racemates, with layer heights of 16—65 cm. As expected, the resolution proved to be better on the longer columns [experiments with racemates *(13a, b)*].

Tables 1 and 2 and so far not investigated on a preparative scale are particularly suitable.

Complete resolution is achieved by repeated chromatography on one and the same adsorbent. To check the efficiency of the resolution the eluate is pumped through the cell of a polarimeter and a differential refractometer and then back into the column. For example after four runs through a column of polyamide *(9j)*, mandelamide *(11a)* is resolved completely and without losses[22].

So far it has only been possible to obtain optically pure *(13b)* by chromatographic resolution of the racemate. Previous attempts to synthesize this optically active amide *via*

Table 3. Optical yields of preparative resolution experiments with compounds of type *(10)*—*(14)* on adsorbents *(9j)* and *(9a—d)* (for explanations see text).



(10) *(11)* *(12)* *(13)* *(14)*

Ph = C_6H_5

Racemate	R^1	R^2	Optical yield [%] of the experiment on:				
			(9j)	*(9a)*	*(9b)*	*(9c)*	*(9d)*
(10a)	H	CH_3	[a]	27	8.5	47	0.9
(10b)	*c*-C_6H_{11}	H	[a]	25	11	4.0	18
(11a)	H	OH [f]	60	39	29	[a]	[a]
(11b)	CH_3	OH	32	39	26	43	63
(12a)	*p*-$HOC_6H_4CH_2$		25	27	33	39	81
(12b)	3-Indolyl-CH_2		29	8.6	20	54	64
(13a)	CH_3		35	26	36 [b] 57 [c]	29	33
(13b)	$CH(CH_3)_2$		6.4	24	44 [d] 58 [e]	22	34
(14)			7.3	0.6	22	10	22

[a] Not determined. Column length [cm]: [b] 43, [c] 116, [d] 39, [e] 107. [f] The discrepancy from the values in Tables 1 and 2 is explained by different solvent system, column length and amount of racemate.

All the compounds in Table 3 can form hydrogen bridges with the amide groups of the optically active adsorbents and can usually be resolved to a considerable extent by chromatography. An example is the resolution of the ethyl ester of *N*-benzoyltyrosine *(12a)* on polymethacrylamide *(9d)* (Fig. 2). Replacement of the benzene in the solvent system by toluene slightly improves the resolution[22].

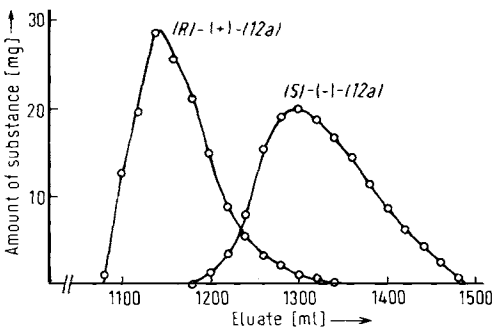


Fig. 2. Chromatographic resolution of 302 mg of racemic *N*-benzoyltyrosine ethyl ester *(12a)* on 65 g of *(9d)* [column: 65 × 2.5 cm; solvent system: benzene/dioxane (80:20)].

In experiments with new racemates it is impossible to predict on which adsorbent they will be resolved best. It may be that for some racemates adsorbents other than those listed in conventional resolution of the racemic amine *(13b)* (with NH_2 instead of $NHCOOH_3$) have been unsuccessful[23]. A dextrorotatory sample of unknown optical purity was finally obtained from an optically active carboxylic acid[23a]. Chromatography of *(13b)* on adsorbent *(9b)* yielded in the initial and final fractions preparations with much higher rotation values, which did not increase when the chromatography of the samples was repeated, thus confirming the optical purity[21]. The resolving action of optically active polyamides remains largely unchanged with higher column loadings. Even with a weight ratio of the adsorbent *(9b)* to the racemate *(13b)* such as 40:1, 12% of the (+)-enantiomer was still obtained in optically pure form[23b].

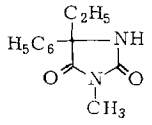
2.3. Preparative Resolution of Racemic Pharmaceuticals

In the case of pharmaceuticals the enantiomers usually differ not only in their physiological action but also in their undesirable side effects. The polyamides of type *(9)* have been developed with the particular aim of resolving such racemates. The polyamides resolve chiral drugs with amide and imide structures, whose enantiomers can only be synthesized with difficulty (if at all) by conventional methods.

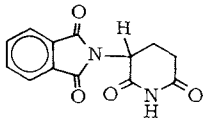
Table 4 demonstrates the extreme differences in the resolving action of those adsorbents in the case of two drugs. Whereas the polyamides *(9j)* and *(9a—d)* resolve racemic

mandelamide *(11a)* almost equally well, the racemic antiepileptic agent mephenytoin *(15)* (Mesantoin®) is resolved well on *(9j)* and poorly on *(9d)*. Conversely, thalidomide *(16)* (Contergan®) is hardly separated into its enantiomers on *(9j)* but completely on *(9d)*.

Table 4. Optical yields of preparative resolution experiments with mephenytoin *(15)* and thalidomide *(16)* on adsorbents *(9j)* and *(9a–d)*. (For explanations see text.)



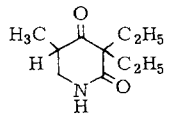
(15)



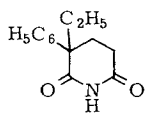
(16)

Racemate	Optical yield [%] of experiment on				
	(9j)	*(9a)*	*(9b)*	*(9c)*	*(9d)*
(15)	55	9.8	34	21	0.6
(16)	3.8	7.2	42	1.5	100

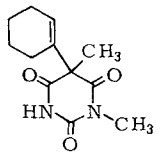
Hitherto it has only been possible to obtain the hypnotic agent methyprylone *(17)* (Noludar®) in optically active form by performing 400 crystallizations (20 kg of initial material), with a yield of less than 0.05%[24]. By means of chromatography on the cyclohexyl polymers *(9c)* and *(9d)*, *(17)* can be resolved partially with optical yields of around 35%.



(17)



(18)



(19)

The hypnotic agents glutethimide *(18)* (Doriden®) and hexobarbital *(19)* (Evipan®) are also resolved to a considerable extent. (+)- and (−)-*(15)* and (+)-*(19)* have both been isolated in optically pure form by repeated chromatography[17]. Of the racemates so far chromatographed on polyamides, thalidomide *(16)* is separated best (Fig. 3)[17,26].

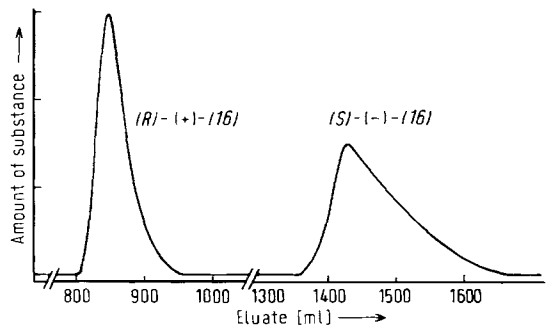
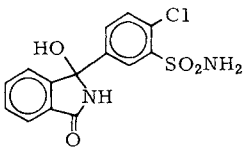


Fig. 3. Chromatographic resolution of 52 mg of racemic thalidomide *(16)* on 65 g of *(9d)* [column: 80 × 2.3 cm; solvent system: benzene/dioxane (80:20)].

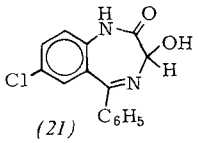
Formerly, the enantiomers of this substance, used at one time as a racemate, were only accessible by synthesis from a costly optically active precursor—a laborious process[25]. Even on a preparative scale it is much simpler to use chromatographic resolution. Although the peaks broaden as the column loading increases, up to 500 mg of racemic *(16)* can be resolved on the same column with 65 g of *(9d)*. In this run a substance-free fraction amounting to at least 120 ml is left between the eluates of dextro- and levorotatory forms. The column packing can be used as often as desired.

Since on the same column small quantities of the substance can also be separated without losses, the optical purity can be determined analytically by means of chromatography. Synthetic optically active thalidomide has been chromatographed on *(9d)*. The ratio of the enantiomers and thus the degree of racemization could be determined exactly by spectrophotometric assay of the two eluate fractions[17].

The chromatographically isolated thalidomide enantiomers have been investigated for teratogenic action[26]. On intraperitoneal administration to mice and rats only (*S*)-(−)-thalidomide displayed teratogenic properties; under the experimental conditions used, (*R*)-(+)-thalidomide did not cause any malformations even at the highest doses.



(20)



(21)

The diuretic chlorthalidone *(20)* (Hygroton®) is completely resolved on the polyacrylamide *(9j)*[22]. In the experiment shown in Figure 4 the column temperature was raised to 40 °C after the elution of (−)-chlorthalidone; this increased the elution rate of the (+)-enantiomer, *i. e.* the time required for the resolution was shortened.

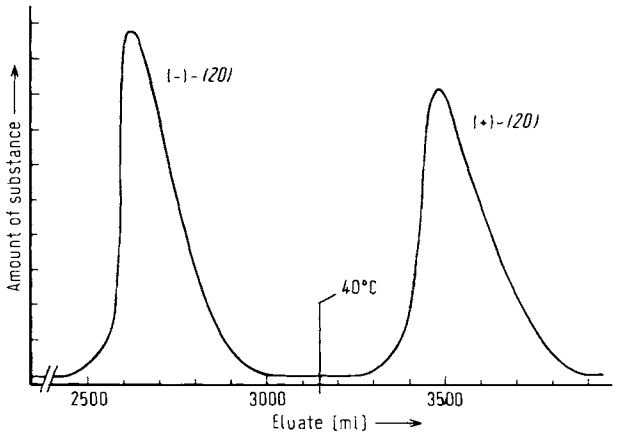
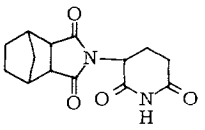


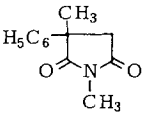
Fig. 4. Chromatographic resolution of 530 mg of racemic chlorthalidone *(20)* on 250 g of *(9j)* [column: 76 × 3.2 cm; solvent system: toluene/dioxane (1:1); pressure 1.2 bar].

The two enantiomers were thus obtained in optically pure form for the first time. However, they racemize very readily in an alkaline solution[22]. The psychopharmaceutical oxazepam *(21)* (Adumbran®) can also be resolved completely by chromatography on polyamide *(9j)*[22], but the enantiomers racemize under the catalytic influence of a glass surface. They must therefore be collected and evaporated in plastic vessels. Compounds that racemize so readily can only be separated into their enantiomers by chromatography.

Other drugs, such as the potential hypnotic biglumide *(22)*[27], have also been separated on polyamides[17]. Both

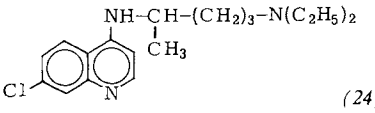


(22)



(23)

enantiomers have been isolated from *(22)*[22]. Compounds with *N*-alkylated imide groups, such as mesuximide *(23)* (Petinutin®), that are unable to form hydrogen bridges with the adsorbent, are eluted with the solvent front and are only slightly resolved[17].



(24)

By means of chromatographic resolution it was possible to test the rotation values for optically active chloroquine *(24)*[29]. As an important antimalarial agent (Resochin®), *(24)* had previously been separated *via* diastereomeric salts into samples considered to be enantiomers, with $[\alpha]_D$ values of $+12.3$ and $-13.2°$[28]. Since these preparations did not differ in their antimalarial action and toxicity, chloroquine has become the textbook example of a drug whose enantiomers, contrary to experience, exhibit the same undesirable and desirable pharmacological effects. By chromatography on polyamide *(9j)*, however, a chloroquine sample with a much higher specific rotation is obtained[29]. The optical purity of the earlier preparations was accordingly only some 10%. Optically pure (+)-chloroquine, which became available by synthetic methods too[29], is more effective against malaria[30,31] and is also less toxic[31] than the racemate.

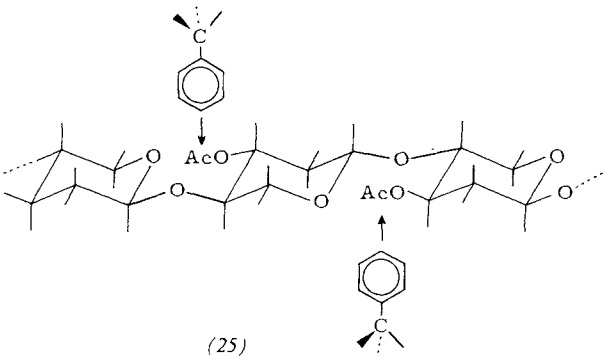
3. Microcrystalline Cellulose Triacetate

3.1. Principle of the Resolution

Microcrystalline cellulose triacetate [cf. *(25)*], introduced by *Hesse* and *Hagel*[32], is an optically active adsorbent that in many cases allows an astonishingly good resolution to be achieved. *Lüttringhaus*[10] had extensively investigated racemate resolutions on a partially acetylated cellulose, "cellulose 2½-acetate", but generally had observed only low degrees of enrichment. These cellulose esters were prepared in a homogeneous solution and then precipitated, the original crystalline structure of the cellulose being broken down.

Cellulose can also be acetylated heterogeneously in a suspension in benzene, the fiber structure with crystalline areas then remaining unchanged. The lamellar arrangement in the manner of a crystalline lattice acts as a two-dimensional molecular sieve, making possible the inclusion of foreign molecules. These are held between two layers in an environment which is asymmetric owing to the sterically fixed ester groups of the cellulose triacetate reaching into the cavities. Since the chromatographic resolution of racemates is based on the different degrees of fit into these cavities, *Hesse* called this process inclusion chromatography.

A phenyl group bearing as few substituents as possible in the vicinity of the chirality center is particularly advantageous for the resolution; this group fits especially well into the gaps between the pyran rings of the cellulose fiber and is thus the anchoring group. The racemate to be separated thus needs no functional group for the absorption on the chiral matrix.

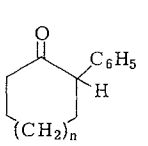


(25)

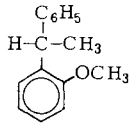
By dissolution and reprecipitation of the microcrystalline cellulose triacetate the crystalline regions are destroyed and the resolving power is almost completely lost. The different resolving capacities of microcrystalline and amorphous cellulose triacetate are similar to those found for the synthetic polyamides. Here too, uniform arrangements of the optically active residues enabling resolutions were formed only in the polymerization step of optically active monomers.

3.2. Resolution of Model Compounds

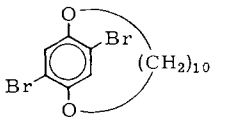
The standard solvent system for chromatography on microcrystalline cellulose triacetate is 95% ethanol, in which the absorbent swells well but is only sparingly soluble. *Hesse* and *Hagel* have chromatographed many racemates on a 40-cm column. Under these conditions the following compounds were completely resolved: Tröger's base *(1)*, 1,2-dithia-4,5:6,7-dibenzocyclooctadiene *(2)*[33], 2-phenylcyclohexanone *(26a)*, 2-phenylcycloheptanone *(26b)*, 2-(1-phenylethyl)anisole *(27)*, and 2,5-dibromo-*O,O'*-decamethylenehydroquinone *(28)*[32].



(26a), n = 1
(26b), n = 2



(27)



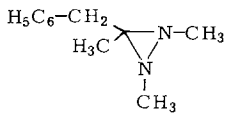
(28)

Other racemates, however, were resolved incompletely or even poorly. Thus, *m*- and *p*-substituents and carboxyl groups impair the separation. *Hesse*[34] evaluated the applicability of microcrystalline cellulose triacetate as follows: "Even with inclusion chromatography on cellulose esters, complete racemate resolution still remains a matter of luck. A measurable activation of chiral compounds, however, is nearly always obtained".

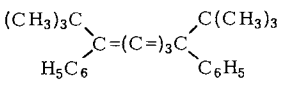
In the author's research group, *Markgraf*[22] chromatographed many racemates only partly resolved on polyamides for comparison with the resolutions on microcrystalline cellulose triacetate. Mostly, racemates with an unsubstituted aromatic group in the direct vicinity of the chirality center

were selected, in accord with previous results the optimal prerequisite for resolution on the triacetate. The 85-cm cellulose triacetate column resolved these racemates with very variable optical yields, sometimes with more success and sometimes with less than the polyamides, but never completely. Thus, the tyrosine derivative *(12a)* extensively separated on the polyamide *(9d)*, was not separated at all on the triacetate, while benzoin *(14)* and benzoin acetate [*(14)*, $OCOCH_3$ in place of OH] were separated better than on polyamides.

Microcrystalline cellulose triacetate has moreover been used for the chromatographic resolution of compounds which easily racemize.



(29)

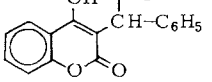


(30)

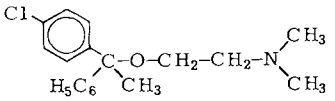
Mannschreck et al.[35] resolved chiral diaziridines such as *(29)* by repeated chromatography on a short column; *Bertsch* and *Jochims*[36] resolved the chiral pentatetraene *(30)* on a cooled column.

3.3. Separation of Drugs and their Synthetic Precursors

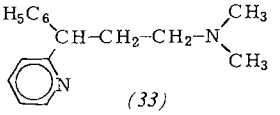
The suitability of microcrystalline cellulose triacetate for the chromatographic separation of enantiomeric drugs has also been investigated by *Markgraf*[22] on some examples. The adsorbent is not suitable for the resolution of thalidomide *(16)*, chlorthalidone *(20)*, oxazepam *(21)*, and chloroquine *(24)*. Other drugs, such as the anticoagulants phenprocoumon *(31a)* (Marcumar®) and warfarin *(31b)* or the antihistamines chlorphenoxamine *(32)*(Systral®) and pheniramine *(33)* (Avil®), are also eluted in fractions displaying no measurable optical activity, although they satisfy the precondition of having an unsubstituted phenyl group at the chirality center.



(31a), R = CH_3
(31b), R = $COCH_3$



(32)



(33)

Glutethide *(18)*, mephenytoin *(15)*, and mesuximide *(23)* are, however, resolved to a considerable extent. A slight effect is observed with the chromatography of methyprylone *(17)*, which does not contain a phenyl group. Surprisingly good results are obtained with the chromatography of *N*-methylated barbiturates on cellulose triacetate. According to *Knabe et al.*[37], these barbiturates are accessible from optically active precursors; the enantiomers frequently exhibit very different pharmacological activity.

Hexobarbital *(19)* (Fig. 5) and the *N*-methylated barbiturates *(34a, b, d—f)* were separated completely on microcrystalline cellulose triacetate, *(34c, g)* only partially, and *(34h, i)* not at all (see Table 5). In the case of *(34h)* the difference in size between the ethyl and the propyl group is presumably insufficient, in the case of *(34i)* the chirality center in the side chain is too far away from the adsorptively active imide group in the heterocycle. As shown by the good separation of some aliphatically substituted barbiturates, however, a phenyl group is not absolutely necessary for resolution.

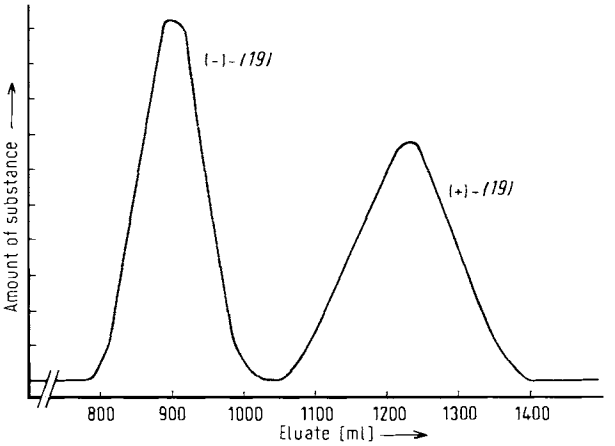
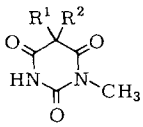


Fig. 5. Chromatographic resolution of racemic hexobarbital *(19)* on cellulose triacetate [column: 85 × 2.5 cm; solvent system: ethanol/water (95:5); pressure 1.2 bar].

Table 5. Preparative resolution experiments with chiral barbiturates on cellulose triacetate [column: 85 × 2.5 cm; solvent: 95-% ethanol]. For some experiments separation and resolution factors are given in addition to the optical yields.

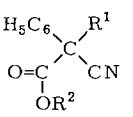


(34a-i)

Racemate	R^1	R^2	Optical yield	Separation factor [a]	Resolution factor [b]
(34a)	Phenyl	CH_3	100		
(34b)	Phenyl	C_2H_5	100	2.3	2.3
(34c)	Phenyl	C_3H_7	48		
(19)	1-Cyclohexenyl	CH_3	100	1.7	1.5
(34d)	1-Cyclohexenyl	C_2H_5	100	2.0	1.7
(34e)	Cyclohexyl	CH_3	100	1.9	1.5
(34f)	Cyclohexyl	C_2H_5	100	2.4	1.7
(34g)	1-Cyclopentenyl	C_2H_5	68		
(34h)	*n*-Propyl	C_2H_5	0		
(34i) [c]	Vinyl	$CH(CH_3)\ C_3H_7$	0		

[a] α = (retention volume of less mobile component minus total dead volume)/(retention volume of more mobile component minus total dead volume).
[b] $R_S = 2$ (retention volume of the less mobile component minus that of more mobile component)/(sum of bandwiths of two peaks).
[c] NH instead of NCH_3.

The cyanoacetic acid esters *(35a—c)*, precursors in the synthesis of chiral barbiturates[37], are also resolved on cellulose triacetate[22]. However, the resolution deteriorates with increasing chain length of the group R^1. For the methyl compound *(35a)* the elution curves of the two enantiomers are far apart. They touch for the ethyl compound *(35b)* and overlap for the butyl compound *(35c)*. The carboxylic acid *(35d)*, however, is not resolved.



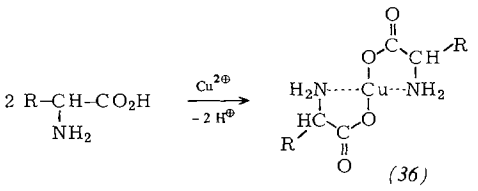
(35a), $R^1 = CH_3$, $R^2 = CH_3$; *(35b)*, $R^1 = C_2H_5$, $R^2 = CH_3$
(35c), $R^1 = C_4H_9$, $R^2 = CH_3$; *(35d)*, $R^1 = CH_3$, $R^2 = H$

With cellulose triacetate too, therefore, as with the polyamides, the outcome of the resolution cannot be reliably deduced from the structure of the enantiomers to be separated.

4. Ligand Chromatography

4.1. Separation Principle

Amino acids in aqueous solution form with Cu^{2+} ions complexes of the structure *(36)*. In these chelates the central atom is bonded to two amino-acid molecules.

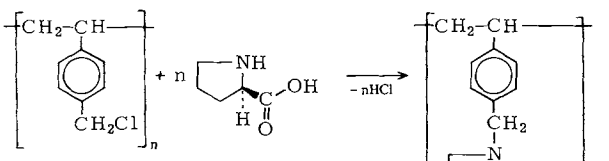


(36)

In ligand chromatography as a method of racemate resolution, an optically active ligand is bonded covalently to an insoluble carrier. After charging this adsorbent with Cu^{2+} ions, the racemate to be resolved is chromatographed. The enantiomers then form diastereomeric complexes with the Cu^{2+} ions and the adsorbent. The differences in complex stability enable chromatographic resolution.

4.2. Performance and Application of Ligand Chromatography

Ligand chromatography particularly has been developed by *Davankov* and his group[38] for the resolution of racemic α-amino acids. A very suitable adsorbent is polymer-bound L-proline; on the one hand it enables good resolution and on the other it practically does not racemize under the conditions of the chromatography, with the result that these adsorbents can be used repeatedly. Polymer-bound L-proline *(39)* is prepared by reacting cross-linked chloromethylated polystyrene *(37)* with L-proline *(38)*[39] or, preferably, with L-proline ethyl ester and subsequent hydrolysis of the ester group[40].

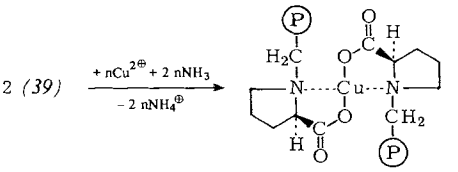


(37) *(38)*

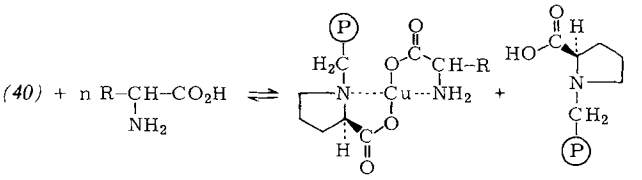
(39)

The light-brown sample *(39)* is washed with ammoniacal copper(II) nitrate solution, whereby it assumes a dark-blue color indicating that the chelate complex *(40)* has been formed between two neighboring polymer-bound proline residues *via* the Cu^{2+} ion. The 2:1 ratio of the amino acid residues to the Cu^{2+} ions has been demonstrated by titration and elementary analysis[40].

After charging with Cu^{2+} ions the adsorbent is ready for use in the resolution experiment. The column packed with the adsorbent is connected to a short column with copper-free adsorbent *(39)* to bind washed-out Cu^{2+} ions. In the chromatography of a racemic α-amino acid on *(40)* each amino acid molecule displaces one of the polymer-bound proline ligands to form the mixed complex *(41)* between the polymer-bound L-proline and the amino acid.



(40)



(41) *(39)*

The two complexes of structure *(41)* with the D- and L-amino acid differ in energy content by up to 825 cal/mol[41]. This difference affects the equilibrium between free and complexed amino acids. The complex *(41)* which contains the L-amino acid is usually less stable, so that the L-amino acid is eluted more rapidly.

Racemic proline can be resolved especially well on the proline polymer *(40)*. The differences in the energy content of the diastereomers are in this case so large that L-proline is already eluted with water and D-proline only with ammonia. In this process ammonia displaces D-proline from the complex *(41)*. Both enantiomers are obtained completely and in an optically pure form by evaporation of the eluates. The resolving capacity is remarkably high. 0.5 g of racemic proline can be completely separated on 12 g of *(40)*[39]. In order to regenerate the column it is only necessary to wash out the excess ammonia with water.

Many other amino acids can be partially or completely resolved into enantiomers on *(40)*[41]. The results of some resolutions on *(40)* are given in Table 6. The separation factor, defined as the ratio of the net retention volumes of the two enantiomers, is given as a measure of the resolution.

Table 6. Resolution factors in the chromatography of some racemic amino acids on *(40)* [41] [solvent: 0.3 M NH_4OH].

Racemate	Separation factor	Racemate	Separation factor
Norvaline	1.40	Phenylalanine	1.63
Norleucine	1.54	Tyrosine	2.46
Proline	4.00	Methionine	1.04
Hydroxyproline	3.85		

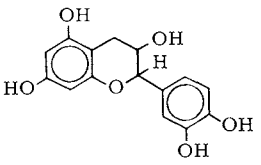
Some other amino acids, such as L-hydroxyproline[42], L-*allo*-hydroxyproline[43], and acetidinecarboxylic acid[41] have also been covalently bound to polystyrene. These adsorbents separate enantiomers, but, like Ni^{2+} complexes[44], generally

to a much lower extent than the Cu^{2+} complex of polymer-bound L-proline. *(40)* also resolves racemates belonging to other classes of compounds, such as diamines, hydroxyamines, and hydroxy acids, at least partly into enantiomers[45].

Thus, by means of ligand chromatography some compounds can be separated very well indeed, the high loading capacity of the adsorbent being particularly advantageous. However, the method is restricted to compounds with amino and/or carboxyl groups that can also be resolved conventionally *via* diastereomeric salts.

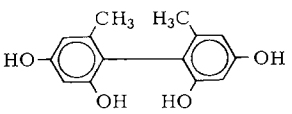
5. Cellulose and Starch

In paper chromatography, the resolution of racemates on the optically active cellulose of the paper has occasionally been observed. Thus, catechol and epicatechol *(42)* are resolved into their enantiomers. This separation can also be used for preparative purposes[46]. Additionally, separations of racemic amino acids[47] and alkaloids[48] by paper chromatography have also been described. However, chromatographic racemate resolution on cellulose requires structural elements such as several neighboring hydroxy groups (*Dalgliesh*'s "three point rule"[47]). The differences in the R_F-values are usually insufficient to obtain preparative amounts of the enantiomers on cellulose columns.

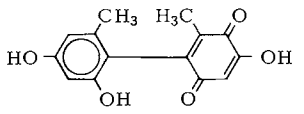


(42)

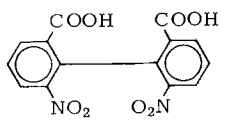
Starch has been particularly used by *Krebs* and *Musso* for the chromatographic resolution of racemates. *Krebs et al.*[7,49] have observed enrichment of the enantiomers of inorganic complexes, hydrophilic camphoric acids, diphenic acids, and amino acids on starch columns. *Musso et al.*[50] have reported on the separation of biphenyl derivatives such as *(43)* and *(44)*. This research group recently succeeded in a complete resolution of 6,6′-dinitrodiphenic acid *(45)*, the alanine derivative *(46)* and its *N*-oxide, and polar orcine derivatives by optimizing the solvent and the temperature. The solvents were aqueous or aqueous-methanolic buffer solutions[51].



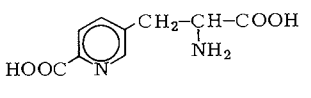
(43)



(44)



(45)



(46)

According to the results hitherto obtained, cellulose seems to be particularly suitable for certain amino acids and starch for polar biphenyl derivatives. Their range of application is thus rather limited. A further disadvantage is the low capacity of these adsorbents.

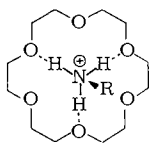
6. Other Optically Active Adsorbents for Liquid Chromatography

The adsorbents discussed in this section have been developed specifically for liquid-chromatographic resolution of racemates belonging to certain substance classes, but, the usually good resolution is obtained at the expense of a narrowly restricted field of application.

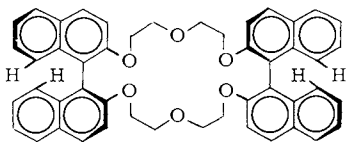
6.1. Chiral Crown Ethers

Crown ethers such as *(47)* form complexes not only with alkali metal ions and alkaline earth metal ions but also with salts of primary alkylamines. In these complexes the hydrogen atoms of the ammonium group are hydrogen bonded to the oxygens of the crown ether.

Optically active crown ethers such as the chiral binaphthyl derivative *(48)* have been developed and utilized for racemate resolution particularly by *Cram* and his co-workers[52]. Binaphthyl derivatives of this type have stable configurations since the rotation around the binaphthyl axis is sterically hindered.



(47)



(48)

Alkylammonium ions of structure R NH_3^+ with a chiral group R are drawn into the asymmetric cavity of the crown ether *(48)* and thus form diastereomeric complexes having various degrees of stability. Such suitably substituted ammonium salts can thus be separated by multiple distribution between an aqueous phase and the solution of *(48)* in a solvent immiscible with water[53].

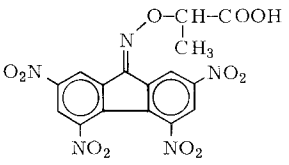
Covalent bonding of optically active crown ethers on cross-linked polystyrene yields optically active adsorbents suitable for the chromatographic racemate resolution of primary alkylammonium ions. With an adsorbent of this kind high-pressure liquid chromatography can be used to resolve several α-amino acids and their methyl esters as perchlorates into enantiomers, the separation factors reaching extremely high values of around 20[54]. With a few exceptions the sequence of the optical forms eluted could be determined in advance using molecule models.

Salts of *p*-hydroxyphenylglycine, phenylalanine, tyrosine, and tryptophan esters have been resolved completely on silica gel substituted with a derivative of the crown ether *(48)* with separation factors of up to 6.4, while salts of 1-phenylethylamine and valine methyl ester have been partly resolved on this adsorbent[55]. These "tailor-made" adsorbents are very well suited for such separations, but the chirality center must be directly adjacent to the ammonium group. Only then do the size differences of the groups at the chirality center come into full play. Unfortunately, such adsorbents are very difficult to prepare.

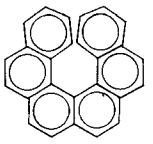
The scope of optically active crown ethers may be extended with macrotricyclic ligands to chiral carboxylic acids whose K^+, Cs^+, and Rb^+ salts also exhibit enantiomer-selective complexation[56].

6.2. Resolution *via* Chiral Charge-Transfer Complexes

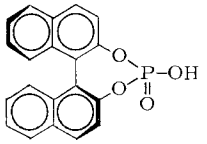
Optically active charge-transfer reagents such as 2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)propionic acid *(49)* ("TAPA") form with chiral arenes such as hexahelicene *(50)* crystalline diastereomeric charge-transfer complexes resolvable by fractional crystallization. Their different stabilities can be utilized for chromatographic separation and racemate resolution of such helicenes. *Gil-Av et al.*[57] first linked optically active *(49)* and similar charge-transfer acceptors to silica gel by adsorption and then resolved helicenes with solvents in which *(49)* is completely insoluble. Resolutions of this kind can also be performed with silica gel to which *(49)* has been bonded covalently *via* the carboxylic group[58]. Not only are racemic helicenes resolved into the enantiomers on such columns, but also mixtures of helicenes are also separated into their components. Since the separation of different helicenes is easier than resolution of the helicene racemates, groups of signals are observed in the chromatogram; each group is split into the two signals of the enantiomers. The (+)-helicene is always bonded more strongly to *R*-(−)-*(49)*. The optically active binaphthyl derivative *(51)*[58] and the dinitrophenyl derivative *(52)*[59] are also suitable charge-transfer acceptors for resolutions. However, resolutions of this type seem to be restricted to helicenes.



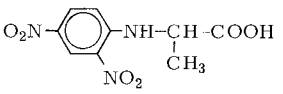
(49)



(50)



(51)



(52)

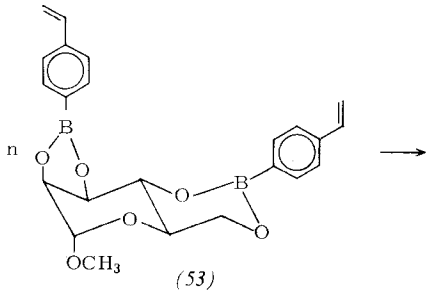
6.3. Optically Active Ion-Exchangers

Chromatographic resolutions of racemic acids and bases have also been attempted on optically active ion-exchangers. Basic ion-exchangers with ephedrine, brucine, and 1-phenylethylamine groups resolve racemic mandelic acid only very poorly[13,14,60]. Pectic acid from sunflowers as well as alginic and polygalacturonic acids have been proposed for the resolution of racemic bases[61]. Ion-exchangers based on Sephadex are also suitable for the enrichment of enantiomers[6,8].

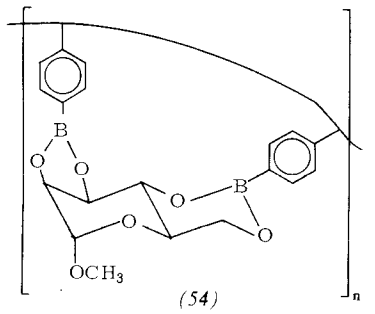
6.4. Polymeric Boronic Acid Derivatives

An interesting possibility for racemate resolution is referred to in a paper by *Wulff et al.*[62]. "Imprinted" silica gels have already been known for some time; these are obtained by precipitation of silica gel from the solution of an optically active compound and its subsequent extraction. In this way asymmetric "prints" of the compound are left behind in the gel particles. This asymmetric imprinting enables the material to adsorb stereoselectively molecules having a similar structure, molecules of the original configuration being bound more strongly. However, so far the resolving powers of such gels have been much too low for practical use[63].

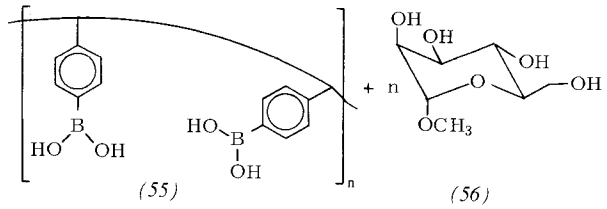
Wulff has obtained such cavitites in the polymeric boronic acid *(55)* by copolymerization of the optically active ester *(53)* with a very high proportion of cross-linked agent to *(54)* and subsequent hydrolytic cleavage of the optically active matrix *(56)*.



(53)



(54)



(55) *(56)*

The asymmetric structure of this boronic acid is extensively stabilized by the high degree of cross-linking. From a solution of racemic methyl-α-mannopyranoside *(56)*, the acid *(55)* takes up in preference the enantiomer originally polymerized-in. In this process the enantiomers are not bound adsorptively but in a reversal of the reaction *(54)* → *(55)* + *(56)* as intermediate boronic esters *(54)*. In suitable solvents an equilibrium is set up between esterified and free *(56)*, and thus almost complete resolution of racemic methyl α-mannopyranoside is possible at very low flow rate on the column. Such experiments have also been performed, with a similar result, on 4-nitrophenyl-α-mannopyranoside.

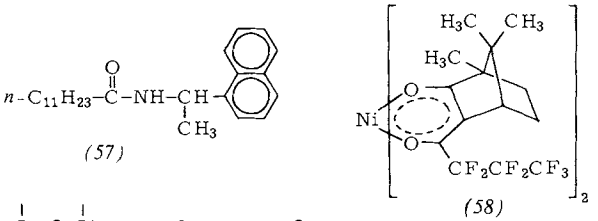
Because of the similarity between the resolution process and partial steps of enzymatic processes, these separation materials are also known as enzyme-analogue polymers.

7. Resolution of Racemates by Gas Chromatography

Gas chromatography on optically active stationary phases is also suitable for resolving racemates. It is used on the ana-

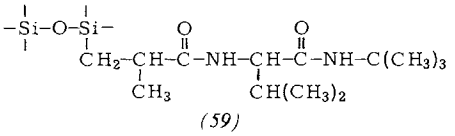
lytical scale for the determination of configurations and optical purity. Since these gas-chromatographic resolutions, developed in particular by *Gil-Av, Lochmüller,* and *Bayer,* have already been reviewed[64], only some new results will be listed here as examples.

Chiral amides such as *N*-trifluoroacetamides, *N*-trifluoroacetylamino acid esters, and α-methyl- and α-phenylcarboxylic acid amides are resolved on (*S*)-*N*-[1-(1-naphthyl)-ethyl]dodecanamide *(57)*[65] and oxiranes on nickel(II) bis(3-heptafluorobutyryl-(1*R*)-camphorate *(58)*[66] as the stationary phase.



(57)

(58)



(59)

Polysiloxanes with covalently bonded L-valine moieties are particularly suitable for the resolution of chiral amides. An example is the L-valine-*tert*-butylamide derivative *(59)* known as Chirasil-Val[67].

Thus, a 20-m long capillary column with *(59)* as the stationary phase separates many *N*-(and also *O*- and *S*-)pentafluoropropionyl derivatives of amino acid isopropyl esters as well as drugs and their metabolites completely into enantiomers[67].

Mixtures of substances can also be analyzed, since such stationary phases at the same time separate mixtures into their components. Good resolutions on *(59)* seem to be largely restricted to amides, since the stereoselective adsorption requires hydrogen bonding between the amide groups of the enantiomers and amide groups of the stationary phase. The resolution deteriorates in the case of racemic *N*-alkylated amides.

8. Outlook

Within a short time chromatographic resolution of racemates has matured into an efficient process, often permitting enantiomers to be obtained for the first time, and there is little doubt that its future development will be equally swift[68]. One particular aim should be the development of adsorbents for racemates not resolvable by conventional means and of adsorbents having a wide range of application.

Thanks are due to Dr. W. Backmann, Dr. F. Donow, Dr. H. P. Kraft, H. Markgraf, Dr. J. Peter, Dr. A. Schwanghart, and Dr. D. Thieme for the results cited from our own working group. We are greatly indebted to Prof. Dr. J. Knabe, University of Saarland, Saarbrücken for suggesting the chromatography of chiral barbiturates and for numerous samples, and to the Deutsche Forschungsgemeinschaft, the Ministerium für Jugend, Familie und Gesundheit, and the Fonds der Chemischen Industrie for supporting the work.

Received: June 6, 1979 [A 299 IE]
German version: Angew. Chem. *92*, 14 (1980)
Translated by AD-EX (Translations) Ltd., London

[1] *E. L. Eliel:* Stereochemie der Kohlenstoffverbindungen. Verlag Chemie, Weinheim 1966; a) p. 63; b) p. 56ff.
[2] *W. H. Pirkle, M. S. Hockstra,* J. Org. Chem. *39*, 3904 (1974).
[3] *G. Helmchen, G. Nill,* Angew. Chem. *91*, 66 (1979); Angew. Chem. Int. Ed. Engl. *18*, 65 (1979).
[4] *R. Willstätter,* Ber. Dtsch. Chem. Ges. *37*, 3758 (1904).
[5] *V. A. Davankov, S. V. Rogozhin, A. V. Semechkin, T. P. Sachkova,* J. Chromatogr. *82*, 359 (1973).
[6] *G. Losse, K. Kuntze,* Z. Chem. *10*, 22 (1970).
[7] *H. Krebs:* Die Trennung von Racematen auf chromatographischem Wege. Westdeutscher Verlag, Köln und Opladen 1956.
[8] *I. S. Krull,* Adv. Chromatogr. *16*, 175 (1978).
[9] *V. Prelog, W. Wieland,* Helv. Chim. Acta *27*, 1127 (1944).
[10] *A. Lüttringhaus, V. Hess, H. J. Rosenbaum,* Z. Naturforsch. *B 22*, 1296 (1967).
[11] *G. Manecke, W. Lamer,* Angew. Makromol. Chem. *24*, 51 (1972); Naturwissenschaften *54*, 647 (1967); *55*, 491 (1968).
[12] *G. Blaschke,* Chem. Ber. *107*, 232 (1974).
[13] *G. Blaschke,* Habilitationsschrift, Universität Kiel 1972.
[14] *G. Blaschke,* Chem. Ber. *107*, 237 (1974).
[15] *G. Blaschke, F. Donow,* Chem. Ber. *108*, 1188 (1975).
[16] *G. Blaschke, F. Donow,* Chem. Ber. *108*, 2792 (1975).
[17] *H. P. Kraft,* Dissertation, Universität Bonn 1978; *G. Blaschke, H. P. Kraft,* unpublished.
[18] *G. Blaschke, A.-D. Schwanghart,* Chem. Ber. *109*, 1967 (1976).
[19] *G. Hesse, R. Hagel,* Justus Liebigs Ann. Chem. *1976*, 996.
[20] *H. J. Rosenbaum,* Dissertation, Universität Freiburg 1967.
[21] *A.-D. Schwanghart, W. Backmann, G. Blaschke,* Chem. Ber. *110*, 778 (1977).
[22] *H. Markgraf,* Dissertation, Universität Bonn, envisaged for 1979; *G. Blaschke, H. Markgraf,* unpublished.
[23a] *O. Cervinka, V. Dudek, L. Hub,* Z. Chem. *9*, 267 (1969); Collect. Czech. Chem. Commun. *35*, 724 (1970).
[23b] *Note added in proof* (Dec. 18, 1979): *(13b)* was also obtained later in optically pure form by *Helmchen et al.* [3].
[24] *K. Vogler, M. Kofler,* Helv. Chim. Acta *39*, 1387 (1956).
[25] *F. Shealy, C. Oplinger, J. Montgomery,* J. Pharm. Sci. *57*, 757 (1968).
[26] *G. Blaschke, H. P. Kraft, K. Fickentscher, F. Köhler,* Arzneim.-Forsch. *29*, 1640 (1979).
[27] *F. Köhler, H. Koch,* Arzneim.-Forsch. *24*, 1616 (1974).
[28] *B. Riegel, L. T. Sherwood,* J. Am. Chem. Soc. *71*, 1129 (1949).
[29] *G. Blaschke, H.-P. Kraft, A.-D. Schwanghart,* Chem. Ber. *111*, 2732 (1978).
[30] *E. Fink, G. Minet, P. Nickel,* Arzneim.-Forsch. *29*, 163 (1979).
[31] *A. Haberkorn, H. P. Kraft, G. Blaschke,* Z. Tropenmed. Parasitol. *30*, 308 (1979).
[32] a) *G. Hesse, R. Hagel,* Chromatographia *6*, 277 (1973); *9*, 62 (1976); b) Justus Liebigs Ann. Chem. *1976*, 996; c) *G. Hagel,* Dissertation, Universität Erlangen-Nürnberg 1976.
[33] *G. Hesse,* personal communication.
[34] See [32b], p. 1003.
[35] *H. Häkli, A. Mannschreck,* Angew. Chem. *89*, 419 (1977); Angew. Chem. Int. Ed. Engl. *16*, 405 (1977); *H. Häkli, M. Mintas, A. Mannschreck,* Chem. Ber. *112*, 2028 (1979).
[36] *K. Bertsch, J. C. Jochims,* Tetrahedron Lett. *1977*, 4379; *K. Bertsch, M. A. Rahman, J. C. Jochims,* Chem. Ber. *112*, 567 (1979).
[37] *J. Knabe, W. Rummel, H. P. Büch, N. Franz,* Arzneim.-Forsch. *28*, 1048 (1978).
[38] *W. Davankov,* Ideen des exakten Wissens *1972*, 319.
[39] *S. V. Rogozhin, V. A. Davankov,* Chem. Commun. *1971*, 490.
[40] *D. Thieme,* Dissertation, Universität Kiel 1975.
[41] *V. A. Davankov, Yu. A Zolotrarev,* J. Chromatogr. *155*, 295 (1978).
[42] *V. A. Davankov, Yu. A. Zolotarev,* J. Chromatogr. *155*, 285 (1978).
[43] *V. A. Davankov, Yu. A. Zolotarev,* J. Chromatogr. *155*, 303 (1978).
[44] *V. A. Davankov, S. V. Rogozhin, A. V. Semechkin,* J. Chromatogr. *91*, 493 (1974).
[45] *V. A. Davankov, A. V. Semechkin,* J. Chromatogr. *141*, 313 (1977).
[46] *W. Mayer, F. Merger,* Justus Liebigs Ann. Chem. *644*, 65 (1961).
[47] *C. E. Dalgliesh,* J. Chem. Soc. *1952*, 3940; *R. Weichert,* Ark. Kemi *31*, 517 (1970); *K. Bach, H. J. Haas,* J. Chromatogr. *136*, 186 (1977).
[48] *B. Franck, G. Schlingloff,* Justus Liebigs Ann. Chem. *659*, 123 (1962); *B. Franck, G. Blaschke, ibid. 695*, 144 (1966).
[49] *H. Krebs, J. A. Wagner, J. Diewald,* Chem. Ber. *89*, 1875 (1956); *H. Krebs, W. Schumacher, ibid. 99*, 1341 (1966).
[50] *H. Musso,* Chem. Ber. *91*, 349 (1958); *W. Steckelberg, M. Bloch, H. Musso, ibid. 101*, 1510, 1519 (1968); *R. K. Haynes, H. Hess, H. Musso, ibid. 107*, 3733 (1974).
[51] *H. Hess, G. Burger, H. Musso,* Angew. Chem. *90*, 645 (1978); Angew. Chem. Int. Ed. Engl. *17*, 612 (1978).

[52] *D. J. Cram, J. M. Cram*, Science *183*, 803 (1974); Acc. Chem. Res. *11*, 8 (1978).
[53] *L. R. Sousa, D. H. Hoffman, L. Kaplan, D. J. Cram*, J. Am. Chem. Soc. *96*, 7367 (1974).
[54] *G. D. Y. Sogah, D. J. Cram*, J. Am. Chem. Soc. *98*, 3038 (1976).
[55] *L. R. Sousa, G. D. Y. Sogah, D. Hoffman, D. J. Cram*, J. Am. Chem. Soc. *100*, 4569 (1978).
[56] *J.-M. Lehn, J. Simon, A. Moradpour*, Helv. Chim. Acta *61*, 2407 (1978).
[57] *F. Mikes, G. Boshart, E. Gil-Av*, J. Chromatogr. *122*, 205 (1976).
[58] *F. Mikes, G. Boshart, J. Chromatogr. 149*, 455 (1978).
[59] *C. H. Lochmüller, R. R. Ryall*, J. Chromatogr. *150*, 511 (1978).
[60] *N. Grubhofer, L. Schleith*, Hoppe-Seylers Z. Physiol. Chem. *296*, 262 (1954); *J. A. Lott, W. Rieman III*, J. Org. Chem. *31*, 561 (1966).
[61] *C. Kratchanov, M. Popova*, J. Chromatogr. *37*, 297 (1968); *C. Kratchanov, M. Popova, T. Obretenov, N. Ivanov, ibid. 43*, 66 (1969); *M. Popova, C. Kratchanov, ibid. 72*, 192 (1972).
[62] *G. Wulff, W. Vesper, R. Grobe-Einsler, A. Sarhan*, Makromol. Chem. *178*, 2799 (1977); *G. Wulff, R. Grobe-Einsler, W. Vesper, A. Sarhan, ibid. 178*, 2817 (1977).
[63] *H. Bartels, H. Erlenmeyer*, Helv. Chim. Acta *48*, 285 (1965); *H. Bartels, B. Prijs, H. Erlenmeyer, ibid. 49*, 1621 (1966).
[64] *C. H. Lochmüller, R. W. Souter*, J. Chromatogr. *113*, 283 (1975).
[65] *S. Weinstein, F. Feibush, E. Gil-Av*, J. Chromatogr. *126*, 97 (1976).
[66] *V. Schurig, B. Koppenhofer, W. Bürkle*, Angew. Chem. *90*, 993 (1978); Angew. Chem. Int. Ed. Engl. *17*, 937 (1978).
[67] *H. Franck, G. J. Nicholson, E. Bayer*, J. Chromatogr. Sci. *15*, 174 (1977); Angew. Chem. *90*, 396 (1978); Angew. Chem. Int. Ed. Engl. *17*, 363 (1978); J. Chromatogr. *146*, 197 (1978).
[68] *Note added in proof* (Dez. 18, 1979): Recent publications on chromatographic resolution of racemates: *e.g. R. Audebert*, J. Liquid Chromatogr. *2*, 1063 (1979) (review); *V. A. Davankov, Yu. A. Zolatarev, ibid. 2*, 1191 (1979) (further examples of ligand exchange chromatography); *W. H. Pirkle, D. W. House*, J. Org. Chem. *44*, 1957 (1979) (separation of sulfoxides and 3,5-dinitrobenzoates *via* high-pressure liquid chromatography on silica-bound 2,2,2-trifluoro-1-(9-anthryl)ethanol); *M. Mintas, A. Mannschreck*, J. Chem. Soc. Chem. Commun. *1979*, 602 (separation of *trans*-1,2-diphenylcyclopropane on cellulose triacetate); *B. Feringa, W. Wynberg*, Rec. Trav. Chim. Pays-Bas *97*, 249 (1978) (separation of arenes on silica gel impregnated with (+)-TAPA).

Determination of Morphological Properties of Swellable Solids by Size Exclusion Chromatography[**]

By István Halász and Peter Vogtel[*]

Many technically interesting porous solids, *e.g.* ion exchangers or adsorbents for catalysis, are swellable polymers, *i.e.* the pore structure depends on the solvent medium. A method based on exclusion chromatography, permits determination of the pore size and pore size distribution in the swollen state.—Size exclusion chromatography, also referred to as gel permeation, gel filtration, or molecular sieve chromatography, is a widely employed method for the separation of dissolved substances—mostly polymer mixtures—according to their molecular size. Porous solids are used as stationary phase. Conversely, pore sizes and other structural data can be determined by exclusion chromatography. This application requires a series of standards (polymer samples) of known molecular weight. As a simple and rapid method, it has already proven valuable for such determinations in the case of rigid solids; in the case of swellable solids, this constitutes the sole method by which the pore structure can be characterized: classical methods require dry samples.

1. Introduction

Rigid solids (*e.g.* silica gels, aluminas) are distinguished by the fact that their pore structure does not depend upon the surrounding medium (gas, liquid). The pore structure of non-rigid solids (*e.g.* polystyrene-divinylbenzene copolymers, polyacrylamides, dextrans), on the other hand, is a function of the swelling medium employed.

Organic gels can be obtained by homogeneous or heterogeneous polymerization[1-3]. In the former case a pore structure is formed only when the three-dimensional cross-linked chains in the dry non-porous material become solvated, *i.e.* an expanded mesh structure is formed only in the swollen state. The mean mesh size can be controlled by the cross-linking component. The porosity of the particles, *i.e.* the ratio of pore volume to particle volume, increases with decreasing amount of cross-linking component; at the same time, however, the mechanical stability decreases. In all cases, homogeneously cross-linked copolymers are microporous on swelling (pore diameters $\phi < 20$ Å).

In the case of heterogeneous polymerization an inert substance is added to the mixture of mono- and difunctional components. During the production process a phase separation takes place leading to copolymers which also contain pores in the unswollen state (permanent porosity). These "semi-rigid" gels are macroporous (pore diameters $\phi > 20$ Å). In addition, a further increase in porosity can also occur on swelling.

The structural data of rigid porous solids—such as specific surface area O_{sp}, pore volume V_p, and pore volume distribution (pore diameter distribution)—can be determined by classical procedures (BET method, nitrogen capillary condensation, and mercury porosimetry; see *e.g.*[4]). For gels exclusively displaying swelling porosity, the classical methods are obviously unsuitable. Though they can of course be used in the case of semi-rigid materials, the results have only limited information value.

[*] Prof. Dr. I. Halász, Dr. P. Vogtel
Angewandte Physikalische Chemie der Universität
D-6600 Saarbrücken (Germany)

[**] Part of the Ph. D. Thesis by *P. Vogtel*, Universität Saarbrücken 1977.

Measurements by the classical methods require special preparation of the polymer samples, including conversion from the swollen state into the dry state, thus influencing the results obtained[5]. Moreover, in the case of exclusively macroporous semi-rigid polymers the pore structure is a function of the swelling agent employed. Finally, the micropores additionally formed on swelling cannot be determined.

The morphological properties of rigid inorganic solids can be conveniently determined by a recently described exclusion chromatography (EC) method[6–8]. The new EC method is simple and fast, leading to results in satisfactory agreement with those of the classical methods, despite the different and disputable boundary conditions.

This review will show that the exclusion method is also suitable for the characterization of swellable solids. The new method is the only one available so far for the investigation of swollen gels, *i.e.* the state in which the material is used in practice. Here the classical methods fail, for they require dry samples.

2. Exclusion Chromatography—Description of the Method[*]

The principles and boundary conditions of the EC method for determination of the structural data of porous solids have already been described in detail elsewhere[7]. The basic model concepts of the method will therefore be presented only briefly here.

When a solvent is passed through a column packed with a porous carrier, axial transport of the eluent takes place exclusively in the interstitial volume V_i. The eluent in the pore volume V_p of the carrier is exchanged only by diffusion between V_p and V_i. For all sample substances, it must be established that they are not adsorbed by the carrier. (This has been shown, for example, for silica gel as solid phase, dichloromethane as eluent, and polystyrene or benzene as sample[7].) Under these conditions the same applies for the samples on the column as for the molecules of the eluent: they flow through the interstitial volume of the column and can diffuse into and out of the pores.

The next condition to be fulfilled is that all sample molecules fully utilize the volume available to them for diffusion, *i.e.* that a concentration equilibrium is established between the "phase" in the pore volume and the phase in the interstitial volume. For samples with small molecules (*e.g.* benzene) the whole pore volume in the column is then—as for the eluent—accessible, *i.e.* this sample is eluted with the greatest possible elution volume.

$$V_{e,max} = V_i + V_p \quad (1)$$

As the molecular size of the sample material increases the smaller pores are not accessible, *i.e.* the elution volume decreases. Finally, for the largest sample molecules the whole pore volume is inaccessible, and for the elution volume we have:

$$V_{e,min} = V_i \quad (2)$$

The measuring procedure for the determination of the total pore volume in the column follows from equations (1) and (2):

$$V_p = V_{e,max} - V_{e,min} \quad (3)$$

If the column is emptied on completion of all the measurements and the mass of the carrier is determined, then the specific pore volume $V_{p,s}$ (referred to one gram of solid) can also be calculated.

The elution volumes (V_e) of the remaining samples lie, according to the above mentioned, between $V_{e,max}$ and $V_{e,min}$. If the sample molecule is assigned an exclusion value (ϕ) then a plot of V_e against ϕ corresponds to the residual sum of the pore volume frequency. The exclusion value ϕ_i [Å] thus describes the diameter of the smallest pores which are accessible for a molecule having a molecular weight M_i. Obviously, all pores with diameters greater than ϕ_i are then likewise accessible. The exclusion values of the samples employed are listed in Table 1. In the case of polystyrene (PS) samples the relationship

$$\phi\ [\text{Å}] = 0.62\ M^{0.59} \quad (4)$$

Table 1. Pore diameter ϕ assigned to standard (sample molecule). (PS = polystyrene; the number indicates the molecular weight.)

Sample	ϕ [Å]	Sample	ϕ [Å]
Benzene	7.4	PS 10000	140
Ethylbenzene	8.5	PS 20800	215
Butylbenzene	10.9	PS 36000	297
Hexylbenzene	13.4	PS 111000	576
Octylbenzene	15.9	PS 200000	815
Dodecylbenzene	20.8	PS 498000	1400
Pentadecylbenzene	24.4	PS 867000	1930
PS 600	26.7	PS 2610000	3700
PS 2100	55.9	PS 3700000	4530
PS 4000	81.6		

was assumed[7]; in the case of the alkylbenzoyl samples the ϕ values correspond to the length of the extended chains[8]. From the residual sum of the pore volume frequency a mean pore diameter of ϕ_{50} can be assumed for 50% accessible pore volume.

Assuming homogeneous, cylindrical and continuous pores, the specific surface area O_{sp} of the solid can be calculated from the specific pore volume $V_{p,s}$ [cm³/g] and the mean pore diameter ϕ_{50} [Å]:

$$O_{sp}\ [\text{m}^2/\text{g}] = 0.04 \times \frac{V_{p,s}\ [\text{cm}^3/\text{g}]}{\phi_{50}\ [\text{Å}]} \quad (5)$$

[*] List of symbols:

M ($\bar{M}_w$)	molecular weight (weight-averaged molecular weight of polymer)
O_{sp}	specific surface area
ϕ	pore diameter (assuming the pores to be cylindrical); also the exclusion value of a polymer standard
ϕ_{50}	mean pore diameter (for 50% accessible pore volume)
V_e	chromatographic elution volume of a test sample
$V_{e,max}$	maximum elution volume in calibration series (elution volume of the standard with the lowest molecular weight)
$V_{e,min}$	minimum elution volume in a calibration series (elution volume of the standard with the highest molecular weight)
V_p	pore volume; volume of eluent that has penetrated the pores
$V_{p,s}$	specific pore volume: pore volume per gram of the solid
V_i	interstitial volume

3. Experimental

The measurements were carried out on a simple apparatus for liquid chromatography[7]. The units comprised a pump (Type M 6000, Waters Associates, Milford, Mass. USA); a sample loop injector (Rheodyne Type 7120; Kontron Technik GmbH, Eching bei München, Germany), a UV detector (254 nm) of our own construction, and a differential diffractometer (Type R 401, Waters).

With this apparatus the pore structure of the following polystyrene-divinylbenzene copolymers was investigated:

1. Bio beads SX 12 (BioRad, Richmond, Calif., USA),
2. Styragel 60, 100, 500, and 1000 (Waters),
3. PSDVB B1 to B4 (Farbenforschung Lewatit, Bayer AG, Leverkusen, Germany).

The first five copolymers are commercially available and are well-known stationary phases for exclusion chromatography. The first material is homogeneously cross-linked, the Styragels are heterogeneously cross-linked. The samples B1 and B4 were kindly supplied by the manufacturer. The average particle diameter of these materials is between 10 and 60 μm. As sample substances we used polystyrenes of various degrees of polymerization and narrow range of molecular weight distribution as well as various alkylbenzenes (Merck-Schuchart, Hohenbrunn bei München, Germany). The eluent employed was dichloromethane. The samples were dissolved in the eluent (*ca.* 10 mg/g); *ca.* 1 μg of sample per gram of solid in the column was used.

To avoid any misunderstanding it must be pointed out once again that the standard substances employed as samples were linear polystyrenes dissolved in dichloromethane; the swellable solids, however, were copolymers of styrene and divinylbenzene.

Stainless steel tubes with a nominal internal diameter of 4 mm were used for the columns. The column length (between 30 and 100 cm) was so chosen that at least 300 theoretical plates[9] were obtained for benzene as sample. The columns were packed by a modified balanced-density method[7]. For a 100-cm column, *ca.* 4 g of copolymer was pre-swollen in 30 ml dichloromethane for *ca.* 12 h (CH_2Cl_2 has a greater density than the copolymer!). Before packing the column a further 14 ml of CH_2Cl_2 and 40 ml of tetrahydrofuran were added. The suspension was stirred, transferred to the packing vessel covered with a layer of 40 ml THF to prevent mixing and then with CH_2Cl_2. Dichloromethane was used as pressure liquid. Packing was carried out a flow rate of *ca.* 3 ml/min. The columns for the measurements were also operated with CH_2Cl_2, but also proved to be stable on changing the solvent. All measurements were carried out at room temperature and a flow rate of 1 ml/min. (A detailed account of the evaluation of SEC measurements for the determination of structural data is given in [7,8].)

4. Results and Discussion

Figure 1 shows semilogarithmic plots of the elution volume of a sample as a function of the molecular weight M for five polystyrene-divinylbenzene copolymers. These plots can be regarded as graphical representations of the measuring procedure. The further the curves are shifted to higher molecular weights the greater is the mean pore diameter ϕ_{50} of the solid. The difference in elution volume between the samples with the smallest and those with the largest molecular weight corresponds to the pore volume V_p in the column [see eq. (3)].

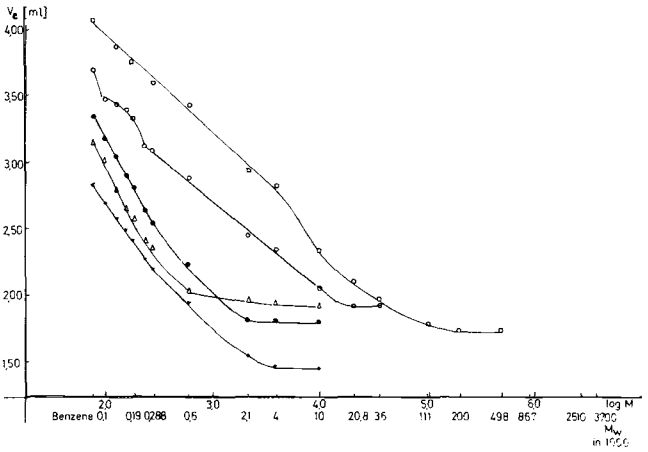


Fig. 1. Elution volumes V_e of the standard substance on five commercial polystyrene-divinylbenzene copolymers. Eluent: dichloromethane; flow rate: 1 ml/min. Standard substances: see Table 1. Solids (copolymers): + BioBeads SX 12; △, ●, ○, □ Styragel 60, 100, 500, 1000.

The integral pore distribution curves are reproduced in Figure 2. The measurements from Figure 1 were so recalculated that the portion of the accessible pore volume V_p is plotted on the ordinate and the exclusion value ϕ (pore diameter) of the sample on the abscissa. From this plot the mean pore diameter ϕ_{50} can be taken for 50% accessibility of the pore volume; the steeper a curve is, the narrower is the corresponding pore distribution. Figure 2 shows that the

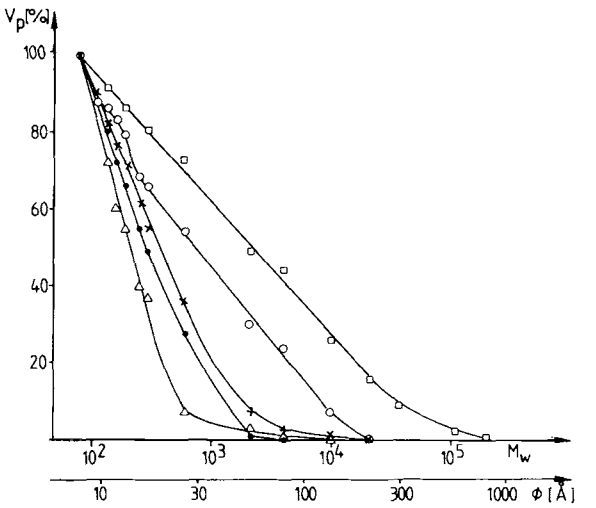


Fig. 2. Sum of residues distribution of the pore diameters (integral distribution curve) for the five copolymers in Fig. 1 (for explanation see text).

samples measured cover the whole range of pore sizes of interest between 10 and 1000 Å. It should be pointed out that—as a result of standardization—no information can be gained from Figure 2 about the absolute size of the pore volume. From the specific pore volume $V_{p,s}$ and the mean pore diameter ϕ_{50}, the surface area of the swollen copolymer in the column can be estimated according to equation (5). Decisive for the use of swellable copolymers is the magnitude of the surface area or pore volume referred to the volume of the

swollen gel. The data in Table 2 are referred to the volume and not the mass of the solid; a knowledge of the packing density makes possible the calculation of these quantities.

Table 2. Pore volumes V_p, mean pore diameters ϕ_{50} and surface areas O referred to the volume of the swollen gel of some swellable copolymers.

Material	V_p [cm³/cm³]	ϕ_{50} [Å]	O [m²/cm³]	Packing density [g/cm³]
SX 12	0.27	17.5	620	0.38
Sty 60	0.35	22.0	636	0.33
Sty 100	0.28	24.0	466	0.31
Sty 500	0.33	29.0	455	0.25
Sty 1000	0.53	53.0	400	—

In Figure 3 the elution volume is plotted as a function of the molecular weight of the sample for four heterogeneously cross-linked PSDVB copolymers manufactured by Bayer AG (Farbenforschung Lewatit). The integral pore distributions derived from these according to the EC method (unbroken line) and according to classical mercury porosimetry (broken line) are shown in Figure 4. The most important data can be taken from Table 3.

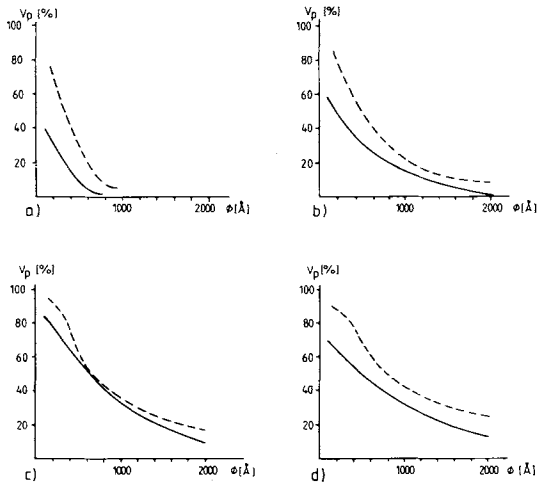


Fig. 4. Sum of residues distribution of the pore diameter (integral distribution curve) according to the EC method (—) and according to the mercury porosimetry method (---) (measurements by the manufacturer). a)—d) PSDVB copolymers B1—B4.

is found to be smaller and the pore volume per grain of solid larger than in the mercury porosimetry measurements. Further, in Table 3 it is shown for sample B1 how strongly the

Table 3. Pore volumes and mean pore diameters ϕ_{50}. The pore volume was calculated from apparent and true density.

Material	Manufacturers data			EC measurements		
	Total pore volume [cm³/g]	Hg-pore volume [cm³/g]	ϕ_{50} [Å]	V_p [cm³/cm³]	$V_{p,s}$ [cm³/g]	ϕ_{50} [Å]
B1 [a]	0.626	0.478	250	0.40	2.50	60
[b]	0.077	0.078	(880)			
B2 [c]	0.881	0.753	260	0.40	2.66	150
B3 [c]	1.211	1.153	270	0.35	2.15	630
B4 [c]	1.639	1.496	210	0.31	2.40	510

[a] Prepared with methanol. [b] Swollen in THF, then THF removed. [c] Dried.

The different results afforded by the two methods are not surprising, since the classical measurements were carried out on dry material and the EC measurements on swollen material. In the EC method the swollen porosity (micropores) is also measured. Thus it would appear reasonable that in the chromatographic measurements the mean pore diameter ϕ_{50} data determined by classical methods can depend on the preparation of the sample prior to carrying out the measurements.

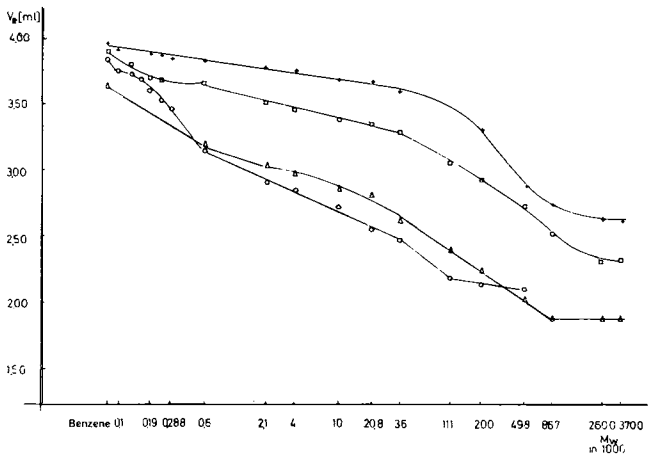


Fig. 3. Elution volumes V_e of the standard substance on four polystyrene-divinylbenzene copolymers from Bayer, Leverkusen. ○, △, □ + PSDVB-copolymers B1—B4. For conditions see Fig. 1.

5. Summary

An exclusion chromatographic method can be used for determination of the structural data of swellable solids. Pore volume, pore distribution, and surface area of swollen materials are measured by this method and reproduce the conditions prevalent in the solids as they are used. This is illustrated by polystyrene-divinylbenzene copolymers of different porosity and having different mean pore diameters. It is suggested that the pore volume and surface area be referred to in terms of the volume of the swollen material, as is usual in catalysis.

When suitable combinations of sample material and eluent are found, it should also be possible to investigate solids which are swollen in different solvents.

We thank the Deutsche Forschungsgemeinschaft for financial support of this work. We are especially indebted to Dr. P. M. Lange and Dr. A. Meyer, Farbenforschung Lewatit, Bayer AG, Leverkusen for supplying some copolymers and the data for these compounds.

Received: November 14, 1979 [A 302 IE]
German version: Angew. Chem. 92, 25 (1980)

[1] *J. C. Moore*, J. Polym. Sci. *A2*, 835 (1961).
[2] *W. Heitz*, Angew. Makromol. Chem. *10*, 115 (1970).
[3] *W. Heitz*, Angew. Chem. *82*, 675 (1970); Angew. Chem. Int. Ed. Engl. *9*, 689 (1970).
[4] *S. J. Gregg, K. S. W. Sing:* Adsorption, Surface Area and Porosity. Academic Press, New York 1967.
[5] *F. Martinola:* Der Einsatz von Kationenaustauschern in der heterogenen Katalyse. Informationsschrift der Bayer AG, Leverkusen 1975.
[6] *I. Halász, K. Martin*, Ber. Bunsenges. Phys. Chem. *79*, 731 (1975).
[7] *I. Halász, K. Martin*, Angew. Chem. *90*, 954 (1978); Angew. Chem. Int. Ed. Engl. *17*, 901 (1978).
[8] *I. Halász, P. Vogtel, R. Groh*, Z. Phys. Chem. (Frankfurt am Main) *112*, 235 (1978).
[9] *H. Engelhardt:* High Performance Liquid Chromatography, Springer, Berlin–New York, 1979.

A Model of Hydrogen-Bonded Liquids

By Werner A. P. Luck[*]

Dedicated to Professor Gustav Kortüm on the occasion of his 75th birthday

The orientation defect model can be used for quantitative estimates and for understanding the properties of H-bonded liquids, such as water and alcohol. The defect concentrations can be determined by vibrational spectroscopy, and the applicability of the approximation procedure derives from considering H-bonds as chemical equilibria. Possible extensions of the simple model are critically discussed.

1. Introduction

1.1. Statement of Problem

A model has recently been described for nonpolar liquids with spherically symmetrical van der Waals forces[1]. Whether attraction or repulsion prevails is determined by the intermolecular distance. This model[1] would remain incomplete if it were not possible to formulate extensions accounting for dipolar forces with attractive *or* repulsive effects depending upon the orientation of the molecule.

Orientation-dependent interactions of this kind are especially pronounced between protons of acidic groups (*e.g.* OH, NH) and lone pairs in H-bonds. The properties of H-bonded liquids are determined by two partition functions, *viz.* of the distances and of the angles; they cannot yet be described exactly. In view of the importance of just such liquids in biochemistry, colloid chemistry, and large areas of chemical technology, it appears pointless to wait for an exact solution of this problem. For the chemist, too, a bird in the hand in generally worth two in the bush. Having a particularly high concentration of strong H-bonds, water is particularly suitable for a simplifying approximation. On the basis of the model for water on the one hand and nonpolar liquids[1] on the other, a wide scale of liquids can be envisaged taking account of the relative contribution of H-bonds (hydrophilic/hydrophobic balance = HHB). Yet more parameters would have to be considered for metallic and ionic melts.

1.2. Hydrogen Bonds

The intermolecular pair potential of nonpolar molecules can be characterized approximately by their critical temperature T_c[1]. The T_c of nonpolar substances is approximately proportional to the square root of the molecular weight or the sum of the number of electrons Z_e (Fig. 1). H-bonds increase T_c. On the other hand, the relation $T_c(C_nH_{2n+1}OH) \approx T_c(C_{n+4}H_{2(n+5)})$ is found to apply for $n \geq 2$. The effect of an alcoholic OH group thus corresponds

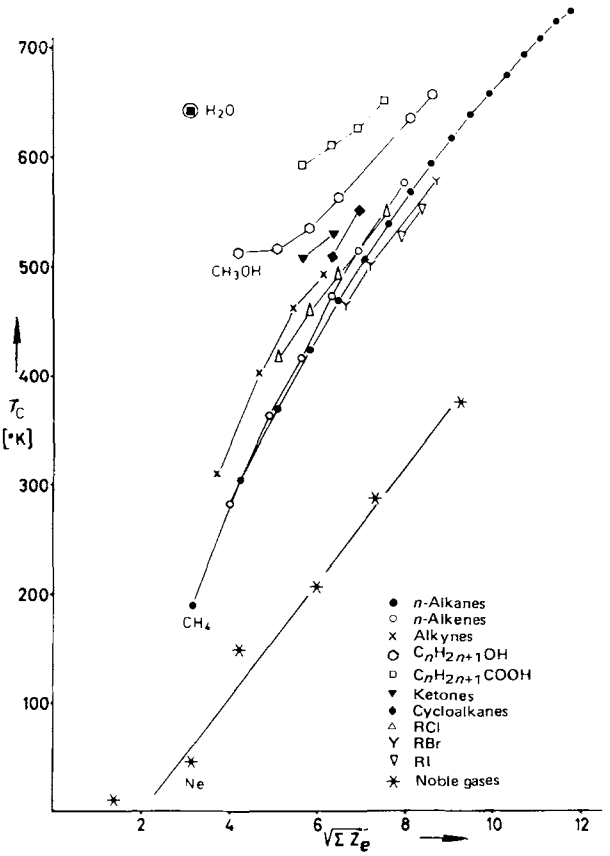


Fig. 1. Critical temperature as a function of the root of the sum of the numbers of electrons Z_e of all the atoms of a molecule. T_c is raised by the presence of H-bonds in carboxylic acids, alcohols, and H_2O.

[*] Prof. Dr. W. A. P. Luck
Fachbereich Physikalische Chemie der Universität
Auf den Lahnbergen, D-3550 Marburg (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0028 $ 02.50/0

approximately to the dispersive interaction of $-(CH_2)_3CH_3$ in *n*-paraffins.

Table 1 shows the contributions of H-bonds and dispersive interactions for water; data for CH_4 are also listed for comparison.

Table 1. Intermolecular interactions in H_2O (values in kcal/mol).

		H_2O	CH_4
(a) Sublimation energy	ΔU_s	11.6	2.2
(b) Difference in internal energies	$U(\text{liq.}, T_c) - U(\text{solid}, T_m)$	10.2	2
(c) Dimer dispersion energy (calc. according to [2])	$W((H_2O)_2)$	1.8	
(d) Ice H-bond energy (from (a) and (c))	$2\Delta H_H \approx \Delta U_s - 2W((H_2O)_2)$	8	
(e) H-bond energy per H-bond	ΔH_H	4	

The energy of 4 kcal/mol estimated for a linear H-bond in ice [Table 1, (e)] from the calculated dispersion energy 2 W agrees with the H-bond energy of 3.7 and 4 kcal/mol determined by spectroscopy in liquid H_2O and CH_3OH, respectively[3,4].

H-bonds differ from normal nonpolar van der Waals interactions by a deeper potential energy minimum and by their angular dependence. The potential-distance function for the optimum H-bond angle of $\beta = 0$ (cf. geometry in Fig. 2a) resembles the Morse curve for a covalent bond[5-7], while it corresponds to the encounter between two H atoms of equal spin in the case of pure repulsion (orientations in Fig. 2e and 2f)[8-10].

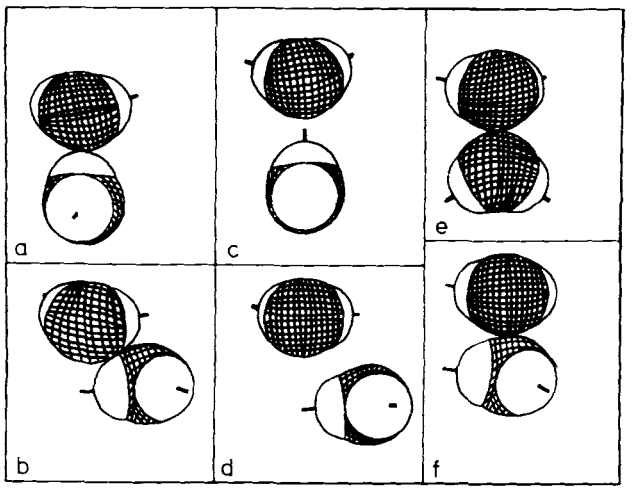


Fig. 2. Orientations of H_2O dimers: a) maximum H-bond interaction for angle $\beta = 0$; b) cyclic dimer, two H-bonds with unfavorable angles β; c) position a with greater intermolecular distance and hence very slight H-bond interaction; d) position b with greater separation and very slight H-bond interaction; e) repulsive orientation of the lone pairs; f) repulsive orientation of the lone pairs.

For $\beta = 0$ (Fig. 2a) a saturation phenomenon is observed. Thus, H-bonds can be regarded as secondary valence effects whose action depends upon the molar concentration of OH groups and of lone pairs.

The c(OH) values listed in Table 2 explain the anomalous values of $T_c(CH_3OH) = 512.5$ K and $T_c(H_2O) = 674.35$ K. Extrapolation of the boiling and melting points of hydrides of type XH_2 to the number of electrons or the molecular weight of H_2O would suggest that water should melt at -90 °C and boil at about -80 °C[11]. The H-bonds cause a drastic rise in the two transition temperatures and thus permit life on our planet.

Table 2. Concentration [mol/l] of OH groups and lone pairs (θ) in water and alcohols at 20 °C.

	H_2O	CH_3OH	C_2H_5OH	n-C_3H_7OH	n-C_4H_9OH
c (OH)	111	24.7	17.1	13.4	10.9
c (θ)	111	49.4	34.2	26.8	21.8

The secondary valence character of H bonds leads in the case of water to a "loose tetrahedral structure of coordination number 4 owing to the charge distribution" as underscored by *Kortüm*[12,13] as a pioneer in the field. This structure is completely different from that of nonpolar liquids, which approach closest packing and coordination numbers of $Z = 12$ between nearest neighbors. Preference for certain spatial directions by H-bonds[14,15] is of fundamental importance for the specificity of higher-order biochemical structures[16].

1.3. Determination of H-Bonds

Apart from higher intermolecular energies detectable by calorimetry, H-bonds lead to anomalously large changes in the frequencies of OH and NH stretching modes and their IR extinction coefficients. This applies particularly to overtones[17-19]. Dilute solutions of H-bonding compounds such as CH_3OH in inert solvents such as CCl_4 exhibit sharp bands (cf. Fig. 3, band at 7122 cm^{-1}) which are due to the so-called "free" OH groups, *i.e.* those not involved in H-bonds[17]. In concentrated solutions, such a band is replaced by a broad band system (cf. Fig. 3, between 7100 and 5600 cm^{-1}, together with some CH bands around 5900 cm^{-1}). This broad overtone induced by OH groups participating in H-bonds differs only slightly in area $\int \varepsilon d\nu$ from the sharp overtone band for the "free" OH groups[20] but significantly in its half-width $\Delta\nu_{1/2}$, and therefore[21,22] in the height of the maximum ε_{max}.

The content O_F of H-bond defect sites can be quantitatively determined from the relative height ε_{max} of the overtone band of the "free" OH groups[*].

$$c_F/c = \varepsilon_c/\varepsilon_0 = O_F; \quad c_B/c = (1 - O_F)$$

or from $\int \varepsilon_c d\nu / \int \varepsilon_0 d\nu$

ε_0 = extinction coefficient for band maximum at concentration c;
ε_0 = extinction coefficient for band maximum at infinite dilution

Methods of calculating chemical equilibria have been successfully applied to c_F and c_B in numerous studies. Equilibrium constants of the association equilibria determined in this way number among the most accurate known in physical chemistry. Thus, for example, H-bonds of lactams with *cis* amide groups have been interpreted quantitatively in the entire solubility range in CCl_4 of 3×10^{-3} to 5 mol/l with the same, and hence true, dimerization equilibrium constant without activity coefficients[14].

The widely differing concentration dependence of O_F for different substances can be interpreted in terms of the angular dependence of H-bonds[14,15]. In solution, the H-bond

[*] Direct quantitative determination of c_B from the H-bond band gives greater errors because of overlap with other bands (OH, CH, or combinations thereof [4]).

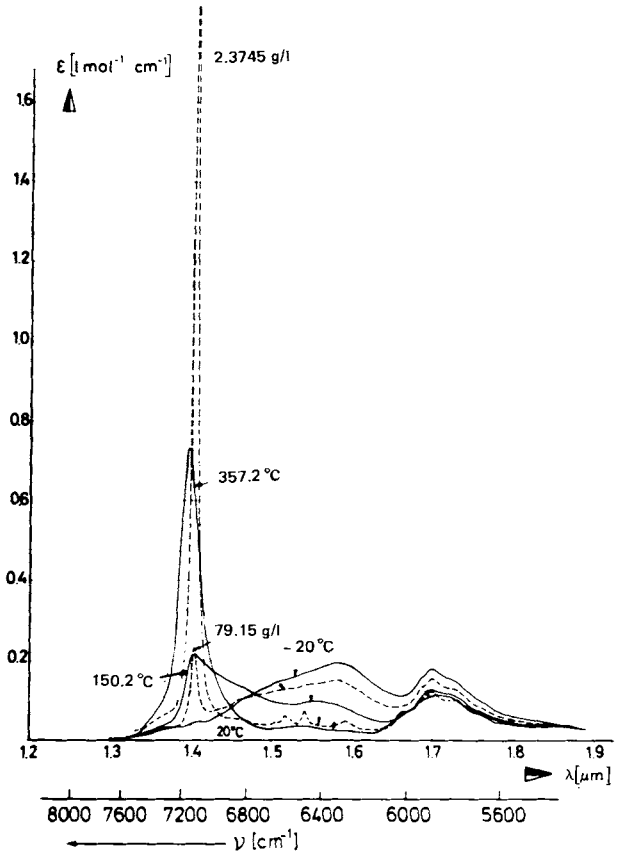


Fig. 3. IR overtone spectra of methanol. Dashed lines: solutions in CCl_4 at 20 °C. Solid lines: liquid at saturation conditions.

angles and lengths essentially have values corresponding to the potential minimum, justifying a treatment as chemical equilibrium between open and closed H-bonds and neglect of intermediate states.—Cyclic aggregates are particularly stable. As a rule, the H-bond angle β is zero in six-membered aggregates (not including protons)—this applies to cyclic dimers of lactams and carboxylic acids, cyclic trimers of oximes and the six-membered H_2O ring in ice[14,15]. If more than two molecules are required in aggregates with $\beta = 0$, then coupled equilibria of various aggregation states will occur[14,15].

H-bonds lead to drastic changes in the intensities of IR fundamental bands[18], in contrast to those of the overtones[3,23-26]. Hence O_F can be determined much less satisfactorily from fundamental modes of liquids exhibiting band broadening; in some cases this can only be done on the basis of considerable experience. This has often been neglected in discussions of the overtone method.

Summary: The content of H-bonds and of their defect sites O_F can be quantitatively determined in solution by IR overtone spectroscopy and treated as chemical equilibria. The resulting equilibrium constants number among the most accurate known.

2. The Model and Its Testing

2.1. Simple H-Bond Defect Model for Liquids

IR overtone spectra of pure liquid alcohols closely resemble those of solutions (cf. Fig. 3). In particular, they also show the band characteristic of "free" OH groups at elevated temperatures[23-26]. Owing to modified environmental conditions (2nd approximation perturbations) this band has a somewhat greater half-width than in solution. According to the rules of spectroscopy[21,22], however, the relation $\varepsilon_{max} \times \Delta\nu_{1/2} = \text{const.}$ still holds. Moreover, $\int \varepsilon d\nu$ is relatively independent of environment for the overtones[20]. The content of "free" OH or NH groups can be determined for pure liquids and for solutions from $\int \varepsilon d\nu$ or, knowing $\varepsilon_{max,0}$, from ε_{max}[3,23-26]. ($\varepsilon_{max,0}$ = extinction coefficient of band for "free" XH groups; it can be determined at elevated temperature[25].)

The overtone spectra of water are very similar to those of alcohols. At elevated temperatures, an identical relatively sharp band appears which is assigned to the "free" OH groups. In the case of H_2O and D_2O, splitting of the stretching band into ν_1 and ν_3 as a result of OH and OD coupling[91,92] also has to be considered. This task is facilitated by the fact that only ν_1 is Raman active and the IR intensity of ν_1 is much lower than that of ν_3, particularly in the overtone range. The difficulties created by two proximate stretching vibrations ν_1 and ν_2 disappear in the case of the monodeuterated HOD spectrum (Fig. 4). Measurements up to 400 °C showed $\nu_{max,0}$ of the "free" OH group in HOD to lie at 7168 cm^{-1}[19,25]. The temperature dependence of O_F agrees for four different H_2O bands, two bands of D_2O, and the first HOD overtone band[3,23,25]. Interference by band overlapping is largely avoided by our method of determining O_F in the frequency range of the narrow band of "free" OH groups. *Schiöberg* was able to show by hitherto unpublished measurements that ΔH_H has a value of -4.1 ± 0.1 kcal/mol both for concentrated alcohol solutions and for the pure alcohol, confirming the validity of the highly successful solution method for pure liquids. The H-bond energy -3.7 kcal/mol of liquid HOD could be established by two different spectroscopic methods: 1) by the overtone band of "free" OH groups[3] or 2) by the band of simultaneous excitation of OH and OD vibrations in two neighboring H-bonded molecules[4].

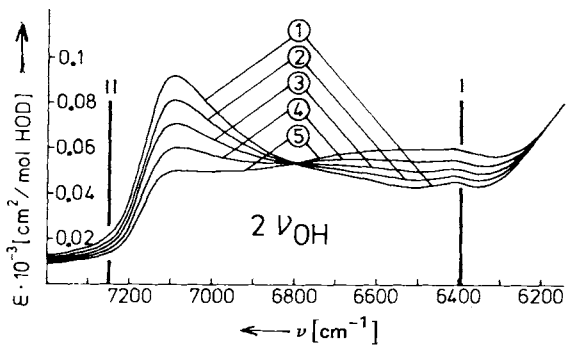


Fig. 4. IR overtone spectra of liquid HOD at various temperatures (HOD in D_2O. D_2O compensated): ① 90 °C; ② 70 °C; ③ 50 °C; ④ 30 °C; ⑤ 10 °C. I: maximum of ice band; II: maximum of vapor band.

Figure 5 shows the O_F values, *i.e.* the fraction of open H-bonds or the so-called orientation defects, for H_2O, CH_3OH, and C_2H_5OH[23,26]. The data pertaining to the alcohols are also obtained by extrapolation of the solution spectra[20]. The analogy with the alcohol spectra also supports the values for water. Close to T_c, strong density gradients[23,24] widen the limits of error. The values given for water in Figure 5 were therefore checked by computer analysis of the spectra[25]. In

order to eliminate the fundamental ambiguity[27] of this analysis, spectra of ice and spectra recorded at supercritical temperatures were chosen as basis. In this way residual H-bonds are found at T_c.

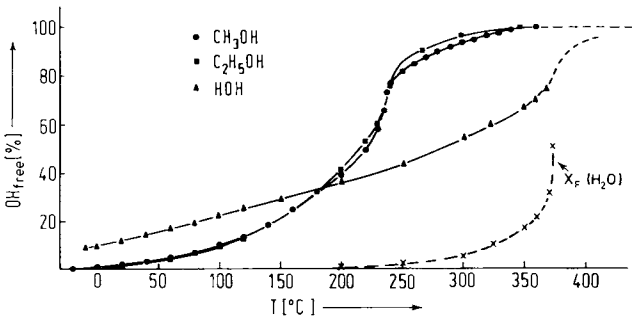


Fig. 5. Fraction of non-H-bonded OH groups in the saturated liquid phase of H_2O, CH_3OH, and C_2H_5OH. Hole defect fraction x_f for H_2O.

According to Figure 5, the fraction of open H-bonds at the melting point T_m is relatively small, and in any case much smaller than assumed in older theories of liquids. Differences between H_2O and the alcohols have the following causes: 1) The concentration of lone pairs θ in alcohols is equal to twice the concentration of OH groups; even for $c(OH_{free})=0$, we find $c(\theta_{free})=c$ [c = concentration of alcohol], whereas for H_2O $c(OH_{free})$ is always equal to $c(\theta_{free})$; 2) the concentration of OH varies; 3) alcohols form branched chain associates whereas H_2O forms an H-bond network with enhanced cooperativity (cf. Section 10.1 in ref. [1]).

On the basis of the existence of "free" OH groups quantitatively demonstrable with high accuracy by the infrared overtones, we have tentatively developed an orientation defect model for H-bonded liquids with the O_F values given in Figure 5. The description of liquids by this simple model is based on the successful description of H-bonds in solution as chemical equilibria. There are two kinds of OH groups in our model: those participating in H-bonds and the "free" OH groups regarded as defects. The following arguments should illustrate the starting point:

1) A description of the bonds with $\Delta H_H > RT$ as a chemical equilibrium between open and closed H-bonds has proved its value in numerous studies.

2) The isosbestic point occurring in all overtone spectra of water (at 6800 cm^{-1}, cf. Fig. 4) is a sensitive indicator that H_2O association can be treated as a simple equilibrium between two OH groups A and B with different stretching vibrations. The frequency range and comparison with spectra of alcohols and their solutions support the formulation of this equilibrium as

$$OH_{free} + \theta_{free} \rightleftharpoons OH_{H\text{-}bond} \quad (1)$$

The isosbestic point becomes unsharp only above 150 °C[19,20,23-25]—this may indicate that smaller aggregates appear at higher temperature and possible inductive effects (cooperative effects involving H-bonds) become less important.

3) The results of our overtone analyses in the range of −70 to 420 °C were confirmed between 0 and 90 °C by difference spectroscopy by *Worley* and *Klotz*[93] and, more recently, by *Paquette* and *Joliceur*[94]. In addition, the somewhat difficult analysis of the fundamental vibrations (IR and Raman spectra) led to agreement[95,96] with our overtone results.

4) It can be assumed from the variation of density with temperature up to 200 °C and from X-ray diffraction experiments[28] that, up to 200 °C, the orientational partition function plays a more important role than the partitioning of the distances. The angular distribution has a relatively sharp minimum for $\beta=0$[14,15]. Recent computer simulations have shown (cf. Section 3.2) that most molecules oscillate about $\beta=0$ in liquid water at low temperature. Replacement of the angular partition functions by the approximation of a two-step function thus appears permissible, especially when it is assumed that the H bonded state observed with the broad H-bond band may be described by angle oscillations around the mean value $\beta=0$.

5) Matrix spectra of H_2O and alcohols in solid Ar or N_2 exhibit only few discrete H-bond bands and no "continuum"; this shows that certain H-bond structures are strongly preferred[29,32].

6) Dielectric relaxation time measurements demonstrate the preponderance of a single relaxation mechanism in liquid water (and suggestions of a second, less pronounced one)[33], indicating the predominant role of two OH states. – Intermediate states between the extremes of closed and open H-bonds admittedly have greater weight in neat liquids than in solutions (greater band half-widths), but they can apparently be neglected to a first approximation because $\Delta H_H > RT$. The practical chemical significance of the liquids considered in this progress report preclude our waiting for a precise knowledge of the partition functions.

The fraction of hole defects x_F in water, methanol, and ethanol formally calculated for $T<0.9\,T_c$ from densities[34,35] according to $x_F=\rho_D/(\rho_L+\rho_V)$ is small in comparison with that of H-bond defects O_F (cf. lower right-hand curve for H_2O in Fig. 5). On a reduced temperature scale T/T_c, the hole defect concentration of water is only slightly lower than that of nonpolar substances (cf. Fig. 2 in ref. [1]). $O_F \gg x_F$ illustrates just how dependent the properties of H-bonded substances should be upon orientation defects.

The fictive occurrence of hole defects in water can be interpreted with the aid of monomeric H_2O molecules in which the random accumulation of thermal energy has led to the breaking of all H-bonds. Such "monomers" should have high vapor pressures, and therefore "evaporate", because their dispersion energy is so small relative to kT. Monomeric fractions greater than 1% should by recognizable from a suggested rotational structure of IR bands. In accord with the estimate of Figure 5, this was not observed for liquid water, in contrast to water vapor. Older theories[36,37] predict values of 65%[36] and 47%[37] (cf. ref. [38]) for O_F at 0 °C. Both spectroscopic studies and a comparative study of the heat of fusion ΔH_m were able to discredit these predictions. Models of water with significant monomer concentrations at room temperature cannot be justified.

2.2. Model for the Properties of H-Bonded Liquids

A simplified model[38-41] can be derived for water (Fig. 6; valid up to about 180 °C) from the results of IR overtone spectroscopy and careful studies of fundamental vibrations:

H-bonds lead to a "liquified ice" structure with coordination numbers of about 4 (cf. the average coordination number of 4.4 from X-ray data[42]). H-bond defects O_F are not distributed entirely randomly (Fig. 6, center) and tend towards closest packing similar to that of nonpolar liquids[1].

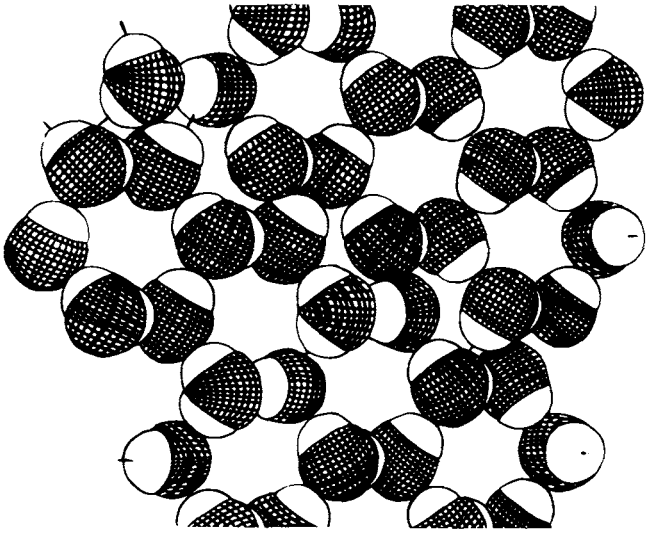


Fig. 6. Idealized two-dimensional model of water. H-bonds of the kind found in ice are assumed to be accompanied by "H-bond defects" with closer packing.

It is the task of models—in a situation that has not been completely elucidated—to describe known and predict unknown properties of substances. As demonstrated by the model underlying the "ideal gas law", stipulating such unreasonable things as force-free, point molecules, models can be sufficiently informative for practical purposes even if they are merely simplifying approximations.

Our simple liquid model which neglects partition functions of angles and distances because the two could not yet be separated will have to prove its worth by quantitative prediction of the properties of materials. After the successes of the hole defect model of nonpolar liquids[1], we shall now test an orientation defect model for H-bonded liquids in which the fraction O_F of H bonds is opened as a result of the random distribution of thermal energy.

2.2.1. Heat of Fusion

When ice melts, the value of O_F changes, increasing by *ca.* 10%. The high heat of fusion of $\Delta H_m = 1.43$ kcal/mol is essentially attributable to the relatively high contribution of H-bond energy: 0.1×7.4 kcal/mol $= 0.74$ kcal/mol (7.4 kcal/mol: H-bond energy per mole of H_2O). If we adopt $\Delta H_m(H_2S) = 0.57$ kcal/mol as a measure for the normal melting process of non-polar substances, and bear in mind that the number of intermolecular degrees of freedom increases on breaking of H-bonds (cf. [1]), then the value of $\Delta H_m(H_2O)$ accords with the prodiction of Figure 5, but contradicts previous theories[36,37]. ΔH_m of the alcohols is lower than the heat of fusion of ice and only slightly higher than for homologous *n*-alkanes (Table 3) in spite of higher molecular weight—*i. e.* greater dispersion forces.

In accord with Figure 1, it can be assumed that the interaction of an OH group which is not due to hydrogen bonding will be greater than that of a CH_2 group. Thus it follows from the spectroscopic findings (Fig. 5) that the contribution of H-bonds to ΔH_m of the alcohols is low.

Table 3. Heat of fusion of alcohols and paraffins.

	C_2H_6	CH_3OH	*n*-C_3H_8	C_2H_5OH	*n*-C_4H_{10}	C_3H_7OH
ΔH_m [kcal/mol]	0.67	0.77	0.84	1.11	1.11	1.24

2.2.2. Heat Content under Saturation Conditions

As in the model of nonpolar or only weakly polar substances[1], we initially consider saturation conditions for the sake of simplicity. Figure 7 shows the enthalpy and internal energy for water as a liquid (H_L, U_L) and as a vapor (H_V, U_V); the zero point is the energy content of the liquid at the melting temperature T_m in equilibrium with ice.

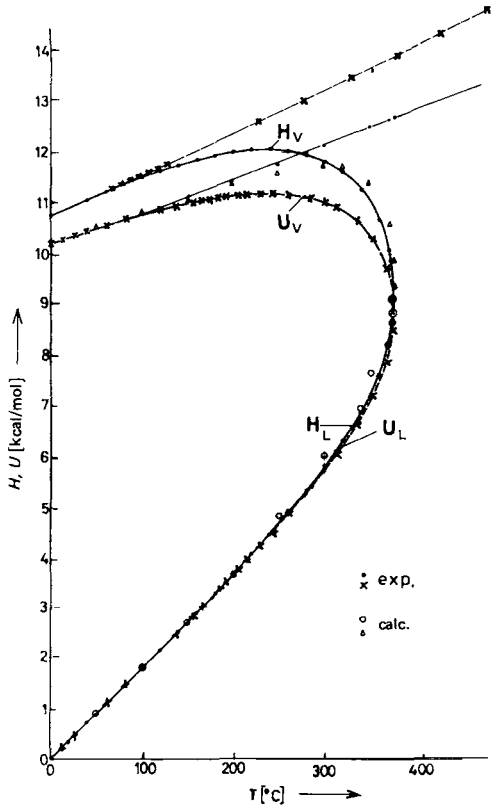


Fig. 7. Heat content of water in liquid/vapor equilibrium (H_L, U_L for liquid; H_V, U_V for vapor), comparison of experimental and calculated values [eqs (2), (4), (6)] (straight lines correspond to ideal gas state).

a) The Liquid State

The energy content of liquid water is made up, according to our simple model, of the following components:

1) Heat content of intramolecular degrees of freedom, obtainable from the specific heat (molar heat capacity) C_V^0 of the ideal gas;
2) the energy required for breaking H bonds $[O_F(T) - O_F(T_m)] \cdot 2\Delta H_H$;
3) heat content of the intermolecular degrees of freedom[1] $(2 + O_F) \times R(T - T_m)$;
4) correction of C_V^0 for loss of translation energy in the liquid phase: $-3R(T - T_m)/2$.

To facilitate comparison with Figure 7, all four terms have been corrected to the chosen zero point at T_m. They are combined in eq. (2).

$$U_L = \int_{T_m}^{T} C_V^0 dT + 2\Delta H_H \cdot [O_F(T) - O_F(T_m)] + \\ + (2 + O_F) \cdot R(T - T_m) - R(T - T_m)3/2 \quad (2)$$

The third summand represents the correction of the intermolecular degrees of freedom. Its contribution to the molar heat was approximated as $C_W = ZR/2$[1,43] (one degree of freedom is attributed to each nearest neighbor with coordination number Z). For our model of water we choose:

$$Z = (1 - O_F)4/2 + O_F 6/2 = 2 + O_F \quad (3)$$

where $Z = 4$ for the ordered regions and $Z'' = 6$ (3 to neighbors with H bonds + 3 for the "free" OH group) for regions with "free" OH groups. We adopt the spectroscopic value of -3.7 kcal/mol for ΔH_H[3,4,25].

The simply derived equation (2), containing only experimentally determinable quantities such as O_F and ΔH_H and no fitted constant, represents the experimental data surprisingly well. Slight deviations at elevated temperatures could be attributed to the hole defects which also occur when the temperature is raised—they are not accounted for in eq. (2). A quantitative correction of these small deviations appears to have little point since the coordination numbers of the sites with "free" OH groups at low T values (existence of larger aggregates with terminal OH groups) would have to be chosen differently from those for high T values (smaller aggregates).

b) The Vapor State

Without any correction for a real gas, the energy of the vapor would be made up of the intramolecular degrees of freedom (first term, eq. (4)) and the heat of evaporation at T_m; this second term can be calculated from the energy of sublimation ΔU_s and the heat of fusion ΔH_m:

$$U_V' = \int_{T_m}^{T} C_V^0 dT + \Delta U_s - \Delta H_m \quad (4)$$

(cf. the straight line shown in Fig. 7, which is a tangent of the experimental curve at T_m).

A real gas correction can first be attempted as with nonpolar substances. 1) At higher vapor densities, intermolecular interaction energies have to be subtracted which can be estimated[1] from the pair potential W and half the coordination number ($12 x_F$ according to the hole defect model[1]). For water that would be

$$W \cdot 4/2 = \Delta U_s - 2\Delta H_H; \quad W = 2.1 \text{ kcal/mol} \quad (5)$$

2) At higher vapor densities an intermolecular component of magnitude $12 RT x_F/2$ has to be added to to the molar heat[1]; however, a loss of translation energy of $3 RT x_F/2$ has to be subtracted in the case of association.

$$U_V = U_V' - 6 W \cdot x_F + \left(\frac{12-3}{2}\right) RT \cdot x_F \quad (6)$$

According to Figure 7, formula (6) gives too small a correction (cf. Table 4); this indicates residual H bonding in the vapor state.

Table 4. Difference between the U_V values calculated by eq. (6) and the experimental values—indication of residual H-bonds?

T [°C]	200	300	350	370
"$\Delta H_{H,V}$" [kcal/mol]	0.23	0.7	1.0	1.1
Vapor pressure P_s [atm]	15.85	87.62	168.01	214.69

A quantitative experimental test of the estimations of H-bonds in the vapor (Table 4) has yet to be performed. It would appear very difficult because of rotational structures[44] and the considerable effort required[22]. The order of magnitude of "$\Delta H_{H,V}$" (Table 4) is in agreement with Figure 5.

2.2.3. Heat of Evaporation

The difference between eq. (2) and (6) corresponds to the energy required for evaporation into the ideal gas state at $V = \text{const.}$, L_V''. The final equation (7) contains the following four terms:

1) Energy for breaking of H-bonds;
2) energy for compensation of dispersion energy $2W$ of the "free" OH groups O_F;
3) heat content liberated on annihilation of intermolecular degrees of freedom in the ideal gas;
4) energy for re-excitation of translation (rotation retained as libration in the liquid, cf. spectroscopy of libration bands[30]).

$$L_V'' = \Delta U_s(1 - O_F) + 2W \cdot O_F - (2 + O_F)RT + RT(1 - x_F) \cdot (3/2) \quad (7a)$$

After rearrangement with $\Delta U_s = 2\Delta H_H + 2W$ (cf. (5))

$$L_V'' = \Delta U_s - 2\Delta H_H \cdot O_F - (2 + O_F)RT + RT(1 - x_F) \cdot (3/2) \quad (7)$$

Instead of L_V'' (ideal gas state) the energy of evaporation L_V (real vapor state) is measured and tabulated. The difference (W_{real}) follows from Section 2.2.2 and more readily from the difference between the straight lines corresponding to eq. (4) or the tangent in Figure 7 and the curve of the experimental H_V values in Figure 7.

As shown by Figure 8, the calculated values of $L_V = L_V'' - W_{real}$ are in good agreement with the data obtained from experiments. Calculation of L_V'' by the model for nonpolar liquids[1] from the hole defects x_F calculated from the densities (Fig. 5) gives only slightly poorer agreement (Fig. 8) than the use of formula (7a). The value of $L_V(0\,\text{K}) = 13.7$ kcal/mol $= L_V^0$ extrapolated for T/T_c gives, by proven methods[1], for water: $Z'f = (3/4)L_V^0/RT_c = 14.1$, *i.e.* a value resembling those for nonpolar substances. The reason is to be found in the (accidently) similar size of $\Delta U_s = 11.6$ kcal/mol; $(12/2) \cdot W = 12.6$ kcal/mol; $(12/2) \cdot (3/2) \cdot RT_c = 11.57$ kcal/mol. Thus in the reduced T/T_c diagram, the anomalous properties of water are not so striking as the greatly increased value of T_c.

For alcohols, L_V can also be calculated from the spectroscopically determined O_F values[39] (cf. Fig. 8). Unfortunately, there are no experimental data available for high temperatures.

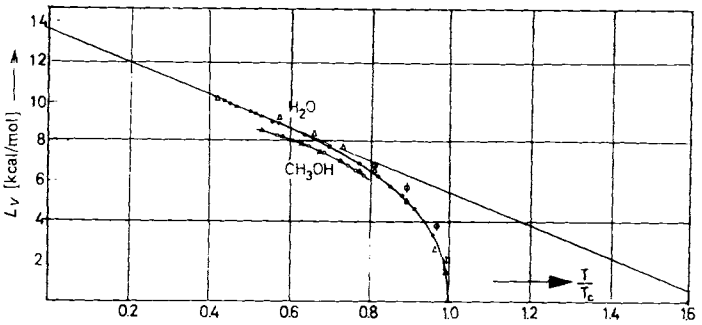


Fig. 8. Heat of evaporation L_V of water and methanol under saturation conditions; ●, ○ experimental; ▲, △ calculated from O_F and eq. (6); ◇ calculated from the hole model and x_F.

2.2.4. Specific Heat

As a differential quantity, the molar heat is a particularly sensitive touchstone for our model. C_σ at the liquid/vapor saturation line (Fig. 7) can be readily represented by the simple two-state model without any modification. The H-bonds induce high values of the heat of evaporation and of the the molar heats of water and the alcohols. Owing to the high relative contributions of H-bonds to the overall forces this has a particularly pronounced effect in the values referred to 1 gram (Table 5).

Table 5. Specific heat capacity c_p and enthalpy of evaporation of selected liquids at 20 °C.

	H_2O	CH_3OH	C_2H_5OH		*n*-Pentane	CH_3COCH_3	Benzene
c_p [cal/g]	0.999	0.57	0.56		0.542	0.51	0.416
ΔH_p [cal/g]	585	287	240		91.4	131	131
	$CHCl_3$	CS_2	CCl_4	HCl	$CHBr_3$		
c_p [cal/g]	0.22	0.237	0.202	0.190	0.128		
ΔH_p [cal/g]	63	89.14	53.8	—	38.28		

As "mobile thermostats", mammals profit from the high heat capacity of water and the high enthalpy of evaporation per unit mass.

The molar heat C_σ of water can be obtained directly by differentiation of eq. (2). The four summands then represent:

1) Intramolecular degrees of freedom;
2) energy required to break H-bonds per degree;
3) increase in heat content of intermolecular degrees of freedom;
4) thawing of translation at defect sites.

Above 200 °C, the fourth term of C_σ has to be increased to account for the hole defects which we could neglect in eq. (2). Neglect of this effect in C_σ would result in a greater error near T_c owing to the differential quotient dx_F/dT giving the energy required for hole defect production per degree (5th term in eq. (8)). Thus, for C_σ we write:

$$C_\sigma = C_V^0 + \frac{dO_F}{dT}[2\Delta H_H + RT] + \\ + (2+O_F)R\bar{A}\frac{3}{2}R(1-x_F) + \frac{dx_F}{dT}\frac{3}{2}RT \qquad (8)$$

The differential quotients dO_F/dT and dx_F/dT are determined from Figure 5. As shown by Figure 9, eq. (8)—again without any adjusted constant—provides a good representation of the experimental values. The second term for the H-bonds in eq. (8) makes a contribution of 50% at room temperature—and explains the anomalously high molar heat of water (cf. Table 5).

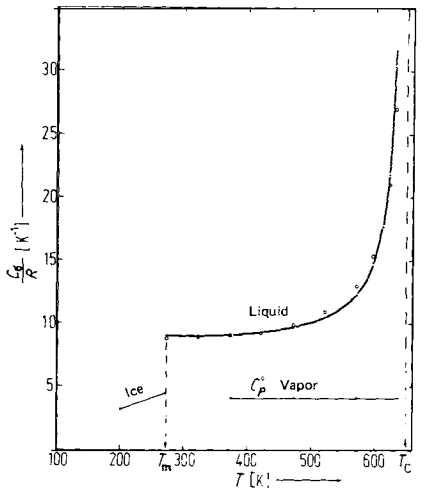


Fig. 9. Molar heat capacity C_σ of liquid water along the saturation line: ●, experimental; ○ calculated according to eq. (8).

The experimental molar heats show a steep maximum for T_c and critical pressure[34,35], the temperature at which it occurs being highly pressure dependent. The maximum corresponds to the point of inflection of O_F at T_c in Figure 5. In semiquantitative experiments we gained convincing evidence that the temperature of the point of inversion of O_F shifts in the same way as the maximum value of the molar heat when the pressure changes. The large pressure gradients[24] in the vicinity of T_c and the start of corrosion of the sapphire window of the IR cell above T_c widen the limits of error of such experiments.

The shift of the point of inversion of O_F with pressure—and thus also of the maximum value of the molar heat—is due to changes of concentration in the H-bond equilibrium. Increase in pressure, and related increases in density and concentration, lower O_F at T=const. and *vice versa*. Spectroscopic studies showed the following O_F values to be similar at temperatures T and densities ρ:

H_2O[3]: $O_F(T_c, 2\rho_c) \approx O_F(325\,°C, \text{saturation})$
$O_F(420\,°C, 2\rho_c) \approx O_F(350\,°C, \text{saturation})$
CH_3OH[24]: $O_F(360\,°C, \rho_c) \approx O_F(310\,°C, \rho_c/2) \approx O_F(230\,°C, \rho_c/4)$

This demonstrates how properties can be determined outside the saturation state.

2.2.5. Density

The anomalously high density of water and its unusual maximum at 4 °C can be readily interpreted with the aid of our model. On breaking of H-bonds, the local structure of coordination number 4 collapses (cf. Fig. 6), leading to higher densities with increasing T. This is opposed by the normal drop in density with increasing temperature as a result of the greater thermal vibration volume. The density of water can be described by the sum of the contributions to the partial molar volumes for OH groups participating in H-bonds (V_b) and for the "free" OH groups (V_F)[39]:

$$1/\rho = V = (1 - O_F)\, V_b + O_F\, V_F \qquad (9)$$

Values somewhat smaller than the data for ice can be used for V_b and its dependence upon T. V_F cannot be determined by spectroscopy, and its values have to be adapted in eq. (9)[39]. Thus, unlike the properties mentioned so far, the density is not a sensitive touchstone for our model. If V_F is fitted for two temperatures, then eq. (9) provides a quantitative description of ρ up to $T = 330$ °C. Additional hole defects have to be considered in eq. (9) at higher temperatures.

2.2.6. Surface Tension and Surface Energy

a) Water

Both the surface tension σ and the surface energy U_σ of water and alcohols can be derived from our simple model. It should initially be noted that the apparently very high surface tension of water $\sigma = 72$ erg/cm^2 (dyn/cm) is not so much a consequence of particularly strong intermolecular forces (as is often assumed) but rather a "consequence" of the unit based on 1 cm^2, which is otherwise most unusual. A discussion of structure again requires conversion to molar units[1,45-47]: $\sigma_M = N_A^{1/3} V^{2/3} \sigma$ (N_A, Avogadro's constant; V, molar volume). The molar surface tension σ_M of water is hardly greater than that of most other liquids (Fig. 10); the high value of σ is due to the large number of H_2O molecules per cm^2. The slightly greater value of σ_M for water, as compared with that for alcohols, is a true indication of its strong molecular interactions.

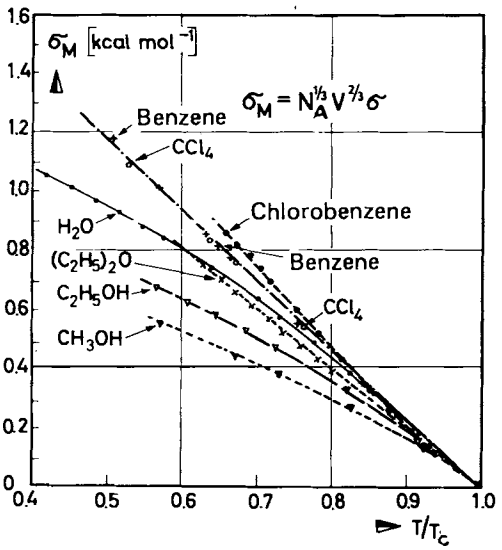


Fig. 10. Molar surface energy: σ_M (energy required to bring 1 mol of molecules to the surface).

Being work measured under isothermal condition, σ and σ_M afford the surface enthalpy by way of the Gibbs-Helmholtz equation:

$$H_\sigma = \sigma_M - T\partial\sigma_M/\partial T \qquad (10)$$

H_σ for liquids differs only slightly from the surface energy U_σ. In contrast to the situation in nonpolar substances, the two quantities are temperature dependent for compounds forming hydrogen bonds (cf. Fig. 11; U_σ calculated from σ values of *Ramsay* and *Shields*[48]; according to [49] for HF, and from our own measurements for alcohols at $T/T_c < 0.65$[45]).

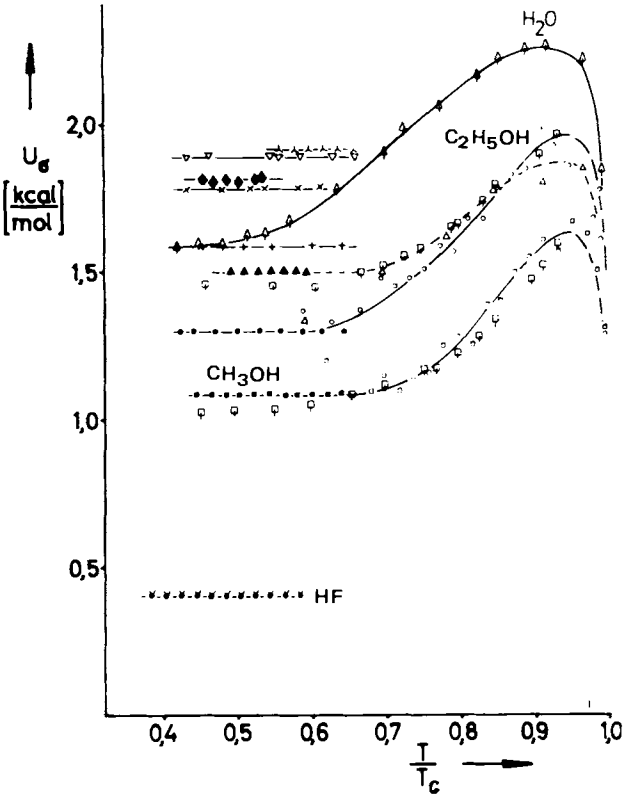


Fig. 11. Surface energy U_σ for H-bonding liquids. Values for alcohols are shown by our own measurements to be independent of T at low temperature, as for nonpolar substances. ⊓ calculated from O_F and eqs (11), (14)

According to the principle of least constraint, mainly "free" OH groups should be brought to the surface when the surface area of water is increased. On breaking "1 mole of pairwise interactions W" there result "2 moles of surface". Thence,

$$U_\sigma = W \cdot Z/2 \cdot 1/2 = 2.1 \cdot 3/4 \text{ kcal/mol} = 1.57 \text{ kcal/mol} \qquad (11)$$

(where $W = 2.1$ kcal/mol, cf. eq. (5), and the coordination number $Z = 3$ between layers of "free" OH groups).

The value of $U_\sigma(H_2O) = 1.58$ kcal/mol determined experimentally at low temperature is in accord therewith. The increase of U_σ with T can be interpreted in terms of the raising of the coordination number of "free" OH groups in smaller aggregates or by model considerations[39]. The maximum for $U_\sigma = 2.22$ kcal/mol corresponds to a coordination number of $Z = 4$ according to eq. (11).

b) Alcohols

The energetically weakest point in alcohols is found in the hydrophobic units associated with the dispersion energy W_d. In the model of chain-like associates (Fig. 12), the coordination number is 6 in the interior of the liquid and 4 at its surface, thus

$$\lim_{T\to 0} U_\sigma = W_d(6/2 - 4/2) = W_d \qquad (12)$$

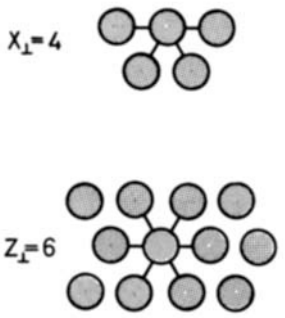


Fig. 12. Model arrangement of alcohol chains perpendicular to OH...OH axis. $Z=6$ for liquid, $Z=4$ at surface.

As for nonpolar substances $\lim_{T\to 0} U_\sigma$ should be independent of T. Since no pertinent experimental data were available, we obtained confirmation of this prediction by performing measurements of our own (difference capillary method)[15,45] (Fig. 11)[*].

$\lim_{T\to 0} U_\sigma(CH_3OH) = 1.08$ kcal/mol $= W_d$ corresponds roughly to the pair potential $W_d = 1.03$ kcal/mol calculated from the limiting value of the heat of evaporation of CH_4 for $T = 0$ K. On resolving the energy of sublimation ΔU_s of the alcohols into H-bond energy ΔH_H and dispersion energy of hydrophobic groups and W of the OH group: $\Delta U_s = \Delta H_H + W_d \cdot (6/2) + W$, then $\Delta U_s(CH_3OH) = 10.7$ kcal/mol and $\Delta H_H = 4$ kcal/mol lead to $W(CH_3OH) = 3.6$ kcal/mol. Taking this value and $\Delta U_s(C_2H_5OH) = 12$ kcal/mol, we calculate $W_d(C_2H_5OH) = 1.47$ kcal/mol—a value which agrees well with $U_\sigma(C_2H_5OH) = 1.3$ kcal/mol for low temperature to within the limits of error[**].

The approximation expression[1] $U_\sigma = 2.85\ RT_c \cdot (3/2)$ applies for nonpolar substances. This expression is also found at low T to apply to alcohols $C_nH_{2n+1}OH$ with $n \geq 2$ if the value of T_c for the n-alkane having the same number of carbon atoms is inserted into the equation[10,45]. The maximum of U_σ at higher temperatures follows from our model with

$$U_\sigma = [(1 - O_F)\Delta H_H + W_d \cdot (6/2) + O_F W] - [(1 - O_{F_0})\Delta H_H + W_d \cdot (4/2) + O_{F_0} W \cdot (2/3)] \qquad (13)$$

The first term in square brackets would be the interaction in the bulk of the liquid, and the second one the interaction at the surface. The coordination numbers are smaller by a factor of $2/3$ at the surface (cf. Fig. 12). As an approximation, we equate the fraction of H-bond defects O_{F_0} at the surface with that of the "free" OH groups in the bulk O_F, and thus obtain from eq. (13) the equation

$$U_\sigma = W_d + O_F W/3 \qquad (14)$$

Eq. (14) satisfactorily reproduces the experimentally observed temperature dependence of U_σ for alcohols (Fig. 11); for $T \to 0$ it assumes the form of eq. (12) because $O_F \to 0$ then applies.

2.2.7. Dielectric Constant

The anomalously high dielectric constant (DC) of water and its drop to the value 7 at T_c has already been explained by *Hasted et al.*[33,50] with the aid of a two-state model closely resembling our own. The values of O_F estimated from the heat of evaporation agree well with those determined experimentally by IR spectroscopy (Fig. 5) up to $T = 250\,^\circ$C; at higher temperatures, deviations result owing to the assumption $O_F(T_c) = 1$, which we had also made in earlier work. In the range $250\,^\circ\text{C} < T < T_c$, the calculated DC values are greater than the experimental values; they could be improved with the experimental O_F values (Fig. 5). Increases in pressure above saturation conditions raise the value of the DC[51], in keeping with our spectroscopic observation that O_F decreases in accord with the H-bond equilibrium[3] under such conditions as a result of the increase in concentration. The DC of ethanol also falls to the value of 2.4[52] at T_c, and, according to Figure 5, should be interpretable with a similar model. The temperature dependence of the magnetic susceptibility[53] or the δ values of NMR signals[54] can likewise be interpreted by the O_F values of Figure 5[41].

2.2.8. Viscosity, Gel Formation, and Cluster Model

Even dynamic quantities such as viscosity and gel formation can be understood, in principle, with the aid of our simple model. Owing to their angular dependence, H-bonds are cooperative[*]. In the vicinity of the defects, the H-bond angles will differ from their optimum values and the energy required to generate further defects will therefore be lower than in ordered regions. It is consequently assumed that owing to this cooperative interaction (cf. Section 10.1 in [1]), the H-bond defects—especially in the network of water—are not randomly distributed but tend to accumulate locally. In the highly idealized limiting case, this leads to a cluster model[3,37] in which ordered regions are separated by zones of H-bond defects. On the basis of Figure 5 and the idealized two-state model, the number N of molecules linked by H-bonds—the size of the cluster—can be estimated[3,15] (cf. upper curve with left-hand scale in Fig. 13).

Substances which undergo only slight interaction with water will preferentially accumulate in these perturbed zones comprising H-bond defects[55,56]. There results a model for solubility[55,56]. The solubility of small molecules dissolved in water by the action of dispersion forces can be arranged according to critical temperature[97] by means of the hole defect model[1]. The relaxation time of 10^{-11} s measured dielectrically for water is regarded as the lifetime of the H-bonds[33].

[*] In this way our model demonstrated its value by predicting *unknown* properties.

[**] The loose network of difunctional water H-bonds is not present here and W for the alcoholic OH groups is therefore higher than the value for HOH.

[*] There may also be a cooperative interaction resulting from charge shifts induced by H-bonds. However, this will hardly change in water up to about 180 °C.

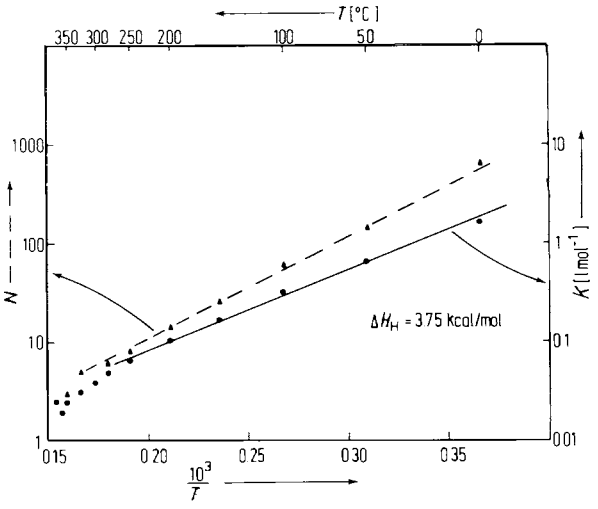


Fig. 13. Upper curve and left-hand scale: mean number N of H_2O molecules linked by H-bonds in water (at saturation, highly idealized model).—Lower curve and right-hand scale: equilibrium constant K of water association.

Perturbed zones will disappear and new ones will be formed on this time scale, leading to what have been called flickering clusters. Larger dissolved molecules will interfere with this mobile mechanism. The anomalous property of gel formation by water on addition of small amounts of foreign matter (*e.g.* 1:1000) thus becomes understandable (cf. the formation of so-called polywater, a gel arising on contamination of water[56]).

The activation energy of the viscosity[42,57] of water (4.8 kcal/mol) or of self-diffusion[57,58] (4.6 kcal/mol) would correspond roughly to the bond energy of an H-bond, *i.e.* the H-bond energy of the water molecules at the perturbed zones. Viscosity and diffusion mechanisms can therefore be envisaged as occurring primarily at the perturbed molecules, at the weak points of the structure.

2.2.9. X-Ray Data

X-ray and neutron diffraction experiments on water in the temperature range of 4 to 200 °C reveal residual "ordered" structures having dimensions of 9 to 4 Å (Table 6)[28,59].

Table 6. Mean radii r of "ordered" regions around a H_2O reference molecule.

T [°C]	4	25	75	200
r [Å] from diffraction data	9	8	6.5	4
r [Å] from O_F values	10.5	9	6.5	4

The radii r of regions with a certain degree of long-range order calculated from distance distribution curves of the diffraction data are in accord with our data regarding the number N of molecules linked by H-bonds (Fig. 13). As early as 1936, *Kortüm*[13] drew attention to ordered regions of 18 to 20 Å in water—*i.e.* containing about 1000 molecules—apparent from X-ray line width measurements by *Scherrer*[60]. On the basis of X-ray diffraction data for alcohols, *Prietzschk*[61] deduced strong association to "chains of considerable length"; according to our IR result of $O_F \approx 1\%$, the $(ROH)_n$ chains should comprise about 100 molecules at room temperature.

2.2.10. Solutions

IR overtone spectra also provide a starting point for a systematic view of aqueous solutions[38,40–42] or even of complicated aqueous systems as in biological cells[10,62] or in membranes[63]. We shall consider just one example: To a first approximation the overtone spectra of water change on addition of electrolyte solutions in the same way as on altering the temperature[10,38,40,64]. The salt series, arranged in the order of the corresponding "structure temperature" T_{str} exhibited by pure water at the same defect content O_F, corresponds to the Hofmeister or lyotropic series of colloid chemistry, which has thus now been identified as a series of modification of the structure of water[38,64]. There are salts in this series whose T_{str} is higher than the solution temperature T_S—so-called structure breakers with O_F (solution, T_S) $> O_F(H_2O, T_S)$—and salts whose T_{str} is lower than T_S—so-called structure makers with O_F (solution, T_S) $< O_F(H_2O, T_S)$. Both groups can also be characterized by NMR spectroscopy (chemical shift, relaxation time)[65]. The first group can exert "salting-in" effects for organic partners, whereas the structure-consolidating ions have a "salting-out" effect, owing to the reduced value of O_F; this is exploited in dyeing and in detergents. The consolidating influence of salts having $T_{str} < T_S$ on the structure of water could be readily appreciated as due to orientation of water dipoles in an ionic field[66], whereas no explanation could be found for the action of the large group of structure breakers.

The frequency shift $\Delta\nu$ of the spectra of water in crystalline hydrates is smaller for most anions than for ice[10,67–70]. Application of the so-called Badger-Bauer rule[18], according to which $\Delta\nu$ is a measure of H-bond energy ΔH_H, to ions as well, raises the question[10,67] whether the field action of numerous anions on OH groups is smaller than that of the lone pairs of the OH groups themselves or similar. The position of the lone pairs close to the "surface" of molecules may cause small distances to OH groups and therefore strong Coulomb interactions. The description of electrolyte solutions could be modified in this respect[67]. The limited solubility of most salts, in spite of their high energy of hydration ΔH_{hyd} would be plausible if H_{hyd} were provided only by a relatively large number of H_2O molecules[67]. Beside ions exerting a hydrolytic action, the ions of strong acids and bases whose spectra show $\Delta\nu$ values greater than that of ice must be treated as exceptions. Their greater solubilities and the tremendous importance of the pH value in chemistry could be attributed by our spectroscopic method to particularly pronounced perturbation of the structure of water as a result of stronger H-bonds than in pure water (for details of aqueous solutions: cf. [10,38,40]; see particularly[97,98]).

2.2.11. H-Bond Energy

In accordance with our two-state model, whose ability to account for many anomalous properties of liquids has been demonstrated in this article, H-bonds in liquids can be described as simple equilibria provided that the temperature is not too high[3].

$$OH_{free} + \theta_{free} \rightleftharpoons OH_{bonded} \tag{15}$$

In the case of water, we have

$$[\theta_{free}] = [OH_{free}] = O_F\, c(OH) \tag{16}$$

$$K = \frac{[OH_{bonded}]}{[OH_{free}]\,[\theta_{free}]} = \frac{(1 - O_F)}{O_F^2\, c(OH)} \tag{17}$$

From $\ln K = f(1/T)$ (cf. lower curve and right-hand scale in Fig. 13) the H-bond energy is found to be $\Delta H_H = -3.4 \pm 0.1$ kcal/mol, in good agreement with the value calculated from an intermolecular (OH + OD) combined frequency of HOD[4]. The literature contains occasional smaller values, during the calculation of which the erroneous assumption of $OH_{free} \rightleftharpoons OH_{bonded}$ was made, neglecting the lone pairs θ_{free}[*]. Eq. (15) and (17) are valid for $T < 250\,^{\circ}C$, a temperature at which $\ln N = f(1/T)$ shows a discontinuity (Fig. 13); smaller aggregates can no longer be neglected at $T > 250\,^{\circ}C$. Of course, they cannot be described by Eq. (15) and (17).

In the case of alcohols, Eq. (16) and (17) are replaced by

$$[\theta_{free}] = [OH_{free}] + c(OH) = (O_F + 1)\,c(OH) \tag{18}$$

$$K = \frac{(1 - O_F)}{(O_F^2 + O_F)\,c(OH)} \tag{19}$$

Up to about 200 °C, $\ln K$ is also a linear function of $1/T$ for alcohols[3]. The successful application of eqs (15) through (19) confirms the utility of the fundamental model.

Summary: The anomalous properties of water and of alcohols and their temperature dependence can be interpreted surprisingly well with the simple two-state model of an equilibrium between open and closed H-bonds.

NB: A model is a simplified system which can describe and predict properties although it may be removed from (frequently unknown) reality (cf. the model underlying the "ideal gas equation"). In the hole model of liquids[1], a model hole may stand for the sum of several real holes which are each smaller than a molecule. In the two-state model of water, the two states could consist of rapid oscillations about certain orientation angles β or molecular distances r, whose mean values lie at $\beta = 0$ and r_{min}, on the one hand, and at very large angles or distances, on the other. The IR overtone spectra show that these mean values (and thus also the mean H-bond energies and the frequencies of the corresponding band maxima) vary only slightly with temperature. Modest increases in the band half-widths with increasing temperature indicate slight increases in the amplitudes of oscillation. It is an advantage of the IR overtone method that the band half-widths contain information about the partition functions of these oscillations. Their accurate analysis is made difficult by the existence of the two parameters β and r. It requires more detailed studies of the—theoretically known—relationships[15, 18] between β, r, and $\Delta\nu$.

3. Improvement of the Simple Model of Water

3.1. The IR Method

Starting from the radial partition functions of diffraction methods, modern research into liquids seeks to acquire an insight into distance and orientation partition functions. The success of our approximation model (with the calculational approach of chemical equilibria) may be a borderline case owing to the relatively high total interaction of water, amounting to 11.6 kcal/mol (cf. standard enthalpies of formation of triethylamine at −11.6 kcal/mol or of ethylene oxide at −12.2 kcal/mol). Nor can details of the overtone spectra be explained by superposition of two bands due to open and closed H-bonds[25]. This requires a third intermediate band whose frequency shift $\Delta\nu$ relative to the band of the "free" OH groups is only 40% of the $\Delta\nu$ value of the ice band. A shift $\Delta\nu$ of 40% of the optimal linear H-bond band has so far been observed: 1) at low concentrations of alcoholic solutions[18]; 2) at low concentrations in the matrix spectra of H_2O and also of alcohols in solid Ar or N_2[18, 29, 32]. Since dipole moment minima occur in the same concentration range[71–75] which were interpreted by analogy with the arrangement in Figure 2b in terms of cyclic dimers, this third band of liquid water and the other two experiments can best be rationalized by assuming configurations with unfavorable H-bond angles. Spectroscopically, only 40% of the energy of a linear H-bond per OH group would correspond to this third state of water with unfavorable H-bond angles of around 100°, *i.e.* for the energy per aggregate with two participating OH groups there would result 80% of the energy of a linear H-bond. Quantum mechanical studies by *Clementi*[5] also ascribed 80% of the energy of a linear dimer to a cyclic dimer. From the trimer upwards, the total energy of cyclic associates is greater, at 12.27 kcal/mol, than that of the linear ones (10.67 kcal/mol).

It should also be noted that the O...O distances become smaller for unfavorable H-bond angles and the dispersive interaction will thus increase relative to linear H-bonds (according to Stuart-Briegleb models, the interaction energy would be *ca.* −3.2 instead of −2.2 kcal/mol for dimers with 7% smaller distances and dispersion forces of $1/r^6$). This increase in energy of 1 kcal/mol may become even greater in condensed phases such as liquids or matrices as a result of increased coordination numbers. The energy difference between H-bonds in the two-state model and such third states with unfavorable angles is thus reduced by an increase in dispersion energy. This would account for the efficacy of our model in the estimation of energetic properties.

Evaluation of computerized band analysis combined with the angular dependence of the frequency shift $\Delta\nu$ of H-bonds and the temperature-dependent half-widths permits estimation of the angular distributions. The area under the curves of Figure 14 corresponds to the percentage angular contributions. In addition, particularly for $T \geq 200\,^{\circ}C$, distance distributions would have to be considered; evidence exists for their influence on the IR frequencies[76–79]. Above 200 °C not only orientation defects (O_F according to Figs. 2b, e, f), but also "distance defects" (Figs. 2c, d) make a significant contribution to the intensity of the band of the "free" OH groups.

Theoretical approaches for the accurate evaluation of IR or Raman bands for partition functions analogous to Figure 14 are being developed[80, 81]. Their application to H-bond bands incurs problems, *e.g.* due to Fermi resonance or to intermolecular coupling with one-quantum excitations of neighboring molecules[4].

In principle, the band shapes of IR and Raman bands and their half-widths contain information about the partition functions of angles and distances and their dynamics. Until methods become available for separating these superposed

[*] A straight line is also obtained for $\ln K = \ln([OH]_{bonded}/[OH_{free}]) = f(1/T)$ since the logarithms of all concentrations are a linear function of $1/T$. The $1/T$ linearity fails to reveal any error in the equilibrium expression!

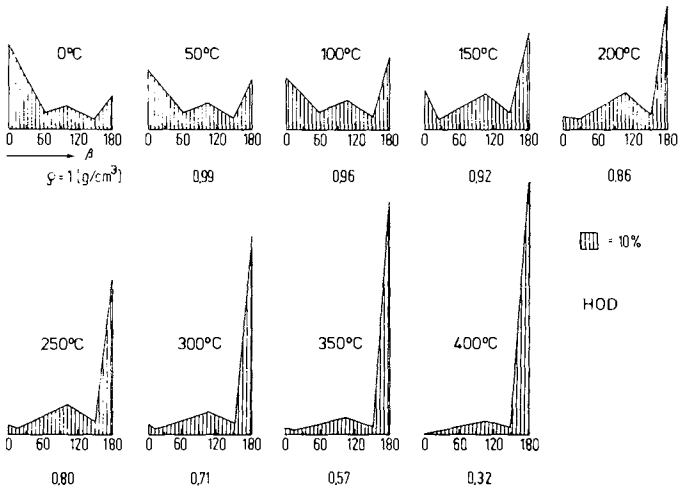


Fig. 14. Estimate of the H-bond defects O_F in water (saturation conditions). At $T<200\,^{\circ}C$ assignment of defects to H-bond angles β; around $\beta=180°$, contributions of "free" OH groups.

functions, use of our model based on mean values appears justified.

3.2. Computer Simulations of Liquids

Computer simulations of the structure of water[82–90] likewise satisfactorily reproduce properties. However, in this approach the potential of the water molecules is "fitted" to the properties. The neon-like dispersion potential used is certainly much too small (cf. in Fig. 1 Ne with CH_4, which is rather H_2O-like); in the range of distances of interest for H-bonds, crucial importance attaches to a "switch potential" which has no physical significance. No contradictions exist between the results of the computer model and those of the model derived from vibrational spectra if the respective nomenclatures are observed. The earlier statement by *Stillinger* and *Rahman*[85] that their calculations would rule out a two-state model of water argues in terms of coordination numbers. Thus it does *not* refer to the model of two different OH groups adopted by us, but rather to different kinds of molecules[*]. The calculated angular distribution[89] between the axis of an OH group and the axes of neighboring lone pairs (Fig. 15) is of interest. The sharpness of the angle partition function around $\beta=0$ accords with our model. A film of a computer simulation by *Geiger*[90] shows most of the molecules to oscillate about $\beta=0$, with rotations being comparatively rare. The second maximum around 100° in Figure 15 arises from the calculation, which simultaneously affords the position of the two OH groups of a H_2O molecule.

The computer model also leads to the conclusion that there is an "unambiguous division of pairs into 'hydrogen bonded' and 'non-hydrogen bonded'"[84] and, for the non-H-bonded states, to the statement that "these entities persist longer than H_2O molecules' vibrational periods"[83].

This corresponds to the observation made with HOD overtone spectra[4] that on increase in temperature the extinction increases in the range of non- or weakly H-bonded OH groups (7200—6800 cm^{-1}) and decreases in the range of bonded OH groups (6800—6200 cm^{-1}) (cf. Fig. 4). The isosbestic point appearing below 150 °C in the overtone spectra of H_2O, HOD, and D_2O supports the approximation of the two-state model. Our experience shows that it is not due to a simple equilibrium between two states but rather to the reluctance of the third state to change in this temperature region.

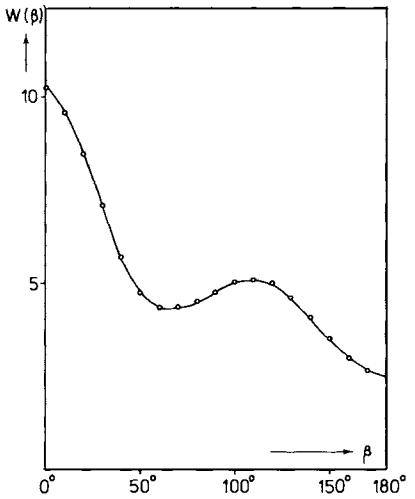


Fig. 15. Probability $W(\beta)$ of the occurrence of the H-bond angle β in water at 32 °C according to computer simulations [89].

The radial partition function calculated from the computer model also indicates residual "ordered" structures up to 7.5 Å from a reference molecule; nearly all the 216 molecules considered exhibit pairwise interaction of at least 3.3 kcal/mol[89]. 216 molecules are fewer than are predicted by the spectra to be linked by H-bonds at room temperature.

Summary: Extensions of the two-state to a three-state model are possible according to vibrational spectra. The spectra also contain information about the angular and distance distribution. In the future we shall learn more about these partition functions. However, the effort involved will probably increase out of proportion to the gain in knowledge.

I am indebted to my teacher Professor G. Kortüm for introducing me to quantitative spectroscopy, which provided an entry to a new field of study in my own contributions reported in this survey. Thanks are also due to my co-workers A. Behrens, C. Buanam-Om, W. Ditter, H. Kleeberg, B. Mann, D. Schiöberg, and O. Schrems for their contributions to our findings.

Received: May 15, 1979;
revised: November 19, 1979 [A 280 IE]
German version: Angew. Chem. 92, 29 (1980)

List of symbols

T_c:	critical temperature
T_m:	melting point
U:	internal energy
H:	enthalpy
ΔU_s:	sublimation energy
ΔH_H:	H-bond energy per H-bond
W:	dispersive interaction energy
W_d:	dispersion energy between hydrophobic moieties of alcohols
U_σ:	surface energy
U_V:	internal energy of saturated vapor
U_L:	internal energy of liquid
H_V:	enthalpy of saturated vapor
H_L:	enthalpy of liquid

[*] I am indebted to Dr. *Stillinger* for clarifying discussions and conformation of this conclusion.

L_V:	heat of evaporation at constant volume
L_V^*:	heat of evaporation into the ideal gas state
C_σ:	molar heat (molar heat capacity) on the liquid/vapor saturation line
C_V^0:	molar heat of ideal gas at V = const.
C_P^0:	molar heat of ideal gas at P = const.
C_W:	molar heat attributable to intermolecular degrees of freedom
σ_M:	surface tension per mole
σ:	surface tension per cm^2
R:	molar gas constant
P:	pressure
V:	molar volume
K_c:	equilibrium constant of H-bond formation
c:	molar concentration
c_F:	concentration of OH groups not participating in H-bonds ("free OH groups")
c_B:	concentration of H-bonds
O_F:	fraction of "free" OH groups
θ:	lone pairs of electrons
θ_F:	lone pairs not participating in H-bonds
N:	number of molecules linked by H-bonds
N_A:	Avogadro's number
Z:	coordination number of nearest neighbors
Z_e:	number of electrons
x_F:	fraction of hole defects
β:	H-bond angle ($\beta = 0$ for linear H-bonds)
ε:	molar extinction coefficient
ε_{max}:	extinction coefficient for band maximum
$\varepsilon_{max,0}$:	extinction coefficient for band maximum extrapolated to $c = 0$
ν:	frequency, wave number
$\Delta\nu_{1/2}$:	half-width

[1] *W. A. P. Luck*, Angew. Chem. *91*, 408 (1979); Angew. Chem. Int. Ed. Engl. *18*, 350 (1979).—The following correction should be made in the article: the term "distance-dependent" ("abstandsabhängig" in German version) in Section 9, line 4, on p. 359 (p. 416 of German version) should read "distance-*in*dependent" ("abstands*un*abhängig").

[2] *G. Briegleb:* Zwischenmolekulare Kräfte und Molekülstruktur. Enke-Verlag, Stuttgart 1937, p. 46.

[3] *W. A. P. Luck:* Structure of Water and Aqueous Solutions. Verlag Chemie, Weinheim 1974, Chapter III.2,3.

[4] *D. Schiöberg, C. Buanam-Om, W. A. P. Luck*, Spectrosc. Lett. *12*, 83 (1979).

[5] *E. Clementi:* Lecture Notes in Chemistry, Vol. 2. Springer-Verlag, Berlin 1976.

[6] *P. Schuster* in [3], p. 115.

[7] *W. Thiel*, Theor. Chim. Acta *48*, 357 (1978).

[8] *W. A. P. Luck*, Z. Elektrochem. *61*, 1057 (1957).

[9] *W. A. P. Luck*, Hochschulskripten No. 715/715a, Bibliographisches Institut AG, Mannheim 1970, p. 101.

[10] *W. A. P. Luck*, Prog. Colloid Polym. Sci. *65*, 6 (1978).

[11] *W. A. P. Luck*, Phys. Bl. *22*, 347 (1966).

[12] *G. Kortüm:* Lehrbuch der Elektrochemie. Dieterichsche Verlagsbuchhandling, Wiesbaden 1948.

[13] *G. Kortüm* in *R. Pummerer:* Sammlung chem. und chem.-techn. Vorträge, No. 26. Enke-Verlag, Stuttgart 1936.

[14] *W. A. P. Luck*, Naturwissenschaften *52*, 25, 49 (1965); *54*, 601 (1967).

[15] *W. A. P. Luck* in *Schuster, Zundel, Sandorfy:* The Hydrogen Bond. North-Holland, Amsterdam 1976, Vol. II, p. 527.

[16] *W. A. P. Luck*, Naturwiss. Rundsch. *21*, 236 (1968).

[17] *R. Mecke*, Wiss. Veroeff. 1937—1960, Festschrift zum 65. Geburtstag, Freiburg 1960; *H. Kempter, R. Mecke*, Z. Phys. Chem. *B46*, 229 (1940).

[18] *W. A. P. Luck* in *F. Franks:* Water, A Comprehensive Treatise, Vol. 2. Plenum, New York 1973, p. 225.

[19] *W. A. P. Luck*, Habilitationsschrift, Universität Heidelberg 1968; *W. A. P. Luck, W. Ditter*, J. Mol. Struct. *1*, 261 (1967/68).

[20] *W. A. P. Luck, W. Ditter*, Ber. Bunsenges. Phys. Chem. *72*, 365 (1968).

[21] *M. Born:* Optik, 2nd Edit. Springer-Verlag, Berlin 1965.

[22] *W. A. P. Luck*, Z. Naturforsch. *A 6*, 191 (1951).

[23] *W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *69*, 626 (1965).

[24] *W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *67*, 186 (1963); *W. A. P. Luck, W. Ditter, ibid. 70*, 1113 (1966).

[25] *W. A. P. Luck, W. Ditter*, Z. Naturforsch. *B 24*, 482 (1969).

[26] *J. R. Scherer* in *R. S. M. Clark, R. E. Hester:* Advances in IR- and Raman-Spectroscopy, Vol. V. Heyden, London 1978.

[27] *W. A. P. Luck, G. Böttger, H. Harders*, J. Phys. Chem. *71*, 459 (1967).

[28] *A. H. Narten*, J. Chem. Phys. *56*, 1185, 5681 (1972); *A. H. Narten, H. A. Levy, ibid. 55*, 2263 (1971); *A. H. Narten* in [3], p. 345.

[29] *M. Thiel, E. D. Becker, G. C. Pimentel*, J. Chem. Phys. *27*, 95, 486 (1957).

[30] *B. Mann, T. Neikes, E. Schmidt, W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *78*, 1236 (1974).

[31] *A. Behrens, W. A. P. Luck, B. Mann*, Ber. Bunsenges. Phys. Chem. *82*, 47 (1978).

[32] *H. Hallam* in *Schuster, Zundel, Sandorfy:* The Hydrogen Bond. North-Holland, Amsterdam 1976, Vol. III, p. 1065.

[33] *J. B. Hasted:* Aqueous Dielectrics. Chapman and Hall, London 1973, p. 74.

[34] VDI-Wasserdampftafeln bis 800 °C und 1000 at, 7th Edit. Springer-Verlag, Berlin 1968.

[35] Gmelins Handbuch der anorganischen Chemie, 8th Edit. Verlag Chemie, Weinheim 1963, System-No. 3. Issue 5.

[36] *A. Eucken*, Nachr. Akad. Wiss. Goettingen Math. Phys. Kl. *1946*, 38; Z. Elektrochem. Angew. Phys. Chem. *52*, 255 (1948).

[37] *G. Némethy, H. A. Scheraga*, J. Chem. Phys. *36*, 3382 (1962).

[38] *W. A. P. Luck*, Fortschr. Chem. Forsch. *4*, 653 (1964).

[39] *W. A. P. Luck*, Discuss. Faraday Soc. *43*, 115 (1967).

[40] *W. A. P. Luck*, Top. Curr. Chem. *64*, 113 (1976).

[41] See [15], Vol. III, p. 1369.

[42] *O. Y. Samoilov:* Struktur wässriger Elektrolytlösungen und die Hydratation von Ionen. Teubner-Verlag, Leipzig 1961.

[43] *W. Ditter, W. A. P. Luck*, Tetrahedron *27*, 201 (1971).

[44] *W. A. P. Luck* in *F. Franks:* Physico-Chemical Processes in Mixed Aqueous Solvents. Heinemann Educ. Books, London 1967.

[45] *W. A. P. Luck* in: Chemie, Physikalische Chemie und Anwendungstechnik der grenzflächenaktiven Stoffe. Ber. VI. Int. Kongr. grenzflächenaktive Stoffe, Zürich 1972. Hanser-Verlag, München 1973, p. 83.

[46] *K. L. Wolf:* Physik und Chemie der Grenzflächen, Vol. 1. Springer-Verlag, Berlin 1957.

[47] *K. Schäfer:* Physikalische Chemie, 2nd Edit. Springer-Verlag, Berlin 1964.

[48] *N. Ramsay, J. Shields*, Z. Phys. Chem. *12*, 433 (1893).

[49] *J. H. Simons, J. W. Bouknight*, J. Am. Chem. Soc. *54*, 129 (1932).

[50] *G. H. Haggis, J. B. Hasted, J. Buchanan*, J. Chem. Phys. *20*, 1452 (1950).

[51] *A. S. Quist, W. L. Marshall*, J. Phys. Chem. *69*, 3165 (1965).

[52] *P. Newton, C. Copeland, S. W. Benson*, J. Chem. Phys. *37*, 339 (1962).

[53] *R. Cini, M. Torrini*, J. Chem. Phys. *49*, 2826 (1968).

[54] *J. A. Glasel* in [3], p. 425.

[55] *W. Schröder*, Z. Naturforsch. *B 24*, 500 (1969).

[56] *W. A. P. Luck*, J. Phys. Chem. *74*, 3687 (1970); Phys. Bl. *26*, 133 (1970); Naturwissenschaften *63*, 39 (1976).

[57] *J. H. Wang*, J. Am. Chem. Soc. *73*, 510, 4181 (1951); *J. H. Wang, C. V. Robinson, I. S. Edelman, ibid. 75*, 466 (1953).

[58] *R. Kosfeld, J. Schlegel*, Adv. Mol. Relaxation Processes *3*, 169 (1972).

[59] *J. Morgan, B. E. Warren*, J. Chem. Phys. *6*, 666 (1938).

[60] *P. Scherrer*, Nachr. Ges. Wiss. Goettingen Math. Phys. Kl. *1928*, 98.

[61] *A. Prietzschk*, Z. Phys. *117*, 482 (1941).

[62] *H. Kleeberg, W. A. P. Luck*, Naturwissenschaften *64*, 223 (1977); *W. A. P. Luck, H. Kleeberg* in *H. Metzner:* Photosynthetic Oxygen Evolution. Academic Press, London 1978, p. 1.

[63] *W. A. P. Luck, D. Schiöberg, U. Siemann*, J. Chem. Soc. Faraday Trans., in press (1979); Ber. Bunsenges. Phys. Chem. *83*, 1085 (1979).

[64] *W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *69*, 69 (1965).

[65] *H. G. Hertz* in [3], p. 439.

[66] *P. Debye:* Polare Molekeln. Hirzel-Verlag, Leipzig 1929.

[67] *C. Buanam-Om, W. A. P. Luck, D. Schiöberg*, Z. Phys. Chem. (Frankfurt am Main), in press.

[68] *M. Falk, O. Knop* in *F. Franks:* Water, A Comprehensive Treatise, Vol. 2. Plenum, New York 1973, p. 55.

[69] *I. M. Straus, M. C. R. Symons*, J. Chem. Soc. Faraday Trans. I *74*, 2581 (1978).

[70] *V. C. Farmer* in *D. J. Greenland, M. H. B. Hayes:* The Chemistry of Soil Constituents. Wiley, New York 1978.

[71] *R. Mecke*, Z. Elektrochem. Angew. Phys. Chem. *52*, 269 (1948); *R. Mecke, A. Reuter*, Z. Naturforsch. *A 4*, 182 (1949).

[72] *R. L. Schupp*, Z. Elektrochem. Angew. Phys. Chem. *53*, 12 (1949).

[73] *D. A. Ibbitson, L. F. Moore*, J. Chem. Soc. *B 1967*, 76, 80.

[74] *R. Van Loon, J. P. Dauchot, A. Bellemans*, Bull. Soc. Chim. Belg. *77*, 397 (1968).

[75] *P. Huyskens, G. Gillerot, Th. Zeegers-Huyskens*, Bull. Soc. Chim. Belg. *72*, 666 (1963); *Th. Clerbaux, Th. Zeegers-Huyskens, ibid. 75*, 366 (1966).

[76] *T. T. Wall, D. F. Hornig*, J. Chem. Phys. *43*, 2079 (1965).

[77] *I. D. Brown*, Chem. Soc. Rev. *7*, 359 (1978).

[78] *R. Allmann*, Monatsh. Chem. *106*, 779 (1975).

[79] *E. R. Lippincott, J. N. Finch, R. Schroeder* in *D. Hadži, H. W. Thompson:* Hydrogen Bonding. Pergamon, Oxford 1959, p. 362.

[80] *S. Bratos*, J. Chem. Phys. *52*, 439 (1970); *63*, 3499 (1975).

[81] *R. G. Gordon*, J. Chem. Phys. *43*, 1307 (1965).

[82] *F. Vesely:* Computerexperimente an Flüssigkeitsmodellen. Physik Verlag, Weinheim 1978.

[83] *A. Rahman, F. H. Stillinger*, J. Chem. Phys. *55*, 3336 (1971).

[84] *F. H. Stillinger, A. Rahman*, J. Chem. Phys. *57*, 1281 (1972).

[85] *F. H. Stillinger, A. Rahman*, J. Chem. Phys. *60*, 1545 (1974).

[86] *F. H. Stillinger, A. Rahman*, J. Chem. Phys. *61*, 4973 (1974).

[87] *A. Geiger, A. Rahman, F. H. Stillinger*, J. Chem. Phys. *70*, 263 (1979).

[88] *K. Heinzinger, W. O. Rieder, L. Schäfer, G. I. Szasz*, Am. Chem. Soc. Symp. Ser. *86*, 1 (1978); *G. Palinkas, W. O. Riede, K. Heinzinger*, Z. Naturforsch. *A 32*, 1137 (1977).

[89] *A. Geiger*, private communication.
[90] *A. Geiger*, Karlsruhe 1979, Institut für Physikalische Chemie.
[91] *D. Schiöberg, W. A. P. Luck*, Spectrosc. Lett. *10*, 613 (1977).
[92] *D. Schiöberg, W. A. P. Luck*, J. Chem. Soc. Faraday Trans. I *75*, 762 (1979).
[93] *J. D. Worley, I. M. Klotz*, J. Chem. Phys. *45*, 2868 (1966).
[94] *J. Paquette, C. Joliceur*, J. Solution Chem. *6*, 403 (1977).
[95] *G. E. Walrafen* in [3], p. 301; *F. Frank*: Water A Comprehensive Treatise, Vol. 1. Plenum, New York 1972, p. 151.
[96] *H. A. Lindner*, Dissertation, Universität Karlsruhe 1970.
[97] *W. A. P. Luck* in *E. G. Belfort*: Membrane Methods in Water and Waste Water Treatment. Academic Press, New York 1980.
[98] *W. A. P. Luck* in "Water in Polymers", Am. Chem. Soc. Symp. Ser., in press.

COMMUNICATIONS

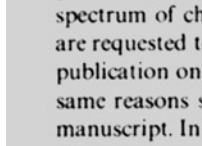
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Synthesis of CH_2-Bridged [4*n*+2]Annulenes by a Building-Block Approach

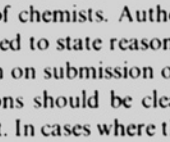
By *Emanuel Vogel, Hans M. Deger, Johannes Sombroek, Jürgen Palm, Arwed Wagner*, and *Johann Lex*[*]

Dedicated to Professor Wolfgang Lüttke on the occasion of his 60th birthday

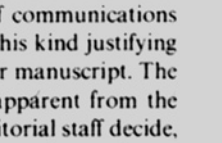
Since the synthesis of the 10π Hückel aromatic compounds 1,6-methano-, 1,6-oxido-, and 1,6-imino[10]annulene[1], we have been concerned with preparative entries to homologous series of bridged [4*n*+2]annulenes with an acene perimeter. With a view to gaining a deeper insight into the Hückel rule, our interest was focused on series in which the members with two and more bridges possess the *syn*- or *all-syn* configuration[2] geometrically favorable for the occurrence of aromatic character. The development of such [4*n*+2]annulene series requires new strategies, for conventional procedures hardly provide a chance of going beyond bridged [14]annulenes[2]. In our current synthetic considerations cycloheptatriene-1,6-dicarbaldehyde *(1)*[3] and the homologous α,ω-dialdehydes *(2)*, *(3)*, and *(4)* constitute the key intermediates.



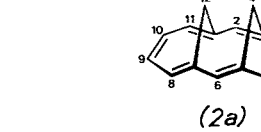
(1)



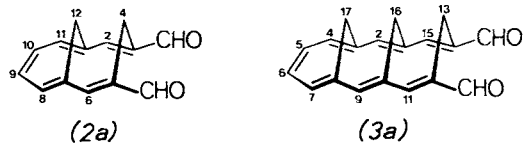
(2)



syn-Isomer
(3)

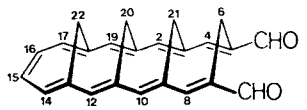


syn,syn-Isomer
(4)



(2a)

(3a)



(4a)

After the dialdehyde *(2)*[4] obtained from 1*H*-3,8-methanocyclopropa[10]annulene had proved to be the *syn* conformer *(2a)*, there was good reason to assume that *(3)* and *(4)* also exist in the *syn* conformation [*(3a)* and *(4a)* respectively]. Arguing from this premise, synthesis of the potentially aromatic 1,6-methano[10]annulene homologues with 14, 18, and 22π electrons and the construction of series of [4*n*+3]annulenylium ions, [4*n*+3]annulenones, [4*n*+1]annulenyl anions and other annulene compounds corresponding to the hydrocarbon series is essentially a question of experimental effort and the ability of the pertinent molecules to exist.

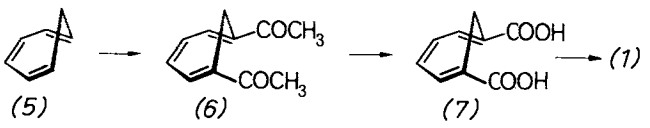
We have now found that the homologous α,ω-dialdehydes *(2)*, *(3)*, and *(4)* having the desired *syn* conformation—and thus most likely many of the [4*n*+2]annulenes and their derivatives listed above—can be obtained by a building-block approach starting from *(1)*.

1) Cycloheptatriene-1,6-dicarbaldehyde (1): The need for a rational synthesis of the previously somewhat inaccessible dialdehyde *(1)*[3] suggested attempts to transform the industrially available compound cycloheptatriene *(5)* by acylation[5] into *(1)* or suitable precursors. A productive entry to *(1)* has now been opened by acetylation of *(5)*.

On treatment with acetyl chloride/zinc chloride in glacial acetic acid/dichloromethane (−30 °C; 4 h), cycloheptatriene *(5)* afforded 1-acetylcycloheptatriene as major product (b.p.

[*] Prof. Dr. E. Vogel, Dr. H. M. Deger, Dr. J. Sombroek, Dipl.-Chem. J. Palm, Dipl.-Chem. A. Wagner, Dr. J. Lex
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

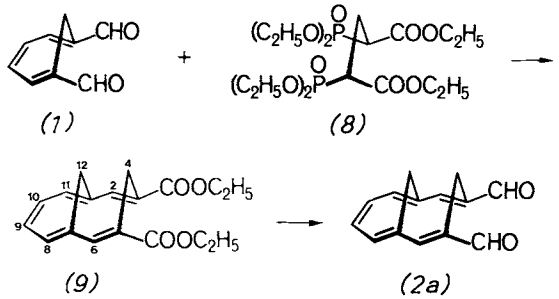
[**] We are grateful to Deutsche Shell Chemie GmbH for inexpensively supplying cycloheptatriene.



(5) (6) (7) (1)

42 44 °C/0.1 torr; yield 45—50%). Introduction of the second acetyl group required isolation of the monoacetyl compound and its treatment with the more aggressive acetylation system acetyl chloride/aluminum chloride in boiling dichloromethane (2 h). There was formed the expected 1,6-diacetylcycloheptatriene *(6)* [b.p. 123—125 °C/0.5 torr, light yellow crystals of m.p. 44—45 °C (pentane), yield 50%; ^{1}H-NMR ($CDCl_3$): $\delta = 2.4$ (s, 6H, $2CH_3$), 3.0 (s, 2H, H-7), 7.0 (AA'BB' system, 4H, H-2, 3, 4, 5); UV (cyclohexane): $\lambda_{max} = 232$ nm ($\varepsilon = 22000$), 309 (5500)]. Haloform reaction (sodium hydroxide/bromine in water/dioxane) degrades *(6)* to the cycloheptatriene-1,6-dicarboxylic acid *(7)*[6] (yield 66%). The dicarboxylic acid→dialdehyde conversion can be accomplished *via* diester and diol, but it was found preferable to prepare the diacyl dichloride from the acid by reaction with thionyl chloride (pyridine catalyzed; 55 °C) and to reduce it with lithium tri-*tert*-butoxyhydridoaluminate in tetrahydrofuran (−70 °C, yield 61%). Compound *(1)* can be prepared in 100g-quantities with comparative ease by this "cycloheptatriene route".

2) Homologization sequence: Carbonyl olefination with the bifunctional Wittig-Horner reagent *(8)* appeared to have potential as the crucial first step in the homologization of *(1)* to *(2a)*. We obtained the heretofore unknown compound *(8)* alongside other products by Michaelis-Arbuzov reaction of diethyl α,α'-dibromoglutarate (*meso* and *rac* form) with triethyl phosphite (8 h; 60 °C). Compound *(8)* can be isolated in sufficient purity for synthetic purposes (*ca.* 95%[7]) by distillation (2×) over a 30-cm Vigreux column [b.p. 185—195 °C/10^{-5} torr; yield 31%; GC/MS: $m/e = 460$ (M^+, < 1%)]. Since the ^{31}P-NMR spectrum of *(8)* exhibits two close peaks, it would appear that *(8)* is likewise a mixture of stereoisomers. On reaction with sodium hydride compound *(8)* affords the bisphosphonate dicarbanion which, on dissolution in benzene, is ready for use in olefination reactions.

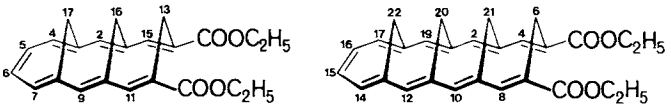


(1) (8) (9) (2a)

The utility of *(8)* was demonstrated by reaction with *(1)* in the molar ratio of 1.1:1 in dichloromethane/benzene (reflux, 3 h). Although ring closures with bifunctional olefination reagents are frequently unsatisfactory[8], the present reaction furnished *(9)* in yields of 48—54% after chromatography of the reaction product on silica gel (ether/pentane, 1:1)[9]. In order to transform *(9)* into *(2a)*, the diester first had to be reduced to the diol (diisobutylaluminum hydride in benzene; room temperature; m.p. 130—131 °C; yield 74%) and the diol oxidized (2,3-dichloro-5,6-dicyanobenzoquinone in dioxane; room temperature; yield 85%).

The three-step sequence considered is just as suitable for converting *(2)* into the next-higher homolog *(3)*; no significant modifications of the reaction conditions are necessary [yields of the various steps are 58%, 71%, and 75%, respectively; see Table 1 concerning the properties of *(3)*]. X-Ray structure analysis[10] and chemical transformations confirm the presence of the expected *syn* conformer *(3a)* in the crystal and in solution.

Table 1. Physical data of the α,ω-polyenedialdehydes *(2a)*, *(3a)*, and *(4a)* and the corresponding diethyl esters *(9)*, *(10)*, and *(11)*.



(10) (11)

(2a), m.p. = 215—216 °C (dec.) (chloroform/ether); yellow crystals; UV (dioxane): $\lambda_{max} = 288$ nm ($\varepsilon = 59300$), 369 (4550); IR (KBr): 1662 cm^{-1} (C=O); ^{1}H-NMR (CD_2Cl_2): $\delta = 0.64$ and 4.18 (AX system, $J = 12.5$ Hz, 2H, H-12), 3.33 and 4.92 (AX system, $J = 16.5$ Hz, 2H, H-4), 7.17 (s, 2H, H-2, 6), 6.78—7.30 (AA'XX' system, 4H, H-8, 9, 10, 11), 9.37 (s, 2H, 2CHO)

(3a), m.p. = 264—267 °C (dec.) (dichloromethane); carmine red needles: UV (dioxane): $\lambda_{max} = 326$ nm ($\varepsilon = 80900$), 334 (81600), 409 (5300); IR (CsI): 1668 cm^{-1} (C=O); ^{1}H-NMR ($C_2D_2Cl_4$): $\delta = -0.22$ and 3.27 (AX system, $J = 13.2$ Hz, 2H, H-17), 3.43 and 4.37 (AX system, $J = 15.3$ Hz, 2H, H-16), 3.53 and 4.85 (AX system, $J = 16.2$ Hz, 2H, H-13), 6.75—7.22 (AA'XX' system with 2 s, 8H, H-2, 4, 5, 6, 7, 9, 11, 15), 9.22 (s, 2H, 2 CHO)

(4a), dec. > 300 °C (dichloromethane); red-violet needles; UV (dioxane): $\lambda_{max} = 251$ nm ($\varepsilon = 28100$), 363 (119000), 463 (sh, 8800); IR (CsI): 1680 cm^{-1} (C=O); ^{1}H-NMR ($C_2D_2Cl_4$): $\delta = -0.64$ and 2.59 (AX system, $J = 13.5$ Hz, 2H, H-22), 2.78 and 3.50 (AX system, $J = 16.4$ Hz, 2H, H-20), 3.43 and 4.88 (AX system, $J = 16.8$ Hz, 2H, H-6), 3.93 and 4.60 (AX system, $J = 15.2$ Hz, 2H, H-21), 6.74 (s, 2H, H-2, 10), 6.83 (s, 2H, H-12, 19), 7.18 (s, 2H, H-4, 8), 7.27 (deg. AA'XX' system, 4H, H-14, 15, 16, 17), 9.27 (s, 2H, 2 CHO)

(9), m.p. = 75—76 °C (hexane); light yellow needles; UV (dioxane): $\lambda_{max} = 278$ nm ($\varepsilon = 42100$), 358 (5000); IR (KBr): 1696 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): $\delta = 0.30$ and 4.00 (AX system, $J = 12.1$ Hz, 2H, H-12), 3.75 and 4.93 (AX system, $J = 16.3$ Hz, 2H, H-4), 6.70—7.12 (AA'XX' system, 4H, H-8, 9, 10, 11), 7.63 (s, 2H, H-2, 6), 1.32 and 4.25 (t and q, 10H, $2\ C_2H_5$)

(10), m.p. = 162—163 °C (methanol); orange-red needles; UV (dioxane): $\lambda_{max} = 317$ nm ($\varepsilon = 81200$), 339 (sh, 68900), 397 (5650); IR (CsI): 1695 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): $\delta = -0.36$ and 3.17 (AX system, $J = 12.9$ Hz, 2H, H-17), 3.35 and 4.22 (AX system, $J = 15.9$ Hz, 2H, H-16), 3.94 and 4.97 (AX system, $J = 16.5$ Hz, 2H, H-13), 6.92 (s, 2H, H-2, 9), 7.20—6.78 (AA'XX' system, 4H, H-4, 5, 6, 7), 7.45 (s, 2H, H-11, 15), 1.29 and 4.22 (t and q, 10H, $2\ C_2H_5$)

(11), m.p. = 168—169 °C (methanol); red needles; UV (dioxane): $\lambda_{max} = 247$ ($\varepsilon = 27000$), 356 (116000), 424 (8400); IR (CsI): 1710 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): $\delta = -0.80$ and 2.50 (AX system, $J = 13.2$ Hz, 2H, H-22), 2.71 and 3.43 (AX system, $J = 16.2$ Hz, 2H, H-20), 3.77 and 4.49 (AX system, $J = 15.4$ Hz, 2H, H-21), 3.99 and 5.00 (AX system, $J = 16.9$ Hz, 2H, H-6), 6.63 (s, 2H, H-2, 10), 7.11 (s, 2H, H-12, 19), 7.20 (deg. AA'XX' system, 4H, H-14, 15, 16, 17), 7.37 (s, 2H, H-4, 8), 1.28 and 4.21 (t and q, 10H, $2\ C_2H_5$)

A second repetition of the homologization process leads from *(3)* to *(4)*. However, the yield of ring closure fell to 22—24%, probably as a result of (i) poorer steric fit between the aldehyde functions of *(3)* and the Wittig-Horner reagent *(8)* as compared with *(1)* and *(2)* and (ii) the need to work at relatively high dilution owing to the lower solubility of *(3)*. The reduction and oxidation steps are again straightforward.

According to the X-ray structure analysis[11] performed by *J. Lex*, compound *(4)* likewise adopts the *syn* conformation *(4a)*. As can be deduced from spectroscopic comparisons, this conformation most likely also applies to the compound in solution. The edge profile of the molecule (Fig. 1) provides more detailed information about the three-dimensional structure of *(4a)* and especially about the significant curva-

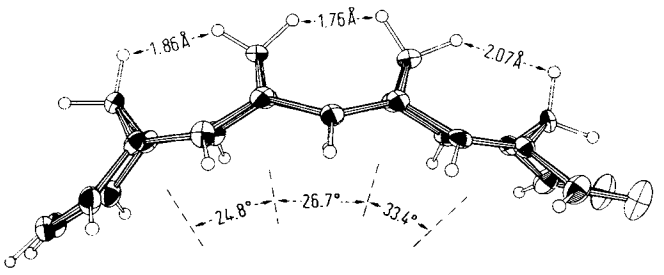


Fig. 1. Edge profile of *(4a)*.

ture of the polyene system which does not appear to greatly affect conjugation.

3) Annulene formation: The general reaction scheme envisaged for transformation of α,ω-polyenedialdehydes *(1)* and *(2a)—(4a)* into the corresponding bridged [4*n*+2]annulenes —and into numerous substitution products not obtainable from the annulenes themselves—is illustrated in the case of the syntheses of *syn*-1,6:8,13-bismethano[14]annulene[4] and *syn,syn*-1,6:8,17:10,15-trismethano[18]annulene[12]. It comprises the following steps (which can be carried out as a one-pot process in specific cases): 1) introduction of the two missing C atoms as C_1 units (these may be linked together by an S atom[4]) by carbonyl olefination with formation of a polyene having (4*n*+2)π electrons; 2) ring closure of the polyene by a thermally allowed disrotatory (4*n*+2)π electrocyclic process, favored by the molecular geometry, which gives a dihydroannulene; and 3) generation of the annulene by β-elimination of an auxiliary substituent introduced on olefination or by (*in situ*) dehydrogenation. The attractiveness of this scheme lies in the range of variation of the initial olefination step, and, methodologically, in the synthetic utilization of hitherto poorly known electrocyclic processes with (4*n*+2) π electrons (*n*>1)[13]. Regarding the synthesis of bridged [4*n*+3]annulenylium ions, [4*n*+3]annulenones, aza[4*n*+2]annulenes, *etc.*, it appears reasonable to look to the chemistry of the synthon phthaldialdehyde.

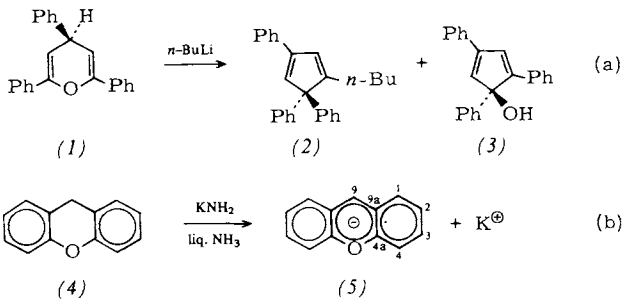
Received: September 11, 1978 [Z 355 IE]
German version: Angew. Chem. *92*, 43 (1980)
Publication delayed at authors' request

[1] *E. Vogel* in: Aromaticity. Chem. Soc. Spec. Publ. No. 21, p. 113 (1967).
[2] *E. Vogel*, Pure Appl. Chem. *28*, 355 (1971).
[3] *E. Vogel, R. Feldmann, H. Düwel*, Tetrahedron Lett. *1970*, 1941.
[4] *E. Vogel, J. Sombroek, W. Wagemann*, Angew. Chem. *87*, 591 (1975); Angew. Chem. Int. Ed. Engl. *14*, 564 (1975).
[5] Acylations of cycloheptatriene to 1-acylcycloheptatrienes are described by *J. A. Blair* and *C. J. Tate*, J. Chem. Soc. *C 1971*, 1592; see also *T. Asao, S. Kuroda, K. Kato*, Chem. Lett. *1978*, 41.
[6] *R. Darms, T. Threlfall, M. Pesaro, A. Eschenmoser*, Helv. Chim. Acta *46*, 2893 (1963). The yield of *(7)* can be raised to 47% (based on 1-acetylcycloheptatriene) if *(6)* is not isolated.
[7] Analysis by gas chromatography on a silicone column (OV 17; 1.5 m; 200—270 °C).
[8] *K. P. C. Vollhardt*, Synthesis *1975*, 765.
[9] Chromatography serves for separation of the olefination product (*ca.* 10%) from *(1)* and the phosphonate-carbanion $[(C_2H_5O)_2PO\ \overset{\ominus}{C}H\ COOC_2H_5]^{\ominus}$ arising from a retro-Michael addition of the monocarbanion of *(8)* which competes with bisphosphonate-dicarbanion formation on reaction of *(8)* with sodium hydride.
[10] *T. Pilati, M. Simonetta*, Acta Crystallogr. *B 33*, 851 (1977).
[11] *(4a)* forms orthorhombic crystals of space group Pnma, with $a = 9.470(2)$, $b = 13.474(2)$, $c = 13.402(3)$ Å; $\rho_{calc} = 1.322$ g/cm³ for $Z = 4$, $\rho_{exp} = 1.326$ g/cm³. Intensities measured with an Enraf-Nonius CAD-4 automatic single crystal diffractometer ($Mo_{K\alpha}$ radiation, $3° \leq \theta \leq 30°$). After refinement (including all H atoms) the conventional *R* value was 0.043 for 1027 independent reflections with $I \geq 2\sigma(I)$.
[12] *W. Wagemann, M. Iyoda, H. M. Deger, J. Sombroek, E. Vogel*, Angew. Chem. *90*, 988 (1978); Angew. Chem. Int. Ed. Engl. *17*, 956 (1978).
[13] Evidence for the occurrence of disrotatory 18π electrocyclic processes in the porphyrin series is reported by *A. W. Johnson*, Pure Appl. Chem. *28*, 195 (1971).

Generation and Direct Observation of the Xanthenide Anion; a Stable 4*n* π-System[**]

By *A. G. Anastassiou* and *H. S. Kasmai*[*]

A major, yet largely unrealized, goal in the area of nonbenzenoid aromatics is the direct observation and possible classification of potentially delocalizable π-systems incorporating a carbanionic center as well as one or more π-excessive heteroatomic units. Particularly challenging of course in this connection is the case of medium-sized, *i. e.* 6-membered, systems associated with a formal count of 4*n* π-electrons, insofar as a number of serious attempts at generating them have led, thus far, to rapid ring-contractive reorganization[1] [for typical example see reaction (a)] believed to be indicative of intrinsic *antiaromatic* instability resulting from the active participation of *all* properly directed lone pairs (homo- as well as heteroatomic) into delocalization[1].



$Ph-\overset{\ominus}{C}H-Ph$ *(6)*

Bearing in mind that the most reliable spectroscopic manifestation of antiaromaticity consistently has been the development of paratropic character, we decided to undertake the generation and direct examination, by NMR, of the carbanion of xanthene *(4)*[2], a molecule which is structurally incapable of undergoing skeletal reorganization without undue expenditure of energy resulting primarily from disruption of benzenoid resonance.

The oxygen-containing carbanion *(5)* was generated upon exposure of xanthene, *(4)*, to potassium amide in liquid ammonia at −30 °C. The NMR data [*(5)*: 60-MHz ^{1}H-NMR (NH_3, *ca.* 34 °C): δ = 3.08 (1H, s, H-9), 4.9—5.4 (6H, m, H-1, 2, 4), 5.78 (2H, dt, H-3, J = 7.0, 6.0, 2.0 Hz); 20-MHz ^{13}C-NMR (NH_3, *ca.* 30 °C, TMS), δ = 68.92 (d, C-9, J_{CH} = 156 Hz), 109.40 (d, J_{CH} = 161 Hz), 118.84 (d, J_{CH} = 153 Hz), 112.32 (d, J_{CH} = 154 Hz), 126.44 (d, J_{CH} = 153 Hz), 143.04 (s, C-9a), 152.37 (s, C-4a)] reveal some interesting features among which the most informative about the nature of the molecule's π system is, no doubt, the dramatic upfield shifts one observes in the ^{1}H-NMR spectrum on passing from *(4)* to *(5)* (Fig. 1). The signals of the "benzenoid" protons of the anion no longer appear in the "aromatic" region of the spectrum but rather in a portion (δ = 5—6) normally reserved for the protons of conventional olefins. Useful insight into the possible cause of this shift may readily be gained upon comparison of the NMR spectra (in NH_3, at *ca.* 34 °C) of *(5)* and *(6)* (diphenylmethanide ion as model compound): the carbanionic center in *(5)* absorbs at substantially higher field (δ = 68.92) than it does in *(6)* (δ = 81.33), and also the major

[*] Prof. Dr. A. G. Anastassiou
Department of Chemistry, Syracuse University
Syracuse, New York 13210 (USA)
Prof. Dr. H. S. Kasmai
Department of Chemistry, Shiraz University, Shiraz (Iran)

[**] The work at Syracuse was supported by the National Science Foundation, the work at Shiraz was supported by the Iranian Ministry of Higher Education.

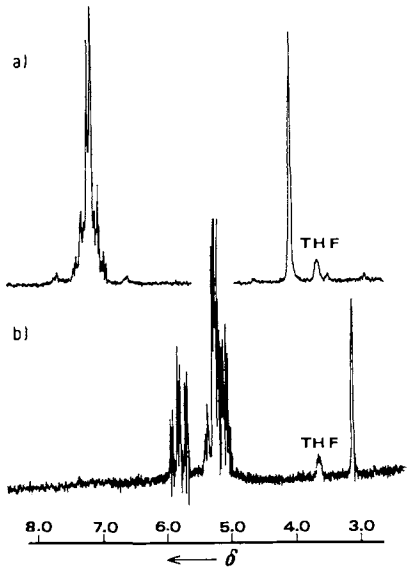


Fig. 1. 60-MHz ^{1}H-NMR spectrum of a) xanthene *(4)* and b) the xanthenide ion *(5)* at *ca.* 34 °C in liquid ammonia containing some THF (<1%; internal standard) as solvent.

group of "benzenoid" protons [6H in *(5)* and 8H in *(6)*] absorbs at a substantially higher field in *(5)* ($\delta = 5.1$) than it does in *(6)* ($\delta = 6.8$). Since the ^{13}C-NMR information convincingly establishes that the carbanionic center of *(5)* retains a significantly larger fraction of the negative charge than its counterpart in *(6)*, it follows that the upfield shift of the signals of the "benzenoid" protons observed on passing from *(6)* to *(5)* cannot be rationally dismissed as an "electron density" effect but may be logically attributed chiefly to the *presence of a paramagnetic ring current.*

The spectra described here would appear to indicate that anion *(5)* is a rather rare example of a remarkably stable[3] species with antiaromatically delocalized π-electrons, *i.e.* paratropic, $4n$-electron π-excessive.

Received: September 5, 1979 [Z 356 IE]
German version: Angew. Chem. 92, 53 (1980)

CAS Registry numbers:
(4), 92-83-1; *(5)*, 72301-71-41; *(6)*, 18802-87-4

[1] For an informative review on the subject see *R. R. Schmidt*, Angew. Chem. *87*, 603 (1975); Angew. Chem. Int. Ed. Engl. *14*, 581 (1975).

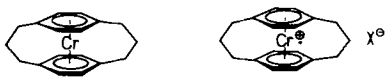
[2] For a discussion of *(4)* and *(5)* in terms of acidity measurements see *H. S. Kasmai, H. W. Whitlock, Jr.*, J. Org. Chem. *37*, 2161 (1972).

[3] The ^{1}H-NMR spectrum of *(5)* (Fig. 1b) shows no qualitative or quantitative deterioration upon prolonged (11 h) exposure to ambient temperature. Subsequent water quench of *(5)* produced *(4)* quantitatively.

Structural Investigations on (η^{12}-[3.3]Paracyclophane)chromium(0) and Its Cation in (η^{12}-[3.3]Paracyclophane)chromium(I) Triiodide[**]

By *Reinhard Benn, Norman E. Blank, Matthias W. Haenel, Jochen Klein, Ali R. Koray, Klaus Weidenhammer,* and *Manfred L. Ziegler*[*]

(η^{12}-[3.3]Paracyclophane)chromium(0) *(1)* was obtained by cocondensation of [3.3]paracyclophane and chromium in a metal evaporator[1]. We report here on the structural investigation of *(1)* by dynamic ^{1}H-NMR spectroscopy and on the X-ray structure analysis of (η^{12}-[3.3]paracyclophane) chromium(I) triiodide *(3)*.

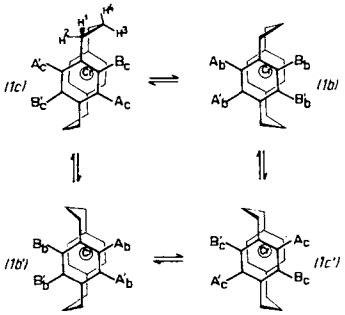


(1) *(2)*, X = PF_6 *(3)*, X = I_3

According to the ^{1}H-NMR spectrum (270 MHz, *ca.* 1% solution in [D_8]toluene) at −70 °C, *(1)* is present in the chair conformation *(1c)* and boat conformation *(1b)* in the ratio 1:1. Accordingly, two AA'BB' systems or, disregarding the long range couplings ($^4J_{HH}$ and $^5J_{HH} \leq 1.5$ Hz), two AB systems are observed between $\delta = 3.6$ and 4.0 for the upfield phenylene proton signals of the [3.3]paracyclophane ligand (cf. Table 1 and Fig. 1). The assignment of the signals to *(1c)* and *(1b)* follows from the coupling constants J_{AB}[2]. The chemical shifts of the methyl protons of the chair and boat form are apparently not resolved: we assign the absorption at $\delta = 2.63$ (8H) to the "equatorial" benzyl protons H^1 of the chair and boat forms[3]; for the "axial" benzyl protons H^2 and the non-benzylic methylene protons H^3/H^4, multiplets are observed in each case around $\delta \approx 1.2$ (8H) and $\delta \approx 2.0$ (16H) (Table 1, Scheme 1). At higher temperatures the two AB systems degenerate to a singlet at $\delta = 3.76$ (8H, 60 °C); between −90 °C and −30 °C the chemical shifts are linearly dependent upon the temperature (Fig. 1). Accordingly, the signals of the benzyl protons H^1 and H^2 coalesce and at 60 °C they coincide with the signal of H^3/H^4 at $\delta = 1.93$ (halfwidth = 5.4 Hz, 12H). A line shape analysis[4] based on the dynamic behavior of the phenylene protons with four exchanging AB systems neglecting direct chair-chair and boat-boat rearrangements (Scheme 1) gave for the flipflop process between chair *(1c)* and boat *(1b)* forms the activation parameters $E_a = 11.68 \pm 0.22$ (48.9 ± 0.9) kcal/mol (kJ/mol), $\Delta H^{\neq} = 11.20 \pm 0.22$ (46.9 ± 0.9) kcal/mol (kJ/mol) and

Table 1. Chemical shift (δ) and coupling constants of *(1b)* (boat) and *(1c)* (chair) [270 MHz, [D_8]toluene, −70 °C, standard solvent ($\delta = 2.03$)].

	(1b)	*(1c)*
H^A	3.79	3.92
H^B	3.77	3.66
$^3J_{AB}$	—	5.2
$^4J_{AB}$	≤1.5	—
H^1(e)	2.63 (dt, $^2J = 13$ Hz, $^3J \approx 3$ Hz)	
H^2(a)	≈1.2 (m)	
H^3, H^4	≈2.0 (m)	



Scheme 1

[*] Priv.-Doz. Dr. M. W. Haenel [+], Dr. R. Benn, J. Klein, Dipl.-Chem. N. E. Blank
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim/Ruhr (Germany)
Prof. Dr. M. L. Ziegler [+], Dipl.-Chem. A. R. Koray, Dr. K. Weidenhammer
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
[+] Authors to whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

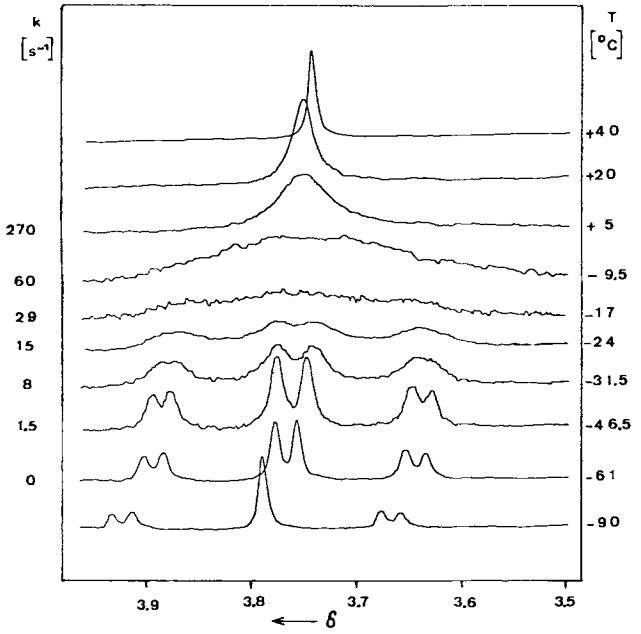


Fig. 1. ^{1}H-NMR spectra (270 MHz, [D$_8$]toluene) of the phenylene protons of *(1)* at various temperatures; values *k* are the calculated exchange rates (cf. Scheme 1).

$\Delta S^{\neq} = -7.7 \pm 0.9$ (-32.2 ± 3.8) cal K^{-1} mol^{-1} (J K^{-1} mol^{-1}).

For comparison the temperature-dependent ^{1}H-NMR spectra of [3.3]paracyclophane were re-examined. Contrary to *Anet* and *Brown*[5a,6], we found the ratio of conformers to be the same as in the case of *(1)*, *i.e. ca.* 1:1[6] [^{1}H-NMR (270 MHz, [D$_8$]toluene, -70 °C) boat: AB system with $\delta_A = 6.62$, $\delta_B = 6.48$, $^4J_{AB} = 1.5$ Hz; chair: AB system with $\delta_A = 6.59$, $\delta_B = 6.50$, $^3J_{AB} = 8.0$ Hz]. However, the line shape analysis[4] of the temperature-dependent ^{1}H-NMR spectra is impaired by the crystallizing out of the chair conformer below -50 °C[6]. Hence, only approximate values can be obtained for E_a and $\Delta H^{\neq}$ of the chair-boat rearrangement of [3.3]paracyclophane which are about 2 kcal/mol (8.4 kJ/mol) smaller than for the rearrangement in the case of *(1)*[7]. The structure of the cation in *(3)* was investigated X-ray crystallographically[1,8]. In the crystal, compound *(3)*, like [3.3]paracyclophane[5b], is present exclusively in the chair conformation. In the cation, the benzene rings, in contrast to the free ligands, are eclipsed. The transannular distances [C(1)···C(4′) = 307.1(17) pm, C(2)···C(5′) = C(3)···C(6′) = 322.2(17) pm], and thus also the boat-shaped deformation of the benzene rings, are somewhat smaller in the cation than in the ligand[8]. The average chromium-carbon distances are 210(1) and 213(1) pm [C(1), C(4) and C(2), C(3), C(5), C(6), respectively] and thus are comparable with those in dibenzenechromium(0) (214 pm)[9a] and dibenzenechromium(I) iodide (213 pm)[9b]. The shortest distance between the central iodine atom of the linear and symmetric triiodide ion [I···I = 291.3(1) pm] and the C(2), C(3), C(5), C(6) (Fig. 2) plane of the benzene ring is 373 pm[8].

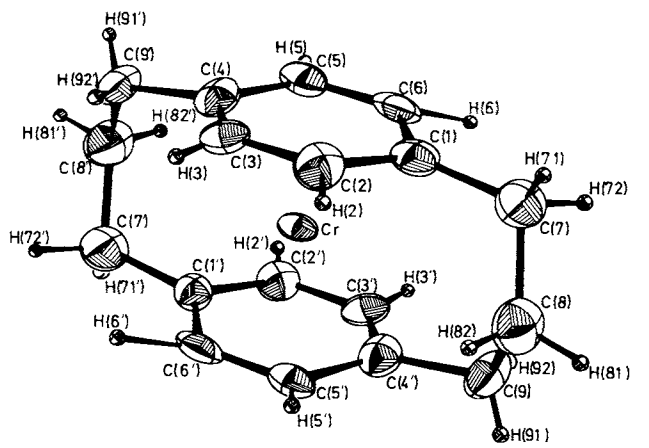


Fig. 2. ORTEP diagram of the cation in (η^{12}-[3.3]paracyclophane)chromium(I) triiodide *(3)* in the crystal.

Received: August 9, 1979 [Z 357 IE]
supplemented: August 20, 1979
German version: Angew. Chem. *92*, 45 (1980)

[1] *A. R. Koray, M. L. Ziegler, N. E. Blank, M. W. Haenel*, Tetrahedron Lett. *1979*, 2465.

[2] For substituted bis(benzene)chromium(0) derivatives, coupling constants $^3J_{HH} \approx 5$ Hz are observed: *V. Graves, J. J. Lagowski*, J. Organomet. Chem. *120*, 379 (1976).

[3] Dihedral angles of about 60° between H^1 H^3 and H^1 H^4 correspond to the triplet with the vicinal couplings $^3J \approx 3$ Hz.

[4] Modified version of the DNMR 2 program of *G. Binsch, D. A. Kleier*, Q. C. P. E. *11*, 140 (1969); *G. Binsch* in *L. M. Jackmann, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975, p. 45.

[5] a) *F. A. L. Anet, M. A. Brown*, J. Am. Chem. Soc. *91*, 2389 (1969); b) *P. K. Gantzel, K. N. Trueblood*, Acta Crystallogr. *18*, 958 (1965).

[6] Concentration-dependent ^{1}H-NMR spectra of [3.3]paracyclophane in [D$_8$]toluene show that the boat/chair ratio of 2:1 as determined by *Anet* and *Brown* [5a] is falsified by incipient crystallization of the chair conformer; according to X-ray structure analysis [5b] only the chair form is present in the crystal.

[7] The activation parameters $\Delta H^{\neq} \approx 9.2$ (38.5) kcal/mol (kJ/mol) and $\Delta S^{\neq} \approx -10$ (-42) cal K^{-1} mol^{-1} (JK^{-1} mol^{-1}) correspond to the value $\Delta G^{\neq} = 11.7 + 0.5$ (49.0 + 2.1) kcal/mol (kJ/mol) measured at the coalescence temperature -33 °C by *Anet* and *Brown* [5a].

[8] The intensely yellow triiodide *(3)* is obtained from *(1)* by atmospheric oxidation in toluene/water and precipitation of the radical cation with potassium iodide. *(1)* crystallizes monoclinically, space group $C_{2h}^5 - P2_1/c$, $a = 748.2(2)$ pm, $b = 764.2(2)$ pm, $c = 1670.1(3)$ pm, $\beta = 102.90(2)°$, 1511 independent reflections, $R = 0.057$, $Z = 2$. The hexafluorophosphate *(2)* [1] exhibits random distribution of both the methylene carbon atoms as well as of the anion; this leads to a factor R of only 0.083 and to rather inaccurate atomic parameters.

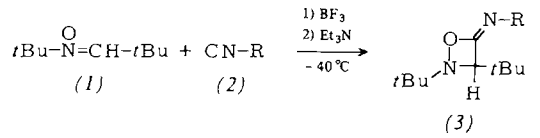
[9] a) *E. Keulen, F. Jellinek*, J. Organomet. Chem. *5*, 490 (1966); cf. *F. Jellinek, ibid. 1*, 43 (1963); *F. A. Cotton, W. A. Dollase, J. S. Wood*, J. Am. Chem. Soc. *85*, 1543 (1963); *J. A. Ibers*, J. Chem. Phys. *40*, 3129 (1964); b) *B. Morosin*, Acta Crystallogr. *B30*, 838 (1974); cf. *O. V. Starovskii, Y. T. Struchkov*, Zh. Strukt. Khim. *2*, 162 (1961); Dokl. Akad. Nauk SSSR *135*, 620 (1961).

Stable 4-Imino-1,2-oxazetidines from *N*-Neopentylidene-*tert*-butylamine *N*-Oxide and Isocyanides

By *Dietrich Moderhack* and *Michael Lorke*[*]

Syntheses of four-membered rings from isocyanides and 1,3-dipoles with internal octet stabilization after the manner of a [3 + 1]cycloaddition are still rare[1]. Although nitrones do react with isocyanides after prior activation with strong Lewis acids such as boron trifluoride[2], the ensuing reaction has so far merely yielded unstable 4-imino-1,2-oxazetidines[3]: alkyl substituents in position 2 with hydrogen attached to the α-C atom promote isomerization to Schiff bases of α-amino acid amides[3]. Stable crystalline products *(3)* have now been obtained, as the very first stable compounds of this type to be isolated[4], on reaction of the nitrone *N*-neopentylidene-*tert*-butylamine *N*-oxide *(1)*.

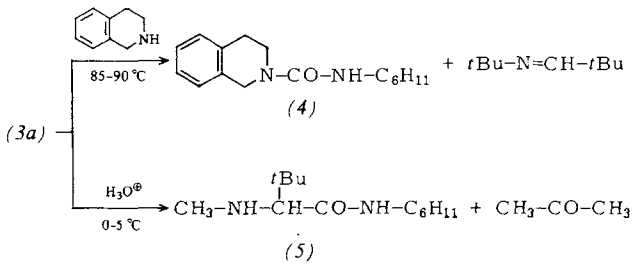
[*] Priv.-Doz. Dr. D. Moderhack, Dr. M. Lorke
Institut für Pharmazeutische Chemie der Technischen Universität
Beethovenstrasse 55, D-3300 Braunschweig (Germany)



Cpd. [a]	R	M.p. [°C]	Yield [%]	IR $\nu_{C=N}$ [cm^{-1}]
(3a)	c-C_6H_{11}	68	67	1758, 1748
(3b)	$CH_2C_6H_5$	48	47	1757
(3c)	C_6H_5	85	25	1735

[a] Correct CHN analyses. [b] Recorded in KBr.

The chemistry of the new heterocycles *(3)* is dominated by reactions involving O–N bond cleavage: these are, on the one hand, the thermally initiated [2+2]cycloreversion typical of 1,2-oxazetidines[5] (here giving isocyanate and azomethine)—heating of *(3a)* with 1,2,3,4-tetrahydroisoquinoline as trapping reagent gives the urea *(4)*, m.p. 122—123 °C, in 90% yield—and, on the other, the proton-catalyzed rearrangement to derivatives of α-amino acids—for example, the action of dilute mineral acid on *(3a)* gives the amide *(5)*, m.p. 135—136 °C, in 94% yield together with acetone.



In their mass-spectrometric fragmentation patterns, which strongly support structure *(3)*, the oxazetidines differ from analogous four-membered ring systems (3-imino-1,2-diazetidines, -1-azetines, -azetidines)[1] primarily in the absence of any elimination of isocyanide *(2)*, as is also observed with 2-iminooxetanes[6]; [2+2]cycloelimination (of isocyanate and azomethine or nitrosoalkane and ketenimine) predominates.

Procedure

A mixture of cyclohexyl isocyanide *(2a)* (1.09 g, 10 mmol) and triethylamine (1.01 g, 10 mmol) in CH_2Cl_2 (10 ml) is added within 2 min to a rigorously stirred solution of *(1)*[7] (1.57 g, 10 mmol) and $BF_3 \cdot OEt_2$ (1.35 g, 9.5 mmol) in anhydrous dichloromethane (20 ml) at −40 °C. The reaction mixture is immediately poured into a saturated solution of $NaHCO_3$ (50 ml) and extracted repeatedly with CH_2Cl_2. 2,3-Di-*tert*-butyl-4-cyclohexylimino-1,2-oxazetidine *(3a)* crystallizes after drying (Na_2SO_4) and removal of solvent; yield after recrystallization from acetone/methanol/water: 1.78 g (67%).—^{1}H-NMR ($CDCl_3$): δ = 1.03 (s, 3 CH_3), 1.10 (s, 3 CH_3), 1.1—1.9 (m, 5 CH_2), 3.46 (m, CH), 3.83 (s, CH).—MS (70 eV; 80 °C): M^+ (5%), $[M-C_6H_{10}]^+$ (7%), $[M-C_4H_9NO]^+$ (16%), $[(CH_3)_2C{=}CHC{\equiv}NC_6H_{11}]^+$ (9%), $[M-C_6H_{11}NCO]^+$ (5%), $[(CH_3)_2C{=}N{=}CHC(CH_3)_3]^+$ (11%), $[(CH_3)_3CCH_2C{\equiv}N]^+$ (27%), $[(CH_3)_2C{=}CHC{\equiv}NH]^+$ (37%), $[C_4H_9]^+$ (100%)[8].

Received: June 18, 1979 [Z 358 IE]
German version: Angew. Chem. *92*, 46 (1980)

CAS Registry numbers:
(1), 12331-68-1; *(2a)*, 931-53-3; *(2b)*, 10340-91-7; *(2c)*, 931-54-4; *(3a)*, 12331-69-2; *(3b)*, 12331-70-5; *(3c)*, 12331-71-6; *(4)*, 12331-72-7; *(5)*, 12331-73-8; 1,2,3,4-tetrahydroisoquinoline, 91-21-4

[1] Cf. references cited in [3], and *K. Burger, R. Ottlinger*, J. Fluorine Chem. *12*, 519 (1978); *J. Charrier, H. Person, A. Foucaud*, Tetrahedron Lett. *1979*, 1381.
[2] *B. Zeeh*, Synthesis *1969*, 37.
[3] *D. Moderhack, M. Lorke*, J. Chem. Soc. Chem. Commun. *1977*, 831; *M. Lorke*, Dissertation, Technische Universität Braunschweig 1979.
[4] Cf. *R. E. Banks, R. N. Haszeldine, D. R. Taylor*, J. Chem. Soc. *1965*, 5602.
[5] *L. L. Muller, J. Hamer*: 1,2-Cycloaddition Reactions. Interscience, New York 1967, pp. 257 ff.
[6] *L. A. Singer, G. A. Davis*, J. Am. Chem. Soc. *89*, 598, 941 (1967).
[7] *G. Zinner, E. Eghtessad*, Arch. Pharm. (Weinheim) *312*, 907 (1979).
[8] We are indebted to the Gesellschaft für Biotechnologische Forschung mbH, Braunschweig-Stöckheim, for recording this spectrum.

Chromium(II)-catalyzed Electrochemical Dehalogenation of β-Hydroxyhalides—Convenient Entry to Deoxynucleosides[1]

By *Josef Wellmann* and *Eberhard Steckhan*[*]

Deoxynucleosides are often prepared from halo-deoxy compounds by catalytic hydrogenation or by reduction with tributyltin hydride. However, the purity of the products and the selectivity of the reduction are not always satisfactory. We have now found that the products formed by chromium(II)-catalyzed electrochemical reduction[2] (indirect electrolysis) can be isolated in high purity and in excellent yield.

In the dehalogenation of β-hydroxyhalides with chromium(II) reagents it is of decisive importance to suppress elimination leading to the olefin. As *Barton et al.* have shown with steroid derivatives[3], this can be achieved with the aid of butanethiol as H-donor if the mild reducing agent chromium(II) acetate in dimethyl sulfoxide is used and the substrates are tertiary bromides or iodides.

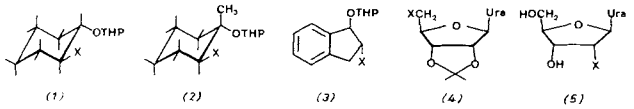
The method failed, however, in the dehalogenation of simple test substrates such as 2-bromocyclohexanol, 2-bromo-1-methylcyclohexanol and 2-bromo-1-indanol with chromium(II) acetate in dimethyl sulfoxide or dimethylformamide (DMF), or with chromium(II) chloride in DMF. Besides the desired alcohols, considerable amounts of olefins were formed; and even with threefold amounts of chromium(II) chloride in DMF only 25%, 30%, and 90% conversions, respectively, could be achieved.

To enforce complete conversion and to increase the selectivity of the reaction we used a strong chromium(II) reducing agent and protected the hydroxy groups in the substrates. Reduction of tetrahydropyranyl ethers *(1a)*—*(3a)* (Table 1) with the very reactive ethylenediamine complex of chromium(II) perchlorate in DMF in the presence of butanethiol led to complete conversion and practically quantitative yields. These results are independent of whether an excess of the reagent is used (molecular ratio of substrate : reagent 1 : 2, Method 1) or whether the chromium(II) complex is electrochemically regenerated in the reactor (Method 2, indirect electrolysis). In the indirect electrolysis, however, only catalytic amounts of reagent are needed; hence, not only is there a saving in costs but also the separation of the products from large amounts of inorganic salts is circumvented. Moreover, handling of the reagent is made easier, since the air-insensitive chromium(III) salt can be used.

[*] Priv.-Doz. Dr. E. Steckhan, Dipl.-Chem. J. Wellmann
Organisch-chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0046 $ 02.50/0

Table 1. Dehalogenation of protected β-hydroxyhalides *(1a)—(3a)* and (protected) halodeoxynucleosides *(4a)*, *(5a)* with $Cr(en)(ClO_4)_2$ to protected alcohols *(1b)—(3b)* and (protected) deoxynucleosides *(4b)*, *(5b)*. Methods 1 and 2, see text. THP = tetrahydropyranyl, Ura = uracil.



(1) (2) (3) (4) (5)

R Halogen → R H
(1a)—(5a) *(1b)—(5b)*

Substrate	X	Product	X	Yield [%] [a] Method 1	Method 2
(1a)	Br	*(1b)*	H [b]	100	92
(2a)	Br	*(2b)*	H	93	98
(3a)	Br	*(3b)*	H	85 [c]	81
(4a)	I	*(4b)*	H	—	93
(5a)	Br	*(5b)*	H	—	60 [d]

[a] Yields referred to substrate employed. [b] Cleavage of protecting group accomplished quantitatively with pyridinium *p*-toluenesulfonate [5]. [c] + 10% indene. [d] Total yield after isolation *via* three steps followed by recrystallization: 1) incorporation of the ethoxyethyl ether protecting group in *(5a)* with vinyl ethyl ether; 2) reduction; 3) cleavage of protecting group from *(5b)* with HOAc (5%).

As typical example for the synthesis of 5′- and 2′-deoxynucleosides, 2′,3′-*O*-isopropylidene-5′-deoxy-5′-iodouridine *(4a)* and 2′-deoxy-2′-bromouridine *(5a)* (protected as the 3′-5′-di-*O*-ethoxyethyl ether) were dehalogenated by indirect electrolysis (Method 2) under the conditions optimized for THP ethers *(1a)—(3a)*. The yield for the reduction step is practically quantitative. From *(5a)* a crude yield of 95% *(5b)* is obtained in three steps (see Table 1); however, only 60% crystalline *(5b)* was isolated.

Experimental

A catholyte of 10 ml DMF, 0.25 ml ethylenediamine, 0.5 ml butanethiol and 1 ml of 0.4 M aqueous solution of chromium(II) perchlorate ($\hat{=}$ 0.4 mmol Cr^{2+}) is transferred to a divided electrolytic cell (Electrolytic vessel EA 876, Metrohm) thermostated at 15 °C and furnished with a 5 mm-thick cathode of glassy carbon (2 cm^2 surface area), a Cd/Hg reference electrode[4] and a platinum mesh anode. A cylindrical glass tube sealed by a G3 glass frit can be used as anode compartment. The anode compartment and the salt bridge of the reference electrode are filled with a 0.2 M solution of $LiClO_4$ in DMF. Electrolysis is carried out at −0.9 V *vs.* Cd/Hg reference electrode. The current density is *ca.* 5 mA/cm^2. After addition of 1.8 mmol of the protected halodeoxynucleoside the current density increases to *ca.* 30 mA/cm^2. The conversion is monitored by thin-layer chromatographic analysis on silica gel F_{254}-plates (Merck) with acetone/benzene/water (60:35:5) as eluent. Conversion of substrate is complete after consumption of 3.2 mF. For workup the catholyte is adjusted to pH = 5 with 10^{-2} M $HClO_4$, extracted with chloroform (5 × 10 ml) and the combined extracts are washed with water (2 × 5 ml). The organic layer is then dried over Na_2SO_4 and the solvent removed in a rotary evaporator.

Received: August 7, 1979 [Z 359 IE]
German version: Angew. Chem. *92*, 47 (1980)

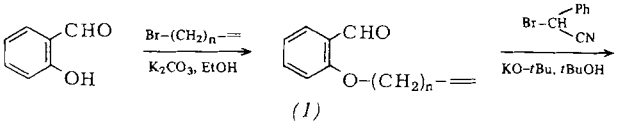
[1] Indirect Electrochemical Processes, Part 9. This work was supported by the Arbeitsgemeinschaft industrieller Forschungsvereinigungen and the Fonds der Chemischen Industrie. We thank Prof. Dr. *H. Witzel* for the supply of the halodeoxynucleosides and the dehalogenated reference compounds. Part 8: *W. Schmidt, E. Steckhan*, Angew. Chem. *91*, 851 (1979); Angew. Chem. Int. Ed. Engl. *18*, 802 (1979).

[2] *J. Wellmann, E. Steckhan*, Synthesis *1978*, 901.
[3] *D. H. R. Barton, N. K. Basu, R. H. Hesse, T. S. Morehouse, M. M. Pechet*, J. Am. Chem. Soc. *88*, 3016 (1966); *O. Gnoj, E. P. Oliveto, C. H. Robinson, D. H. R. Barton*, J. Org. Chem. *31*, 2749 (1966); *M. Akhtar, D. H. R. Barton, P. G. Sammes*, J. Am. Chem. Soc. *87*, 4601 (1965).
[4] *L. W. Marple*, Anal. Chem. *39*, 844 (1967).
[5] *M. Miyashita, A. Yoshikashi, P. A. Grieco*, J. Org. Chem. *42*, 3773 (1977).

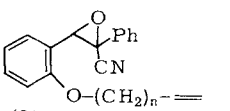
Intramolecular Cycloadditions of Carbonyl Ylides[**]

By *Wolfgang Eberbach, Jürgen Brokatzky*, and *Hans Fritz*[*]

The scope of 1,3-dipolar cycloaddition reactions for the stereoselective synthesis of heterocyclic systems has been extended considerably by the intramolecular approach[1]. However, to our knowledge, no such examples have been reported so far with the use of carbonyl ylides as dipoles[2]—except for the special case of the cyclization of 2-oxapentadienyl dipoles to 2,3-dihydrofurans[3]. We have investigated this type of reaction with two derivatives of a model system and report here on intramolecular trapping of the carbonyl ylides *(3a)* and *(3b)* and on their relative reactivity in the presence of external dipolarophiles.



(1)



(a), n = 1; *(b)*, n = 2 *(2)*

As educts we used the trisubstituted oxiranes *(2a)* and *(2b)*, which were obtained sterically pure by Darzens condensation of the alkenyl ethers *(1)*, the latter in turn being readily accessible from salicylaldehyde [*(2a)*: m.p. 52 °C (methanol); UV (ethanol): λ_{max} (ε) = 282 (4200), 274 (3860, sh), 234 (12400, sh), 217 nm (19200, sh); ^{1}H-NMR ($CDCl_3$): δ = 4.44 (oxirane-H); *(2b)*: m.p. 38—39 °C (methanol); UV (ethanol); λ_{max} (ε) = 282 (4260), 274 (3760, sh), 231 (11900, sh), 217 nm (19850, sh); ^{1}H-NMR ($CDCl_3$): δ = 4.41 (oxirane-H)][4].

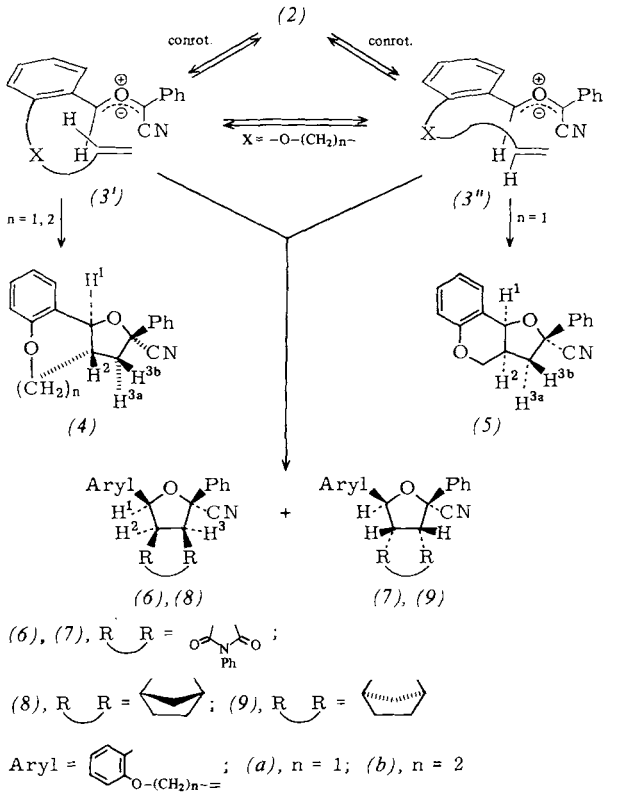
On heating in bromobenzene or isooctane, the ene-oxirane *(2a)* slowly isomerized above *ca.* 170 °C[5] to the intramolecular cycloadducts *(4a)* and *(5)*, which were isolated as a crystalline 2:1 mixture after thin-layer chromatography [yield after 9 h at 175 °C (40% conversion) 75%][6]. Under the same conditions the homologue *(2b)* gave only the *trans*-diastereomer *(4b)* (yield 66% at 30% conversion)[6].

Evidence for the ring fusion as indicated in *(4)* and *(5)*[4] is provided principally by the NMR coupling constants between H^1 and H^2 (Table 1), which are consistent with the dihedral angles of *ca.* 180° in *(4)* and 40° in *(5)*.

The formation of *(4)* and *(5)* is most likely initiated by a conrotatory opening of the oxirane ring[7] to carbonyl ylides of type *(3)*. Depending on the conformation of the alkenyloxy group, addition to the C=C-group then leads to the *trans*- *(4)* or to the *cis*-annelated ring system *(5)*. Consideration of models shows—in agreement with the preferred and

[*] Univ.-Doz. Dr. W. Eberbach [†], Dipl.-Chem. J. Brokatzky, Prof. Dr. H. Fritz
Chemisches Laboratorium der Universität Freiburg
Albertstr. 21, D-7800 Freiburg (Germany)
[†] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



exclusive formation, respectively, of *trans*-products—that the transition state *via (3')* leading to *(4)* is energetically more favorable than that *via (3")* to *(5)*. However, despite the entropic advantage of intramolecularity, this cycloaddition step is not especially favored, either electronically or sterically, as shown by the following experiments: 1) With *N*-phenylmaleimide, which externally is a particularly powerful dipolarophile owing to the electron deficient C=C-bond[8], *(2a)* and *(2b)* react almost quantitatively even at 120 °C, giving in each case a *ca.* 3:1 mixture of the bimolecular adducts *(6a)/(7a)* and *(6b)/(7b)*, respectively [14 h, yields *ca.* 90%, ^{1}H-NMR data in Table 1; *(6a)* was isolated pure by fractional crystallization from methanol (m.p. 169 °C[4])]; *i.e.* the oxirane ring apparently is opened already at a temperature which is too low for the formation of *(4)* and/or *(5)*[9]. 2) The reaction of *(2a)* and *(2b)* with norbornene as electron-rich dipolarophile is also more rapid than the intramolecular addition: Whereas *(2a)* or *(2b)* upon heating with a fivefold excess of norbornene (in bromobenzene, 180 °C, 12 h, *ca.* 90% conversion) gave rise to the formation of *(4)/(5)* as well as *(8)/(9)* [1.5:1 for *(2a)*, 3:1 for *(2b)*], the reaction carried out in norbornene as solvent afforded *(8)* and *(9)* as the sole products (ratio 3:1; yield of isolated mixtures 50—60%; ^{1}H-NMR data in Table 1). Our investigations have shown that carbonyl ylides are indeed capable of undergoing intramolecular cycloadditions with a C=C-bond. By modifying the educts (*e.g.* incorporating electron-withdrawing groups in the ene unit) the activation barrier of this reaction might be lowered considerably.

Table 1. Selected ^{1}H-NMR data of the compounds *(4)—(9)* (in $CDCl_3$).

Cpd.	δ-values [a]				Coupling constants [Hz]			
	H^1	H^2	H^{3a}	H^{3b}	$J_{1,2}$	$J_{2,3a}$	$J_{2,3b}$	$J_{3a,3b}$
(4a)	4.98	2.42	2.72	2.57	10.6	12.2	6.9	12.2
(4b) [b]	5.02	1.60	2.24	2.06	10.1	11.2	7.5	13.0
	5.26	2.1	2.76	2.66				
(5)	5.33	2.96	3.08	2.09	6.3	8.1	5.9	13.5
(6a)	6.05	4.22	4.15		7.1	8.0		
(6b)	6.03	4.24	4.15		7.1	8.0		
(7a)	5.71	4.17	3.93		6.0	10.0		
(7b)	5.75	4.13	4.01		6.7	10.0		
(8a)	5.67	2.87	2.92		7.0	7.5		
(8b)	5.65	2.87	2.91		6.9	7.5		
(9a)	~5.3	2.25	2.38		9	9.1		
(9b)	~5.2	2.29	2.42		8	9.2		

[a] 360 MHz.—With the exception of the data for *(5)* and *(6a)*, the values are taken from the spectra of the isomeric mixtures. [b] In $CDCl_3/C_6H_6$ (2:1).

Received: July 23, 1979 [Z 360 IE]
German version: Angew. Chem. *92*, 48 (1980)

[1] Reviews: *A. Padwa*, Angew. Chem. *88*, 131 (1976); Angew. Chem. Int. Ed. Engl. *15*, 123 (1976); *W. Oppolzer, ibid. 89*, 10 (1977) and *16*, 10 (1977).

[2] Likewise, intramolecular additions of azomethine ylides have been reported only recently: *C. L. Deyrup, J. A. Deyrup, H. Hamilton*, Tetrahedron Lett. *1977*, 3437; *A. Padwa, H. Ku*, J. Org. Chem. *44*, 255 (1979).

[3] *W. Eberbach, B. Burchardt*, Chem. Ber. *111*, 3665 (1978); *W. Eberbach, W. Seiler*, Tetrahedron Lett. *1978*, 4875; *W. Eberbach, J. C. Carré, ibid. 1976*, 3299.

[4] The new compounds gave correct elemental analyses and characteristic mass spectra.

[5] The Claisen rearrangement only competes above *ca.* 190 °C.

[6] The chromatographic fractions from the educts *(2a)* and *(2b)* each contained small amounts of the *cis*-isomeric oxirane.

[7] *R. Huisgen*, Angew. Chem. *89*, 589 (1977); Angew. Chem. Int. Ed. Engl. *16*, 572 (1977).

[8] Example: *K. N. Houk, J. Sims, R. E. Duke, R. W. Strozier, J. K. George*, J. Am. Chem. Soc. *95*, 7287 (1973).

[9] In accord with this finding, the photochemically generated ylide *(3a)* does indeed react with dimethyl fumarate, but not—at least up to 80 °C—to give the intramolecular adducts *(4a)* and/or *(5a)*; *J. Brokatzky*, Diplomarbeit, Universität Freiburg 1979.

Stereospecific Syntheses of Cycloheptatriene Trioxides[**]

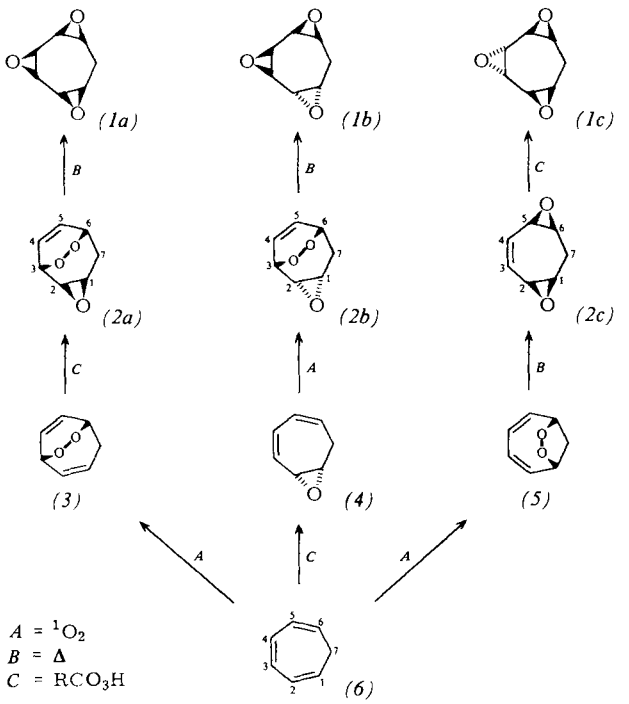
By *Waldemar Adam* and *Metin Balci*[*]

Three stereoisomers are possible for the trioxides of 1,3,5-cycloheptatriene, namely the *syn,syn- (1a)*, the *syn,anti- (1b)*, and the *anti,anti* structures *(1c)*. The thermal or photochemical formation of *syn*-dioxides from endoperoxides, which are readily available through singlet oxygenation of conjugated dienes, should serve as a convenient and effective synthetic approach for the stereospecific design of such complex molecules[1]. Scheme 1 illustrates how 1,3,5-cycloheptatriene *(6)* can be transformed into each one of the trioxides *(1a—c)* by judicious choice of the sequence of singlet oxygenation (step *A*), endoperoxide-dioxide rearrangement (step *B*), and peracid epoxidation (step *C*). To the best of our knowledge, such permutation of these reaction steps has not been utilized before for the stereospecific synthesis of polyoxides.

syn,syn-Trioxide (1a) (sequence A, C, B): Treatment of the [2+4]-endoperoxide *(3)*, readily obtained by singlet oxygenation of *(6)*[2], with *m*-chloroperbenzoic acid in CH_2Cl_2 at 40 °C afforded the *syn*-oxide *(2a)* as the major product (35% yield); it was isolated by chromatography (silica gel/CH_2Cl_2) as colorless plates, m.p. 101—103 °C (n-C_5H_{12}/CH_2Cl_2). Inspection of Dreiding models of the [2+4]-endoperoxides suggests that peracid approach is least encumbered from the *syn* side of the C_3 bridge.

[*] Prof. Dr. W. Adam (NIH Career Awardee, 1975—80), Dr. M. Balci, Department of Chemistry, University of Puerto Rico Rio Piedras, Puerto Rico 00931 (USA)

[**] Acknowledgments are made to the Donors of the Petroleum Research Fund (11022-AC1), administered by the American Chemical Society, the National Science Foundation (CHE-78-12621), and the National Institutes of Health (GM-00141-05 and RR-8102-07) for financial support.



Scheme 1. Permutation of the reaction steps *A*, *B*, and *C* for stereospecific synthesis of the cycloheptatriene trioxide *(1a—c)*. ^{1}H- and ^{13}C-NMR data, see Tables 1 and 2.

Table 1. ^{1}H-NMR data of compounds *(1a—c)* and *(2a—c)* (TMS standard).

(1a) ($CDCl_3$): δ = 1.7—2.1 (m, 1 H, *endo*-H^7), 2.4—2.8 (m, 1 H, *exo*-H^7), 2.9—3.6 (m, 6 H)
(1b) ($CDCl_3$): δ = 1.6—2.0 (m, 1 H, *endo*-H^7), 2.4—3.4 (m, 7 H)
(1c) (CCl_4): δ = 0.7—1.25 (m, 1 H, *endo*-H^7), 2.45—3.25 (m, 7 H)
(2a) ($CDCl_3$): δ = 2.06 (ddd, 1 H, *endo*-H^7), 2.7 (dd, 1 H, *exo*-H^7), 3.1 (t, 1 H, H^1), 3.35 (t, 1 H, H^2), 4.5—4.8 (m, 1 H, H^6), 4.8—5.1 (m, 1 H, H^3), 6.3—6.8 (m, 2 H, $H^{4,5}$); J_{12} = 4.0, J_{23} = 4.3, $J_{67(exo)}$ = 3.6, $J_{17(endo)}$ = 5.5, $J_{67(endo)}$ = 3.4, J_{77} = 16.7, $J_{17(exo)} \approx 0$ Hz
(2b) ($CDCl_3$): δ = 2.2—2.4 (m, 2 H, H^7), 3.0—3.4 (m, 2 H, $H^{1,2}$), 4.2—4.5 (m, 1 H, H^6), 4.8—5.2 (m, 1 H, H^3), 5.8—6.4 (m, 2 H, $H^{4,5}$)
(2c) (CCl_4): δ = 1.0—1.4 (m, 1 H, *endo*-H^7), 2.3—2.8 (m, 1 H, *exo*-H^7), 3.0—3.3 (m, 4 H, $H^{1,2,5,6}$), 5.65 (s, 2 H, $H^{3,4}$)

Table 2. ^{13}C-NMR data of the isomeric cycloheptatriene trioxide *(1a—c)*.

Trioxide [a]	δ values ($CDCl_3$) [b]						
	C^1	C^2	C^3	C^4	C^5	C^6	C^7
(1a)	52.61	53.11	50.56	50.56	53.11	52.61	28.19
(1b)	1.39	53.19	50.35	50.39	52.83	50.70	27.36
(1c)	51.86	52.29	50.61	50.61	52.29	51.86	32.25

[a] We are grateful to Dr. *Obenauf* (JEOL Company, New Jersey) for the spectra of *(1a)* and *(1b)* and to Dr. *D. Scheutzow* (Würzburg, Germany) for that of *(1c)*; [b] The numbering of the C atoms is based on cycloheptatriene *(6)*.

On heating (190 °C in toluene, 1 h, sealed tube), *(2a)* rearranges to *(1a)* in 32% yield, colorless plates, m.p. 159—162 °C (m.p. 165 °C[3]). This trioxide isomer *(1a)*, the only one of the three possible isomers hitherto isolated, purified, and characterized (X-ray analysis), was prepared by *Prinzbach* and *Rücker*[3] *via* a classical sequence starting from cycloheptatriene oxide. Its ^{13}C-NMR spectrum shows four distinct carbon resonances, which can only be reconciled with a symmetrical structure.

syn,anti-Trioxide (1b) (sequence *C, A, B*): Photo-oxygenation of cycloheptatriene oxide *(4)*, readily available by peracetic acid epoxidation of *(6)*[4], in CCl_4 at 0 °C with tetraphenylporphyrin as sensitizer (see ref. [2a]) gave the endoperoxide *(2b)* in 68% yield after chromatography (silica gel/CH_2Cl_2) as colorless needles, m.p. 125—127 °C. On heating (190 °C in toluene, 1 h, sealed tube), *(2b)* gave *(1b)* in 44% yield after chromatography (silica gel/1:1 $CHCl_3$/*n*-C_5H_{12}) as colorless plates, m.p. 66—67 °C (1:2 CH_2Cl_2/ether). The ^{13}C-NMR spectrum reveals seven distinct carbon atoms, which is only consistent with the unsymmetrical structure *(1b)*.

anti,anti-Trioxide (1c) (sequence *A, B, C*): The [2+6]-endoperoxide *(5)*, obtained alongside *(3)* on photo-oxygenation of *(6)*[2a], served as starting point for the preparation of *(1c)*. On thermolysis, but more conveniently on photolysis at λ = 350 nm in benzene, the *syn*-dioxide *(2c)* was obtained in 57% yield after chromatography (silica gel/$CHCl_3$), colorless needles, m.p. 55—56 °C (2:1 *n*-hexane/ether). Inspection of Dreiding models suggested that peracid epoxidation should take place preferentially *anti* to the existing epoxide rings because *syn* approach appears to be blocked by the *endo*-methylenic hydrogen. Indeed, after treatment of *(2c)* with *m*-chloroperbenzoic acid (CH_2Cl_2, 3 d) *(1c)* was isolated in 31% yield as colorless plates, m.p. 100—102 °C (1:2 CH_2Cl_2/*n*-C_5H_{12}). The ^{13}C-NMR spectrum reveals four distinct carbon resonances, as expected for the symmetrical structure *(1c)*.

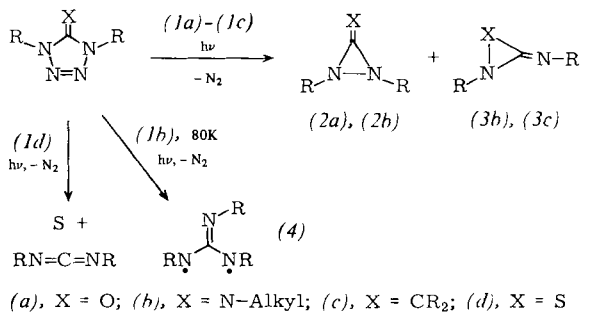
Received: August 23, 1979 [Z 362 IE]
German version: Angew. Chem. *92*, 54 (1980)

[1] a) *W. Adam*, Angew. Chem. *86*, 683 (1974); Angew. Chem. Int. Ed. Engl. *13*, 619 (1974); b) *E. Vogel, H. J. Altenbach, C. D. Sommerfeld, ibid. 84*, 986 (1972) and *11*, 939 (1972), respectively; c) *C. H. Forster, G. A. Berchthold*, J. Org. Chem. *40*, 3743 (1975).
[2] a) *W. Adam, M. Balci*, Angew. Chem. *90*, 1014 (1978); Angew. Chem. Int. Ed. Engl. *17*, 954 (1978); b) *T. Asao, M. Yagihara, Y. Kitahara*, Bull. Chem. Soc. Jpn. *51*, 2131 (1978); c) *A. Mori, H. Takeshita*, Chem. Lett. *1978*, 395.
[3] *H. Prinzbach, C. Rücker*, Angew. Chem. *88*, 611 (1976); Angew. Chem. Int. Ed. Engl. *15*, 559 (1976). Exhaustive epoxidation of cycloheptatriene oxide with peroxy acid should also give *(1b)* and *(1c)*, which, however, could not be isolated pure from the complicated product mixture.
[4] *P. Schiess, M. Wisson*, Helv. Chim. Acta *57*, 980 (1974).

Cyclopropanimines by Photolysis of Pyrazolinimines; Thermal Reaction of an Excited State[**]

By *Helmut Quast, Andreas Fuss,* and *Alfred Heublein*[*]

Photochemical elimination of nitrogen from 1,4-dialkyltetrazolines *(1a)—(1c)* yields diaziridinones *(2a)*, diaziridinimines *(2b)*, *(3b)*, and aziridinimines *(3c)*, while elimination from *(1d)* gives carbodiimides and sulfur[1]. Matrix photolysis of the tetrazolinimines *(1b)* at 80 K has been shown by ESR spectroscopy to generate triplet trisiminomethanes *(4)*[2].



(a), X = O; *(b)*, X = N–Alkyl; *(c)*, X = CR_2; *(d)*, X = S

[*] Prof. Dr. H. Quast, Dipl.-Chem. A. Fuss, Dr. A. Heublein
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Photochemical Formation of Methylenecyclopropane Analogs, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The results constitute part of the doctoral dissertation of *A. H.*, Universität Würzburg 1976, and of the planned doctoral dissertation of *A. F.*—Part 2: [2].

Table 1. Data of pyrazolinimines *(5e)*—*(5g)*, cyclopropanimine *(6f)*, and pyrazolidinimines *(7e)* and *(7f)*.

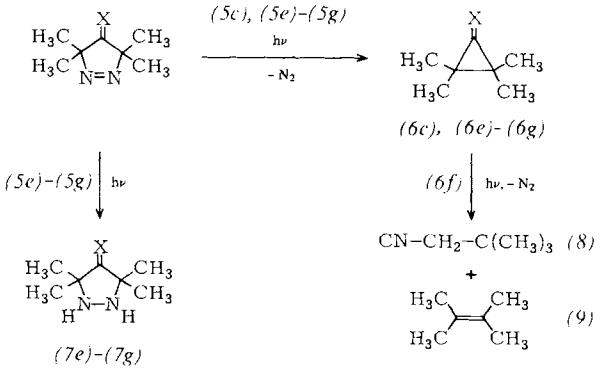
Cpd.	B.p. [°C/torr] (M.p. [°C])	IR [cm^{-1}] (CCl_4) $\tilde{\nu}$(C=N)	$\tilde{\nu}$(N=N)	^{1}H-NMR δ values (C_6D_6) $C(CH_3)_2$		X	NH	UV (*n*-Hexane) λ_{max} [nm] (log ε)
(5e)	$23/10^{-2}$ (3—4)	1696	1545	1.25	1.35	3.06	—	273 (1.926), 342 (2.308)
(5f)	$0/10^{-5}$ (18.5—19)	1697	1546	1.28	1.33	0.94, 3.06	—	275 (1.911), 342 (2.308)
(5g)	$55/10^{-5}$ (75—75.5)	1693	1545	1.30	1.37	1.1—1.9 (m) 3.33 (broadened quintet, J = 6.0 Hz)	—	273 (1.871), 342 (2.282)
(6f)		1772 [a]	—	1.08	1.10	1.06, 3.24	—	
(7e) [b]				1.07	1.17	3.13	3.58 (br.)	
(7f)	(61—62)	1692	—	1.08	1.15	0.98, 3.11	3.62 (br.)	

[a] Cf. [8]. [b] Only identified by ^{1}H-NMR spectroscopy.

Depending on the reaction conditions, methylenecyclopropanes or trimethylenemethanes and their consecutive products are obtained on photolysis of 4-alkylidene-1-pyrazolines[3] such as *(5c)*[4a,b]. In contrast, the pyrazolinone *(5a)* *resisted* photochemical conversion into *(6a)*[4c]. We have now prepared the cyclopropanimines *(6e)*—*(6g)* by irradiation of the pyrazolinimines *(5e)*—*(5g)* at elevated temperature.

The reactants *(5e)*—*(5g)* were obtained by prolonged heating of the pyrazolinone *(5a)*[4a,c] with the relevant primary alkylamine without solvent in an autoclave in the presence of a molecular sieve and an acidic SiO_2/Al_2O_3 catalyst (BASF catalyst D10-10)[5] [*(5e)*, 90 h, 110 °C, yield 53%; *(5f)*, 114 h, 150 °C, yield 85%; *(5g)*, 95 h, 150 °C, yield 70% (Table 1)].

The fluorescence of *(5e)*—*(5g)* indicated the necessity of modifying the conventional photolysis conditions for efficient loss of nitrogen[6]. Irradiation of *(5f)* in [D_6]benzene at 90 °C with light of wavelength exceeding 340 nm[7] produces 68% of cyclopropanimine *(6f)* within 2 h. The cyclopropanimine structure of the principal product *(6f)* is deduced from its IR and ^{1}H-NMR spectrum (Table 1) and its fast, quantitative decomposition to 2,2-dimethylpropyl isocyanide *(8)* and 2,3-dimethylbutene *(9)* on irradiation of the photolysis product in [D_6]benzene *without* filter (2 h, 5 °C). The smooth photochemical cleavage into isocyanide and alkene under these conditions is typical of cyclopropanimines, as we have demonstrated with an authentic cyclopropanimine, *viz.* 2-*tert*-butylcyclopropylidene-*tert*-butylamine[8].



(a), X = O; *(c)*, X = CR_2; *(e)*, X = N–CH_3;
(f), X = N–CH_2–$C(CH_3)_3$; *(g)*, X = N–cC_6H_{11}

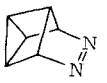
The second photolysis product could be identified as pyrazolidinimine *(7f)* by comparison with an authentic sample prepared from the pyrazolidinone *(7a)*[4a,c] and 2,2-dimethylpropylamine. Moreover, the decomposition products of *(6f)*, *i.e.* the isocyanide *(8)* and the alkene *(9)*, were also detectable in small amounts (Table 2).

The rate and course of photolysis of *(5f)* are surprisingly dependent upon the temperature, but hardly dependent upon solvent in all cases examined so far (Table 2). The much greater amount of *(7f)* formed in [D_{12}]cyclohexane, as compared with [D_6]benzene, suggests H abstraction from the solvent; however, the reason may also lie in formation of degradation products eluding detection by ^{1}H-NMR spectroscopy (polymers?), since the mass balance was only 80—90% after prolonged irradiation. The situation may resemble that encountered with the tetracyclic azo compound *(10)*: S_1 *(10)* gives $(CH)_6$ isomers by thermally activated nitrogen elimination while T_1 *(10)* rearranges to 1,2-diaza-2,4,6,8-cyclooctatetraene regardless of temperature and solvent[9]. Compounds *(5e)* and *(5g)* behave similarly to *(5f)*.

Table 2. Product ratio and mass balance (determined by ^{1}H-NMR spectroscopy (90 MHz)) on photolysis of pyrazolinimine *(5f)* in [D_6]benzene and [D_{12}]cyclohexane at 5 and 90 °C.

T [°C]	*t* [h]	Product ratio *(5f)*	*(6f)*	*(7f)*	*(8)*, *(9)*	Mass balance [%]
[D_6]Benzene [a]						
90	2	3	87	8	2	78
5	5	91	6	3	—	95
5	46	61	29	9	1	83
[D_{12}]Cyclohexane [b]						
5	5	92	3	5	—	98
5	20	71	13	16	—	88
5	46	49	22	28	1	85

[a] TMS as internal standard. [b] Dioxane as internal standard.


(10)

Received: August 6, 1979 [Z 363 IE]
German version: Angew. Chem. *92*, 55 (1980)

[1] *H. Quast, L. Bieber*, Angew. Chem. *87*, 422 (1975); Angew. Chem. Int. Ed. Engl. *14*, 428 (1975).
[2] *H. Quast, L. Bieber, W. C. Danen*, J. Am. Chem. Soc. *100*, 1306 (1978).
[3] *P. Dowd*, Acc. Chem. Res. *5*, 242 (1972), and references cited therein; *J. A. Berson, ibid. 11*, 446 (1978), and references cited therein.
[4] a) *R. J. Crawford, H. Tokunaga*, Can. J. Chem. *52*, 4033 (1974); b) *R. J. Bushby, M. D. Pollard*, Tetrahedron Lett. *1978*, 3855; c) *W. L. Mock*, Ph. D. Thesis, Harvard University, Cambridge, Mass. 1965; *P. S. Engel, L. Shen*, Can. J. Chem. *52*, 4040 (1974).
[5] Cf. *H. Quast, A. Heublein*, Chem. Ber. *108*, 2574 (1975), and references cited therein.
[6] *N. J. Turro, K.-C. Liu, W. Cherry, J.-M. Liu, B. Jacobson*, Tetrahedron Lett. *1978*, 555.
[7] All photolyses were performed with 50 μl *(5f)*/0.5 ml solvent in NMR sample tubes repeatedly degassed at 10^{-3} torr and sealed under nitrogen. Osram HBO 500 W/2 high pressure focused lamp, quartz optics, Schott u. Gen. WG 345 edge filter.
[8] Cf. *H. Quast, E. Schmitt, R. Frank*, Angew. Chem. *83*, 728 (1971); Angew. Chem. Int. Ed. Engl. *10*, 651 (1971).
[9] *N. J. Turro, V. Ramamurthy*, Rec. Trav. Chim. Pays-Bas *98*, 173 (1979), and references cited therein.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0050 $ 02.50/0

Short-Path Pyrolysis: Silabenzene[**]

By *Bahman Solouki, Pavel Rosmus, Hans Bock,* and *Günther Maier*[*]

Photoelectron spectroscopy has proved to be of immense value as a probe in flow systems for the analysis and optimization of gas phase reactions[1,2]. Thus it is possible to determine the decomposition temperature[3a], to improve the yield[3b], and to characterize the products[3c] of a pyrolysis reaction in a single experiment. However, unstable species with a mean lifetime below about 1 s can only be observed[4] if the distance between the heating and measuring zones [some 30 cm on use of an external furnace[2]] is drastically reduced (Fig. 1).

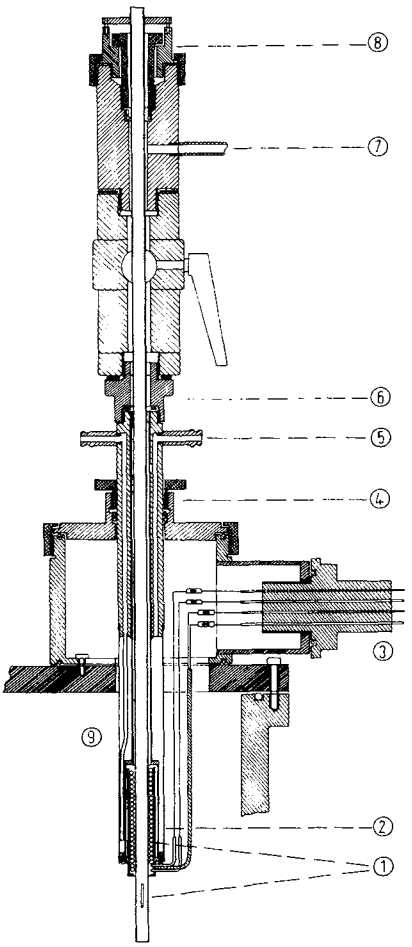


Fig. 1. Newly developed short-path pyrolysis set-up for a Perkin Elmer PS 16 PE spectrometer, designed by *B. Solouki* and built in the mechanical workshops of the Universities of Frankfurt and Mainz. Key: ① furnace of variable length with a high-output miniature heating element (stainless steel jacket, nickel-chromium core) at variable distance above the entry slit of analyzer; ② water cooling jacket for removal of furnace heat (max. temp. 1300 K); ③ current leads (up to 4 A/30 V) for furnace and thermoelement; ④ locking nut for sliding furnace with separate sliding internal tube; ⑤ supply and removal of water; ⑥ centering device; ⑦ vacuum pump connection with stopcock for change of inner tube; ⑧ adjusting device for inner tube; ⑨ PES target chamber. Overall height of apparatus 0.5 m.

During development of the short-path pyrolysis set-up (Fig. 1), a special difficulty encountered was the accommodation of the furnace and the cooling zone in the existing cylindrical jacket of only 7 mm internal diameter. It was first used for elimination of propene[5] from the 1-allyl-1-sila-2,4-cyclohexadiene derivatives *(1a)* and *(1b)* to form silatoluene *(2a)*[6a,b] and silabenzene *(2b)*[6c] (see Fig. 2).

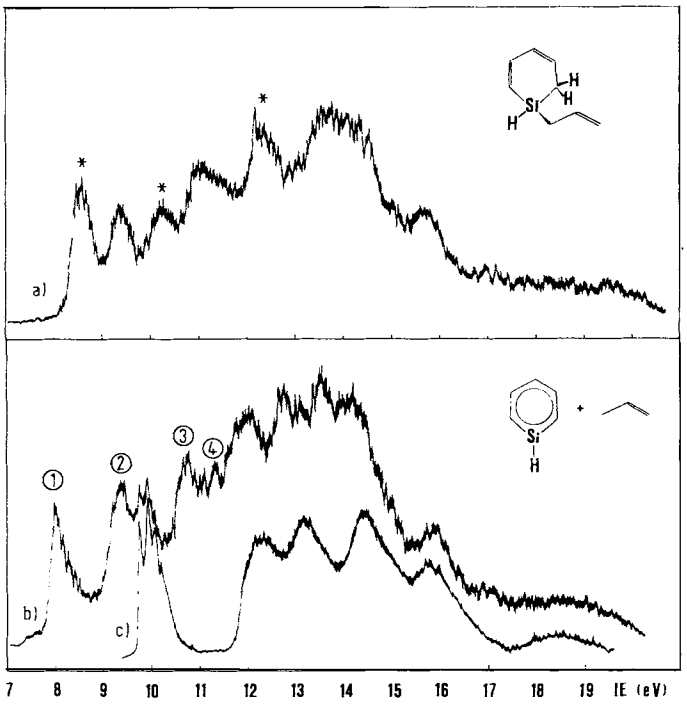
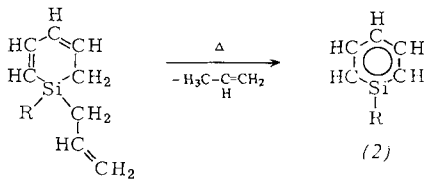


Fig. 2. He(I) PE spectra of (a) 1-alkyl-1-sila-2,4-cyclohexadiene *(1b)*, (b) of the pyrolysis mixture at 1000 K furnace temperature, and (c) of propene. Disappearing reactant bands are marked by an asterisk; the spectrum of the pyrolysis mixture (b) is assigned to silabenzene *(2b)* on the basis of a Koopmans' correlation $IE_n/-\varepsilon_j^{SCF}$ ① $\tilde{X}(^2B_1)$; ② $\tilde{A}(^2A_2)$; ③ $\tilde{B}(^2B_2)$; ④ $\tilde{C}(^2B_1)$.

Assignment of the short-path pyrolysis PE spectrum to silabenzene *(2b)* is supported by SCF calculations[7] and can be explained with the aid of perturbation arguments[8]: in the series of heterobenzene derivatives $(HC)_5X$, the perturbation X = SiH corresponds roughly to that of X = Sb, and, therefore, π-ionization energies $IE_1 \approx 8.2$, $IE_2 \approx 9.2$, and $IE_4 \approx 11.5$



(1) *(2)*

(a), R = CH_3; *(b)*, R = H

eV are expected—in satisfactory agreement with the experimental values of 8.0, 9.3, and 11.3 eV, respectively. The additional methyl-perturbation for silatoluene[6a], which lowers IE_1 to 7.7 eV and leaves IE_2 almost unchanged at 9.2 eV, is in full accord with prediction, as is the UV spectrum recorded in an argon matrix (see ref. [6c]) which is expected to correspond in its features to that of unperturbed benzene[9].

Received: October 8, 1979 [Z 364a IE]
German version: Angew. Chem. 92, 56 (1980)

[*] Prof. Dr. H. Bock, Dr. B. Solouki, Dr. P. Rosmus
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. G. Maier
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] Analysis and Optimization of Gas-Phase Reactions, Part 15.—Part 14: ref. [1]. Also: Photoelectron Spectra and Molecular Properties, Part 92.

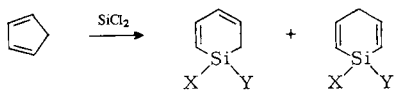
[1] *H. Bock, B. Solouki, S. Aygen, T. Hirabayashi, S. Mohmand, P. Rosmus, H. Wittmann*, J. Mol. Spectrosc., in press.
[2] Cf., *e.g., H. Bock, B. Solouki, G. Bert, T. Hirabayashi, S. Mohmand, P. Rosmus*, Nachr. Chem. Tech. Lab. *26*, 634 (1978), and references cited therein.
[3] Cf., *e.g.*, a) *H. Bock, S. Mohmand*, Angew. Chem. *89*, 105 (1977); Angew. Chem. Int. Ed. Engl. *16*, 104 (1977); b) *H. Bock, B. Solouki, J. Wittmann, H.-J. Arpe, ibid. 90*, 986 (1978) and *17*, 933 (1978), respectively; c) *H. Bock, B. Solouki, G. Bert, P. Rosmus*, J. Am. Chem. Soc. *99*, 1663 (1977).
[4] *A. Houle, J. L. Beauchamp*, J. Am. Chem. Soc. *100*, 3290 (1978); *J. Dyke, N. Jonathan, A. Morris*, J. Electron Spectrosc. Relat. Phenom. *15*, 45 (1979), and references cited therein.
[5] In general, propene is a favorable leaving molecule; *S. Mohmand*, Thesis, Frankfurt 1979; cf. also *E. Block, K. Revelle*, J. Am. Chem. Soc. *100*, 1630 (1978).
[6] a) *H. Bock, A. Bowling, B. Solouki, T. Barton, G. T. Burns*, J. Am. Chem. Soc., in press; b) Cf. also *C. L. Kreil, O. L. Chapman, G. T. Burns, T. J. Barton*, J. Am. Chem. Soc., in press; c) *G. Maier, G. Mihm, H. P. Reisenauer*, Angew. Chem. *92*, 58 (1980); Angew. Chem. Int. Ed. Engl. *19*, 52 (1980).
[7] The unknown structure of silabenzene was approximated by a MNDO geometry optimization calculation, which gave, *e.g.*, $d_{CSi}=172$ pm and $\sphericalangle$ CSiC = 109°. The total energy of the neutral molecule $\tilde{X}(^1A_1)$ was calculated to be −481.1428 a.u. with the basis set [2 s for H, 7 s/3 p for C, and 9 s/5 p for Si] which must be strongly contracted in view of the size of the molecule.
[8] Cf. *H. Bock*, Angew. Chem. *89*, 645 (1977); Angew. Chem. Int. Ed. Engl. *16*, 627 (1977), based on *C. Batich, E. Heilbronner, H. Hornung, A. J. Ashe III, D. T. Clark, D. Kilcast, I. Scanlan*, J. Am. Chem. Soc. *95*, 928 (1973).
[9] A CNDO/CI calculation predicts 34400 cm^{-1}, 38400 cm^{-1}, 51400 cm^{-1}, and 52500 cm^{-1}, respectively; *H. Bock* and *B. Roth*, unpublished results.

Silabenzene[**]

By *Günther Maier, Gerhard Mihm,* and *Hans Peter Reisenauer*[*]

If it is true that silabenzene is characterized by a considerable delocalization energy[1a] and previous attempts at its synthesis[2] were merely thwarted by the pronounced reactivity of the polar C=Si double bond, then the molecule should be isolable in a matrix at low temperature. We now report the experimental realization of this concept[3,4].

Starting from 1,1-dichloro-1-sila-2,4-cyclohexadiene *(2a)*[5a,b] [accessible in 25% yield by copyrolysis of the dimer of cyclopentadiene *(1)* with hexachlorodisilane[5c] at 540 °C (together with 5—10% of *(3a)*[1b])], reduction with $LiAlH_4$ in ether at room temperature afforded the dihydro derivative *(2b)*[5c,d] (80%; b.p. 97 °C). Reaction of *(2b)* with phosphorus pentachloride[6] in carbon tetrachloride at 0 °C leads to the monofunctionalized silacyclohexadiene *(2c)* (55%; b.p. 62 °C/40 torr)[7]. Treatment with sodium acetate (ether, 12 h, 20 °C) affords the monoacetate *(2d)* (80%; b.p. 50 °C/0.3 torr) while treatment with allylmagnesium bromide (ether, 90 min reflux) gives the even more promising[4,8] silabenzene precursor *(2e)* (75%; b.p. 90 °C/75 torr)[9].



(1) *(2)* *(3)*

(a), X = Y = Cl; *(b)*, X = Y = H; *(c)*, X = H, Y = Cl; *(d)*, X = H, Y = O–CO–CH_3; *(e)*, X = H, Y = CH_2–CH=CH_2

Apart from the molecular peaks, the mass spectra of *(2d)* and *(2e)* show an intense signal at the mass number of silabenzene ($m/e=94$). If *(2e)* is pyrolyzed immediately in front of the inlet of the mass spectrometer, characteristic changes are seen in the spectrum. At 500 °C the mass peaks at $m/e=136$ [*(2e)*], 95 [*(2e)*-allyl], and 94 [*(4)*] diminish, and that at 42 (propene) increases in intensity. This suggests that the desired elimination of propene starts under these conditions.

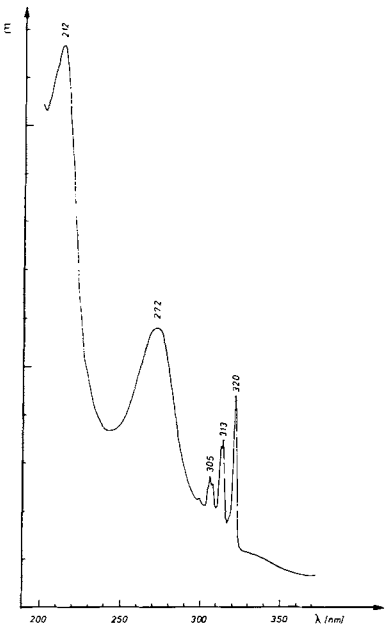
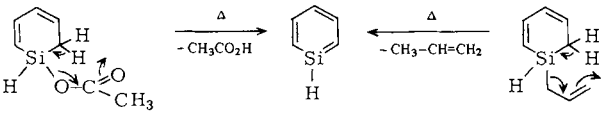


Fig. 1. UV spectrum of silabenzene *(4)* in argon at 10 K [pyrolysis of *(2d)* or *(2e)*; extinction coefficients cannot be given for methodological reasons].

With this in mind we subjected *(2d)* and *(2e)* to flash pyrolysis[10] and condensed the products with argon onto a window at 10 K. The UV spectrum of the pyrolyzate has the habit expected for a π-perturbed benzene. The three bands at $\lambda=212$, 272, and 320 nm fit into the series of bathochromic shifts observed[2,11] with other donor-substituted heterobenzenes. The absorptions are no longer visible after even brief irradiation[12].



(2d) *(4)* *(2e)*

Monitoring of the thermolysis of *(2e)* by IR spectroscopy is no less instructive. The IR spectrum of the matrix-isolated products exhibits bands at $\tilde{\nu}=418$, 566, 598, 886, 1259, 1353, 1500, 1526, and 2217 cm^{-1}, in addition to the characteristic bands of propene. We assign them to silabenzene *(4)* because they disappear both on irradiation in argon at 10 K[12] and on thawing of the matrix[13]. The Si—H stretching vibration of *(4)* lies at 2217 cm^{-1}, *i.e.* between that of a hydrogen atom attached to an sp^3-hybridized silicon atom [*(2b)* and *(2e)*: 2140 cm^{-1}] and that calculated for silaethene (2480 cm^{-1})[14].

These observations, together with the results of PE studies[3], show that ester pyrolysis of *(2d)* and the retro-ene cleavage of *(2e)* lead to the long-sought silabenzene *(4)*. This molecule is stable in an argon matrix at extremely low temperature.

Received: October 8, 1979 [Z 364b IE]
German version: Angew. Chem. *92*, 58 (1980)

[*] Prof. Dr. G. Maier, G. Mihm, Dr. H. P. Reisenauer
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] a) *M. J. S. Dewar*, Lecture at the ISNA II Meeting at Lindau, 1974; Pure Appl. Chem. *44*, 767 (1975); *M. J. S. Dewar, D. H. Lo, Ch. A. Ramsden*, J. Am. Chem. Soc. *97*, 1311 (1975); b) *R. O. W. Baumgärtner*, Dissertation, Universität Marburg 1978.

[2] Survey: *P. Jutzi*, Angew. Chem. *87*, 269 (1975); Angew. Chem. Int. Ed. Engl. *14*, 232 (1975).

[3] PE study: *B. Solouki, P. Rosmus, H. Bock, G. Maier*, Angew. Chem. *82*, 56 (1980); Angew. Chem. Int. Ed. Engl. *19*, 51 (1980).

[4] Indirect proof of intermediacy of silatoluene: *Th. J. Barton, D. S. Banasiak*, J. Chem. Soc. *99*, 5199 (1977); *Th. J. Barton, G. T. Burns, ibid. 100*, 5246 (1978); b) PE study: *B. Solouki, A. Bowling, H. Bock, Th. J. Barton, G. T. Burns, ibid.*, in press.

[5] a) *R. Benkeser, R. F. Cunico*, J. Organomet. Chem. *4*, 284 (1965); b) *E. A. Chernyshev, N. G. Komalenkova, S. A. Bashkirova*, Dokl. Akad. Nauk SSSR (Engl.) *205*, 642 (1972); c) *H.-J. Hwang, R. T. Conlin, P. P. Gaspar*, J. Organomet. Chem. *94*, C38 (1975); d) the structures of the silacyclohexadienes *(2)* have been confirmed by ^{1}H-NMR, UV, and high-resolution mass spectra.

[6] *S. Mawaziny*, J. Chem. Soc. *A 1970*, 1641.

[7] The dimethoxy-, diphenoxy-, diacetoxy-, bis(methylthio)-, bis(phenylthio)-, and bis(dimethylamino) derivatives can easily be prepared by bisfunctionalization of *(2a)*. Elimination to give correspondingly substituted silabenzenes has not yet been accomplished [1b]. Only in the case of thermolysis of 1,1-bis(methylthio)-1-sila-2,4-cyclohexadiene can UV spectra resembling that of unsubstituted silabenzene *(4)* be observed (albeit with a bathochromic shift) which could be due to silathioanisole.

[8] Elimination of propene in a kind of retro-ene reaction has proved of great value for introduction of C=Si double bonds: *H. Block, K. Revelle*, J. Am. Chem. Soc. *100*, 1630 (1978); *H. Bock*, personal communication.

[9] *(2e)/(3e)* can be completely separated by gas chromatography at room temperature on a 4 m polypropylene glycol column.

[10] Pyrolysis furnace coupled directly to a low temperature cell (Displex Closed Cycle Refrigeration System CSA 202 from the Air Products company); 780 °C/10^{-5} torr; quartz pyrolysis tube (8 × 50 mm); distance between furnace exit and window 50 mm.

[11] Phospha- and arsabenzene: *A. J. Ashe, III*, J. Am. Chem. Soc. *93*, 3293 (1971); stibabenzene: *ibid. 93*, 6690 (1971); survey Acc. Chem. Res. *11*, 153 (1978).

[12] Light of wavelength 254 or 320 nm. Silabenzene is presumably transformed into Dewar-silabenzene (new bands at $\tilde{\nu}$ = 559, 591, 689, 728, 761, 818, 1084, 1263, 1890, 2142 cm^{-1}). Owing to its preferred sp^3-type hybridization silicon favors the Dewar form with Si in a bridgehead position. According to STO-3G calculations ([1b]; *R. O. W. Baumgärtner, G. Maier, M. T. Reetz*, unpublished) the energy difference between the benzene and Dewar-benzene (75.7 kcal/mol) is reduced to 29.5 kcal/mol in the case of silabenzene and Dewar-silabenzene.

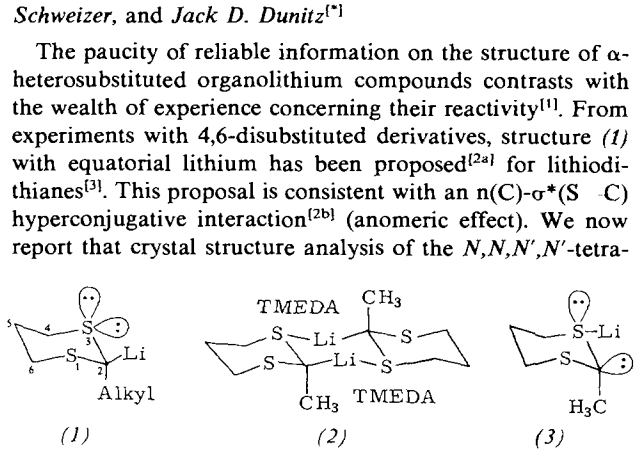
[13] Silabenzene can still exist at 37 K when the matrix is soft enough to permit intermolecular reactions. After warming to ≈ 80 K—the argon evaporates completely—propene can still be detected but no *(4)*.

[14] *B. Schlegel, S. Wolfe, K. Mislow*, J. Chem. Soc. Chem. Commun. *1975*, 246.

Crystal Structure of 2-Lithio-2-methyl-1,3-dithiane · Tetramethylethylenediamine

By *René Amstutz, Dieter Seebach, Paul Seiler, Bernd Schweizer*, and *Jack D. Dunitz*[*]

The paucity of reliable information on the structure of α-heterosubstituted organolithium compounds contrasts with the wealth of experience concerning their reactivity[1]. From experiments with 4,6-disubstituted derivatives, structure *(1)* with equatorial lithium has been proposed[2a] for lithiodithianes[3]. This proposal is consistent with an n(C)-σ*(S–C) hyperconjugative interaction[2b] (anomeric effect). We now report that crystal structure analysis of the *N,N,N',N'*-tetramethylethylenediamine (TMEDA) complex of 2-lithio-2-methyl-1,3-dithiane[4] leads to a *dimeric*[5a] structure *(2)* in which pairs of dithiane molecules are doubly bridged by Li atoms in equatorial positions.



(1) *(2)* *(3)*

Crystalline *(2)* was obtained by allowing a solution of 2-methyl-1,3-dithiane and TMEDA (each 3.7×10^{-2} molar) in hexane/cyclohexane (1:1), to which an equivalent amount of butyllithium (1.6 molar in hexane) had been added at −30 °C, to stand for several days at −20 °C. A single crystal was coated with tetradecane as adhesive and inserted into a 0.3-mm diameter capillary. All operations were carried out under nitrogen. X-ray measurements (3406 independent reflections) were made at −150 °C. The analysis (R = 0.028, with isotropic hydrogens, other atoms anisotropic) leads to the structure shown in Figure 1; Table 1 gives bond lengths and angles.

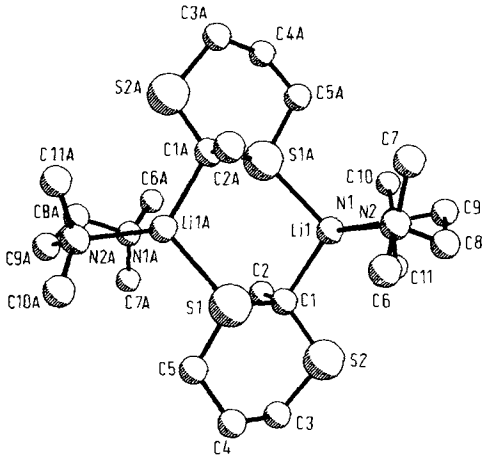


Fig. 1. Structure of the dimer *(2)* with H-atoms excluded (PLUTO program, Cambridge Crystallographic Data Centre); see Table 1.

Table 1. Structural data for complex *(2)*. Bond lengths [pm, σ ≤ 0.5 pm], bond angles [deg, σ ≤ 0.1°]. Space group $P2_1/n$; Z = 2, a = 976.0, b = 1379.6, c = 1109.7 pm; β = 88.64°. The measurements were carried out with an automated Enraf-Nonius CAD4 diffractometer equipped with a graphite monochrometer ($Mo_{K\alpha}$ radiation) and a cooling device.

Bond lengths

C1 C2 153.0, C1 S2 178.2, C1 S1 180.3, C1 Li1 218.6, C3 C4 152.6, C3 S2 183.0, C4 C5 152.6, C5 S1 182.5, C6 N1 146.9, C7 N1 146.8, C8 C9 151.4, C8 N1 147.8, C9 N2 147.7, C10 N2 146.8, C11 N2 147.1, N1 Li1 213.8, N2 Li1 217.0, S1 Li1 251.6

Bond angles

C2 C1 S2 111.9, C2 C1 S1 112.1, C2 C1 Li1 108.9, S2 C1 S1 109.4, S2 C1 Li1 111.4, S1 C1 Li1 102.9, C4 C3 S2 113.0, C3 C4 C5 112.7, C4 C5 S1 112.7, C9 C8 N1 111.9, C8 C9 N2 110.8, C6 N1 C7 109.1, C6 N1 C8 109.6, C6 N1 Li1 111.1, C7 N1 C8 110.4, C7 N1 Li1 117.1, C8 N1 Li1 99.1, C9 N2 C10 110.7, C9 N2 C11 110.3, C9 N2 Li1 103.7, C10 N2 C11 108.4, C10 N2 Li1 118.1, C11 N2 Li1 105.4, C1 S2 C3 105.4, C1 S1 C5 104.8, C1 S1 Li1 110.3, C5 S1 Li1 107.3, C1 Li1 N1 120.1, C1 Li1 N2 116.2, C1 Li1 S1 103.0, N1 Li1 N2 86.1, N1 Li1 S1 120.5, N2 Li1 S1 110.7

The centrosymmetric dimer can be concisely described as having a *trans-trans*-perhydroanthracene type skeleton with spiro junctions at the Li atoms. The dimensions of the dithiane rings and of the five-membered chelate rings are similar to those in non-metalated dithianes[4] and TMEDA-Li derivatives[5b], respectively. The new feature is the central six-membered ring. The difference of 33 pm between the Li···C and Li···S distances is practically the same as the difference between the covalent single-bond radii of carbon and sulfur (27 pm). Furthermore, the Li–C and Li–S vectors both lie in tetrahedral directions with respect to the two

[*] Prof. Dr. D. Seebach, Dipl.-Chem. R. Amstutz, P. Seiler, Dr. B. Schweizer, Prof. Dr. J. D. Dunitz
Organisch-chemisches Laboratorium der ETH
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

atoms[6]. This lithium atom thus interacts about equally strongly with the carbanionoid carbon of the one ring and a sulfur of the other so that it is hardly possible to decide between the alternative descriptions of the complex as a dimer of the C–Li monomer *(1)* or of the S–Li monomer *(3)*. Although the equatorial position of the lithium in this type of compound has been interpreted as a consequence of the anomeric effect[2], the structure of the complex shows that steric factors are probably at least as important. Since the methyl group is the smallest of the three substituents on the dithiane ring, it can be expected to adopt the axial position[7]. This type of structure may well be preserved in THF solutions of lithiodithianes where the oxygen atoms of the solvent molecules can take over the role of the TMEDA nitrogen atoms.

Received: September 21, 1979 [Z 366 IE]
German version: Angew. Chem. 92, 59 (1980)

[1] Cf. *D. Seebach, K.-H. Geiss*, J. Organomet. Chem. Library *1*, 1 (1976).
[2] a) *A. G. Abatjoglau, E. L. Eliel, L. F. Kuyper*, J. Am. Chem. Soc. 99, 8262 (1977), and earlier work cited therein; b) *J.-M. Lehn, G. Wipff, ibid. 98*, 7498 (1976); *J.-M. Lehn, G. Wipff, J. Demuynck*, Helv. Chim. Acta *60*, 1239 (1977); *N. D. Epiotis, R. L. Yates, F. Bernardi, S. Wolfe*, J. Am. Chem. Soc. *98*, 5435 (1976).
[3] *D. Seebach*, Synthesis *1969*, 17; *D. Seebach, E. J. Corey*, J. Org. Chem. *40*, 231 (1975); *B.-Th. Gröbel, D. Seebach*, Synthesis *1977*, 357.
[4] The latest version of the Cambridge Crystallographic Data File lists 13 dithiane structures.
[5] a) Cf. the crystal structure of Li-bicyclo[1.1.0]butane · TMEDA: *R. P. Zerger, G. D. Stucky*, J. Chem. Soc. Chem. Commun. *1973*, 44; b) see the Cambridge Crystallographic Data File on Li-TMEDA complexes.
[6] A study of non-bonded contacts with divalent sulfur shows that strong interactions with electrophiles occur preferentially approximately along an sp^3 lone-pair direction: *R. E. Rosenfield, Jr., R. Parthasarathy, J. D. Dunitz*, J. Am. Chem. Soc. 99, 4860 (1977).
[7] Experimental information (X–X electron-density maps [8]) on the nature of the bonding in this type of complex is under way: *D. Seebach, J. D. Dunitz*, to be published.
[8] *P. Coppens*, Angew. Chem. *89*, 33 (1977); Angew. Chem. Int. Ed. Engl. *16*, 32 (1977).

Preparation of 1-*tert*-Butyl-3-methyl-2-phenyl-Δ^3-1,2-azaboroline and Utilization of Its Anion as a Complex Ligand Analogous to Cyclopentadienyl

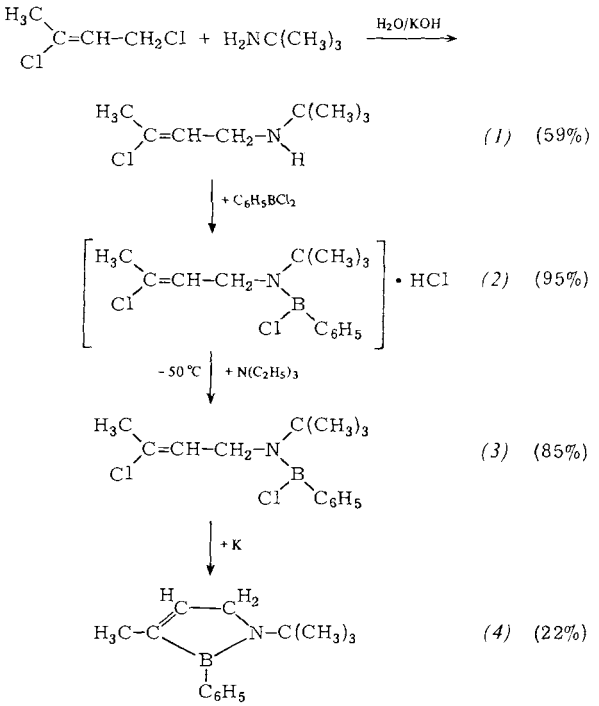
By *Joachim Schulze* and *Günter Schmid*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

1,2-Azaborolines derive from cyclopentadiene by replacement of a C=C moiety by a BN group. We have now synthesized the first 1,2-azaboroline, the title compound *(4)*.

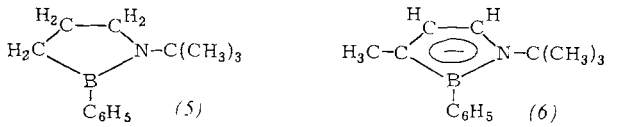
Reaction of 1,3-dichloro-2-butene with *tert*-butylamine leads to *(1)*, b.p. 61—63 °C/15—20 torr, which affords the aminoborane *(3)*, b.p. 103 °C/1 torr, *via* the hydrochloride *(2)* with phenylboron dichloride in light petroleum. In boiling dioxane, *(3)* can be dehalogenated and cyclized to 1,2-azaboroline in 22% yield by potassium. One reason for the relatively low yield is the reaction of *(4)* with potassium to give a solid product which is still being investigated. Moreover, it is not known how large the *trans* component is of 1,3-dichlorobutene[1] and of *(1)*, *(2)*, and *(3)*. Compound *(4)* is a colorless liquid of b.p. 52—53 °C/1 torr; it is soluble in inert organic solvents but somewhat sensitive to moisture.

In addition to the molecular peak at $m/e = 213$, the mass spectrum of *(4)* contains readily characterizable fragments formed by ligand elimination: $m/e = 198$ $(M-CH_3)^+$, 156 $(M-C(CH_3)_3)^+$, 136 $(M-C_6H_5)^+$. The C=C stretching mode appears at 1610 cm^{-1} in the IR spectrum and is thus



(1) (59%) *(2)* (95%) *(3)* (85%) *(4)* (22%)

shifted by 60 cm^{-1} towards longer wavelengths relative to that in the open-chain aminoborane *(3)*. The ^{1}H-NMR spectrum of *(4)* (int. TMS in $CDCl_3$) shows five signals in the intensity ratio 9:3:2:1:5 at $\delta = 1.20$ (s, $C(CH_3)_3$), 1.61 (m, CH_3), 3.84 (m, CH_2), 6.55 (m, CH), and 7.22 (br. s, C_6H_5). The ^{11}B-NMR signal lies at $\delta = 41$ (ext. $BF_3 \cdot O(C_2H_5)_2$). Transition from the unsaturated *(4)* to the saturated *(5)*[2] ($\delta = 46$) is accompanied by a significant downfield shift. The boron atom in *(4)* is better shielded by the stronger delocalization of the π-electrons.

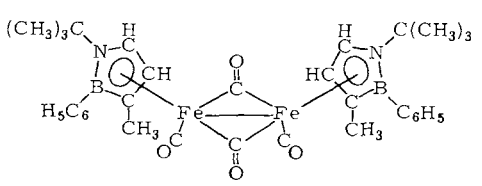


(5) *(6)*

Attempts to prepare an alkali metal salt of the anion *(6)* derived from *(4)* have so far remained unsuccessful. In contrast, the utilization of *(6)* as ligand in complex *(7)* succeeded. Compound *(7)* is formed in analogy to the known cyclopentadienyl complex $[(C_5H_5)Fe(CO)_2]_2$[3] from $Fe(CO)_5$ and *(4)*. The ν(CO) frequencies of *(7)* in solution essentially correspond in number and intensity to those of the dissolved cyclopentadienyl complex: 2000 sh (2054 w)[4], 1980 vs (2005 vs), 1938 s (1958 vs), 1758 vs (1786 s) cm^{-1} (in CH_2Cl_2 and $CHCl_3$); ^{1}H-NMR: five signals in the intensity ratio 9:3:1:1:5 at $\delta = 1.35$ (s, $C(CH_3)_3$), 1.90 (s, CH_3), 4.90 (br. s, CH), 5.45 (d, CH), 7.35—7.70 (m, C_6H_5); ^{11}B-NMR (int. TMS in [D$_8$]THF) $\delta = 22 \pm 1$. A strong upfield shift of the ^{11}B signal expectedly attends the transition from *(4)* to the complex-bonded species *(6)*.

The X-ray structure analysis of *cis-(7)* shows that *(6)* is η^5-bonded, as expected[5].

The crude product appears to contain the *trans* compound too.



(7)

[*] Prof. Dr. G. Schmid, Dipl.-Chem. J. Schulze
Fachbereich Chemie der Universität Essen—GHS
Universitätsstrasse 5—7, D-4300 Essen 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0054 $ 02.50/0

Procedure

(4): $CH_3(Cl)C{=}CH{-}CH_2Cl$ (12.5 g, 0.1 mol) is added dropwise to an ice-cooled solution of *tert*-butylamine (37.0 g, 0.5 mol). After reaction for 1 h at the boiling point, a solution of KOH (16.8 g, 0.3 mol) in H_2O (100 ml) is added slowly to the cooled mixture. The organic phase is separated off, the aqueous phase is extracted three times with ether, and the organic phases are dried over $CaCl_2$. Compound *(1)* (9.5 g, 59%) distills over at 61—63 °C/15—20 torr. All further operations are carried out under N_2 in anhydrous solvents. Compound *(1)* (9.4 g, 58.2 mmol) is dissolved in light petroleum (50 ml) and added dropwise at −30 °C to a solution of $C_6H_5BCl_2$ (9.3 g, 58.6 mmol) in light petroleum (400 ml). Stirring is continued for 1 h and the product *(2)* (17.7 g, 95%) is filtered off. Compound *(2)* is added to light petroleum (500 ml); a solution of $N(C_2H_5)_3$ (5.92 g, 58.6 mmol) in light petroleum is then added dropwise at −50 °C. After reaction for 12 h at room temperature, the mixture is heated to boiling for 1 h, filtered, and the filtrate subjected to fractional distillation; 13.2 g (85%) of *(3)* are obtained at 103 °C (1 torr). Compound *(3)* (36.5 g, 128.6 mmol; prepared in several batches) is dissolved in dioxane *(1l)* and treated with pieces of potassium (8.0 g, 204.4 mmol). The mixture is refluxed for 1 h, and the cooled solution filtered and fractionally distilled to give 6.0 g of *(4)* (22%)[6].

(7): Compound *(4)* (0.8 g, 3.75 mmol) is dissolved in $Fe(CO)_5$ (20 ml) and heated to boiling for 10 h. All volatile components are removed *in vacuo* and the residue is washed with ether (10 ml). It is then taken up in tetrahydrofuran, filtered, evaporated down to 5 ml and light petroleum is slowly added. Compound *(7)* precipitates as reddish-brown crystallites. Precipitation is brought to completion by cooling to 0 °C. The precipitate is separated, recrystallized from CH_2Cl_2, and dried *in vacuo*; yield 0.72 g (56%), dec. above 150 °C.

Received: January 29, 1979
Supplemented: August 31, 1979 [Z 368 IE]
German version: Angew. Chem. 92, 61 (1980)

[1] $ClHC{=}CH{-}CH_2Cl$ can be resolved into its *cis* and *trans* isomers. Attempts to synthesize 3-unsubstituted 1,2-azaboroline from the *cis* compound failed for unknown reasons in the last step.

[2] Colorless liquid, b.p. 52–54 °C/1 torr, prepared by reaction of $CH_2{=}CH{-}CH_2{-}NH(t\text{-Bu})$ with $C_6H_5BCl_2$ to give $CH_2{=}CH{-}CH_2N(t\text{-Bu})B(Cl)C_6H_5$, further reaction with $n\text{-}C_4H_9Li$ to form $CH_2{=}CH{-}CH_2{-}N(t\text{-Bu})B(C_4H_9)C_6H_5$, and subsequent thermolysis at 200–210 °C with loss of butene.

[3] *B. F. Hallam, O. S. Mills, P. L. Pauson,* Inorg. Nucl. Chem. *1*, 313 (1955); *S. Piper, F. A. Cotton, G. Wilkinson, ibid. 1*, 165 (1955).

[4] *F. A. Cotton, A. D. Liehr, G. Wilkinson,* Inorg. Nucl. Chem. *1*, 175 (1955).

[5] Triclinic space group $P\bar{1}$, cell constants: $a = 8.107(20)$, $b = 10.246(16)$, $c = 25.515(23)$ Å; $\alpha = 115.90(10)$, $\beta = 99.30(15)$, $\gamma = 113.18(14)°$, $Z = 2$, $V = 1604(4)$ Å^3.

[6] Correct elemental analysis (C, H, N, B).

Synthesis and Properties of the First Organosilyl-Gallium Compounds[**]

By *Lutz Rösch* and *Heinrich Neumann*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

Tris(trimethylsilyl) derivatives are known for all Group IIIB metals except gallium, for which not a single organosilyl compound has yet been reported. We have now succeeded in synthesizing lithium tetrakis(trimethylsilyl)gallate and tris(trimethylsilyl)gallium.

Lithium tetrakis(trimethylsilyl)gallate *(1)* coordinated with diethyl ether arises formally according to eq. (a) at room temperature.

$$5\,Li + 4\,Me_3SiCl + Ga \xrightarrow[-4\,LiCl]{Hg/Et_2O;\ 14d} \underset{(1)\cdot x\,Et_2O}{Li[Ga(SiMe_3)_4]\cdot x\,Et_2O} \qquad (a)$$

Heating fails to accelerate reaction, as has been observed on preparation of the analogous aluminum compound[1]; decomposition occurs instead. $(1)\cdot x\,Et_2O$ dissolves in diethyl ether and on removal of this solvent it is recovered as a colorless compound, contaminated with small amounts of LiCl, and pyrophoric in air. On vacuum sublimation, $(1)\cdot x\,Et_2O$ undergoes partial decomposition to a colorless, pentane-insoluble fraction and a yellow, pentane-soluble compound. The former product is shown by elemental analysis and spectroscopy to be $(1)\cdot 3\,Et_2O$; it closely resembles the analogous aluminum compound in its properties[1].

Cooling of the pentane solution precipitates yellow needles which ignite spontaneously on exposure to air. They contain gallium as the sole metal and afford trimethylsilane on treatment with hydrogen chloride. The ^{1}H-NMR spectrum consists of just one signal close to that of TMS. These observations indicate that solvate-free tris(trimethyl)gallium *(2)* is liberated from $(1)\cdot x\,Et_2O$ on sublimation. Elemental analysis and the mass spectrum, which exhibits the molecular ion with the calculated isotopic satellites and the signals of the expected fragmentation products, confirm the composition. In the range of expectation for Ga–Si stretching vibrations, the Raman spectrum contains two bands at 312 cm^{-1} ($\nu_s GaSi_3$) and 349 cm^{-1} ($\nu_{as} GaSi_3$); of these two bands only that at higher wavenumber also appears in the IR spectrum. This confirms the planar structure of the $GaSi_3$ group, as expected for a monomeric molecule. In this respect, *(2)* resembles the higher homologue tris(trimethylsilyl)indium, which shows a comparable vibrational spectrum[2], more closely than solvate-free tris(trimethylsilyl)aluminium, whose spectra suggest formation of associates[3].

Thermal decomposition (50 °C) gives, besides gallium, hexamethyldisilane as major product; no evidence was obtained for loss of dimethylsilanediyl, as is observed with trimethylsilylaluminum compounds[4]. Attempts to prepare *(2)* from gallium and bis(trimethylsilyl)mercury were unsuccessful. In contrast, good yields of the desired product are obtained according to eq. (b).

$$GaCl_3 + 6\,Li + 3\,Me_3SiCl \xrightarrow[-6\,LiCl]{THF;\ -10\,°C} \underset{(2)\cdot THF}{Ga(SiMe_3)\cdot THF} \qquad (b)$$

The adduct with tetrahydrofuran (THF) loses solvent on vacuum sublimation. The analogous reaction in diethyl ether does not give *(2)*.

Procedure

All operations are to be performed under argon and with exclusion of air and moisture.

(1)·3 Et_2O and *(2):* Short pieces of lithium wire (3.5 g), gallium (7 g), and mercury (1.5 ml) are heated with stirring for 1 h in diethyl ether (25 ml). After addition of diethyl ether (175 ml) and chlorotrimethylsilane (50 ml), the mixture is stirred at room temperature for 14 d. It is then filtered over a glass frit and the volatile components are removed at room temperature under oil-pump vacuum. The resulting colorless

[*] Priv.-Doz. Dr. L. Rösch, Dr. H. Neumann
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

powder contains *(1)*·2—3 Et_2O and small amounts of LiCl (crude yield 17 g). The product is purified by sublimation at 40 °C/10^{-5} torr. A yellowish substance collects on the cold finger; it is washed with pentane until the washings are colorless. The residue is dried under oil-pump vacuum and consists of *(1)*·Et_2O; yield *ca.* 3 g, m.p. 50 °C (dec.). The yellow washings are concentrated and cooled to −78 °C. Long yellow needles of *(2)* precipitate; yield 7 g, m.p. 52 °C (dec.).

Direct synthesis of *(2)*: Small pieces of lithium wire (1.2 g) are added at −20 °C to sublimed $GaCl_3$ (5 g) dissolved in pre-cooled THF (150 ml). After dropwise addition of chlorotrimethylsilane (22 ml) with cooling, the mixture is stirred at −20 °C for 2 h and *ca.* 8 h (until disappearance of the lithium) at −10 °C. The solution is decanted off, and the volatile components removed at oil-pump vacuum. Sublimation at 50 °C/10^{-5} torr gives 4.3 g of *(2)* (yield 65%). Any gallate that has also sublimed over can be removed by recrystallization from pentane.

Received: July 25, 1979 [Z 369 IE]
German version: Angew. Chem. 92, 62 (1980)

CAS Registry numbers:
(1), 72428-79-6; *(2)*, 72428-56-9; chlorotrimethylsilane, 75-77-4; $GaCl_3$, 13450-90-3

[1] *L. Rösch, G. Altnau*, Chem. Ber., in press.
[2] *H. Bürger, U. Goetze*, Angew. Chem. *81*, 122 (1969); Angew. Chem. Int. Ed. Engl. *8*, 140 (1969).
[3] *L. Rösch, G. Altnau*, unpublished.
[4] *L. Rösch*, Angew. Chem. *89*, 497 (1977); Angew. Chem. Int. Ed. Engl. *16*, 480 (1977).

Stabilization of Diborane(4) Derivatives by *tert*-Butyl Groups: The First Tetraalkyldiborane(4)

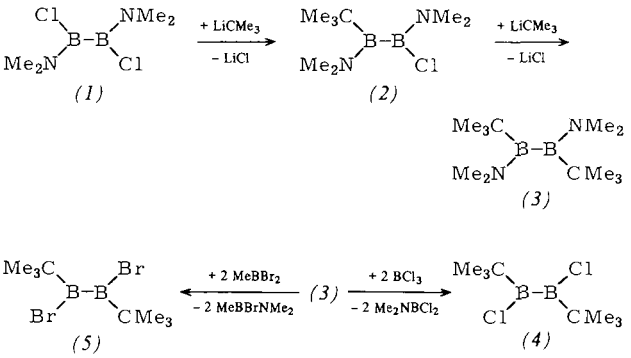
By *Werner Biffar, Heinrich Nöth,* and *Hans Pommerening*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

Increasing electronic shielding of boron in diborane(4) derivatives hinders their characteristic decomposition to BX_3 and polyboron compounds and thereby enhances their thermal stability. This is illustrated by the series $B_2Cl_4 < B_2F_4 < B_2(OR)_4 \ll B_2(NR_2)_4$. Consistent with this observation is the finding that the methyldiboranes(4) $B_2Me_{4-n}X_n$ become increasingly more unstable the greater the number of methyl groups and the weaker the π-back bonding by the group X: B_2Me_4 is unknown[1], $B_2Me_2Cl_2$[2] decomposes above −20 °C, $B_2Me_2(NMe_2)_2$[3] above 150 °C, and $B_2(NMe_2)_4$[4] survives heating for several hours at 200 °C. R_2N groups not only raise the electron density at boron by way of BN (pp)π bonds, but also hinder nucleophilic attack at that site by steric effects. This suggests that diborane(4) derivatives may be stabilized with regard to disproportionation by the highly bulky *tert*-butyl group.

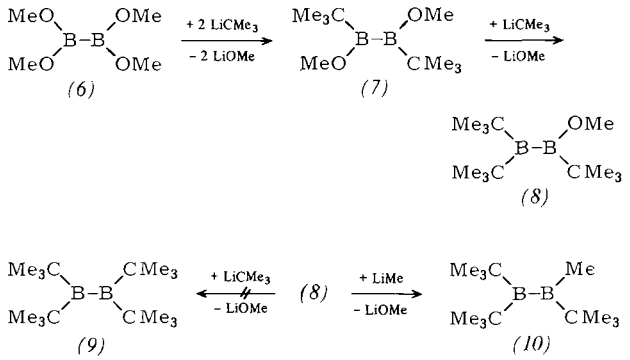
tert-Butyllithium reacts with dichlorobis(dimethylamino)-diborane(4) *(1)* to give di-*tert*-butylbis(dimethylamino)diborane(4) *(3)* *via* *tert*-butylchlorobis(dimethylamino)diborane(4) *(2)*. Treatment of *(3)* with PCl_3 or BCl_3 gives the dichloride *(4)*. $MeBBr_2$ is particularly well suited for synthesis of the dibromide *(5)*. In contrast, attempts to transform *(3)* into di-*tert*-butyldifluorodiborane(4) by reaction with BF_3 were unsuccessful. Only $(Me_2NBF_2)_2$, Me_3CBF_2, and $(Me_3C)_2BF$ were isolated.

Further alkylation of *(4)* or *(5)* with $LiCMe_3$ proceeds in an unclear manner: nucleophilic attack by CMe_3^- leads not



only to alkylation but also to B B bond cleavage and to isomerization of the *tert*-butyl groups. In order to avoid the latter reaction we attempted the preparation of higher alkylated diborane(4) derivatives starting from the less acidic $B_2(OMe)_4$ *(6)*[5].

(6) reacts with $LiCMe_3$ *via* di-*tert*-butyldimethoxydiborane(4) *(7)* to give tri-*tert*-butylmethoxydiborane(4) *(8)*. Attempted conversion of *(8)* by $LiCMe_3$ into tetra-*tert*-butyldiborane(4) *(9)* failed[6]. Under forcing conditions (1 day, 80 °C) B B cleavage occurred to give, *inter alia*, $B(CMe_3)_3$[7].



However, the less bulky $LiCH_3$ reacts with compound *(8)* to form tri-*tert*-butylmethyldiborane(4) *(10)*, the first tetraalkyldiborane(4). Likewise, $LiSiMe_3$ reacts with *(8)* to give $(Me_3C)_2B$ $BCMe_3(SiMe_3)$ *(11)*, the first silylborane which is not resonance stabilized.

The thermal stability of *tert*-butyldiboranes(4) greatly exceeds that of the comparable methyl- and ethyldiboranes(4). This suggests that diboranes(4) decompose *via* intermolecu-

Table 1. Boiling points and NMR data (in CH_2Cl_2) [a] of *tert*-butyldiboranes(4).

Cpd.	B.p. [°C/torr]	δ(¹H) $N(CH_3)_2$	OCH_3	$C(CH_3)_3$	CH_3	δ(¹¹B)
(2)	38/10^{-2}	2.87	—	0.97	—	49.0
		2.82				42.0
(3)	56/10^{-2}	2.76	—	0.95	—	54.8
		2.83				
(4)	34/4	—	—	1.07	—	84.3
(5)	36/0.5	—	—	1.14	—	88.0
(7)	41/2	—	3.81	0.88	—	63.7
(8)	46/10^{-2}	—	3.68	1.09(2)	—	64.7(1)
				0.90(1)	—	105.5(1)
(10)	41/10^{-2}	—	—	1.04(1)	0.86	103.0
				1.02(2)	(0.33)	
(11)	65/10^{-3} [b]	—	—	1.06(2)		102.0(1)
				1.22(1)	0.21(1) [c]	126.9(1)

[a] Standards: TMS internal, BF_3·$O(C_2H_5)_2$ external. (1) or (2) in the case of $C(CH_3)_3$ signifies 9 and 18H, resp. [b] Sublimation point. [c] $Si(CMe_3)_3$ group.

[*] Prof. Dr. H. Nöth, Dipl.-Chem. W. Biffar, H. Pommerening
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

lar processes subject to steric hindrance by the bulky *tert*-butyl groups. The dichloride *(4)* decomposes more readily than *(5)*[8], while the tetraalkyl compounds *(10)* are thermally stable up to at least 50 °C, and the oxygen-stable silyl derivative *(11)* up to at least 80 °C.

Table 1 lists some characteristic data of *tert*-butyldiboranes(4). $\delta(^{11}B) = 126.9$ for the B atom in the B*B*CSi group of *(11)* is the greatest downfield shift yet observed for tervalent boron; it is only 102.0 for B*B*C_2.

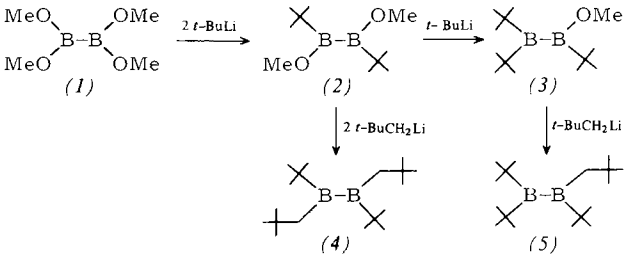
Procedure

(3): A 1.57 M solution of $LiCMe_3$ in pentane (40 ml) is slowly added dropwise to a stirred solution of *(1)*[9] (5.7 g, 31 mmol). The reaction mixture is refluxed for two days, and LiCl is filtered off. Fractional distillation affords *(3)* (6.21 g, 88%) as a colorless liquid showing little sensitivity to moisture.

(10): A solution of *(8)* (1.71 g) in ether (10 ml) is cooled to −30 °C, and a 0.685 M solution of LiMe in ether (22.3 ml) is then added dropwise with stirring. The reaction mixture is warmed to room temperature and stirred for 6 h. After filtration, the ether is removed *in vacuo*; *(10)* (0.48 g, 30%) is isolated as an oxidation-sensitive liquid at b.p. 41 °C/10^{-2} torr.

Received: May 30, 1979;
Supplemented: June 21, 1979 [Z 371a IE]
German version: Angew. Chem. 92, 63 (1980)
Publication delayed at authors' request

Reaction of tetramethoxydiborane(4) *(1)* with two or three equivalents of *tert*-butyllithium at room temperature leads to *(2)* and *(3)*, the first diboranes(4) which contain both alkyl



and alkoxy groups. We were unable to produce tetra-*tert*-butyldiborane(4) from *(3)* and *tert*-butyllithium, either by recourse to reaction times of several days or at higher reaction temperature (50 °C). We obtained, however 1,2-di-*tert*-butyl-1,2-dineopentyldiborane(4) *(4)* and tri-*tert*-butylneopentyldiborane(4) *(5)* from neopentyllithium and *(2)* and *(3)*.

Table 1. Properties of the diboranes(4) *(2)*—*(5)*. NMR data in $CDCl_3$.

Cpd.	B.p. [°C/torr]	Yield [%]	^{1}H-NMR [a] *t*-Bu	*t*-Bu	CH_2	OCH_3	^{11}B-NMR [d] $B(OCH_3)$	BR_2
(2)	45—48/0.3	36	0.87	—	—	3.77	64	—
(3)	40—43/0.01	57	0.88 [b]	1.07 [c]	—	3.65	65	106
(4)	67—69/0.001	26	0.98	1.00	1.65	—	—	103
(5)	91/0.01	67	0.99 [b]	1.01 [b] 1.08 [c]	1.59	—	—	104

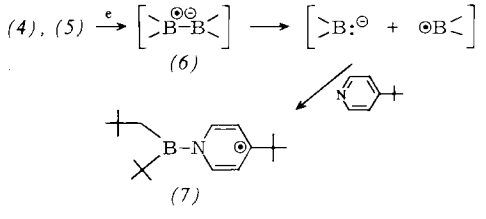
[a] δ-values, internal TMS, all peaks are singlets. [b] 9H. [c] 18H. [d] *d*-values rel. to external $BF_3 \cdot OEt_2$.

Some of the properties of the new compounds are shown in Table 1. The structure of the diboranes(4) *(2)*—*(5)* follows from the NMR data, that of *(4)* and *(5)* also from their mass spectra.

The ^{11}B-chemical shifts of *(4)* and *(5)*, *i.e.* 103 and 104 ppm, lie in the range predicted for tetramethyldiborane(4) by extrapolation[5].

The tetraalkyldiboranes(4) *(4)* and *(5)* are thermally persistent up to *ca.* 90 and *ca.* 100 °C, respectively; at 120 °C in *o*-dichlorobenzene/[D_8]toluene, *(5)* decomposes with cleavage of the B—B bond with a half-life of *ca.* 30 min into products of unknown structure.

The diboranes *(4)* and *(5)* also exhibit unusual chemical persistence: they do not react at room temperature with methanol, ammonia, hydrazine, or pyridine; the sterically well shielded *(5)* is even persistent towards oxygen.



On reduction at a cathode or with potassium, the B–B bond of *(4)* and *(5)* is readily cleaved; even at −70 °C, we could not detect the expected radical anions *(6)*, which are isoelectronic with the radical cations of correspondingly substituted ethylenes, by ESR spectroscopy. On reduction in the presence of 4-*tert*-butylpyridine, *(4)* and *(5)* give the same persistent radical which we assign structure *(7)* on the basis of its ESR coupling constants ($a^B = 2.2$ G, $a^N = 6.0$ G, $a^H = 4.4$ G for 2H and $a^C = 19.6$ G for 1C). Apparently, the

[1] Gmelin: Handbuch der Anorganischen Chemie. Ergänzungswerk zur 8. Aufl. Borverbindungen. Springer, Berlin 1977, Band 48, Teil 16, pp. 24ff.
[2] *P. L. Timms*, Chem. Commun. *1968*, 1525.
[3] *H. Schick*, Dissertation, Universität München 1966.
[4] *R. J. Brotherton, A. L. McCloskey, L. L. Petterson, H. Steinberg*, J. Am. Chem. Soc. *82*, 6242 (1960).
[5] *R. J. Brotherton, A. L. McCloskey, J. L. Boone, H. M. Manasevit*, J. Am. Chem. Soc. *82*, 6245 (1960).
[6] An ion of mass equivalent to *(9)* can be detected by mass spectrometry in the reaction mixture, but *(9)* cannot be isolated.
[7] *H. Nöth, T. Taeger*, J. Organomet. Chem. *142*, 281 (1977).
[8] *(4)* decomposes at room temperature, *(5)* above 40 °C.
[9] *H. Nöth, H. Schick, W. Meister*, J. Organomet. Chem. *1*, 401 (1964).

Persistent Tetraalkyldiboranes(4)[**]

By *Kaspar Schlüter* and *Armin Berndt*[*]

The only diboranes(4)[1] known so far are those in which each boron atom possesses at least one substituent with a lone pair of electrons which contributes to resonance stabilization by donation to the boron[2–4].

We have now synthesized the first tetraalkyldiboranes(4). They owe their persistence to shielding of the boron atoms by bulky groups.

[*] Prof. Dr. A. Berndt, Dipl.-Chem. K. Schlüter
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by Hoechst AG.

radical anions *(6)* rapidly decompose to anions and radicals. The latter are trapped with pyridine to give the *N*-(dialkylboryl)pyridinyl radical *(7)*[6].

The ready reductive cleavage of tetraalkyldiboranes(4) may explain why previous attempted syntheses carried out under reducing conditions[8,9] were unsuccessful.

Received: June 8, 1979;
Revised: June 26, 1979 [Z 371 b IE]
German version: Angew. Chem. *92*, 64 (1980)

CAS Registry numbers:
(1), 7318-94-7; *(2)*, 72428-49-0; *(3)*, 72428-50-3; *(4)*, 72428-53-6; *(5)*, 72428-54-7; *(7)*, 72428-55-8; 4-*tert*-butylpyridine, 3978-81-2

[1] a) Gmelin: Handbuch der anorganischen Chemie. Ergänzungswerk zur 8. Aufl. Borverbindungen. Springer, Berlin 1977, Band 48, Teil 16, pp. 24ff.; b) *T. D. Coyle, J. J. Ritter*, Adv. Organomet. Chem. *10*, 237 (1972).
[2] *H. Nöth, P. Fritz*, Z. Anorg. Allg. Chem. *324*, 129 (1963), and references cited therein.
[3] *R. J. Brotherton, H. M. Manasevit, A. L. McCloskey*, Inorg. Chem. *1*, 749 (1962).
[4] *P. L. Timms*, Chem. Commun. *1968*, 1525.
[5] *H. Nöth, B. Wrackmeyer:* NMR of Boron Compounds. Springer, Berlin 1978, p. 62.
[6] Radicals of type *(7)* have been discussed in the literature [7], but not unequivocally characterized by ESR spectroscopy.
[7] *R. Köster, H. Bellut, G. Benedikt, E. Ziegler*. Justus Liebigs Ann. Chem. *724*, 34 (1969), and references cited therein.
[8] *E. Wiberg, W. Ruschmann*, Chem. Ber. *70*, 1583 (1937).
[9] *R. W. Auten, Ch. A. Kraus*, J. Am. Chem. Soc. *74*, 3398 (1952).

Tetrakis(trimethylsilyl)borate and Other Trimethylsilylborates

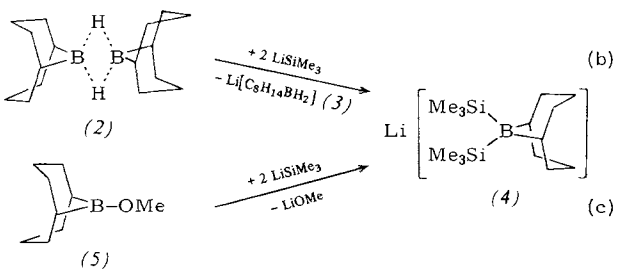
By *Werner Biffar* and *Heinrich Nöth*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

The assumption that tri-*tert*-butylborane cannot be isolated for steric reasons proved to be erroneous[1]. The Si-homologue tris(trimethylsilyl)borane should therefore also be isolable since the steric effect of the Me_3C group is greater than that of the Me_3Si group. So far, however, only silylboranes with electron-rich boron atoms[2] are known, apart from $Cl_3Si—BCl_2$[3] and $(Me_3C)_2B—BCMe_3(SiMe_3)$[4].

Our attempts to prepare $B(SiMe_3)_3$ from $LiSiMe_3$ and BX_3 did not lead to silylboranes, but instead to silylborates. No substitution occurs at the boron atom if the borane derivative BX_3 contains poor leaving groups (hydride, alkyl) or the boron atom is subject to strong steric or electronic shielding. In the latter case addition is also suppressed, *e.g.* when $LiSiMe_3$ acts upon 9-*tert*-butyl-9-BBN[5], whereas in the former case the reaction stops at the adduct stage *(1)*, as shown by quantitative reactions in hexane at 0 °C.

$$R_3B + LiSiMe_3 \longrightarrow Li[R_3B{-}SiMe_3] \quad (a)$$
$$R = CH_3,\ C_2H_5 \qquad (1)$$



(2) (b) (4) (c) (5)

LiSiMe$_3$ cleaves the hydride bridges of dimeric 9-BBN *(2)* asymmetrically[6], resulting in a 1:1 mixture of lithium dihydrido-9-boratabicyclononane *(3)* and lithium bis(trimethylsilyl)-9-boratabicyclononane *(4)*, as demonstrated by a 1:2:1 triplet and a singlet in the ^{11}B-NMR spectrum. While LiSiMe$_3$ reacts in a very unclear manner with MeS-9-BBN, MeO-9-BBN *(5)* reacts smoothly to give *(4)*. In neither case could the silylborane Me_3Si-9-BBN be detected. In general, methyl esters of alkylboric acids give trimethylsilylborates in hexane according to reaction (d). These reactions are accompanied, however, by alkyl group transfers, hydridoborate formation, and disproportionation. Thus the 2:1 reaction of LiSiMe$_3$ with Me_2BOMe gives, for example BMe_3 and $Li[(Me_3Si)_3BMe]$ in addition to $Li[(Me_3Si)_2BMe_2]$ as the major product.

$$R_{3-n}B(OMe)_n + (n+1)LiSiMe_3 \rightarrow n\,LiOMe + Li[R_{3-n}B(SiMe_3)_{n+1}] \quad (d)$$

Increasing Me_3Si substitution obstructs borate formation for steric reasons. Nevertheless, silylation of $B(OMe)_3$ according to reaction (e) surprisingly leads to lithium tetrakis(trimethylsilyl)borate *(6)* as a microcrystalline powder soluble in pentane and benzene. Even a substoichiometric amount of LiSiMe$_3$ fails to give $B(SiMe_3)_3$ since it apparently reacts faster with LiSiMe$_3$ than $B(OMe)_3$ and the intermediates $(MeO)_2BSiMe_3$ and $MeOB(SiMe_3)_2$.

$$4\,LiSiMe_3 + B(OMe)_3 \rightarrow 3\,LiOMe + \underset{(6)}{Li[B(SiMe_3)_4]} \quad (e)$$

LiSiMe$_3$ accordingly provides a strongly nucleophilic $SiMe_3$ anion in hexane. The formation tendency of trimethylsilylborates thus far exceeds that of *tert*-butylborates. Trimethylsilylboranes therefore appear to be stronger Lewis acids than their *tert*-butyl analogs. This is due mainly to steric reasons as shown by the non-existence of $Li[B(CMe_3)_4]$[1]. However, if the steric conditions hinder borate formation, as in the $(Me_3C)_2B—BOMe(CMe)_3$/LiSiMe$_3$ system then silylboranes are also capable of existence[4].

Trimethylsilylborates show an increasing Si—B coupling constant and upfield shift of the ^{11}B-NMR signal as the extent of Si-substitution increases. The sign of the coupling constant $^1J(^{11}B^{29}Si)$ is negative. Characteristic NMR data are listed in Table 1. *(6)* contains 36 magnetically equivalent protons whose ^{1}H-NMR signal is split into a quartet by coupling with the ^{11}B nucleus.

Table 1. Some NMR spectroscopic data of trimethylsilylborates (standard: $BF_3 \cdot OEt_2$) [a].

	$\delta(^{11}B)$	$^1J(^{11}B^{29}Si)$ [Hz]	Solvent	M.p. [°C]
$Li[Me_3BSiMe_3]$	−28.5	−74	C_6D_6	127
$Li[Me_2B(SiMe_3)_2]$	−36.1	−61	Hexane	—
$Li[MeB(SiMe_3)_3]$	−45.3	−53	C_6D_6	81
$Li[B(SiMe_3)_4]$ [b] *(6)*	−53.4	−48	C_6D_6	81
(4)	−25.0	−65	THF	—

[a] ^{1}H- and ^{13}C-NMR data correspond to the constitution of these borates. [b] A single ^{1}H-NMR signal was found for *(6)* at $\delta(^1H) = +0.09$, which is split by coupling with ^{11}B to form a 1:1:1:1 quartet, $^3J(^{11}B^1H) = 1$ Hz.

Procedure

(6): $B(OMe)_3$ (10 mmol) in 10 ml *n*-hexane is slowly added dropwise to a stirred solution of LiSiMe$_3$ (40 mmol) in *n*-hexane (64 ml) at −70 °C. After warming to room temperature, the precipitate is separated and the filtrate evaporated down to half its volume. The product crystallizes at −78 °C. Re-

[*] Prof. Dr. H. Nöth, Dipl.-Chem. W. Biffar
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0058 $ 02.50/0

crystallizing three times from pentane gives colorless crystalline *(6)*, m.p. 85—87 °C.

Received: June 28, 1979 [Z 371 c IE]
German version: Angew. Chem. 92, 65 (1980)
Publication delayed at authors' request

[1] *T. Taeger, H. Nöth*, J. Organomet. Chem. *142*, 281 (1977).
[2] *R. W. Kirk, D. L. Smith, W. Asley, P. O. Timms*, J. Chem. Soc. Dalton Trans. *1972*, 1392; *H. Nöth, G. Höllerer*, Chem. Ber. *99*, 2197 (1966); *E. Amberger, R. Römer*, Z. Anorg. Allg. Chem. *345*, 1 (1966); *D. Seyferth, H. P. Kögler*, J. Inorg. Nucl. Chem. *15*, 99 (1960); *A. H. Cowley, H. H. Sisler, G. E. Ryschkewitsch*, J. Am. Chem. Soc. *82*, 501 (1960).
[3] *A. G. Massey, D. S. Urch*, Proc. Chem. Soc. (London) *1964*, 284.
[4] *W. Biffar, H. Nöth, H. Pommerening*, Angew. Chem. *92*, 63 (1980); Angew. Chem. Int. Ed. Engl. *19*, 56 (1980).
[5] 9-BBN = 9-borabicyclo[3.3.1]non-9-yl.
[6] *J. L. Hubbard, G. W. Kramer*, J. Organomet. Chem. *156*, 81 (1978), also observed asymmetric cleavage of the hydride bridges on reaction of H-9-BBN with alkyllithium compounds.

The First Optically Active Cluster: Resolution of Enantiomers and Absolute Configuration of $SFeCoMoCp(CO)_8$[**]

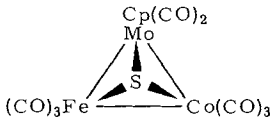
By *Felix Richter* and *Heinrich Vahrenkamp*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

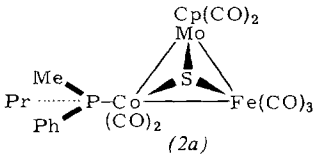
Tetrahedrane-type chiral molecules with four different corner atoms have not been known for long. Having synthesized such transition metal clusters[1], we have now resolved *(1)* into the pure enantiomers *(1a)* and *(1b)*.



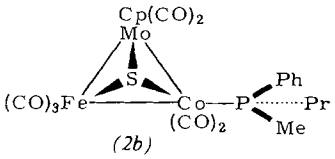
(1a)



(1b)



(2a)



(2b)

The optically active phosphane (*R*)-PMePrPh[2] was introduced into *(1)* as ligand to facilitate resolution. The resulting diastereomers *(2a)* and *(2b)* could be separated by crystallization. The phosphane was subsequently trapped as phosphonium salt by methyl iodide under CO pressure, leaving pure *(1a)* and *(1b)*.

The IR spectra of *(2a)* and *(2b)* cannot be distinguished in the CO stretching region[3]. The ^{1}H-NMR signals of the phosphane ligands recorded in benzene are also identical, whereas the signal of the cyclopentadienyl ligand appears at $\delta = 4.72$ for *(2a)* but at $\delta = 4.71$ for *(2b)*: The molar rotations $[\Phi]_D$ are $-14700 \pm 400°$ for *(2a)* and $10050 \pm 300°$ for *(2b)*. The optical data of *(1a)* are shown in Figure 1.

[*] Prof. Dr. H. Vahrenkamp, Dipl.-Chem. F. Richter
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the University Computing Center at Freiburg. We are grateful to Prof. Ullrich, Biochemisches Institut der Universität Freiburg, for the optical measurements.

Crystal-structure analysis of *(2b)*[4] provided a means of determining the absolute configuration of *(1a)* and *(1b)*. The configuration of the cluster could then be deduced from the

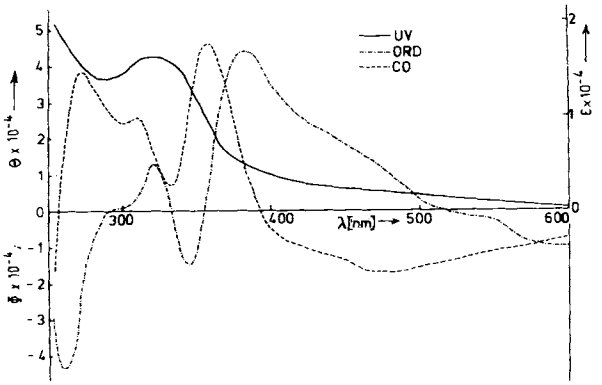


Figure 1. UV, ORD, and CD spectra of optically pure *(1a)*.

known configuration of the phosphane. The structural parameters of *(2b)*[5] should also apply to the clusters *(1)* and *(2a)*.

Like the phosphane, the enantiomers of *(1)* have an optical purity of about 98—100%. This was deduced from the NMR spectrum of the product mixture resulting on renewed reaction of isolated *(1a)* with the (*R*)-phosphane; it consisted almost exclusively of *(2a)*. Thus it was also established that elimination of phosphane from *(2)* is not accompanied by inversion or partial racemization.

The relatively facile synthesis and enantiomeric resolution and the thermal and configurational stability of the cluster *(1)* up to *ca.* 100 °C predestinate it for numerous reactions. The ready accessibility of the metal atoms resulting from the large number of substitutable CO ligands raises considerable hopes regarding optical induction in catalyses and inorganic syntheses.

Procedure

(2a) and *(2b)* can be obtained by known methods[6] from *(1)*[1] and (*R*)-PMePrPh[2]. Recrystallization twice from *n*-hexane affords the less soluble *(2b)* (m.p. 133 °C) in about 40% yield and the more soluble *(2a)* (m.p. 119 °C) in about 65% yield. The phosphane is removed by stirring the pure diastereomer *(2a)* or *(2b)* (120 mg, 0.18 mmol) in cyclohexane (30 ml) with methyl iodide (5 ml) for one week under CO pressure (60 atm). After filtration, the solution is chromatographed with pentane/benzene (2:1) over a 1.5 cm × 20 cm silica gel column. The first red fraction gives 65—75 mg (on average 73%) of *(1a)* or *(1b)* after recrystallization from *n*-hexane; m.p. 105 °C.

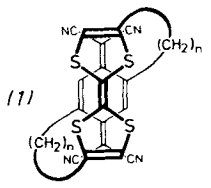
Received: July 3, 1979 [Z 372 IE]
German version: Angew. Chem. 92, 66 (1980)

[1] *F. Richter, H. Vahrenkamp*, Angew. Chem. *90*, 916 (1978); Angew. Chem. Int. Ed. Engl. *17*, 864 (1978).
[2] *K. Naumann, G. Zon, K. Mislow*, J. Am. Chem. Soc. *91*, 7012 (1969).
[3] In cyclohexane 2052 vs, 1999 vs, 1979 sh, 1967 m, 1957 sh, 1944 sh, 1890 cm^{-1} w.
[4] Orthorhombic, $P2_12_12_1$, $Z = 4$, $a = 1290.7(8)$, $b = 1381.8(1)$, $c = 1426.3(3)$ pm, 2048 reflections, $R = 0.039$.
[5] Principal bond lengths: Mo—Co 275.0(2), Mo—Fe 279.3(2), Fe—Co 256.8(2), Mo—S 236.3(3), Co—S 217.0(3), Fe—S 218.2(3), Co—P 224.0(3) pm.
[6] *S. Aime, L. Milone, R. Rossetti, P. L. Stanghellini*, Inorg. Chim. Acta *25*, 103 (1977).

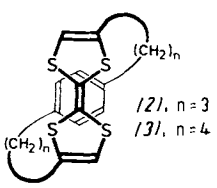
Tetrathiafulvalenoparacyclophanes[1]

By *Heinz A. Staab, Joachim Ippen, Chu Tao-pen, Claus Krieger,* and *Barbara Starker*[*]

Owing to its "metallic conductivity"[2] the crystalline 1:1 molecular complex of tetrathiafulvalene (TTF) and tetracyanoquinodimethane (TCNQ) is one of the most interesting organic electron donor-acceptor compounds. Other than in the usual crystal lattices of strong donor-acceptor complexes, in which the donor and acceptor molecules alternate within a stack, in the TTF-TCNQ crystal the components form separate stacks[3]. Whether the special conducting properties are connected with this difference in molecular structure cannot be established experimentally owing to the lack of other crystal modifications of the same complex. Since it appeared *a priori* very unlikely that the crystal structure of the TTF-TCNQ complex is optimal with respect to the electrical conductivity we tried to effect other TTF-TCNQ arrays in the crystal lattice by changing the molecular architecture. For example crystallization in alternating donor-acceptor stacking should be enforced if TTF and TCNQ are bonded to each other cyclophane-like as in *(1)* ($n=3$ or 4). Donor-acceptor cyclophanes with TCNQ as acceptor component have already been synthesized[4]. For the incorporation of TTF in cyclophane structures, however, a novel reaction sequence had to be developed. As example we describe here the synthesis of the parent compounds of *(1)*, namely [3]tetrathiafulvaleno[3]paracyclophane *(2)* and [4]tetrathiafulvaleno[4]paracyclophane *(3)*.

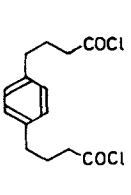


(1)

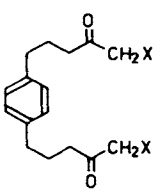


(2), n = 3
(3), n = 4

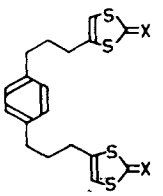
For the synthesis of *(2)*, 4,4'-(*p*-phenylene)dibutyryl chloride *(4)*[5] (prepared by reaction of the corresponding dicarboxylic acid[6] with thionyl chloride, 2 h, 90 °C; 83% yield) was converted *via* the bis(diazoketone) (obtained on reaction with diazomethane in ether) into the bis(chloroketone) *(5)*[5] (m.p. 70—71 °C; 51% yield) (sodium chloride, hydrochloric acid, methanol)[7]. Reaction of *(5)* with potassium *O*-isopropyldithiocarbonate (acetone, 30 minutes' reflux) afforded the corresponding bis(*O*-isopropyldithiocarbonate) *(6)*[5] (m.p. 63—64 °C; 89% yield). Subsequent cyclization (70% perchloric acid, chloroform/ether, 1:1)[8] furnished the bis(1,3-dithiol-2-one) *(7)*, which on reaction with phosphorus(v) sulfide (xylene, 2.5 h, 140 °C) gave the bis(1,3-dithiol-2-thione) *(8)*[5] [m.p. 99—100 °C; 10% yield based on *(6)*].



(4)

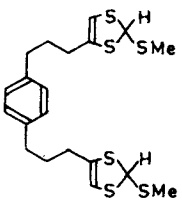


(5), X = Cl
(6), X = S-CS-OiPr

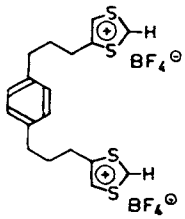


(7), X = O
(8), X = S
(9), X = SMeI$^{\ominus}$

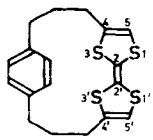
Methylation of *(8)* (methyl iodide in nitromethane, 2.5 h, 70 °C) to give the bis(sulfonium iodide) *(9)* followed by hydride reduction (sodium tetrahydridoborate, tetrahydrofuran/methanol, −78 °C) afforded the bis(methylthio) derivative *(10)*[5] in 91% yield. Reaction of *(10)* with tetrafluoroboric acid in acetic anhydride gave the bis(1,3-dithiolium tetrafluoroborate) *(11)*, which on treatment with triethylamine in acetonitrile in a variation of the TTF synthesis by *Wudl et al.*[9] in dilute solution underwent intramolecular cyclization. The two possible structural isomers *(2)* and *(12)* are formed in a ratio of about 1:1 (^{1}H-NMR). The isomer *(2)* could be obtained pure from the isomeric mixture by repeated recrystallization from cyclohexane.



(10)



(11)



(12)

The product (yellow prisms, m.p. 180—182 °C)[5] was shown by its mass spectra and ^{1}H-NMR spectra[10a] to have the [3]tetrathiafulvaleno[3]paracyclophane structure. Differentiation between the two possible structural isomers *(2)* and *(12)* was accomplished by X-ray structure analysis, which was consistent with the isomer *(2)*[10a]. Figure 1a shows that the electron-rich central double bond of the TTF group is centered almost above the middle of the benzene ring (deviations: $L=7.5$, $M=10.4$ pm). The long axis of the TTF group and the *para*-axis of the benzene ring are twisted by an angle of 15° to each other. The transannular distance of 373 pm, however, is surprisingly large (Fig. 1b). This arises from the fact that the TTF group in *(2)* deviates considerably from planarity owing to ring strain: the S(1A) C(5A) C(4A) S(3A) and S(1B) C(5B) C(4B) S(3B) planes form angles of 28 and 33°, respectively, with the mean plane through the four S-atoms; the S(1A) C(2A) S(3A) and S(1B) C(2B) S(3B) planes are also bent at a slight angle (*ca.* 4°) to the C(2A) C(2B) double bond, and exhibit a mutual twisting of 7° about this bond. The benzene ring is slightly boat-shaped with the bridgehead atoms C(9) and C(12), unlike in normal paracyclophane structures, bending *outwards* from the C(10) C(11) C(13) C(14) plane (the planes C(11) C(12) C(13) and C(14) C(9) C(10) each form an angle of 2° to this basal plane); the exocyclic bonds on C(9) and C(12) are bent outwards by a further 4° (Fig. 1c).

Owing to the unusual ring strain effects in *(2)*, interest was aroused in its higher homolog, for which a more strictly parallel arrangement of donor and acceptor with on average shorter transannular distance was expected. *(3)* was synthesized analogously to *(2)*. Starting from 5,5'-(*p*-phenylene)divaleric acid[11], the bis(chloroketone) *(13)*[5] (m.p. 86—87 °C, 53% yield) was obtained *via* the bis(diazoketone) generated by reaction of the dicarboxylic chloride with diazomethane. *(13)* was then converted into the bis(*O*-isopropyl dithiocarbonate) *(14)*[5] (m.p. 114—115 °C; 75% yield). Subsequent cyclization with perchloric acid gave the bis(1,3-dithiol-2-one) *(15)*[5] (m.p. 86—88 °C; 78% yield), which on reaction with phosphorus(v) sulfide afforded the bis(1,3-dithiol-2-thione) *(16)*[5] (m.p. 104—105 °C; 59% yield). Methylation of *(16)* to *(17)* followed by hydride reduction furnished the

[*] Prof. Dr. H. A. Staab, Dr. J. Ippen, Chu Tao-pen, C. Krieger, B. Starker
Abteilung Organische Chemie,
Max-Planck-Institut für medizinische Forschung
Jahnstrasse 29, D-6900 Heidelberg 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0066 $ 02.50/0

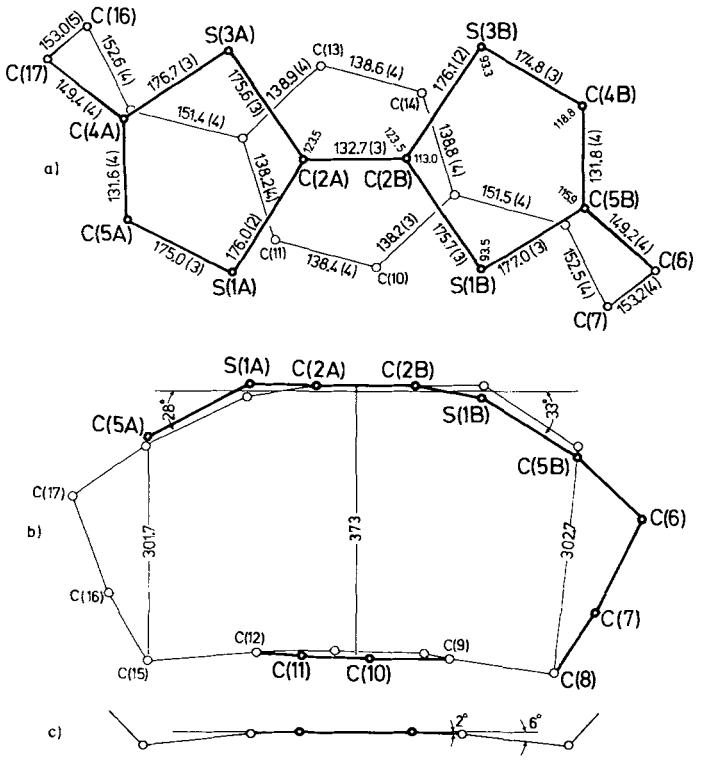
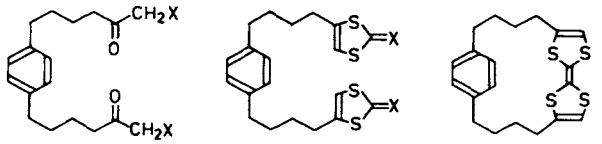


Fig. 1. Molecular structure of *(2)*. a) front view vertical to the C(10)—C(11)—C(13)—C(14) plane of the benzene ring; b) side view vertical to C(2A)—C(2B) within the mean plane defined by the four S-atoms; c) side view in the C(10)—C(11)—C(13)—C(14) plane vertical to C(9)—C(12). Bond lengths and transannular distances in pm (in brackets, standard deviations in units of the decimal place given); angles given for the TTF group are the mean values for the rings A and B.

bis(methylthio) derivative[5] (95% yield) analogous to *(10)*. Reaction of the bis(1,3-dithiolium tetrafluoroborate) analogous to *(11)* with trimethylamine in acetonitrile gave, in contrast to the synthesis of *(2)*, only a single intramolecular cyclization product in remarkably good yield (63%).



(13), X = Cl
(14), X = S-CS-OiPr

(15), X = O
(16), X = S
(17), X = $\overset{\oplus}{S}Me\ I^{\ominus}$

(18)

The mass spectra and ^{1}H-NMR spectra of the product (yellow prisms, m.p. 157—158 °C)[5] are consistent with the [4]tetrathiafulvaleno[4]paracyclophane structure[10b]. However, differentiation between the structural isomers *(3)* and *(8)* was possible only by means of an X-ray structure analysis[10b]. Surprisingly, the main product of the cyclization is not *(3)* but the isomer *(18)*. In *(18)* the benzene ring is displaced sideways to the TTF group and forms an angle of 63.5° with the plane of the TTF central double bond. In contrast to *(2)*, in *(18)* the central part of the TTF group [S(1A)—C(2A)—S(3A)/S(1B)—C(2B)—S(3B)] is coplanar, yet here also the planes defined by S(1A)—S(3A)—C(4A)—C(5A) and S(1B)—S(3B)—C(4B)—C(5B) are each at an angle of about 22° to this plane.

Received: August 13, 1979 [Z 361a IE]
German version: Angew. Chem. 92, 49 (1980)

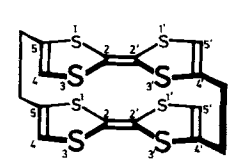
[1] Electron-Donor-Acceptor Compounds, Part 25.—Part 24: *H. A. Staab, M. Jörns, C. Krieger*, Tetrahedron Lett. *1979*, 2513.
[2] *J. Ferraris, D. O. Cowan, V. Walatka, Jr., J. H. Perlstein*, J. Am. Chem. Soc. *95*, 948 (1973); *D. B. Tanner, C. S. Jacobsen, A. F. Garito, A. J. Heeger*, Phys. Rev. Lett. *32*, 1301 (1974); *P. A. Berger, D. J. Dahm, G. R. Johnson, M. G. Miles, J. D. Wilson*, Phys. Rev. *B 12*, 4085 (1975); and references cited therein; see also *J. H. Perlstein*, Angew. Chem. *89*, 534 (1977); Angew. Chem. Int. Ed. Engl. *16*, 519 (1977).
[3] *T. J. Kistenmacher, T. E. Phillips, D. O. Cowan*, Acta Crystallogr. *B 30*, 763 (1974).
[4] *H. A. Staab, H.-E. Henke*, Tetrahedron Lett. *1978*, 1955; *H. A. Staab, G. Knaus*, Tetrahedron Lett. *1979*, 4261; cf. also *M. Yoshida, H. Tatemitsu, Y. Sakata, S. Misumi*, Tetrahedron Lett. *1976*, 3821.
[5] These compounds gave correct analyses and characteristic spectra.
[6] *D. J. Cram, N. L. Allinger, H. Steinberg*, J. Am. Chem. Soc. *76*, 6132 (1954).
[7] In analogy to *E. Fahr*, Justus Liebigs Ann. Chem. *638*, 1 (1960); references cited therein.
[8] Cf. *A. K. Bhattacharya, A. G. Hortmann*, J. Org. Chem. *39*, 95 (1974).
[9] *F. Wudl, M. L. Kaplan, E. J. Hufnagel, E. W. Southwick, Jr.*, J. Org. Chem. *39*, 3608 (1974).
[10] a) *(2)*, M^+ calc. 362.0291, obs. 362.0287; m/e = 364 (18%, $M+2$), 362 (100, M^+), 329 (1), 285 (1), 181 (3, M^{2+}), 117 (3), 91 (1); ^{1}H-NMR (CS_2): δ = 1.9—2.35 (m, 4H), 2.4—3.05 (m, 8H), 5.95 (s, 2H), 6.78 (s, 4H); space group $P2_1/n$, a = 1419.3(4), b = 1280.4(3), c = 983.2(2) pm, β = 105.5(1)°, Z = 4; R = 0.034, 2414 observed reflections. b) *(18)*, M^+ calc. 390.0604, obs. 390.0594; m/e = 392 (18%), 390 (100, M^+), 357 (1), 313 (1), 195 (1, M^{2+}), 181 (1); ^{1}H-NMR (CS_2): δ = 1.5—1.9 (m, 8H), 2.35—2.75 (m, 8H), 5.93 (s, 2H), 6.96 (s, 4H); space group C2/c, a = 1812(1), b = 913.7(5), c = 2358(2) pm, β = 100.2(1)°, Z = 8; R = 0.06; *C. Krieger, J. Ippen, H. A. Staab*, unpublished results.
[11] *D. J. Cram, H. U. Daeniker*, J. Am. Chem. Soc. *76*, 2743 (1954).

[2.2]- and [3.3]Tetrathiafulvalenophanes[1]

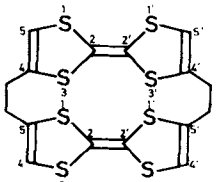
By *Joachim Ippen, Chu Tao-pen, Barbara Starker, Dieter Schweitzer*, and *Heinz A. Staab*[*]

In order to systematically vary the crystal lattice in charge transfer systems which could be of interest as electrical semiconductors or conductors by changing the molecular architecture[1], we synthesized [2.2]- and [3.3]tetrathiafulvalenophanes ("TTF-phanes"). For these compounds the following structural and stereo-isomers are possible: 1) "paracyclophane-like" compounds with diagonal 4',4'- and 5,5-linkage, which may exist as an achiral stereoisomer with approximately parallel TTF "axes" and all corresponding C- and S-atoms of the two TTF groups [*(1)* and *(3)*, respectively] in the eclipsed position as well as a chiral stereoisomer with crossed TTF axes which formally is derived from *(1)* and *(3)*, respectively, by 180° rotation of one of the TTF units about the axis through the C-4'/C-5 points of linkage; 2) "metacyclophane-like" compounds with 4,5- and 4',5'-linkage [*(2)* and *(4)*, respectively], whose TTF groups, as in the metacyclophanes, could be in a step-like *anti*-conformation and—less likely—in a *syn*-arrangement; 3) finally, TTF-phanes in which one TTF group is linked metacyclophane-like, the other paracyclophane-like (4,5-/4',4'-linkage). In the synthetic method employed by us, in which the central C=C double bonds of the TTF groups were formed in the last step[1], in principle, all the structural and stereo-isomers could be formed. Although only a few of them have so far been isolated in pure form and unequivocally characterized, we should like to report some preliminary results even at this stage since representatives of this type of compounds in combination with tetracyanoquinodimethane (TCNQ) show interesting properties.

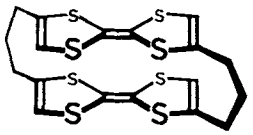
[*] Prof. Dr. H. A. Staab, Dr. J. Ippen, Chu Tao-pen, B. Starker
Abteilung Organische Chemie,
Dr. D. Schweitzer
Abteilung Molekulare Physik,
Max-Planck-Institut für medizinische Forschung
Jahnstrasse 29, D-6900 Heidelberg 1 (Germany)



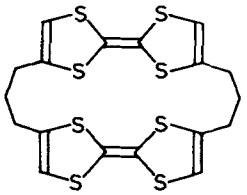
(1)



(2)

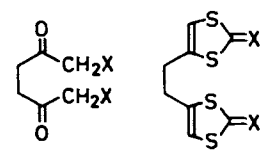


(3)



(4)

For the synthesis of the [2.2]tetrathiafulvalenophanes *(1)/(2)*, 1,6-bisdiazo-2,5-hexanedione was converted, in analogy to the method given in [2], into 1,6-dichloro-2,5-hexanedione *(5)*[3] (m.p. 87—88 °C; 23%), which on reaction with potassium *O*-isopropyldithiocarbonate (acetone, 20 °C, 3 h) gave the bis(*O*-isopropyldithiocarbonate) *(6)*[3] (m.p. 82—83 °C; 84%). Cyclization of *(6)* with conc. sulfuric acid afforded 4,4′-ethylenedi(1,3-dithiol-2-one) *(7)*[3] (m.p. 135—136 °C; 87%). On boiling with phosphorus(v) sulfide (xylene, 6 h, 140 °C), *(7)* was converted into the bis(thione) *(8)*[3] (m.p. 172—174 °C; 80%). *(8)* was methylated with methyl iodide

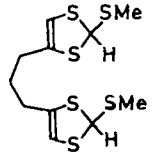


(5), X = Cl
(6), X = S-CS-OiPr

(7), X = O
(8), X = S



(9)



(10)

(nitromethane, 2.5 h, 50 °C) and the crude product was reduced with sodium tetrahydridoborate (tetrahydrofuran/methanol, −78 °C; overall yield 27—40%) to the bis(methylthio) derivative *(9)*[3]. Analogously to the synthesis of tetrathiafulvalenoparacyclophane, the bis(thiolium ion) was then prepared from *(9)* by reaction with tetrafluoroboric acid in acetic anhydride. On dropwise addition of its solution in acetonitrile to a solution of triethylamine in acetonitrile under argon the bis(thiolium ion) underwent dimerization and cyclization to [2.2]tetrathiafulvalenophane.

After removal of oligomeric and polymeric reaction products, fractional crystallization from carbon disulfide afforded *(2)*[3] as yellow, cubic crystals (dec. >210 °C) in 10—15% yield. Besides *(2)*, an isomer [presumably *(1)*] could also be enriched, but not completely purified. The mass spectra essentially agree with those of *(2)*[4].

The structure of *(2)* is confirmed by X-ray structure analysis[4]. The molecule has the step-like *anti*-conformation. As in the case of [3]tetrathiafulvaleno[3]paracyclophane[1] the TTF units deviate considerably from a planar arrangement: The S(1)···C(5)···C(4)···S(3) planes in all five-membered rings of *(2)* are bent at an angle of 20° to the planes through the four sulfur atoms and central double bond of the two TTF units.

The [3.3]tetrathiafulvalenophanes *(3)/(4)* were synthesized analogously to *(1)/(2)* *via* the homologs of *(5)*[2], *(6)*[3] (m.p. 98—100 °C; 74%), *(7)*[3] (63—64 °C; 93%) and *(8)*[3] (m.p. 101—102 °C; 52%). Methylation of the bis(dithiolthione) analogous to *(8)* with methyl iodide in nitromethane and subsequent reduction of the almost quantitatively formed methylation product with sodium tetrahydridoborate (tetrahydrofuran/methanol, −78 °C) afforded 4,4′-trimethylenedi(2-methylthio-1,3-dithiol) *(10)*[3] (yellow oil; 77%). Like *(9)*, *(10)* can undergo dimerizing cyclization. Oligomers and polymers can be removed by extraction with carbon disulfide. After evaporating *in vacuo* (9% yield) the extract consisted essentially of one isomer[6], which, however, has not yet been obtained free from isomers.

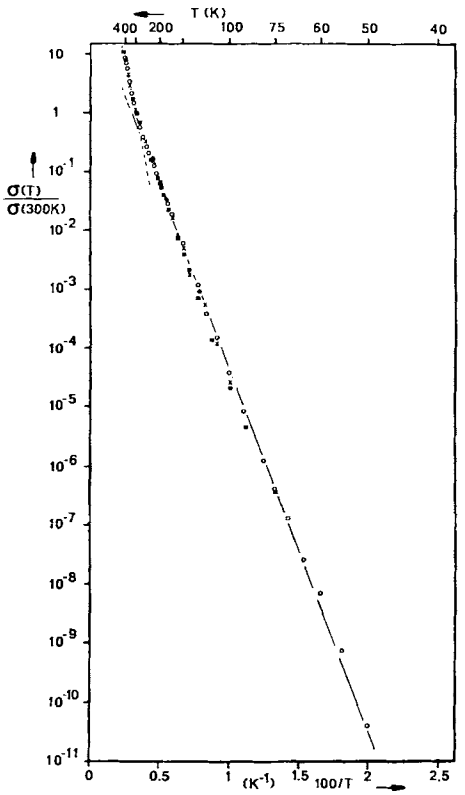


Fig. 1. Conductivities $\sigma(T)/\sigma(300\ K)$ of four single crystals of the 1:4 complex of [3.3]tetrathiafulvalenophane and TCNQ as a function of temperature. σ (300 K) of the four single crystals ▪ 5×10^{-3}, * 5.3×10^{-3}, ▲ 6×10^{-3}, ○ 7.5×10^{-3} [Ω cm]$^{-1}$.

Treatment of the [3.3]tetrathiafulvalenophane obtained with tetracyanoquinodimethane (TCNQ) in carbon disulfide/acetonitrile (room temperature, under argon, exclusion of light) afforded black-needles of a complex, which, according to elemental analysis, has the composition [3.3]tetrathiafulvalenophane/TCNQ = 1:4. The following crystallographic data were determined on a single crystal (0.4 × 0.1 × 0.08 mm) of this complex[5]: triclinic, space group $P\bar{1}$, $a=780$, $b=1393$, $c=2873$ pm, $\alpha=92.9$, $\beta=88.9$ and $\gamma=91.9°$; $\rho_{calc}=1.39\ g\cdot cm^{-3}$; a structure elucidation has not yet been completed. Conductivity measurements (4-contact measurements) on single crystals of this complex showed conductivities between 5×10^{-3} and 10^{-2} $[\Omega\ cm]^{-1}$ along the long axis of the needles at 300 K. Figure 1 shows for four different single crystals the excellent reproducibility of the conductivities measured and their temperature-dependence. Between 40 and 400 K, σ varies by more than ten orders of magnitude. Pellets of the complex (diameter 2.5 mm, thickness 0.5—1.0 mm) show a conductivity very similar to that of the single crystals at room temperature, with $\sigma=6\times10^{-3}$ $[\Omega\ cm]^{-1}$.

Received: August 13, 1979 [Z 361 b IE]
German version: Angew. Chem. 92, 51 (1980)

[1] Electron Donor-Acceptor Compounds, Part 26.—Part 25: *H. A. Staab, J. Ippen, T. Chu, C. Krieger, B. Starker*, Angew. Chem. *92*, 49 (1980); Angew. Chem. Int. Ed. Engl. *19*, 66 (1980).

[2] *E. Fahr*, Justus Liebigs Ann. Chem. *638*, 1 (1960).

[3] These compounds gave correct elemental analyses and characteristic spectra.

[4] M^+ calc. 459.8705, obs. 459.8708; MS: $m/e = 462$ (35, $(M+2)^+$), 460 (100, M^+), 230 (20, M^{2+}); cf. *(2)*: 462 (36, $(M+2)^+$), 460 (100, M^+), 230 (19, M^{2+}). *(2)*, space group $P2_1/c$, $a = 1001.3(2)$, $b = 973.1(2)$, $c = 1118.5(2)$ pm, $\beta = 121.00(3)$, $Z = 2$, 1383 observed reflections, $R = 0.043$) [5].

[5] *C. Krieger*, unpublished results.

[6] $m/e = 490$ (36, $(M+2)^+$), 488 (100, M^+), 244 (16, M^{2+}); ^{1}H-NMR (80 MHz, CD_2Cl_2/CS_2): $\delta = 5.88$ (s, 4H), 2.25—2.80 (m, 12H).

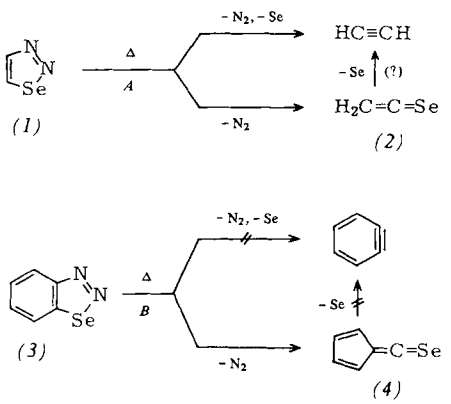
6-Fulveneselone[**]

By *Reinhard Schulz* and *Armin Schweig*[*]

Dedicated to Professor Hans Kuhn on the occasion of his 60th birthday

On heating, cycloalkeno-1,2,3-selenadiazoles are converted into cycloalkynes[1]. 1,2,3-Selenadiazole *(1)*[2] can be transformed photochemically[3] (in matrix) and thermally[4] (in the gas phase) into the reactive selenoketene *(2)*. We have now been able to generate for the first time the highly reactive 6-fulveneselone *(4)* from 1,2,3-benzoselenadiazole *(3)*[6] in the gas phase by variable temperature photoelectron spectroscopy and flash vacuum thermolysis (VTPES[5a] and FVT[5b], respectively).

The decomposition reactions A and B take place in the reactor of the spectrometer at *ca.* 5×10^{-2} mbar between *ca.* 450 °C (start of reaction) and *ca.* 700 °C (completion of reaction). In the temperature range investigated acetylene in reaction A is always formed together with *(2)*, while at



800 °C it is the sole product. Dehydrobenzene is not observed in reaction B, even at 800 °C. From these experiments it cannot be decided whether acetylene is formed by direct fragmentation of *(1)* or *via (2)*, or in both ways concurrently. Figure 1 shows the PE spectra of the reactants *(1)* and *(3)* as well as those of the products *(2)* and acetylene and of *(4)*.

The PE spectra of *(1)* to *(4)* very closely resemble those of the corresponding sulfur compounds (1,2,3-thiadiazole[7a], thioketene[7b], 1,2,3-benzothiadiazole[7c] and 6-fulvenethione[7d], respectively). A comparison of the respective PE spectra and of the HeI and HeII spectra[8] provided a basis for the identification of *(2)* and *(4)* and for the following

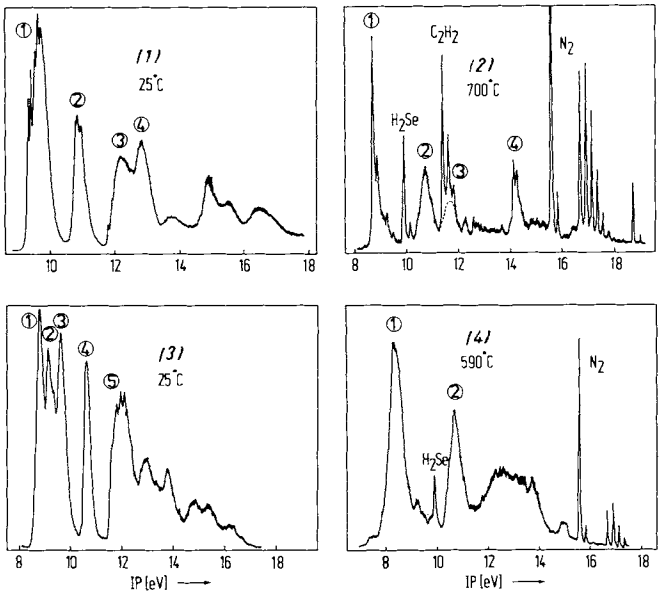


Fig. 1. HeI photoelectron spectra of 1,2,3-selenadiazole *(1)*, selenoketene *(2)* (band ③ is superposed by the $^2\Pi_u$ band of acetylene), 1,2,3-benzoselenadiazole *(3)*, and 6-fulveneselone *(4)*.

band assignments (band positions in eV): *(1)* ① 9.69 $^2A''(\pi)$, $^2A'(\sigma_N)$, ② 10.88 $^2A''(\pi)$, ③ 12.25 $^2A'(\sigma)$, ④ 12.88 $^2A'(\sigma)$; *(2)* ① 8.72 (1300 cm^{-1}) $^2B_1(\pi)$, ② 10.75 $^2B_2(\pi)$, ③ *ca.* 11.6 $^2B_1(\pi)$, ④ 14.15 (950 cm^{-1}) $^2A_1(\sigma)$; *(3)* ① 8.83 $^2A''(\pi)$, ② 9.16 $^2A'(\sigma_N)$, ③ 9.65 $^2A''(\pi)$, ④ 10.66 $^2A''(\pi)$, ⑤ 11.99 $^2A'(\sigma)$ and *(4)* ① 8.34 $^2B_1(\pi)$, $^2A_2(\pi)$, ② 10.76 $^2B_2(\pi)$. Further evidence for the identity of *(4)* can be obtained from Figure 2.

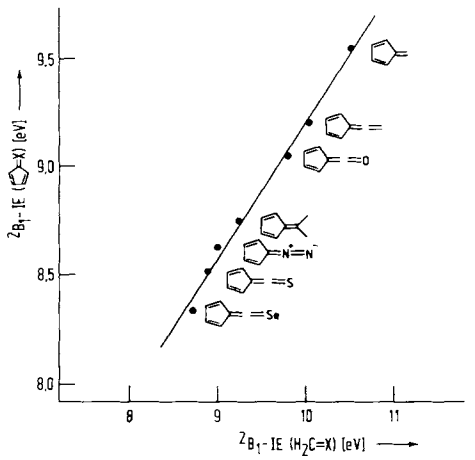


Fig. 2. $^2B_1$ ionization energies (*IE*) of fulvene-like molecules as a function of the $^2B_1$ ionization energy of the respective $H_2C{=}X$ system [fitted line: *IE* (fulvene analog) $= 2.93 \pm 0.25$ eV $+ 0.63 \pm 0.03$ *IE*($H_2C{=}X$); for the LCMO model cf. *E. Heilbronner, H.-D. Martin*, Chem. Ber. *106*, 3376 (1973)]. The measured ionization energy of *(4)* and the value expected from this expression are in good agreement.

6-Fulveneselone *(4)* can be briefly observed as a red deposit on the cold-finger (−196 °C) of a FVT apparatus (600 °C/5×10^{-3} mbar). On growth of a thicker layer, *(4)* reacts spontaneously (explosively) to give a brown polymer. Under conditions which facilitate trapping of *(2)* with dimethylamine[4] no identifiable trapping product of *(4)* could be obtained[9].

Received: August 20, 1979 [Z 365 IE]
German version: Angew. Chem. *92*, 52 (1980)

[*] Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Straße, D-3550 Marburg 1 (Germany)

[**] Theory and Application of Photoelectron Spectroscopy, Part 85. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 84: *J. Kreile, A. Schweig*, Chem. Phys. Lett., in press.

[1] *H. Meier, E. Voigt*, Tetrahedron *28*, 187 (1972).
[2] *I. Lalezari, A. Shafiee, M. Yalpani*, J. Org. Chem. *36*, 2836 (1971).
[3] *J. Laureni, A. Krantz, R. A. Hajdu*, J. Am. Chem. Soc. *98*, 7872 (1976).
[4] *A. Holm, C. Berg, C. Bjerre, B. Bak, H. Svanholt*, J. Chem. Soc. Chem. Commun. *1979*, 99.
[5] a) *V. Eck, C. Müller, R. Schulz, A. Schweig, H. Vermeer*, J. Electron Spectrosc. Relat. Phenom. *17*, 67 (1979), and references cited therein; b) *G. Seybold*, Angew. Chem. *89*, 377 (1977); Angew. Chem. Int. Ed. Engl. *16*, 365 (1977).
[6] *S. Keimatsu, I. Satoda*, J. Pharm. Soc. Jpn. (Yakugaku Zasshi) *55*, 233 (1935).
[7] a) *M. H. Palmer, R. H. Findlay, J. Neil, A. Ridyard, A. Barrie, P. Swift*, J. Mol. Struct. *39*, 189 (1977); b) *P. Rosmus, B. Solouki, H. Bock*, Chem. Phys. *22*, 453 (1977); c) *R. A. W. Johnstone, F. A. Mellon*, J. Chem. Soc. Faraday Trans. II, 1155 (1973); *M. H. Palmer, S. M. F. Kennedy*, J. Mol. Struct. *43*, 203 (1978); d) *R. Schulz, A. Schweig*, Tetrahedron Lett. *1979*, 59.
[8] *P. Dechant, A. Schweig, W. Thiel*, Angew. Chem. *85*, 358 (1973); Angew. Chem. Int. Ed. Engl. *12*, 308 (1973).
[9] Also the trapping product of 6-fulvenethione has not been isolated in pure form.

μ-Alkylthio- and μ-Arylthio-μ-chlorodicarbonylbis(tri-*tert*-butylphosphane)dirhodium: Dinuclear Rhodium Complexes with Different Bridging Ligands[**]

By *Herbert Schumann, Guy Cielusek,* and *Joachim Pickardt*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

Carbonylrhodium complexes having sulfur bridges can be readily prepared in good yield by reaction of tetracarbonyldi-μ-chlorodirhodium with alkali metal thiolates[1]. Both chlorine bridges are always replaced by sulfur bridges, irrespective of the ratio of the reactants; the latter bridges are more stable towards bridge-breaking nucleophilic ligands[2]. Complexes having one chlorine and one sulfur bridge have so far only been suggested[3] or assumed[4] on the basis of IR spectroscopy as intermediates in exchange reactions.

We have now found that such complexes *(3)* are formed as stable yellow crystals on cleavage of the complex dicarbonyldi-μ-chlorobis(tri-*tert*-butylphosphane)dirhodium *(1)* by alkyl- and aryl-trimethylsilylsulfanes *(2)*.

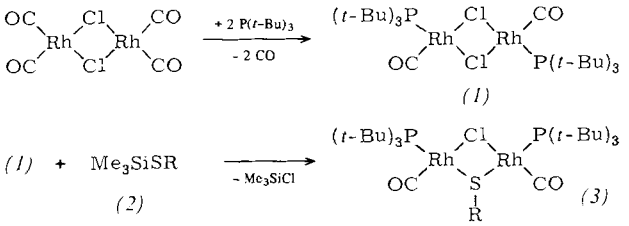


Table 1. NMR spectroscopic data of complexes *(3)* (δ values, ^{1}H-NMR: TMS int.; ^{31}P-NMR: 85% H_3PO_4 ext.; *J* in Hz).

Cpd.	R	δ(*t*-Bu)	^3J(HP)	δ(P)	^1J(PRh)
(3a)	*i*-Pr	1.55 (d)	12	91.2 (d)	143.9
(3b)	*n*-Bu	1.54 (d)	11.8	92.4 (d)	143.9
(3c)	*t*-Bu	1.41 (d)	11.7	89.4 (d)	142
(3d)	Ph	1.44 (d)	11.8	94.8 (d)	148.8
				94.8 (d)	154.9
(3e)	*p*-$CH_3C_6H_4$	1.53 (d)	12	93.8 (d)	148.2
				93.8 (d)	154.9
(3f)	*p*-ClC_6H_4	1.50 (d)	12	94.4 (d)	147.9
				94.4 (d)	153.1

[*] Prof. Dr. H. Schumann, Dipl.-Chem. G. Cielusek,
Priv.-Doz. Dr. J. Pickardt
Institut für Anorganische und Analytische Chemie der Technischen Universität Berlin
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

X-Ray structure analysis (Fig. 1) of the *tert*-butylthio derivative *(3c)* shows that each phosphane ligand is bonded to rhodium in *trans* position relative to the sulfur atom. Thus *(3c)* has a *cis* configuration. Transformation of the *trans* configuration of *(1)* into the *cis* configuration of *(3c)* is attributable to the steric influence of the *tert*-butyl group on the sulfur. We had already deduced from IR and NMR data that such a transformation occurs for steric reasons in corresponding reactions of *(1)* with trimethylsilyldi-*tert*-butylphosphane[5].

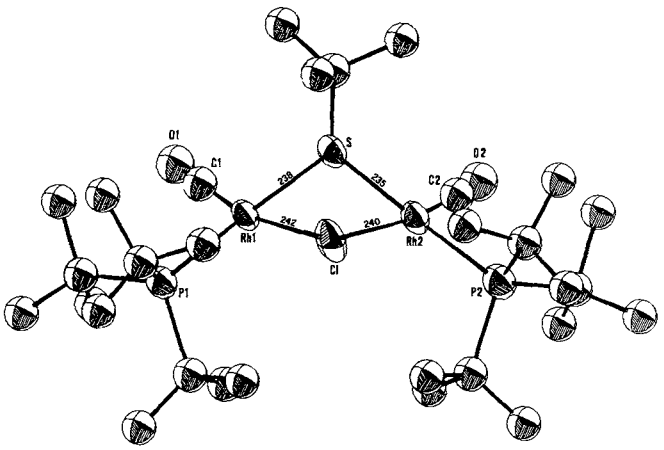


Fig. 1. Structure of $P(t\text{-}Bu)_3(CO)Rh(\mu\text{-}Cl)(\mu\text{-}S\text{-}t\text{-}Bu)Rh(CO)P(t\text{-}Bu)_3$ *(3c)*. Crystal data: orthorhombic, space group Pbca, $Z=8$; $a=2735.6(8)$, $b=1771.1(5)$, $c=1534.7(5)$ pm, $V=7.424\times10^9$ pm^3, $\rho_{calc.}=1.62$, $\rho_{exp.}=1.5$ g/cm^3; 1509 independent reflections: Syntex $P2_1$ four-circle diffractometer, $R_1=0.065$.

In the IR spectrum of *(3c)* (Nujol suspension), the equal-intensity νCO bands of the two *cis* carbonyl groups are observed at 1963 and 1954 cm^{-1}. Field desorption mass spectrometry gives the molecular ion $m/e=790$ as strongest peak. A sharp singlet at $\delta=2.08$ in the ^{1}H-NMR spectrum (benzene, rel. to int. TMS) is assigned to the protons of the *S-tert*-butyl group, and a doublet at $\delta=1.41$ with $^3J(HP)=11.7$ Hz to those of the tri-*tert*-butylphosphane ligands. The proton-decoupled ^{31}P-NMR spectrum contains a doublet at $\delta=89.4$ (C_6D_6, rel. to 85% H_3PO_4) with $^1J(PRh)=142$ Hz for the two equivalent phosphorus atoms. While the NMR spectra of *(3a)* and *(3b)* exhibit only slightly different parameters, the ^{31}P-NMR spectra of *(3d)*, *(3e)*, and *(3f)* show a second doublet of almost half intensity at the same chemical shift but with slightly different coupling constant (Table 1), suggesting two isomers with axial and equatorial substituents R[3].

Complexes *(3)* are excellent hydrogenation, decarbonylation, and isomerization catalysts. They prove highly active in conversion of 1-decen-3-ol into the ketone, in hydrogenation of cyclohexene, in decarbonylation of benzaldehyde, and in isomerization of allylbenzene and allyl alcohols. Thus 1-octen-3-ol could be isomerized almost quantitatively into 3-octanone in the presence of *(3b)*[6].

Procedure

All operations were performed under argon in oxygen- and water-free solvents. Tri-*tert*-butylphosphane (300 mg, 1.48 mmol) is added to tetracarbonyldi-μ-chlorodirhodium (300 mg, 0.77 mmol) in pentane (10 ml). After evolution of CO a clear solution is obtained which is stirred for 5 h at room temperature. *(2c)* (125 mg, 0.77 mmol) is then added slowly, and a yellow precipitate of *(3c)* appears immediately which is collected on a glass frit. A further crop of *(3c)* crys-

tallizes from the mother liquor within 48 h; yield 340 mg (56%), dec. 90 °C.

Received: May 28, 1979;
supplemented: September 14, 1979 [Z 367 IE]
German version: Angew. Chem. 92, 60 (1980)

[1] E. S. Bolton, R. Havlin, G. R. Knox, J. Organomet. Chem. 18, 153 (1969).
[2] P. Kalck, R. Poilblanc, Inorg. Chem. 14, 2779 (1975).
[3] G. Palyi, A. Vizi-Orosz, L. Marko, F. Marcati, G. Bor, J. Organomet. Chem. 66, 295 (1974).
[4] L. D. Rollman, Inorg. Chim. Acta 6, 137 (1972).
[5] H. Schumann, M. Heisler, Chem. Ber. 112, 541 (1979).
[6] J. Blum, G. Cielusek, A. Zoran, H. Schumann, to be published.

Synthesis and Reactions of Diorganophosphinite Complexes of Gold

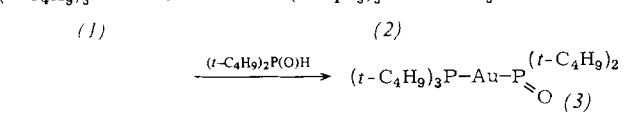
By *Hubert Schmidbaur* and *Aref A. M. Aly*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

The complexing properties of diorganophosphinite ions $[R_2(O)P:]^{\ominus}$ and the reactions of these species in complexes have hardly been examined, although the excellent donor properties of phosphorus are but little impaired by the oxygen atom[1]. The O atom is frequently also coordinated as well as the P atom, leading to bridge formation[2], and thus gold(I) dialkylphosphinites $[R_2(O)PAu]_3$[3], e.g., form trimers having a nine-membered ring.

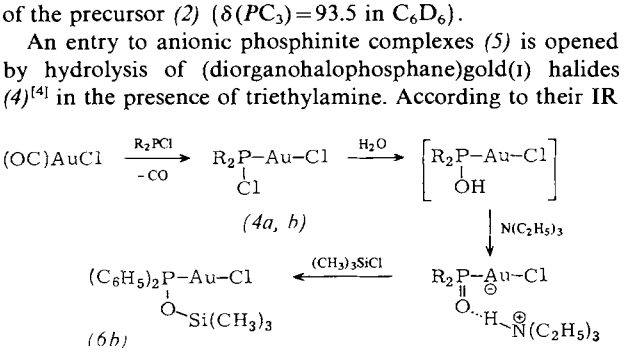
We have now discovered further specific modes of reaction of the diorganophosphinite group in gold complexes.

Methylation of (phosphane)gold(I) chloride *(1)*[4] to give *(2)* and its subsequent reaction with $(t\text{-}C_4H_9)_2P(O)H$ by several hours' refluxing in benzene readily affords (phosphane)gold(I) phosphinite *(3)* in high yield.



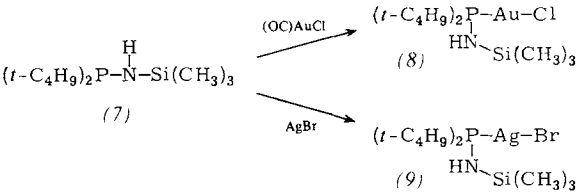
Compound *(3)* forms air- and moisture-stable crystals shown by DTA not to decompose at their melting point (356 °C). The linear PAuP structure unit leads to a high coupling constant of $J(PP) = 308$ Hz in the ^{31}P-NMR spectrum ($\delta(PC_3) = 93.3$, $\delta(PO) = 124.1$, AX, in C_6D_6). In the IR spectrum $\nu(P{=}O) = 1090$ cm^{-1} reveals an uncoordinated PO function. The observation of a PAuC coupling ($^2J(PAuC) = 89$ Hz) was possible in the ^{13}C-NMR spectrum of the precursor *(2)* ($\delta(PC_3) = 93.5$ in C_6D_6).

An entry to anionic phosphinite complexes *(5)* is opened by hydrolysis of (diorganohalophosphane)gold(I) halides *(4)*[4] in the presence of triethylamine. According to their IR spectra, the thermally stable, salt-like products *(5)* contain hydrogen bonds in the solid state and in solution. In the ^{1}H-NMR spectrum ($CDCl_3$), $\delta(CH_3P)$ is shifted upfield by 0.65 ppm on going from *(4a)* to *(5a)* while $J(PH)$ remains unchanged. Conservation of the AuCl group is established by IR absorption bands at 301/310 *(4a)* and 312/320 cm^{-1} *(5a)*.—Compound *(4)*, R = t-C_4H_9, does not hydrolyze.



(a), R = CH_3; *(b)*, R = C_6H_5

Several hours' refluxing with $(CH_3)_3SiCl$ in benzene transforms the complex *(5b)* into the siloxyphosphane complex *(6b)*. Compound *(6b)* is thermally stable; its IR absorption at 1020 cm^{-1} indicates the presence of a POSi bridge; $\nu(AuCl) = 330/335$ cm^{-1}.



The analogous silylaminophosphane complex *(8)* and the silver derivative *(9)* are directly accessible from (OC)AuCl and AgBr, respectively, and the ligand *(7)*[5] in benzene. The sharp IR bands at 3260 and 3340 cm^{-1} observed for *(8)* and *(9)* rule out hydrogen bonding. Table 1 lists selected physical data of the compounds synthesized.

Table 1. Some physical data of the compounds synthesized. Coupling constants J in Hz.

(2), m.p. 194 °C; yield 60%; IR: 535, RE: 535 cm^{-1}, ν(AuC); ^{1}H-NMR ($CDCl_3$): $\delta = 0.23$ (d, CH_3Au, $^3J(PH) = 7$), 1.50 (d, CH_3C, $^3J(PH) = 13$); ^{13}C-NMR ($CDCl_3$): 8.01 (d, CH_3Au, $^2J(PC) = 89$), 32.31 (d, CH_3C, $^2J(PC) = 5$), 38.52 (d, CP, $^1J(PC) = 12$)
(3), m.p. 356 °C (toluene); yield 80%, ^{1}H-NMR (C_6D_6): $\delta = 0.58$ (d, 27H, $^3J(PH) = 12$), 1.03 (d, 18H, $^3J(PH) = 13$)
(4a), m.p. 125 °C (dec.); IR: 520, ν(PCl), 380 cm^{-1}, ν(AuP); ^{1}H-NMR ($CDCl_3$): $\delta = 2.3$ (d, $^2J(PH) = 10$)
(4b), m.p. 177 °C (dec.); IR: 550, ν(PCl), 370 cm^{-1}, ν(AuP)
(5a), m.p. 189 °C (dec.); yield 75%; ^{1}H-NMR ($CDCl_3$): $\delta = 1.66$ (d, CH_3P, $^2J(PH) = 10$), IR: 1001, ν(PO), 2620 cm^{-1}, ν(NH) (broad)
(5b), m.p. 144 °C (dec.); yield 70%; IR: 2260 cm^{-1}, ν(NH) (broad)
(6b), m.p. 208 °C (benzene/pentane); ^{1}H-NMR ($CDCl_3$): $\delta = 0.43$ (CH_3Si)
(8), m.p. 289 °C; yield 95%; ^{1}H-NMR ($CDCl_3$): $\delta = 0.26$ (s, CH_3Si), 1.20 (d, CH_3C, $^3J(PH) = 16$); ^{13}C-NMR ($CDCl_3$): $\delta = 2.13$ (d, CH_3Si, $^3J(PC) = 2$), 28.83 (d, CH_3C, $^2J(PC) = 29$), 37.29 (d, $^1J(PC) = 33$); ^{31}P-NMR ($CDCl_3$): $\delta = 89.1$
(9), m.p. 192 °C; yield 70%; ^{31}P-NMR: $\delta = 69$ ($^1J(^{109}Ag^{31}P) = 686.6$)

Procedure

(2): Compound *(1)* (0.85 g, 2 mmol) is metalated in diethyl ether at −50 °C with a slight excess of CH_3Li. After warming to room temperature, the reaction mixture is stirred for 15 h and hydrolyzed at −50 °C. *(2)* is obtained from the ethereal phase.

(4): On addition of an equimolar amount of R_2PCl, benzene solutions of (OC)AuCl immediately evolve CO; pure *(4)* can be isolated in quantitative yield from the reaction solution.

(5a, b): Solutions of *(4a)* in acetone/CH_2Cl_2 or of *(4b)* in acetone/dioxane are treated with $(C_2H_5)_3N$ and the product carefully hydrolyzed with a stoichiometric amount of H_2O. Compound *(5a)* is formed as an oil which can be crystallized from $CHCl_3$/pentane, while *(5b)* precipitates in crystalline form.

[*] Prof. Dr. H. Schmidbaur, A. A. M. Aly (M. A.)
Anorg.-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

Received: June 1, 1979 [Z 370 IE]
German version: Angew. Chem. 92, 66 (1980)
Publication delayed at authors' request

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0101-0071 $ 02.50/0

CAS Registry numbers:
(1), 69550-28-3; *(2)*, 72428-68-3; *(3)*, 72428-69-4; *(4a)*, 72428-70-7; *(4b)*, 72428-71-8; *(5a)*, 72428-73-0; *(5b)*, 72428-75-2; *(6b)*, 72428-76-3; *(7)*, 17858-29-6; *(8)*, 72428-77-4; *(9)*, 72428-78-5

[1] Surveys: *D. M. Roundhill, R. P. Sperline, W. B. Beaulieu*, Coord. Chem. Rev. *26*, 263 (1978); *F. E. Nifant'ev*, Russ. Chem. Rev. *1978*, 835; Usp. Khim. *1978*, 1565.

[2] This tendency is even more pronounced in the thiophosphinites $[R_2(S)P:]^{\ominus}$: *E. Lindner, B. Schilling*, Chem. Ber. *110*, 3889 (1977) and earlier work.

[3] *H. Schmidbaur, A. A. M. Aly, U. Schubert*, Angew. Chem. *90*, 905 (1978); Angew. Chem. Int. Ed. Engl. *17*, 846 (1978).

[4] *H. Schmidbaur, A. A. M. Aly*, Z. Naturforsch. *B 34*, 23 (1979).

[5] *O. J. Scherer, G. Schieder*, Angew. Chem. *80*, 83 (1968); Angew. Chem. Int. Ed. Engl. *7*, 75 (1968).

Activation and Sulfur-Atom Transfer Reaction of Cluster-Bonded S_2^{2-}-Bridge Ligands: Synthesis of the New Cluster $[Mo_3^{IV}S_4(CN)_9]^{5-}$ from $[Mo_3^{IV}S(S_2)_6]^{2-}$ and CN^-

By *Achim Müller* and *Uta Reinsch*[*]

Reactions of complex- or cluster-bonded activated ligands are of topical interest in view of their bio-inorganic and catalytic relevance. Very little is known about reactions of S_2^{2-} ligands. Especially interesting is the fact that "labile sulfur" is removed from the Mo-containing enzyme xanthine-oxidase on addition of CN^-, resulting in deactivation of the enzyme function and formation of NCS^-[1]; the following reaction types have been postulated[1b]:

$$Mo^m\text{—}(S_2^{2-}) + CN^- \rightarrow Mo^m\text{—}(S^{2-}) + SCN^- \quad (I)$$

(atom transfer without reduction of the Mo center)

and

$$Mo^m\text{—}(S^{2-}) + CN^- \rightarrow Mo^{m-2} + SCN^- \quad (II)$$

(atom transfer with reduction of the Mo center)[2]

We report here on the first model reaction of type I: In H_2O, $[Mo_3S(S_2)_6]^{2-}$ *(1)*[3] undergoes nucleophilic attack by CN^- at the three S_2^{2-} bridge ligands, which cleave with quantitative formation of the new cluster[4] $[Mo_3S_4(CN)_9]^{5-}$ *(2)*. On addition of ethanol to the aqueous solution, dark-green crystalline $K_5[Mo_3S_4(CN)_9]\cdot n\,KCN\cdot m\,H_2O$ *(3)* is precipitated, which is diamagnetic and extremely soluble in water. The salt $K_5[Mo_3S_4(CN)_9]\cdot 3\,KCN\cdot 4\,H_2O$ *(4)* was characterized, not only by elemental analysis, TG and magnetic measurements, and IR, UV/VIS, and ESCA spectra, but also by a complete crystal structure analysis[5].

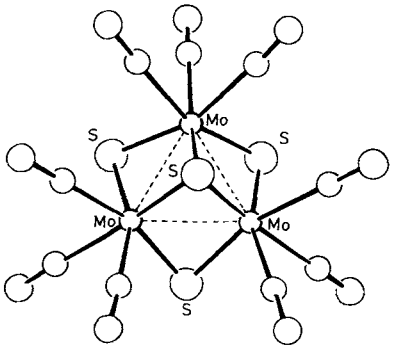


Fig. 1. Structure of the anion *(2)* in crystals of *(4)*.

[*] Prof. Dr. A. Müller, Dipl.-Chem. U. Reinsch
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)

In the IR spectrum (solid, Nujol) the bands of greatest intensity (with exception of the H_2O bands) lie at 2118 [ν_{as}(CN· –E)], 367 and 337 cm^{-1} [ν(MoSMo)]; the bands in the ν(CN) region indicate high symmetry of the anion *(2)* (ideal symmetry C_{3v}; site symmetry, however, C_s). In the trinuclear cluster (Mo—Mo 2.773 Å) each Mo atom is surrounded by a distorted octahedral array of three CN^- groups and three S atoms (Fig. 1). The central $\{Mo_3S_4\}$-skeleton may be regarded as an incomplete, distorted cube[6] (comparable with the $\{Fe_3MoS_4\}$-cage in the model system of nitrogenase[7]), in which the incorporation of a $FeSR^+$ would be interesting.

From the vibration frequencies and SS distances of *(1)* it follows that the S_2^{2-} bridges in the educt are activated for attack (low population of the π_v^* level through reduced electron density) by nucleophiles such as CN^-[3,8]. Remarkably, the oxidation number of the molybdenum is not altered by an atom transfer of *neutral sulfur* from S_2^{2-} (experimental evidence for the presence of a S_2^{2-} ligand and not S_2 has frequently been discussed![8]).

A reaction of Type II, with reduction of the molybdenum, was first observed in the synthesis of $[(CN)_6MoS\text{-}Mo(CN)_6]^{6-}$[9]. The mechanism of the "formal exchange" of each of the three terminal S_2^{2-} ligands by three CN^- in the conversion into *(2)* is still unclear. During the reaction, the coordination of the Mo center changes (octahedral → pseudotetrahedral) and consequently a different number of d-functions is available for bonding in the Mo_3-unit of product and reactant [*(2)*: d_{xy}, d_{xz}, d_{yz}; MOs: $(1a_1)^2(1e)^4$, $2a_1$, $(2e)^*$, $(3e)^*$, $(1a_2)^*$.—*(1)*: $d_{x^2-y^2}$, d_{z^2}; MOs: $(1a_1)^2(1e)^4$, $(a_2)^*$, $(2e)^*$]. As a result of the different density in the MO state in the Mo_3-cluster, the LUMO a_2 in *(1)* is strongly antibonding, while the corresponding MO $2a_1$ in *(2)* is weakly bonding. This explains the different influence of the Mo_3 units on the optical, electrochemical and chemical properties of *(1)* and *(2)*. Thus, in contrast to *(1)*, compound *(2)* should undergo reversible reduction.

Experimental

On addition of KCN (5 g) to an aqueous suspension (20 ml) of $(NH_4)_2[Mo_3S_{13}]$[3] (0.5 g), a deep-green solution of $[Mo_3S_4(CN)_9]^{5-}$ is obtained. (The isolation of solid *(3)* and separation of the "by-product" KSCN and excess KCN is complicated owing to high solubility.) After 1 h, the mixture is filtered and ethanol is added to the filtrate until clouding occurs (precipitation of a colorless substance). After filtration of the precipitate the process is repeated. The filtrate is then treated with 2—5 ml ethanol, and no more turbidity should occur. After several hours have elapsed, the precipitated needle-shaped, dark-green crystals of *(3)* are washed with ethanol, ether, and *n*-pentane and dried over P_4O_{10} (yield *ca.* 70%).

Received: August 21, 1979 [Z 373 IE]
German version: Angew. Chem. *92*, 69 (1980)

[1] Cf. a) *E. I. Stiefel*, Prog. Inorg. Chem. *22*, 1 (1977); b) *R. J. P. Williams*: The Biological Role of Molybdenum. Climax Molybdenum, London 1978; and references cited therein.

[2] An alternative reaction course is:

$$Mo^m\text{—}(S^{2-}) + CN^- + H_2O \rightarrow Mo^m\text{—}(O^{2-}) + SCN^- + 2H^+ + 2e^-$$

cf. *W. E. Newton, J. W. McDonald, K. Yamanouchi, J. H. Enemark*, Inorg. Chem. *18*, 1621 (1979).

[3] *A. Müller, S. Sarkar, R. G. Bhattacharyya, S. Pohl, M. Dartmann*, Angew. Chem. *90*, 564 (1978); Angew. Chem. Int. Ed. Engl. *17*, 535 (1978); *A. Müller, S. Pohl, M. Dartmann, J. P. Cohen, J. M. Bennet, R. M. Kirchner*, Z. Naturforsch. *B 34*, 434 (1979) [X-ray structure analysis]; *A. Müller, R. G. Bhattacharyya, B. Pfefferkorn*, Chem. Ber. *112*, 778 (1979) [very simple synthesis].

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0101-0072 $ 02.50/0*

[4] For interesting aspects of the chemistry of electron-deficient trinuclear clusters of the early transition elements see: *A. Bino, F. A. Cotton, Z. Dori*, Inorg. Chem. Acta *33*, L133 (1979); *A. Müller, R. Jostes, F. A. Cotton*, unpublished results.

[5] *(4)* forms monoclinic crystals with $a = 15.661(3)$, $b = 18.807(3)$, $c = 6.552(1)$ Å, $\beta = 116.39(2)°$, space group Cm, $Z = 2$, $\rho_{calc} = 2.14$ g·cm^{-3}; 1985 independent reflections (Syntex $P2_1$ diffractometer, $2\theta_{max} = 54.0°$, $Mo_{K\alpha}$); $R = 3.1\%$.

[6] Cf. *H. Vahrenkamp*, Angew. Chem. *87*, 363 (1975); Angew. Chem. Int. Ed. Engl. *14*, 322 (1975).

[7] *T. E. Wolff, J. M. Berg, C. Warrick, K. O. Hodgson, R. H. Holm, R. B. Frankel*, J. Am. Chem. Soc. *100*, 4630 (1978); *G. Christou, C. D. Garner, F. E. Mabbs, T. J. King*, J. Chem. Soc. Chem. Commun. *1978*, 740.

[8] *A. Müller, W. Jaegermann*, Inorg. Chem. *18*, 2631 (1979).

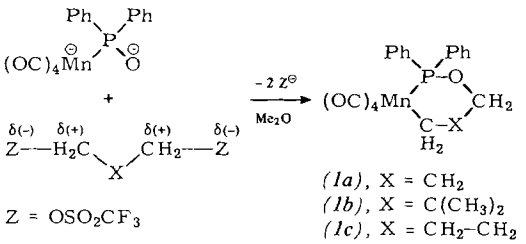
[9] *A. Müller, P. Christophliemk*, Angew. Chem. *81*, 752 (1969); Angew. Chem. Int. Ed. Engl. *8*, 753 (1969); cf. also *M. G. B. Drew, P. C. H. Mitchell, C. F. Pygall, ibid. 88*, 855 (1976) and *15*, 784 (1976), respectively.

Nucleophilic Elimination-Cycloaddition of α,ω-Alkanediyl Bis(triflates), a Novel Method for the Synthesis of Metallacycles with Reactive Metal-Carbon σ Bonds[1]

By *Ekkehard Lindner* and *Hans-Jürgen Eberle*[*]

Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

Heterocycles with metal-carbon σ bonds have recently been the subject of numerous detailed investigations, since they play an important role as intermediates in transition metal catalyzed reactions[2] and in organic syntheses[3]. In the search for new general methods for the synthesis of such compounds having aliphatic ring systems of various sizes we have examined the reaction of dianionic manganese complexes[4] $[(OC)_4Mn(PR_2O)]^{2-}$ with alkane derivatives containing the carbenium ion-stabilizing trifluoromethanesulfonate moiety ("triflate") in the α,ω-position as favorable leaving group.



At 20 °C the variously nucleophilic centers of $[(OC)_4Mn(PPh_2O)]^{2-}$ attack the terminals of the hydrocarbon chain almost simultaneously with elimination of $CF_3SO_3^-$. This pseudosynchronous mechanism hinders β-hydrogen elimination. Owing to the chelate effect, the colorless metallacycles *(1)* are thermally stable; they sublime in a high vacuum and are soluble in all the common organic solvents. They were characterized by complete elemental analysis, IR, mass spectra (Table 1), and ^{1}H-NMR spectra [*e.g. (1a)*, C_6D_6 rel. to TMS: $\delta = 1.04$ (td; $J = 6.4$ Hz, Mn—CH_2—CH_2; $J = 2.1$ Hz, P—Mn—CH_2), 1.92 (m; CH_2—CH_2—CH_2), 3.79 (dt; $J = 15.3$ Hz, P—O—CH_2; $J = 4.7$ Hz, O—CH_2—CH_2)]; *(1a)* was additionally characterized by an X-ray crystal structure analysis[5].

The six-membered ring of *(1a)* has a distorted chair shape with dihedral angles of 130.6 and 164.2°. The Mn3···C4 distance is markedly greater than the sum of the single bond radii. Substantial widening of the tetrahedral angle is indicative of a highly strained ring. The deviation of C6 from the plane formed by C4, C5, O1, P2 effects slight distortion of the tetrahedral angle. The *trans* CO-ligands are bent inwards to the heterocycle (C10···Mn3···C8 164.9(2)°).

The MnC σ bond is extremely reactive. Thus the action of liquid SO_2 or CO on *(1b)* and *(1c)* leads *via* an insertion reaction to the expanded, colorless heterocycles *(2b)* and *(2c)* which are soluble only in polar solvents (cf. Table 1).

We have thus demonstrated the first instance of CO insertion in the M···C bond of a metallacycloalkane.

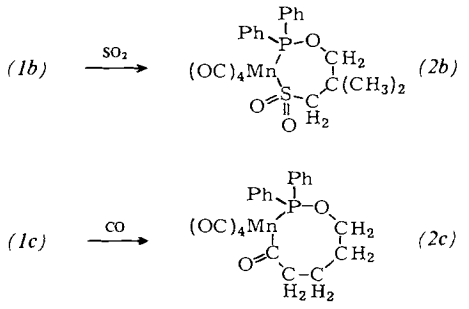


Table 1. IR and MS data and melting points of the heterocycles *(1)* and *(2)*.

	(1a)	*(1b)*	*(1c)*	*(2b)*	*(2c)*
ν(CO) [cm^{-1}]	2060 m [a] 1993 s 1976 vs 1946 s	2062 m [a] 1996 s 1978 vs 1944 s	2059 m [a] 1995 s 1973 vs 1943 s	2098 m [b] 2046 s 2022 vs 1984 s	2072 m [c] 2008 s 1985 vs 1960 s
ν(SO$_2$), ν(C=O)				1170 s [d] 1035 s	1611 m [c]
m/e (M^+)	410	438	424	502 [e]	452
M.p. [°C]	118	108	94	102 (dec.)	

[a] In *n*-hexane. [b] In $CHCl_3/CCl_4$ (1:1). [c] In CCl_4. [d] In KBr. [e] Field desorption.

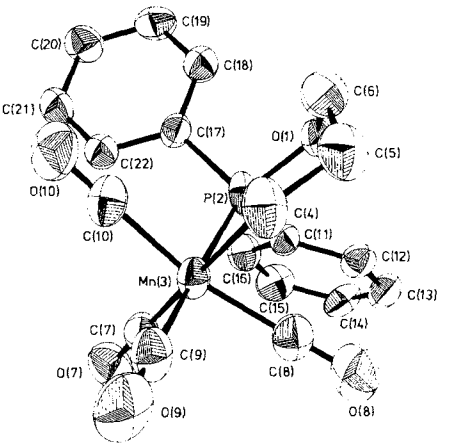


Fig. 1. ORTEP diagram of *(1a)* (vibrational ellipsoids correspond to 50% probability density).

Bond lengths [pm]			Angles [°]			
Mn3	C4	221.0(3)	P2	Mn3	C4	92.1(1)
C4	C5	151.8(7)	Mn3	C4	C5	118.7(2)
C5	C6	148.0(7)	C4	C5	C6	117.2(4)
C6	O1	144.4(4)	C5	C6	O1	112.8(3)
O1	P2	161.1(2)	C6	O1	P2	120.2(2)
P2	Mn3	227.1(1)	O1	P2	Mn3	116.4(1)

Experimental

The heterocycle *(1)* is obtained by dropwise addition of a solution of $Na_2[(OC)_4Mn(PPh_2O)]$ (1 mmol) in dimethyl

[*] Prof. Dr. E. Lindner, Dipl.-Chem. H.-J. Eberle
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

ether (DME) (50 ml) to a solution of ZCH_2-X-CH_2Z (1 mmol) in DME (30 ml) at 20 °C. After 1 h the solvent is removed in a high vacuum and the residue is extracted with *n*-heptane at 40 °C. After filtration (D3), the *n*-heptane is removed and *(1)* is sublimed at *ca.* 100 °C in a high vacuum. Yield 15—56%.

(1b) (0.5 mmol) is allowed to react in 30 ml of liquid SO_2 for 1 h at −60 °C. After removal of SO_2, *(2b)* is obtained in quantitative yield.

A solution of *(1c)* (0.5 mmol) in *n*-heptane (15 ml) is transferred to an autoclave and subjected to a CO pressure of 300 bar at 80 °C. After 16 h, analytically pure *(2c)* crystallizes from the solution in 80% yield.

Received: July 24, 1979 [Z 374 IE]
German version: Angew. Chem. *92*, 70 (1980)

[1] Preparation and Properties of, and Reactions with, Metal-Containing Heterocycles, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: *E. Lindner, G. Funk, S. Hoehne*, Angew. Chem. *91*, 569 (1979); Angew. Chem. Int. Ed. Engl. *18*, 535 (1979).

[2] *D. E. Webster*, Adv. Organomet. Chem. *15*, 147 (1977); *R. H. Grubbs, A. Miyashita*, J. Am. Chem. Soc. *100*, 7416 (1978); *U. Schubert, A. Rengstl*, J. Organomet. Chem. *166*, 323 (1979).

[3] *M. I. Bruce*, Angew. Chem. *89*, 75 (1977); Angew. Chem. Int. Ed. Engl. *16*, 73 (1977).

[4] *E. Lindner, G. von Au, H.-J. Eberle*, Z. Naturforsch. *B 33*, 1296 (1978).

[5] *(1a)* forms monoclinic crystals from *n*-hexane (space group $P2_1/c$), $a = 913(2)$, $b = 1371(2)$, $c = 1646.4(3)$ pm, $\beta = 115.39(2)°$, $Z = 4$, $\rho_{calc} = 1.462$ g·cm^{-3}. The structure was solved by Patterson and difference Fourier syntheses and anisotropically refined to $R = 0.036$ (apart from H) for 2318 independent reflections with program system SHEL-76.

Lithium Nitride Halides—New Solid Electrolytes with High Li^+ Ion Conductivity

By *Peter Hartwig, Werner Weppner, Winfried Wichelhaus,* and *Albrecht Rabenau*[*]

Dedicated to Professor Harry Hahn on the occasion of his 65th birthday

Hahn et al.[1] have examined the existence of ternary lithium-nitrogen-halogen compounds on the quasibinary Li_3N-LiX cut (X = Cl, Br, I) of the Gibbs phase triangle Li-N-X. For $Li_9N_2Cl_3$, the LiCl-richer phase of the two lithium nitride chlorides, an antifluorite structure was found in which 10% of the lithium sites are vacant while the anionic partial lattice is almost completely occupied by N and Cl. In order to underscore the cationic underoccupation of the antifluorite phase, we choose the designation $Li_{1.8}N_{0.4}Cl_{0.6}$.

On interchanging the anionic and the cationic lattices, an analogy is seen to exist with a series of known solid oxygen and fluorine ion conductors, *e.g.* ZrO_2 doped with 20 mol-% of CaO.

Coordination		
Cubic	Tetrahedral	
$Zr_{0.8}Ca_{0.2}$	$O_{1.8}\square_{0.2}$	Fluorite type O^{2-} ion conductor
$N_{0.4}Cl_{0.6}$	$Li_{1.8}\square_{0.2}$	Antifluorite type Li^+ ion conductor

[*] Prof. Dr. A. Rabenau, Dipl.-Chem. P. Hartwig, Dr. W. Weppner, Dr. W. Wichelhaus [**]
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
[**] Present address: Jenaer Glaswerk Schott & Gen., D-6500 Mainz, Germany.

In neither case does the fluorite structure occur with the ideal composition ZrO_2 and "$Li_2N_{0.5}Cl_{0.5}$".

These structural properties prompted us to characterize lithium nitride chloride with respect to ionic conductivity[2] and thermodynamic properties. The studies were extended to other lithium nitride halides for purposes of comparison. We found all the compounds listed in Table 1 to have a high lithium ion conductivity and negligible electronic conduction.

Table 1. Activation energy E_A (products of ionic conductivity and absolute temperature), decomposition potentials U_{dec}, and free energy of formation ΔG_f^0 of the lithium nitride halides from the elements in their standard states [a]. $Li_{6.67}N_{1.98}I$ and $Li_{9.27}N_{2.76}I$ are different stoichiometries of the same phase. LT = low temperature modification, HT = high temperature modification.

	E_A [eV]	U_{dec} [V]	ΔG_f^0 [kJ/gAtom]	T [°C]
$Li_{1.8}N_{0.4}Cl_{0.6}$	0.49	2.52	−185	101
$Li_{11}N_3Cl_2$	0.83	1.86	−154	332
Li_6NBr_3	0.46	>1.30		176
$Li_{13}N_4Br$ (LT)	0.73	1.32		146
$Li_{13}N_4Br$ (HT)	0.47	0.66		300
Li_5NI_2 (LT)	0.50	1.96	−138	98
Li_5NI_2 (HT)	0.44	1.63	−124	287
$Li_{6.67}N_{1.89}I$	0.55	0.92	− 90	313
$Li_{9.27}N_{2.76}I$	0.80	0.92		316

[a] The energies of formation of the binary lithium halides were taken from standard tabulations [5].

The logarithms of the product of the conductivities (obtained by AC measurements) and the absolute temperature are plotted as a function of the reciprocal temperature in Figure 1. The relation obeys an Arrhenius law for the diffusion constant of the ions.

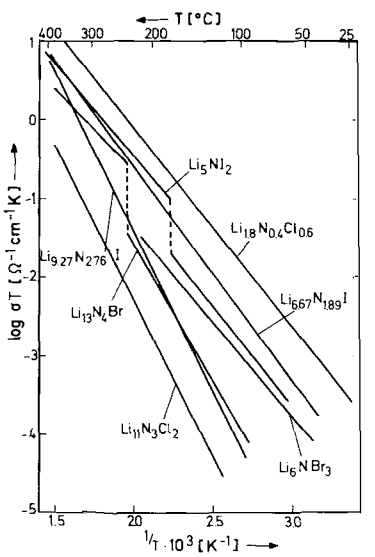


Fig. 1. Temperature dependence of the product of electrical conductivity and absolute temperature of the lithium nitride halides.

It is seen that the conductivity of the antifluorite phase $Li_{1.8}N_{0.4}Cl_{0.6}$ is greatest over the entire temperature range; at the same time, the activation energy of 0.49 eV is comparatively low. The discontinuities in the conductivities of $Li_{13}N_4Br$[3] and Li_5NI_2 are attributed to kinetically strongly inhibited phase transitions which are confirmed by calorimetric measurements. The Li_3N-richer phase of the two lithium nitride iodides is the only compound to exhibit a relatively wide phase width, extending at least from $Li_{6.67}N_{1.89}I$ to $Li_{9.27}N_{2.76}I$ ($Li_3N:LiI = 1.89$ to 2.76). The ionic conductivity increases by several orders of magnitude with increasing

LiI content in the lower temperature range, while the activation energy falls from 0.80 to 0.53 eV. The pre-exponential factor of the Arrhenius equation $\sigma T = A \exp(-E_A/kT)$ remains approximately constant, *i.e.* the jump frequency is independent of the composition.

Transfer experiments were undertaken with lithium to establish that the electrolytic current is indeed due to lithium ions. EMF measurements on lithium concentration cells with $Li_{1.8}N_{0.4}Cl_{0.6}$ as electrolyte and Li and Li_xTiS_2 as electrodes also confirmed practically pure ionic conduction.

All the ternary compounds lying on the quasibinary cuts Li_3N-LiX are thermodynamically stable towards pure lithium, which can therefore be used as anode in electrolytic cells. Moreover, all lithium nitride halides decompose only at low lithium activities. This leads to high decomposition potentials, *e.g.* more than 2.5 V for $Li_{1.8}N_{0.4}Cl_{0.6}$ at 100 °C (cf. Table 1). The high thermodynamic stability permits use of thin low-resistance layers, *e.g.* in printed circuits.

The free energy of formation of lithium nitride halides from the elements can be calculated from the decomposition potentials given a knowledge of the ternary phase diagrams Li-N-X. Applying the experimental result that all ternary compounds are in equilibrium with nitrogen and no other chlorides and iodides occur, the values listed in Table 1 were obtained. Measurement of the specific heat of $Li_{1.8}N_{0.4}Cl_{0.6}$ gave the standard enthalpy as $H^0(298\,K) - H^0(0\,K) = 9.57$ kJ/mol.

Experimental

The lithium nitride chlorides were produced by annealing tablets pressed from a mixture of finely ground Li_3N[4] and LiCl [Fluka AG] for 48 hours at 450 °C under N_2; the lithium nitride bromides and iodides were prepared analogously by annealing at 300 °C or by 3 hours' fusion of the binary compounds in tungsten vessels. The conductivity was determined by AC measurements over the frequency range of 1 Hz to 150 kHz. The frequency dependence could be analyzed by way of Debye equivalent circuits. The electronic partial conductivities were determined with DC by blocking the ion flux with molybdenum electrodes.

Received: September 26, 1979 [Z 375 IE]
German version: Angew. Chem. *92*, 72 (1980)

[1] *H. Sattlegger, H. Hahn,* Naturwissenschaften *51*, 534 (1964); Z. Anorg. Allg. Chem. *379*, 293 (1970).
[2] *P. Hartwig, W. Weppner, W. Wichelhaus,* Mater. Res. Bull. *14*, 493 (1979).
[3] *P. Hartwig, W. Weppner, W. Wichelhaus, A. Rabenau,* Solid State Commun. *30*, 601 (1979).
[4] *E. Schönherr, G. Müller, E. Winkler,* J. Cryst. Growth *43*, 469 (1978).
[5] *I. Barin, O. Knacke:* Thermochemical Properties of Inorganic Substances, 1973, and *I. Barin, O. Knacke, O. Kubaschewski:* Supplement 1977. Springer-Verlag, Berlin; Verlag Stahleisen, Düsseldorf.

BOOK REVIEWS

Strained Organic Molecules. By *A. Greenberg* and *J. F. Liebman.* Organic Chemistry. A Series of Monographs. Vol. 38. Academic Press, New York 1978. xi, 406 pages. Bound, $ 41.50.

This is a long-awaited book. There has been no monograph on this subject since *A. von Baeyer* coined the term "strain" for angle deformations relative to the tetrahedral arrangement at carbon. The volume and the variety of the material collected is overwhelming; the huge number of strained compounds being scarcely conceivable.

In accordance with the authors' claim of aiming somewhere between a textbook for advanced students and a monograph focused on a special field, one would expect a clear taxonomy of strained compounds from thermodynamic and kinetic points of view, and portrayal (with examples) of the types, causes, and chemical consequences of strain.

To be perfectly honest, the book does not live up to all these expectations. For example, thermodynamic and kinetic stability are not discussed until the penultimate chapter, though the lability of many strained compounds is referred to much earlier. Stability and instability are discussed in terms of thermochemical concepts—and it is clear that conformational enthalpy differences have been ignored—yet one becomes suspicious, if the dissociation enthalpy $CH_4 \rightarrow CH_3^{\bullet} + H^{\bullet}$ is used as a basis and hence methane would have 19 kcal/mol of strain. The unsolved problem of the *mean* bond enthalpy of a C–H bond is dealt with by reference to the difference in the bond energy (dissociation energy) in methane and toluene. Not all readers will agree with a choice of bond and group increments according to which ethylene and tetrafuoroethylene become strained compounds. Also, one has to get accustomed to the conclusion that conjugative destabilization of anti-aromatic annulenes amounts to strain.

The report about the tranformations of strained carbocycles under the influence of transition metals is undoubtedly of great interest. Other current topics touching upon our concepts of bonding and reactivity in general are only indicated: the slow isomerization of prismane in solution may be a forbidden reaction according to the Woodward-Hoffmann rules, but the substance itself is explosive; cyclopropene has a short and thus stable double bond, but it is highly strained and reactive as a dienophile; the influence of fluorine substituents on stability and lability; lithium as a "strain-reducing" substituent on a carbon atom; and the significance of steric hindrance for the properties of strained compounds. The importance of quantum-chemical results is not always clearly recognizable. A sentence such as "Calculational evidence supporting the intermediacy of ..." (p. 287) is unlikely to find undivided agreement.

While the book hardly offers a modern treatment of "The present state of strain theory"[*], it contains what is promised in the title—a comprehensive catalog of strained and labile organic compounds.

Reinhart Keese [NB 485 IE]

Luminescence Spectroscopy. Edited by *M. D. Lumb.* Academic Press, New York 1978. ix, 375 pp., bound, $ 49.75.

The book consists of five independent contributions: 1) Inorganic Luminescence (*G. F. Imbush,* 92 pp.), 2) Organic Luminescence (*M. D. Lumb,* 56 pp.), 3) Luminescence Instrumentation (*T. D. S. Hamilton, I. H. Munroe, G. Walker,* 90 pp.), 4) Magnetic Effects in Organic Molecular Spectroscopy (*N. E. Geacintov, C. E. Swenberg,* 60 pp.), 5) Magneto-optical Investigations of Recombination Radiation in Inorganic Crystals (*B. C. Cavenett,* 70 pp.).

[*] *W. Hückel,* Fortschr. Chem., Phys., Phys. Chem. *19* (4), 1 (1927).

In his foreword, the editor writes: "The subject of luminescence spectroscopy has in recent years been divided into the two specific areas of organic luminescence and inorganic luminescence. This monograph attempts to merge these two areas within the common ground of experimental physics. ...The aim of this monograph is to provide sufficient theoretical and experimental groundwork for experimental physicists, chemists, or biologists entering this field for the first time to grasp the essentials of luminescence spectroscopy". In terms of these claims, the book must regarded as a failure. The authors of contributions 1, 2, 4, and 5 have made not the slightest attempt to present organic and inorganic luminescence as areas of the same discipline. There is no coordination between contributions 1 and 5 and between 2 and 4. In the following, I shall restrict my comments to contributions 2, 3, and 4, which correspond to my own field of study.

The second contribution reads like an unsuccessful precis of the book "Photophysics of Aromatic Molecules", by *J. B. Birks*. It contains numerous inaccuracies and errors. Only one example will be mentioned: the structural formula of azulene (p. 117) contains a *six*-membered ring and a five-membered ring, and in the text (p. 115) only the five-membered ring is mentioned as a special feature of azulene. I consider this contribution to be completely superfluous because the very same topic has already been treated far better by other authors.

The third contribution comes closest to fulfilling the aims of the book. However, the presentation is probably insufficiently detailed for the real newcomer. This section can be recommended to the more advanced worker on the strength of its good survey of experimental methods and the sound discussion of possible sources of error in luminescence studies.

The fourth contribution is a revised version of the article "Exciton Interactions in Organic Solids" in "Organic Molecular Photophysics" (Editor: *J. B. Birks*). It is concerned with the influence of an external magnetic field on pairwise interaction of triplet excitons in molecular crystals and is a good introduction to this special field.

Bernhard Nickel [NB 488 IE]

Organic Liquids: Structure, Dynamics, and Chemical Properties. Editors: *A. D. Buckingham, E. Lippert,* and *S. Bratos.* John Wiley & Sons, London 1978, 352 pp., bound, £ 18.00.

This book contains the 20 lectures presented at the Euchem conference of the same name. They are concerned with the methodology and results of techniques for the study of liquids (scattering experiments, flash spectroscopy, other dynamic methods, computer simulations, dielectric and thermodynamic properties, *etc.*).

The contributions provide a good survey of research into liquids, which is becoming increasingly topical. Up till now, physical chemistry had rather neglected the liquid state, which is actually the most important phase for most chemists. Regrettably, only few research groups have set themselves the task of providing chemists with information of value in practice. In the present book, such aims remain in the background (the article by *Reichardt* about solvent scales is an exception). Much more effort is devoted to the study of complicated partition functions of liquids which are of relatively little practical help to most chemists. While nobody will deny physical chemistry the right to conduct research for its own sake, it should not be forgotton that chemists need approximate models of the liquid phase for their work.

W. A. P. Luck [NB 491 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Chemisorption of Gases on Metals. By *F. C. Tompkins.* Academic Press, London 1978. xii, 370 pp., bound, £ 16.80.

A plethora of new methods has led to a vigorous development in studies on the interaction between gases and metal surfaces during the past decade. A glance at the bibliographies given in some publications could even create the impression that the field was non-existent just a few years ago, which is of course incorrect.

One of the past-masters of this discipline, *F. C. Tompkins,* has made a laudable attempt to survey the entire field, including modern developments, in a terse monograph—with mixed success. Non-uniform presentation of theoretical principles and experimental aspects is a disturbing feature of this work. (In this respect, *Wedler*'s book is certainly more suitable for newcomers.) The references hardly go beyond 1974, *i. e.* the very latest developments are not included. The choice of examples is sometimes rather unfortunate, and errors are also to be found. On the other hand, the historical development of various concepts receives fitting treatment and a comprehensive overview of the field is actually given. However, in view of the other monographs available in this field, the book cannot be unreservedly recommended.

Gerhard Ertl [NB 489 IE]

Radicals. By *D. C. Nonhebel, J. M. Tedder,* and *J. C. Walton.* Cambridge University Press, Cambridge 1979. 200 pp., paperback, £ 11.95.— ISBN 0-521-22004-1

Spin Labeling, Vol. 2. Theory and Applications. Edited by *L. J. Berliner.* Academic Press, New York 1979. xiii, 357 pp., bound, $ 32.00.—ISBN 0-12-092352-1

Environmental Science Research, Vol. 12. Pentachlorophenol. Edited by *K. Ranga Rao.* Plenum Press, New York 1978. xiv, 402 pp., bound, $ 45.00.—ISBN 0-306-36312-7

Einführung in die Aromaforschung. By *M. Rothe.* Akademie-Verlag, Berlin 1978. vi, 115 pp., bound, *ca.* DM 47.00

Corrosion of Stainless Steels. By *A. J. Sedriks.* John Wiley & Sons, Chichester 1979. xv, 282 pp., bound, $ 38.95.— ISBN 0-471-05011-3

Nothing but Motion. Vol. 1 of a revised and enlarged edition of The Structure of the Physical Universe. By *D. B. Larson.* North Pacific Publ., Portland 1979. xvi, 292 pp., bound, $ 9.50.—ISBN 0-913138-07-X

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 2
February 1980
Pages 79–150

Raw Material–Polymer Interrelationships — Today and Tomorrow[**]

By Klaus Weissermel[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Against the background of increasing demand and limited availability of fossil, non-regenerative fuel reserves and resources, ways are indicated of ensuring future supplies of raw materials and energy. The ambivalence of petroleum, natural gas, and coal in the energy and chemical sectors is demonstrated and opportunities for the gradual separation of their dual function are indicated. Taking into account the time factor, the necessary restructuring processes are analyzed critically with respect to their impact on the raw material–polymer relationship.

1. Fossil Organic Raw Materials: Combustion or Upgrading?

In no other branch of industry is the interrelationship between fossil energy sources and organic raw materials as intimate as in the chemical industry, for more than 90% of the energy and raw materials consumed throughout the world are based on petroleum, natural gas, and coal.

There are signs that the two most important chemical feedstocks—petroleum and natural gas—will already be threatened with exhaustion in the medium term and coal in the long term, unless it is possible for their dual function as sources of energy and raw materials to be gradually disengaged in good time and ultimately eliminated.

The switchover from coal, the most common fossil source of energy, to petroleum and natural gas was only possible because the latter have hitherto been available on world markets at prices well below their value as energy and upgraded product and because they are easier to transport, utilize, and upgrade. In the wake of this economic development, a far-reaching process of restructuring has taken place throughout the world in the last thirty years, as shown in Figure 1.

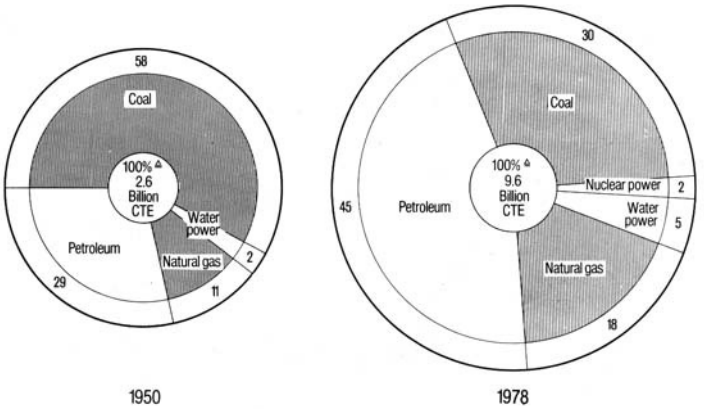


Fig. 1. Primary global energy consumption in 1950 and in 1978.

[*] Prof. Dr. K. Weissermel
Hoechst Aktiengesellschaft
Postfach 800320, D-6230 Frankfurt am Main 80 (Germany)

[**] Extended version of the paper delivered at the plenary session of the 26th International Symposium on Macromolecules, September 20, 1979 in Mainz.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0202-0079 $ 02.50/0*

As a result of rapid economic growth, particularly in the highly developed countries, world consumption of primary energy has changed considerably, not only in terms of quantity, but also in the proportions of the individual fossil energy sources used. Especially affected by this development is petroleum, which now bears by far the chief burden of the energy supply. In comparison with its geological age of around 500 million years, we are in the process of consuming this valuable, non-regenerative raw material "in a matter of seconds".

In spite of geological limitations, political restrictions, and economic factors related to its availability, the consumption of petroleum is at present continuing to rise and inevitably this has greatly increased the supply risks and the dependence of many countries on imports. On a national and a regional level, however, it is possible to ascertain important differences in the energy consumption structure (cf. Fig. 2).

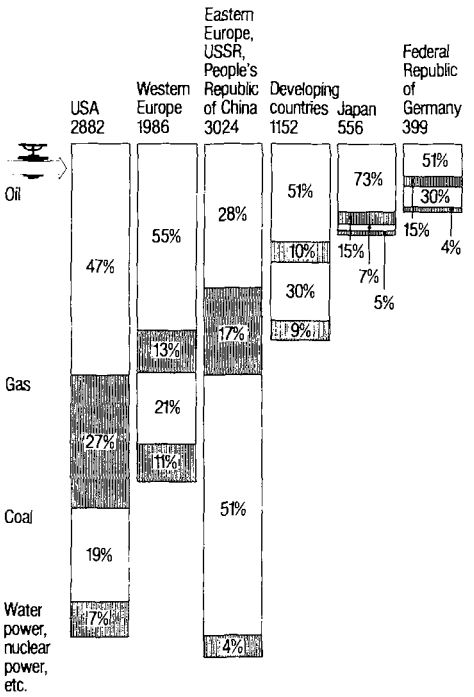


Fig. 2. Regional annual energy consumption for 1978 (in million CTE).

According to Figure 2, Eastern Europe, the USSR, and China have been largely spared the repercussions of the oil crisis, since it is in these regions that the greatest equilibrium in consumption exists between the individual sources of energy. At the same time, this diagram shows clearly the tremendous efforts that are required in order to direct patterns of consumption, especially in the Western industrialized countries, into new channels. It must be assumed that the introduction of a new energy system or the changeover to a new raw material basis will, according to past experience with coal, petroleum, as well as with nuclear energy, take at least 20 to 30 years from the time of its availability on a technical scale to the attainment of a large market share.

Up to the turn of the millenium we shall thus only be able to avail ourselves of those energy sources and raw materials, the recovery of which has already reached an advanced technological stage, which are economically and ecologically acceptable, and which can be reliably controlled. From this it follows that we must be clear as to the possible alternatives for future supply of energy and raw material and that regulative perspectives must determine the rules of action. Long-term strategies cannot be derived from short-term demand considerations.

The widespread crisis of acceptance that we are at present experiencing in the utilization and urgently needed development of nuclear energy is a typical example of the fact that we are not prepared, or not yet prepared, to initiate developments affecting the period beyond the year 2000. This is by no means based on a factually substantiatable assessment of the technological consequences, but is marked by an irrational fear of technology. Uncertain, and in some cases contradictory statements on the exhaustion of fossil reserves and its effect on the existence of human life is an additional factor that has hampered orientation. It is in fact frequently overlooked that there is a considerable difference between reserves and resources of fossil sources of energy. By definition, reserves are proven supplies of fossil materials that are recoverable under modern production conditions. Resources are geologically probable deposits which will be recoverable at considerably greater expense at some time in the future. They include the reserves. As a result of technological progress, the boundaries between reserves and resources will continuously shift. Nevertheless the recoverable proportion amounting to some 3200 billion CTE is still far below the estimated world deposits of fossil energy sources of 12000 billion CTE[1]. If the energy potential provided by nuclear energy and the so-called inexhaustible energy sources are included in the considerations, it should be sufficient for any growth rate.

The safeguarding of energy and raw material supplies in the long-term is thus less a question of resources, but is concentrating more and more on making them available in good time. Scarcity thus has many causes—we should on no account underestimate the time factor. Recent experience, in particular, has shown that changes often take place more rapidly than the development of alternative means of combating them.

The modern power industry has only been in existence for three generations. If it is not to end in an impasse in the fourth and fifth generation, we must break with the present pattern of energy consumption, as shown in Figure 3[2].

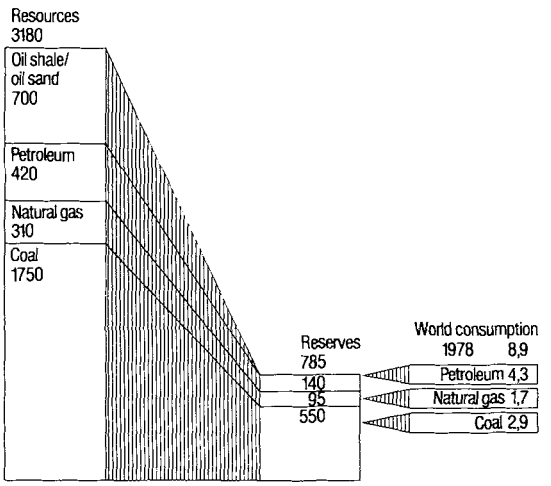


Fig. 3. Recoverable fossil fuels from reserves and resources (billion CTE).

Although the recoverable coal deposits are four times, and probably even five times as large as those of petroleum, this diagram illustrates the crass discrepancy between reserves and consumption. At the same time, Figure 3 makes it possible to estimate how long the predatory exploitation of natural resources can continue. If consumption were to remain unchanged, petroleum resources would only last a period of decades and coal would be exhausted in a few centuries. The problems are intensified still further if we bear in mind the future growth in energy demand.

At all events we require more energy, particularly if we are to preserve the environment and utilize sparingly the valuable, non-regenerative natural products. However how much does this "more" imply? Past experience has shown that there can be a wide gap between estimates and reality and that nothing is as constant as the changes that occur in the data used in forecasts and estimates of demand. Nevertheless it appears to me possible to make a qualitative statement as to the trend.

The main difficulty lies in predicting the energy and raw material demand per head of the world's population. This leads us to the crucial issue: for how many people when and in which region do we expect what demand? Figure 4 illustrates the problems of forecasting. It provides information on the current *per capita* consumption of primary energy and the breakdown by countries and regions[3].

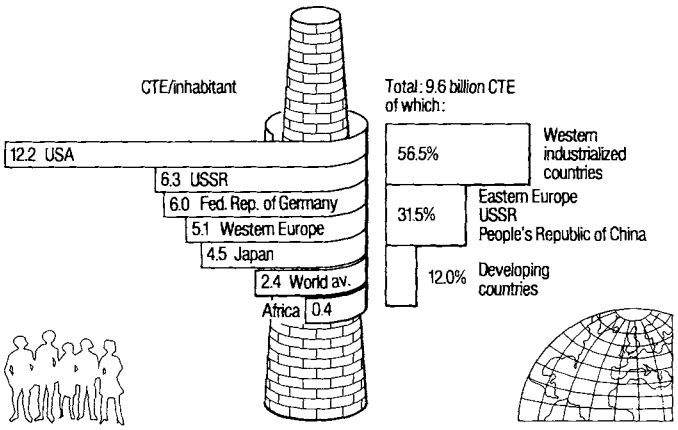


Fig. 4. World consumption of primary energy in 1978. (5.1 CTE/inhabitant for Western Europe includes the Federal Republic of Germany.)

Currently some 4 billion people have to be supplied with energy and raw materials; at the turn of the millenium the number will have reached 6 billion and in 50 years the 8 billion will probably have been reached or exceeded[4].

Advancing industrialization, in particular in the developing countries, inevitably leads to a continuing rise in the consumption of primary energy. It can be assumed, however, that economic growth will in future proceed more slowly in the industrialized countries and be accompanied by a more gradual rise in energy consumption. This is based on the assumption that there is still considerable scope for reducing energy utilization, especially in the non-industrial area.

According to studies carried out by *Keyfitz*[5], an increase in primary energy consumption from 2 CTE to 3—5 CTE per person per year is to be anticipated during the next 50 years. This would then mean a total annual consumption of 24—40 billion CTE compared to 9.6 billion CTE in 1978. Although these figures may appear excessive, energy consumption must nevertheless be expected to at least double within a few decades. However, the attempt to present the estimated development of primary energy demand and supply, broken down by energy sources, is worthy of consideration[6].

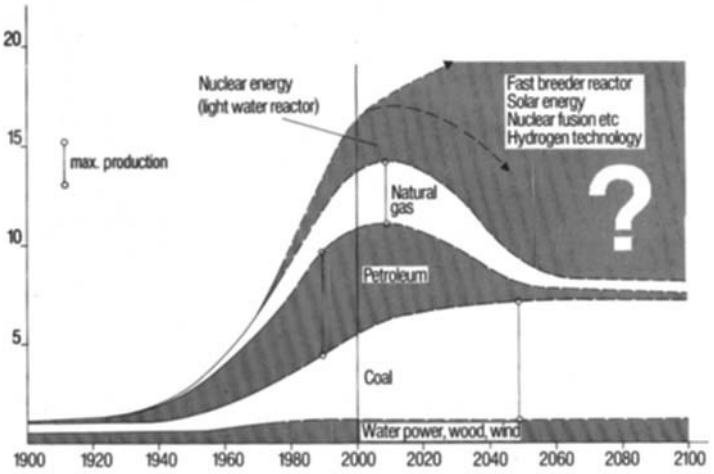


Fig. 5. Development of the world consumption of primary energy (billion CTE).

Figure 5 is intended to show that the further we are removed from the year 2000, the more difficult it is to make a tangible statement as to the proportionate usage of conventional sources of energy and those still to be developed. In my view, however, it is important to observe that the extent to which the fossil resources will last beyond the year 2000 is also decisively influenced by scientific and technical progress, *i. e.* by our ability to open up new sources of energy and develop their utilization to technical maturity at an early stage.

Although a greater degree of probability can be attached to forecasts of the development of primary energy demand in the eighties and nineties, the energy supply trend can by no means be regarded as satisfactory. Figure 5 makes plain that we shall probably have to abandon any hopes in the short-term of being able to make any lasting changes in the pattern of energy consumption. It could be rated a success if oil consumption were to be further reduced during this period. Nevertheless, petroleum will continue in the year 2000 to be the largest single source of energy.

This statement finds confirmation in a recently published study by Deutsche Shell AG on the development of demand for primary energy and the pattern of consumption in the Federal Republic of Germany up to the year 2000[7]. For the sake of completeness, it is presented here in the form of a graph (Fig. 6), which requires no further comment.

Stretching the use of all fossil, non-regenerative energy sources over a longer period remains of vital importance. If rapidly expanded, both at national and global level, the utilization of nuclear energy could already contribute to this objective in the medium-term. After thirty years of development, this source of energy has reached industrial maturity; from the environmental pollution aspect it is preferable to coal and petroleum and is economically superior to energy production from fossil sources[8]. At present it offers the only alternative source of energy that can replace petroleum and

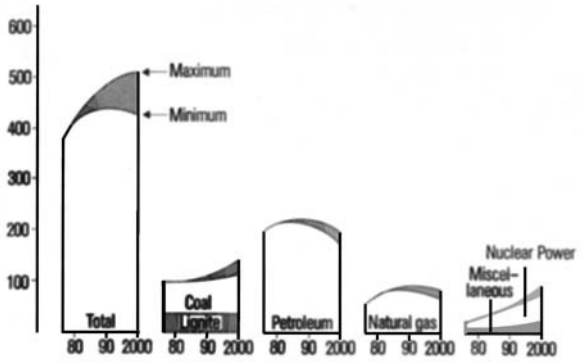


Fig. 6. Predicted primary energy and energy sources in the Federal Republic of Germany between 1978 and 2000 (million CTE).

natural gas on a scale that would be quantitatively significant.

Coal, too, in the form of its conversion products, will have to make a greater contribution towards meeting the demand for energy. In view of its limited availability, natural gas should, however, be largely reserved for processing by the chemical industry.—Unfortunately, even in the medium term this aim would appear scarcely achievable, even though for energy policy reasons the use of natural gas in electric power stations is probably on the decline *vis-à-vis* hard coal.

The development in demand forecast for the period beyond the year 2000 underlines the urgency of the need to separate the interrelationship between energy and raw materials. It requires a radical restructuring and not simply a corrective adjustment. Above all it calls for courage and an awareness of the need for change. A power industry based both on hydrogen and electricity—utilizing inexhaustible sources of energy—would be a worthwhile although distant aim, in order that the fossil reserves will long remain available for applications yielding a higher net product and for instances where there is no alternative source of supply. The future doubtless lies in an integrated energy set-up, utilizing all sources of energy—and in particular in a partnership between coal and nuclear energy.

2. Safeguarding Raw Materials through Structural Changes

Compared to the world consumption of petroleum amounting to 3 billion tonnes in 1978, the share of petroleum-based raw materials for the chemical industry of the order of 5—6% appears to be insignificant.

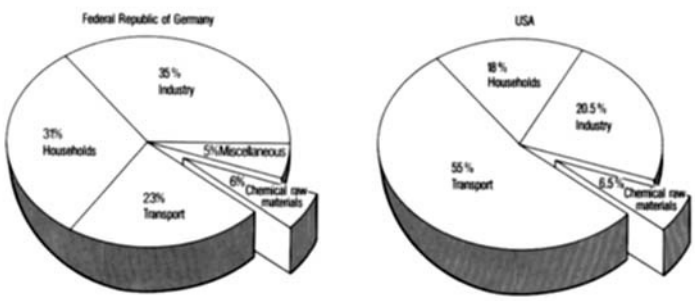


Fig. 7. Petroleum consumption by sectors (Federal Republic of Germany 1976 [9], USA 1975 [10]).

The data (cf. Fig. 7) can easily give rise to misinterpretation, since they do not reveal the true dependence of the chemical industry on petroleum. This dependence only becomes clear on considering the fact that the primary chemicals of organic chemistry are based almost entirely on petrochemicals. This development, which initially commenced in the USA and became established in Europe at the start of the fifties, had two main causes: on the one hand, the petroleum and natural gas fractions, in the main crude naphtha, ethane, propane, and LP gas, which were favored by the chemical industry, were available cheaply in increasing quantities and accelerated the development of pyrolysis processes for the production of the most important olefinic and aromatic building blocks for the chemical industry. On the other hand, new processes were discovered for the polymerization of olefins and the production of monomers on an olefin basis. Both developments were closely linked to one another by a large number of reciprocal relationships and feedbacks and gradually initiated the replacement of acetylene as the starting material for the classical monomers.

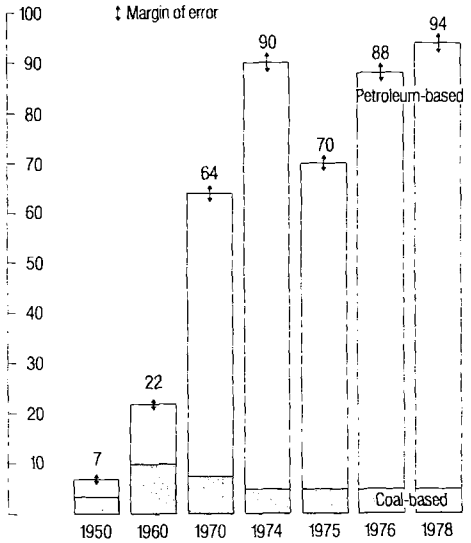


Fig. 8. World production of organic primary chemicals in millions of tonnes (without Eastern Europe, the USSR, and the People's Republic of China).

Figure 8 shows the development in the last three decades and underlines the importance of petroleum-based products in the chemical industry and the extent to which they are used. Only 5% of the primary chemicals are at present still based on coal.

The dependence of the organic speciality products and polymer products on specific petroleum or natural gas fractions that are limited in quantity is evident, particularly since it must be assumed that as intermediates for many branches of industry both will continue to grow at an above-average rate.

There are several possibilities of safeguarding energy supplies; for safeguarding supplies of organic raw materials it may be many times more difficult to replace petroleum. The upgrading of petroleum must always take priority over combustion, since hydrogen-containing carbon compounds are not necessary for energy production, whereas for upgrading processes they are essential and are already present in petroleum in the desired C/H ratio.

The logical consequences as regards the competitiveness of an alternative chemical feedstock are thus indicated. It is not only a function of the cost price of the basic product, but includes the upgrading, finishing, and capital costs involved in the manufacture of primary chemicals.

Under present economic conditions and the latest state of conversion technology, coal cannot compete with petroleum as a chemical feedstock. Exceptions to this are the polycyclic ring systems which, however, are not significant from the volume aspect. Following the establishment of a coal producing and processing infrastructure adapted to meet the increased demand, coal is, however, doubtless able in the medium term to contribute to a marked easing of the pressure on petroleum and natural gas in the form of coal gasification and coal liquefaction products for the heating fuel and motor fuel sector.

Although exploitation of oil shale and oil sand deposits has been initiated it is proving to be more difficult from the technological and the ecological standpoint than at first expected, and will have no appreciable impact on raw material supplies in this century.

The much discussed possibilities of producing raw materials from regenerative natural products are in my view highly overrated. They will not make any decisive global contribution to the supply of primary chemicals but will be confined to a few products at regional level. The upgrading of natural products and the processing of their waste materials will be of prime importance. This is a sphere of activity that opens up future-oriented opportunities for the biotechnology field at present at the development stage.

All factors considered realistically, the chemical industry is still far removed from a "post-petroleum economy". It will begin by way of a more intimate interrelationship between petroleum and coal, while taking into account the possibilities of upgrading that are specific to both raw materials. From the present viewpoint, the following developments and priorities are emerging:

2.1. Optimizing the Upgrading of Crude Oil

A marked rise in the degree of crude oil upgrading for the purposes of the chemical industry would appear possible and urgently necessary within the coming decade.

A prerequisite of this change is a restructuring into petrochemical refineries of refineries which in Western Europe are primarily operated on conventional lines; this will permit the naphtha yield to be increased from 23 to a maximum of 60%. This measure permits the specific crude oil demand for petrochemical primary chemicals to be reduced to one-third (cf. Fig. 9)[11]. However, this reorientation of the refinery structure, such as is practised in the USA, necessitates additional capital expenditure.

In addition to the increased yield of primary chemicals, the petrochemical refinery enjoys the additional advantage over the conventional refinery that its production structure enables it to be extensively adapted to the chemical industry's requirements for different primary chemicals. The increase in yield outlined is attained by operating crackers with naphtha and gas oil and furthermore by the use of plants for converting heavy mineral oil fractions into lighter fractions and also by resorting increasingly to heavy oil for the production by partial oxidation of synthesis gases rich in hydrogen. The flow diagram of Figure 10 illustrates the main process characteristics for the optimum utilization of crude oil as a chemical raw material[12].

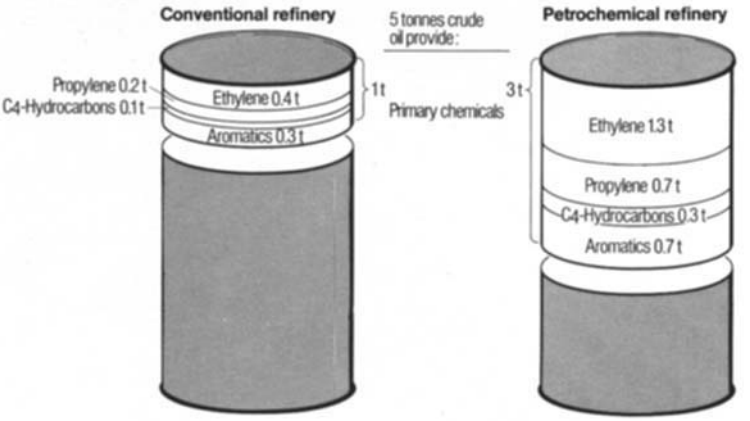


Fig. 9. Primary chemicals from petroleum: influence of the refinery structure [11].

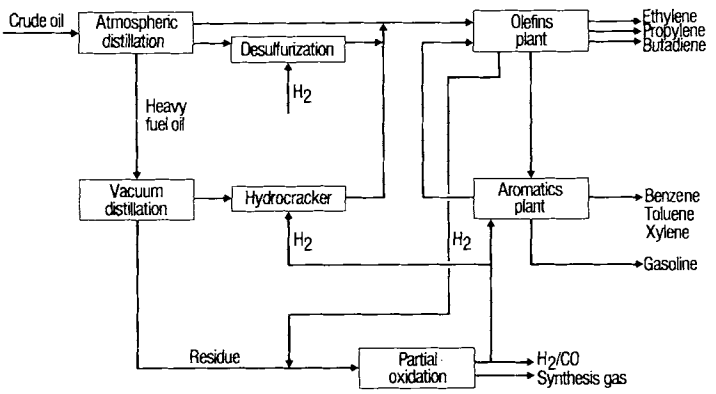


Fig. 10. Flow diagram of a petrochemical refinery.

2.2. Optimization of Crude Oil Production

Exploration and production techniques are being continuously developed to more advanced stages. It is foreseeable that they will increasingly extend to offshore areas and regions that are difficult to exploit. This requires considerable effort in the technical field and a high capital commitment. Of equal importance is the field of drilling and petroleum auxiliaries for secondary and tertiary production. By means of suitable chemical additives that have different tasks to fulfil, the objective of raising exploitation of the deposits from 25—30% to 40—50% and more is already aimed at in the medium term.

2.3. Expansion of Coal Upgrading

As crude oil becomes scarcer and more expensive, increasing importance will attach to the symbiosis of petroleum and coal as a basis for chemical feedstocks.

The production of primary chemicals from coal is fundamentally possible and is based on processes developed during the twenties and thirties in Germany and also employed on a large industrial scale in that country during the Second World War. Conversion of the coal takes place using two methods, one entirely different from the other.

In the Fischer-Tropsch synthesis, it is first necessary to convert the coal into synthesis gas, *i. e.* into carbon monoxide and hydrogen, which in the presence of suitable catalysts is in turn converted into aliphatic hydrocarbons of different structures and chain lengths.

Hydrogenation of coal by means of the Bergius/Pier method or extraction by hydrogenation in the Pott/Broche or IG/Uhde processes are based on the addition of hydrogen to the coal, effecting a partial cleavage and a consequent liquefaction. This process, which does not require the total degradation of the coal, is mainly suited for hydrocarbon fractions with a high aromatics content. The thermal efficiency is higher than in the Fischer-Tropsch synthesis[13].

Up to 1945, 12 hydrogenation plants and 9 Fischer-Tropsch plants were in operation in Germany. The average capacity of the hydrogenation plants was 400000 tonnes per annum, that of the synthesis plants using the Fischer-Tropsch process was below 100000 tonnes per annum. In the fifties, a consortium consisting of Ruhrchemie and Lurgi concluded an agreement with the South African firm of Sasol for the erection of a Fischer-Tropsch plant (Arge process). This plant in South Africa draws upon readily workable coal reserves and today represents the world's only industrial-scale Fischer-Tropsch unit (fixed bed reactor) with an annual capacity of 270000 tonnes of coal chemicals[14]. Coal chemicals are understood to mean the total of all gaseous, liquid, and solid hydrocarbons. A second plant employing the Synthol process of Kellogg (fluidized dust reactor) is shortly to come into operation with a capacity of 2 million tonnes per annum. A further plant of the same size is at the planning stage.

Although the technology of coal gasification and liquefaction has since been developed further[15], and synthesis gas chemistry would also appear capable of additional development, the upgrading potential of coal remains far below that of petroleum.

From the aspect of regulative perspectives that are not only determined by the economic, geological, and political availability, but also by the technological availability, it seems to me that, as mentioned earlier, coal upgrading should pre-eminently be directed towards meeting the expected shortage in supply and easing the pressure on liquid secondary energy sources (naphtha, motor fuel, heating fuel).

The entry to coal upgrading will preferably be by way of coal gasification and the latter must thus be given top priority. The process to be used must be determined by the nature of the coal available and the intended application of the gasification products. In every process, the coal consumption for maintaining the required temperature level of the coal gasification could be reduced by introducing process heat from high-temperature nuclear reactors[16]. The decisive advantage of this future-oriented technology lies in the fact that coal is only used as a raw material, whereby under optimum conditions a coal utilization efficiency of 0.8 and higher appears attainable. An appreciable reduction in coal consumption is a desirable objective, not only to stretch the coal resources over a longer period, but also to counter the rising concentration of carbon dioxide in the atmosphere and the possible climatic changes associated therewith. This could in general become a limiting factor[17].

Because of its low calorific value and high carbon monoxide content, synthesis gas cannot, however, replace natural gas in domestic heating. In the industrial sector there are only limited substitution opportunities for lean gas in energy production. Further processing into synthetic natural gas (SNG) or coal gasification by hydrogenation are possible alternatives that should be given priority in future development activities.

The classical method of carbon monoxide hydrogenation using the Fischer-Tropsch synthesis is extremely capital-intensive and only acceptable in cases where the cost price of the coal used for the production of gasoline and other hydrocarbon fractions is highly favorable. It requires at least 4 tonnes of hard coal for each tonne of coal chemicals.

The Mobil Oil process[18], in which synthesis gas is first converted into methanol, appears to be more promising, even though it has not yet been tested on an industrial scale. The methanol is converted in the presence of zeolite-containing catalysts with concomitant dehydration *via* dimethyl ether into hydrocarbons with a high aromatics content. If one assumes a specific coal consumption of 1.3—1.5 tonnes of hard coal, a total coal consumption of about 3.4 tonnes can be calculated for the production of 1 tonne of coal chemicals.

The production of C_2—C_4 olefins from methanol with high selectivity likewise appears possible with modified catalysts. However, as long as petroleum fractions are still burnt, the production of hydrocarbons and olefins from synthesis gas not only represents a devious route involving a higher expenditure of energy, raw materials, and capital, but its conversion technology is also much more complicated. The unfavorable thermal efficiency is, however, an incentive to bypass the olefin stage for a number of oxygen-containing products during the transition from petroleum to coal.

Special opportunities exist for those synthesis gas derivatives in which carbon monoxide is wholly or partly present in the final product. The process chain of coal–synthesis gas–methanol–acetic acid derivatives is a typical example that is already capable of computation.

Although in view of the present cost-price ratio, the use of lignite instead of methane in the production of synthesis gas still involves appreciable cost increases, it is already superior to naphtha and can be almost compared with the use of heavy petroleum fractions for gasification.

The conversion of heavy and light petroleum fractions through cracking by hydrogenation also offers an alternative to light fuel oil for the domestic sector. As the shortages continue, the further development of coal liquefaction in two directions must ultimately be considered: First, low-sulfur and low-ash fuels for power stations and industrial heating could be produced from coal by slight hydrogenation and extraction by hydrogenation. On the other hand, the route of catalytic high-pressure hydrogenation of coal results in a coal oil with a higher hydrogen content which could be converted into gasoline, naphtha, and primary chemicals in a refinery designed for the production of coal chemicals[19]. In the development of the individual process sequences and upgrading stages it will be possible to build on the extensive experience gained in the processing of petroleum.

The advantages of direct conversion of coal into liquefied coal products are partly offset by the disadvantages, in particular, of a high hydrogen consumption and complex technol-

ogy. This circumstance could be allowed for by using a practical combination of coal extraction by hydrogenation and coal gasification for the production of hydrogen and synthesis gas. According to our present knowledge, the specific coal consumption for the production of 1 tonne of coal chemicals by direct hydrogenation of coal is 3.6 tonnes of hard coal[20]. Of this, 1 tonne alone is used for energy production and 1.36 tonnes for producing the hydrogen required.

The direction pursued in coal upgrading and in coal chemistry and their development potential in comparison to petroleum are thus indicated. The former is directed at the substitution of petroleum-based energy sources for the domestic, industrial, and transport sectors, the latter at the much more elaborate techniques for the production of specific organic primary chemicals. This is illustrated in Figure 11[21].

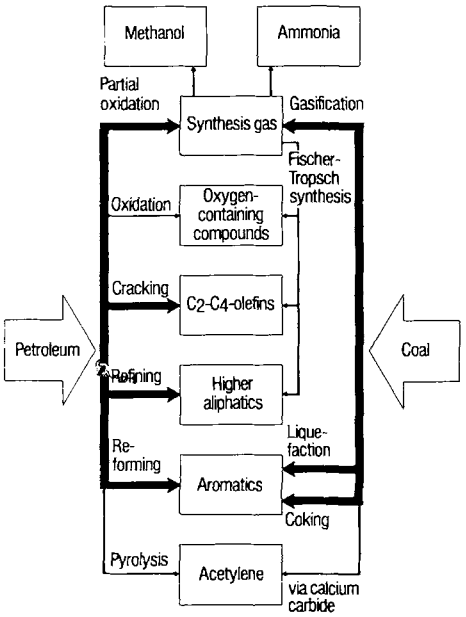


Fig. 11. Upgrading of petroleum and coal.

If the possibilities of substitution are realistically assessed, the transition to new supply patterns which result from the symbiosis of petroleum and coal will be gradual and partially overlap. It is not possible within the scope of this paper to deal with the economic conditions which differ greatly from region to region.

Changes in the pattern and availability of raw materials based on petroleum and coal, as they are to be expected in the medium and long term, are not without an influence on the intertwined system of starting products and intermediates of the chemical industry. These are problems that can be solved if they are recognized and tackled in good time. In view of the high state of development of the chemical industry, rising raw material and energy costs can only to a limited extent still be absorbed by savings in consumption. These costs will in future have a lasting influence on the price structure of all chemical products and, depending on the situation, will also cause processes to be changed.

3. Is Resubstitution of Plastics Foreseeable?

The increase in the price of raw materials will undoubtedly make itself felt most of all in respect of the products with the least number of upgrading stages. A large number of polymers are involved. This raises the question of resubstitution by alternative methods of inorganic or organic origin such as glass, wood and metal, since the introduction of a new material is normally undertaken for reasons of price. Under the pressure of costs, non-utilized properties of materials are not appreciated. The regulating mechanism in the resubstitution of plastics is, however, not determined by the price-property relationship of the raw material alone, but by the final cost of the finished products. The extent of a possible substitution thus depends on several cost factors which result among other things from the processing, shaping, and finishing operations. From the present-day viewpoint, no substantial resubstitution is to be expected, since the cost advantages of plastics products with regard to capital expenditure and labor and energy costs predominate in comparison with finished goods made from natural products.

The multiplicity of properties and combinations of properties have thrown open large markets and opened up new fields of application for plastics, synthetic resins, elastomers, and man-made fibers. In their range of applications they are far superior to all natural products. This explains the steep world-wide increase in the consumption of polymers (cf. Fig. 12).

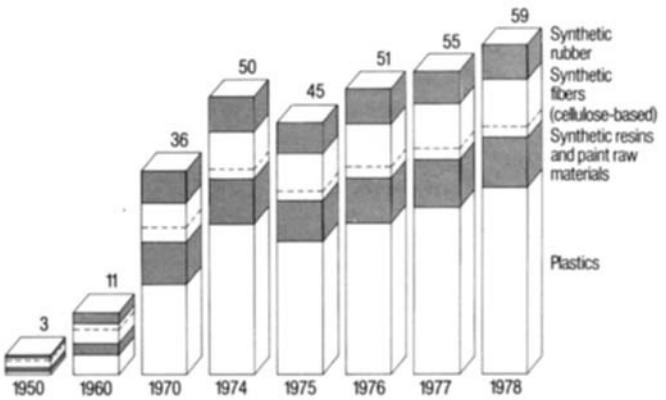


Fig. 12. World consumption of organic polymers between 1950 and 1978 in million of tonnes (without Eastern Europe, the USSR and the People's Republic of China).

In the area of thermoplastics the situation is marked by the commodity resins, namely the polyolefins (HDPE, LDPE, PP), polyvinyl chloride (PVC), and polystyrene (PS and EPS). If one traces the development of the consumption of commodity resins back to 1970, it is evident that pronounced shifts have taken place in the proportions accounted for by the individual types of plastic (cf. Fig. 13).

This development is an expression of the fact that the incentive to substitute commodity resins for one another is determined to a great extent also by the relationship between price and properties, providing that the processability and shaping characteristics are equal. The possibilities of varying the property profiles had considerably extended the application spectrum of plastics and thus facilitated their interchangeability. This trend will continue and is a mark of the dynamism of the market and of creativity.

Fundamentally new commodity resins are not to be expected. Further development of these classes of plastics by

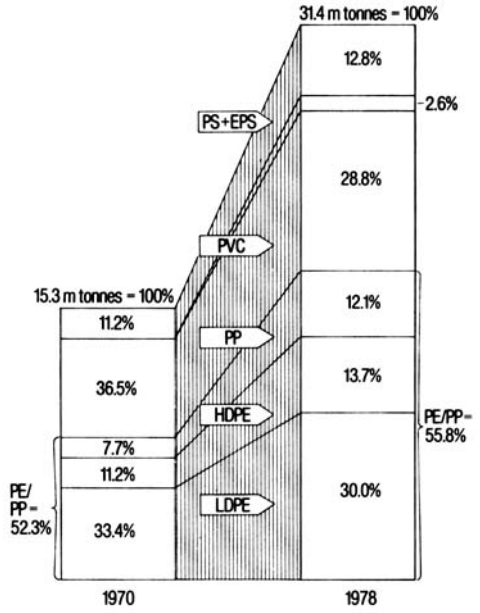


Fig. 13. Development of the world consumption of commodity resins 1970 and 1978 (without Eastern Europe, the USSR and the People's Republic of China).

specific combination and variation of the mechanical and physical properties, tailored to the respective application, will be of primary importance. It is difficult to predict the changes that may occur in the consumption pattern. In most cases, the price-cost gap referred to earlier on will be decisive in the large fields of application.

Commodity resins are appropriately complemented by a large number of high-quality engineering plastics. They are gaining increasing importance as polymer materials and are marked by a high development potential. Narrow limits are placed on their possible substitution for one another, since very specific property combinations are called for in polymer materials, which for reasons of safety and serviceability do not permit any compromise.

On the other hand, the substitution of metals such as zinc, aluminum, copper, and iron by polymer materials will continue, especially in the housing sector and in vehicle and machinery production. This process of substitution was triggered off by the higher energy consumption of metal production (cf. Fig. 14) and processing[22,23].

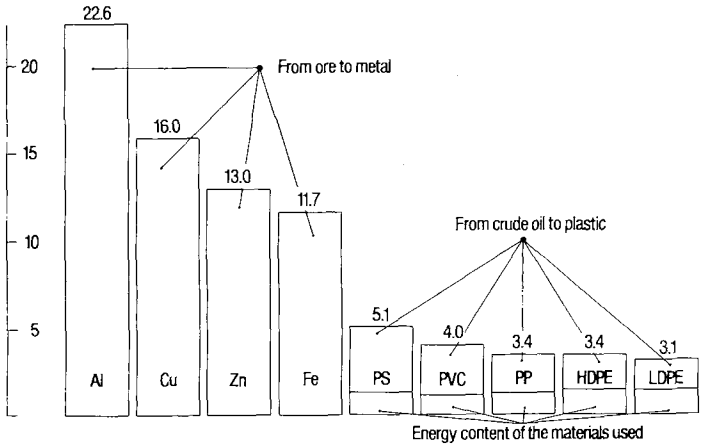


Fig. 14. Consumption of materials and energy (CTE/m³).

Designs of plastic moldings that take into account the properties of the material result in savings in finishing and assembly costs as compared to mass-produced metal parts. These savings are also reflected in the processing costs, particularly the labor costs. In the face of rising energy costs there is an economic incentive to increase the substitution of polymer materials for conventional materials. This is demonstrated with the aid of three examples in Figure 15[24].

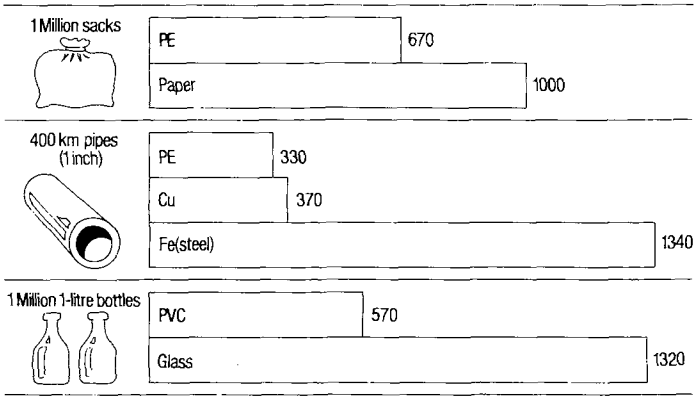


Fig. 15. Finished products and energy consumption (CTE).

Hand in hand with the production of more and more sophisticated products, reinforced thermoplastics and thermosets will continue to gain ground as materials of construction. Since the development of an injection molding process for thermosetting molding compounds and the surmounting of other processing problems, the substitution of thermoplastics for thermosets is no longer of such prime importance. Moreover, in their range of properties they differ markedly from the thermoplastic materials.

For reasons of raw material and energy saving, the applications for highly filled plastics, *i. e.* combinations of polymers with inorganic fillers, will be extended. This applies also to plastics foams, especially those based on polystyrene and polyurethane. They are being increasingly used for thermal insulation in the housing sector and in the form of structural foam as materials for lightweight constructions. In the wide and versatile field of packaging, the process of substitution in favor of plastics film based on petrochemicals is making further progress. This applies mainly to polypropylene due to its low price, its high dimensional stability under heat, and its low permeability to water vapor.

The incentive to re-use plastics and recover waste will be stimulated in respect of all types of plastics. Several technically and economically feasible methods are emerging both for re-use and the indirect utilization of plastics waste by pyrolysis or hydrolysis to obtain low molecular weight hydrocarbon compounds. The potential for innovation is by no means exhausted. I have merely cited examples in order to underline the statement that the polymer field will continue to gain in scope and importance.

Temporary bottlenecks in the supply of raw materials can never be excluded. The great variability of plastics is a characteristic of this area of production which has already proved in the past that it can rapidly adjust itself to changed raw material situations.

4. Summary

Let us return to the starting point of our reflections about raw material-polymer interrelationships—present and future. What final conclusions can be drawn?

Under no circumstances may we continue in the future in the way we started. It would then no longer be possible to safeguard supplies of energy and raw materials even in the medium term. We must therefore follow new paths that will result in radical changes of a structural nature. Above all, we must not lose any time if we are to win the race against tomorrow's problems.

It is my hope that something can be accomplished by determination and not just by necessity,
it is my wish that an awareness of the essentials can accomplish much,
it is my belief that intelligence and prudent restraint can accomplish everything.

I wish to thank Dr. F. Kluge and Dr. W. Scheibitz for their assistance with the content and graphic presentation of the diagrams.

Received: November 13, 1979 [A 308 IE]
German version: Angew. Chem. *92*, 75 (1980)

[1] *W. Oehme,* Umschau *79*, 495 (1979).
[2] *F. Barthel, P. Kehrer, J. Koch, F. K. Mixius, D. Weigel* in "Die zukünftige Entwicklung der Energienachfrage und deren Deckung", Studie der Bundesanstalt für Geowissenschaften und Rohstoffe, Hannover 1976.
[3] Die Zeit, Vol. 34, July 20, 1979.
[4] *W. Häfele,* Vortrag, ACHEMA 79, Frankfurt am Main, June 19, 1979.
[5] *N. Keyfitz:* Population of the World and its Regions 1975—2030. International Institute for Applied Systems Analysis, Laxenburg 1977.
[6] Based on *E. Edye,* Erdoel Kohle *31*, 68 (1978).
[7] Aktuelle Wirtschaftsanalyse, Deutsche Shell AG, August 1979.
[8] *W. Schüller,* Umschau *77*, 41 (1977).
[9] *G. Winter,* Tech. Rundsch. *71*, No. 27, p. 2 (July 3, 1979).
[10] *R. L. Loftness:* Energy Handbook 1978. Van Nostrand Reinhold Co., New York 1979, p. 147.
[11] In Anlehnung an *K. Stork, M. A. Abrahams, A. Rhoe,* Hydrocarbon Process. *54*, Nov. *1974*, 157.
[12] *H. J. Madsack, U. Buskies,* Erdoel Kohle *30*, 31 (1977).
[13] Review: *K. F. Schlupp, H. Wien,* Angew. Chem. *88*, 348 (1976); Angew. Chem. Int. Ed. Engl. *15*, 341 (1976).
[14] *J. C. Hoogendorn,* Gas Waerme Int. *25*, 283 (1976).
[15] *H. Franke,* Chem. Ing. Tech. *50*, 917 (1978).
[16] *R. Schulten,* Erdoel Kohle *24*, 334 (1971).
[17] *J. Williams:* Carbon Dioxide, Climate and Society, Proc. IIASA Workshop, February 21—24, 1978. Pergamon, Oxford 1978.
[18] *S. L. Meisel, J. P. McCullough, C. H. Lechthaler, P. B. Weisz,* Chem. Technol. *6*, 86 (1976).
[19] *H. G. Franck,* Chem. Ind. (Duesseldorf) *XXXI*, 377 (1979).
[20] *H. Jüntgen,* Glueckauf *115*, 329 (1979).
[21] Cf. Nachr. Chem. Tech. Lab. *25*, 227 (1977).
[22] *A. H. Smolders,* Kunststoffe *69*, 419 (1979).
[23] Chem. Week, Ausgabe vom 28. 3. 1979, S. 20.
[24] *P. J. Bakker,* Lecture, Assoc. Plast. Manuf. Europe, Amsterdam, June 19, 1979.

Chemistry and Function of Human Plasma Proteins

By Hans-Gerhard Schwick and Heinz Haupt[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Human blood plasma contains a large number of proteins. New analytical and preparative techniques have so far permitted the isolation of more than one hundred such proteins; about ninety percent of these were first characterized in the last 30 years. The plasma proteins include components of the clotting and complement systems as well as proteinase inhibitors, immunoglobulins, lipoproteins, and carrier proteins. The biological function of some of the plasma proteins is not yet known. Deficiency of one or more plasma proteins usually causes serious health disorders, the best known example being hemophilia. Several biologically active proteins can be gained from blood plasma; these proteins—for example the blood clotting factors—are of great prophylactic and therapeutic importance and allow a better exploitation of the valuable plasma than can be obtained by means of transfusion.

1. Introduction

30 years ago *H. E. Schultze*[1] published a report on "Die Plasmaeiweisskörper im Blickfeld des Chemikers". At that time, approximately ten proteins had been purified from human blood plasma and had been well characterized by physicochemical techniques. The number of proteins isolated from human blood plasma now amounts to more than 100. Their identification and purification were made possible, mainly in the last 15 years, by the development of new analytical and preparative techniques; the great diversity of the plasma proteins was revealed in particular by immunological detection methods and many human plasma proteins were then soon purified by preparative chromatographic methods (see Table 1).

There are three main reasons for the fractionation and purification of plasma proteins:

1) the isolation of protein preparations with prophylactic and therapeutic properties from human blood plasma;
2) the utilization of pure proteins for obtaining plasma protein antisera which are nowadays indispensible reagents for clinical diagnoses; and
3) the utilization of pure proteins in structural analyses, *e.g.* determination of amino acid sequences and X-ray structure analyses in order to elucidate the functions of these proteins at a molecular level.

[*] Prof. Dr. H. G. Schwick, H. Haupt
Behringwerke AG, D-3550 Marburg/Lahn (Germany)

Table 1. A century of plasma protein fractionation. Analytical and preparative techniques which have had a major influence on the preparation of highly purified plasma proteins.

Year	Method	Approx. number of highly purified plasma proteins
1880	Mineral salt precipitation	1
1890		2
	Euglobulin precipitation	
1900		2
1910	Electrodialysis	2
	Alcohol precipitation	
1920		3
	Ultracentrifuge	
1930		3
	Free electrophoresis	
1940	Perchloric acid precipitation	5
	Amino acid analysis	
	Paper electrophoresis	
	Immunoelectrophoresis	
	Affinity chromatography	
1950	Hydroxyl-apatite chromatography	10
	Starch gel electrophoresis	
	Rivanol® precipitation	
	DEAE-, CM-cellulose	
	Radioimmunoassay	
	Gel filtration	
1960	Polyacrylamide gel electrophoresis	30
	Electrofocusing	
1970	Isotachophoresis	55
1980		100

Whereas at the time of *Schultze*'s publication no complete amino acid sequence analyses of human plasma proteins were known, the entire sequences of some and partial sequences of many of these proteins have now been established (Table 2).

Table 2. Amino acid sequence analyses of human plasma proteins.

1. Plasma proteins, for which complete or almost complete sequences have been determined:	*2. Plasma proteins, for which detailed partial sequences, amino terminal sequences, and sequences of the active center have been determined:*
Prealbumin	Transferrin
Albumin	Ceruloplasmin
α_1-Acid glycoprotein	Complement-component C1q
Haptoglobin: α_1^S-, α_1^F-, α_2-, β-chain	Complement-component C1r
Apolipoproteins A-I, A-II, C-I, C-II, C-III	Complement-component C1s
Fibrinogen; α-, β-, γ-chain	Retinol-binding protein
β_2-Microglobulin	β_2-Glycoprotein I
C3a-Anaphylatoxin	9.5S α_1-Glycoprotein
C5a-Anaphylatoxin	Prothrombin
C-reactive protein	α_1-Antitrypsin
IgG; γ-chain	α_1-Antichymotrypsin
IgA; α-chain	Plasminogen and plasmin
IgM; μ-chain	Hemopexin
IgE; ε-chain	Factor XIII
κ-chain	Secretory component
λ-chain	
J-chain	

As there is so much information available concerning the chemistry and function of plasma proteins, this review cannot be complete. We shall concentrate on reporting more recent findings and otherwise refer to comprehensive reviews.

2. Classification of the Plasma Proteins

2.1. Definition of the Plasma Proteins

Putnam[2b] recently compiled a list of criteria which characterize the true plasma proteins (Table 3).

Table 3. Criteria for classification as a true plasma protein [2b].

1. Presence in the plasma (after the neonatal period)
2. Synthesis in liver or RES system rather than in specialized tissues
3. Primary function (including transport function) mediated in the vascular system rather than in a target organ
4. Protein actively secreted into blood rather than by leakage through tissue damage
5. Protein concentration highest in blood of all body fluids
6. Appreciable half-life in plasma rather than just a short transit time
7. Protein may exhibit genetic polymorphism or variant forms but polymorphism not due to tissue of origin, as with some isozymes
8. Protein not derived by catabolic proteolytic cleavage in plasma (as Fab or Fc) but may be proteolytic cleavage product of physiological pathways such as complement or coagulation

These criteria are fulfilled, for example, by proteins which are components of multienzyme systems (such as the clotting or complement systems), by immunoglobulins, lipoproteins, proteinase inhibitors, and carrier proteins. In addition, human plasma contains a large number of proteins which cannot be assigned to any of these systems or groups and whose functions are still not known.

This definition of the plasma proteins thus excludes hormones, enzymes originating in the tissues, erythrocyte proteins, and numerous proteins which only circulate temporarily in the blood plasma under physiological or pathophysiological conditions without exercising any function. The latter were termed "passenger proteins" by *Putnam*[2b].

2.2. Concentration of the Plasma Proteins

There are enormous differences between the normal mean concentrations of the plasma proteins. This is shown particularly well in a diagram by *Putnam*[2b] which we have modified somewhat and completed by adding proteins which have been recently described (Fig. 1).

In this diagram the normal mean concentrations of 63 plasma proteins are plotted on the logarithmic scale as functions of their electrophoretic mobility (u).

Proteins which belong to the same system or group are denoted by the same color. The large differences between the concentrations of proteins within a system or group should be noted. The range extends from 4 g per 100 ml plasma for albumin to 5 μg per 100 ml plasma for IgE (immunoglobulin E). The concentration of most plasma proteins is less than 100 mg/100 ml. This means that the few plasma proteins which are found in quantities of more than 100 mg/100 ml already account for about 90% of the protein content of human plasma; the remainder of approximately 10% contains more then 100 plasma proteins. It is thus understandable that great difficulties are encountered when purifying trace proteins (1 to 10 mg/100 ml) from human plasma; many trace and ultra-trace proteins (up to 1 mg/100 ml) with important physiological functions are certainly still not known today.

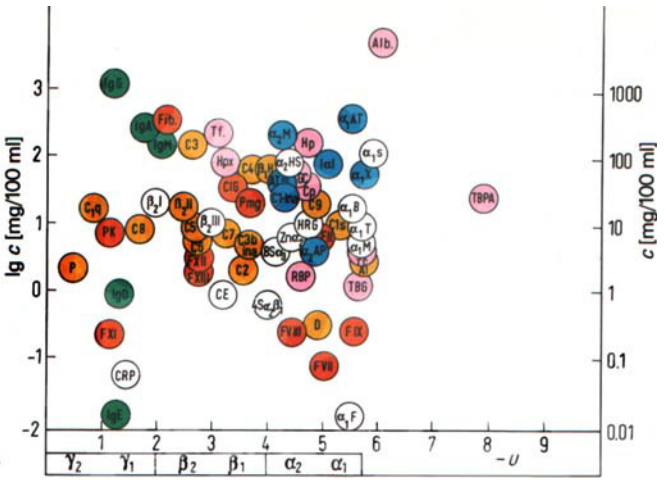


Fig. 1. Distribution diagram (without lipoproteins) of human plasma proteins (modified according to [2b]). Red: blood clotting system; Fib. = fibrinogen, CIG = cold-insoluble globulin (fibronectin); PK = prekallikrein, Pmg = plasminogen, F = factor in F II, F VII, F VIII, F IX, F XI, F XII, F XIII. Pink: carrier proteins; Alb. = albumin, Tf. = transferrin, Hp = haptoglobin, Hpx = hemopexin, GC = Gc globulin, Cp = ceruloplasmin, TBPA = prealbumin, TC = transcortin, RBP = retinol-binding protein, TBG = thyroxine-binding globulin. Yellow: complement system; proteins C1q, C1s, C2, C3, C4, C5, C6, C7, C8, C9, β_1H; AI = anaphylatoxin inactivator. D = C3 proactivator convertase, C3b ina = C3b inactivator, P = properdine, β_2II = C3 activator. Green: immunoglobulins IgA, IgD, IgE, IgG, IgM. Blue: proteinase inhibitors; α_1AT = α_1-antitrypsin, α_2M = α_2-macroglobulin, IαI = inter-α-trypsin inhibitor, α_1X = α_1-antichymotrypsin, ATIII = antithrombin III, C1 ina = C1 inactivator, α_2AP = α_2-antiplasmin. White: other plasma proteins; α_1s = α_1-acid glycoprotein, α_2HS = α_2HS-glycoprotein, α_1B = α_1B-glycoprotein, β_2I = β_2-glycoprotein I, β_2III = β_2-glycoprotein III, HRG = histidine-rich 3.8Sα_2-glycoprotein, α_1T = α_1T-glycoprotein, Znα_2 = Zn-α_2-glycoprotein, α_1M = 9.5Sα_1-glycoprotein (α_1-macroglobulin), 8Sα_3 = 8S-α_3-glycoprotein, CE = cholinesterase, 4S$\alpha_2\beta_1$ = 4S$\alpha_2\beta_1$-glycoprotein, α_1F = α_1-fetoprotein, CRP = C-reactive protein.—u = electrophoretic mobility, barbital buffer, pH 8.6, μ = 0.1.

ber of proteins in plasma is age-dependent[3,4]. In the case of newly born infants and in early childhood, the concentrations of a series of plasma proteins (including components of the complement and clotting systems and the immunoglobulins) are lower than those of adults. In the case of older individuals there may also be an increase or decrease in the concentrations of certain plasma proteins under normal physiological conditions[5–7]. Finally, the concentrations of several proteins in human plasma are sex-dependent: for example women have higher mean values for immunoglobulin M (IgM), α_2-macroglobulin, and apolipoprotein A[8].

3. Plasma Protein Systems and Groups

3.1. The Clotting System

Like the complement system, the blood clotting system is a very complex multienzyme system. Both systems involve activation and cascade reactions, which lead to intermediate products or new components.

Excluding the inhibitors, 14 protein components are involved in blood clotting. Most of them have been highly purified and physicochemically well characterized within the last few years (see Table 4)[9–12]. They differ considerably in their molecular weights, electrophoretic mobilities, and plasma concentrations. Apart from fibrinogen, plasminogen, and fibronectin, all clotting proteins are trace or ultra-trace proteins.

The blood clotting factors can be functionally classified into enzymes (factors II, IX, X, XI, XII, prekallikrein, and plasminogen), accessory factors (factors III, V, and VIII,

Table 4. Blood clotting factors: nomenclature and properties.

Factor	Conventional name	Molecular weight	u_{rel} [a]	c [mg/100 ml] [b]
Factor I	Fibrinogen	340000	β	200—450
Factor II	Prothrombin	72000	α_1	5—10
Factor III	Tissue factor			
Factor IV	Calcium ions			
Factor V	Proaccelerin	250000—300000	β	
Factor VII	Proconvertin	56000	α	*ca.* 0.1
Factor VIII	Antihemophilic globulin	*ca.* 2×10^6	β	*ca.* 0.1—1
Factor IX	Christmas factor	57000—70000	α_1	0.1—0.7
Factor X	Stuart factor	60000	α_1	
Factor XI	Plasma-thromboplastin-antecedent (PTA)	160000—210000	γ	*ca.* 0.6
Factor XII	Hageman factor	80000	β	1.5—4.7
Factor XIII	Fibrin stabilizing factor	340000	β	1.0—4.0
	Prekallikrein	80000—127000	γ	4—5
	HMW kininogen (high molecular weight kininogen)	120000	α	6
	Plasminogen	87000	β	10—15
	Fibronectin	440000	β	25—40

[a] Relative electrophoretic mobility, pH 8.6; see also Fig. 1. [b] Normal mean concentration in plasma.

The ultra-trace protein IgE which belongs to the immunoglobulins was, for example, only discovered because it occurred in the serum of a very small number of patients suffering from multiple myeloma in concentrations which were increased 50000 fold.

The present state of our knowledge of the diversity and concentrations of the plasma proteins has been strongly affected by the development of qualitative and quantitative immunological techniques. Very soon after the introduction of electrophoresis and immunological plasma protein determination, it was found that the concentration of a large number of proteins in plasma is age-dependent[3,4]. In the case of newly born infants and in early childhood, the concentrations of a series of plasma proteins (including components of the complement and clotting systems and the immunoglobulins) are lower than those of adults. In the case of older individuals there may also be an increase or decrease in the concentrations of certain plasma proteins under normal physiological conditions[5–7]. Finally, the concentrations of several proteins in human plasma are sex-dependent: for example women have higher mean values for immunoglobulin M (IgM), α_2-macroglobulin, and apolipoprotein A[8].

high molecular weight kininogen, and fibronectin), catalysts (phospholipid, Ca^{2+} ions), substrates (fibrinogen), and proteinase inhibitors.

It is impossible to describe the entire physiology of clotting in detail here, however prothrombin activation will be used as an example to show how well the protein chemistry of the reactions of the blood clotting system is now understood. The upper part of Figure 2[13] schematically demonstrates the fixation of prothrombin to a phospholipid vesicle; this is brought about *via* the Ca^{2+} binding sites in the amino terminal of the prothrombin molecule. It has been shown that the

clotting factors in the wound are also concentrated and activated according to this reaction principle.

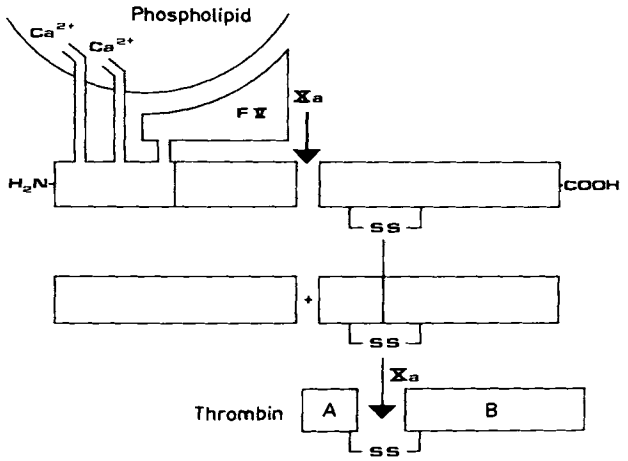


Fig. 2. Activation of prothrombin by factor Xa, catalyzed by Ca^{2+} and phospholipid (modified according to [13]). For details see text.

It is also evident from Figure 2 that thrombin is liberated from prothrombin by two successive peptide cleavages which are catalyzed by factor Xa. In the absence of factor V this activation proceeds very slowly, in the presence of factor V the reaction is accelerated a thousand-fold, *i.e.* factor V has an accessory function. Factor V apparently binds to the prothrombin molecule and the phospholipid and brings the two molecules so close together that charge transfer is possible, resulting in cleavage of the peptide bond by factor Xa. The prothrombin-activator complex is thus only formed to promote the activation of prothrombin. Even after the first cleavage of prothrombin by factor Xa the residual molecule is already separated from the activation complex. The resulting cleavage product does not contain any γ-carboxyglutamic acid residues and thus no longer differs in this respect from other serine esterases.

As regards the proteins involved in the clotting system, we will merely mention a protein which was already isolated more then 30 years ago[14], the function of which, however, was recognized only recently; this protein, which is insoluble in the cold, has now been called fibronectin[15]. It is a glycoprotein (molecular weight 440000) consisting of two subunits linked by disulfide bridges[16]. Fibronectin has an affinity for collagen, fibrin, heparin, and the cell surface[15, 17]. During the last phase of blood clotting it is cross-linked with itself and fibrin by factor XIII. The cross-linking with fibrin favors adhesion of fibroblasts to the fibrin matrix, this is an important prerequisite for the colonization of these cells in the wounded area, for their survival and collagen synthesis[18].

3.2. The Complement System

The importance of the complement system in plasma lies in its "complementation"—hence the name—of humoral and cellular immunity. Disregarding the inhibitors or inacti-

Table 5. Properties of the proteins of the complement system.

Protein	Molecular weight [a]	Chains [b]			c [mg/100 ml] [c]	u_{rel} [d]
1. Early activating proteins of the classical pathway						
$C1_q$	410000		6A	24000	15	γ_2
		18	6B	23000		
			6C	22000		
C1r	166000	2	[e]	83000	5	β
C1s	83000		1		5	α
C2	110000		1		1.5	β_1
C3	180000	2	α	105000	120	β_2
			β	75000		
C4	206000		α	93000	40	β_1
		3	β	78000		
			γ	33000		
C4 bp (C4-binding protein)	540000—590000	several		70000	?	β_2
2. Proteins of the alternative pathway						
C3	180000	2	α	105000	120	β_2
			β	75000		
B(C3-proactivator)	93000		1		20	β_1
D(C3-proactivator convertase)	24000		1		0.25	α
P(Properdin)	184000	4	[e]	46000	2	γ
C3b INA	93000	2	α	55000	3.4	β
(C3b-Inactivator)			β	42000		
β_1H	150000		1		50	β
3. Proteins of the terminal pathway						
C5	180000	2	α	105000	8	β_1
			β	75000		
C6	128000		1		7.5	β_2
C7	121000		1		5.5	β_2
C8	174000		α	77000	8	γ_1
		3	β	63000		
			γ	13700		
C9	79000		—		23	α

[a] Intact molecule. [b] After reduction and alkylation of the disulfide bonds. [c] Normal mean concentration in serum. [d] Relative electrophoretic mobility, pH 8.6. [e] The subunits are held together by non-covalent bonds.

vators, 17 proteins belong to this system (see Table 5)[19–22]. Although most complement components are trace proteins, all of them have been isolated and physicochemically characterized. They differ, like the proteins of the blood clotting system, in their molecular weights and electrophoretic mobilities. Their subunit composition has been extensively investigated. As far as is known, all complement components are glycoproteins.

From the chemical point of view the protein C1q is one of the most unusual proteins of the complement system and of the entire human blood plasma, for it resembles collagen. C1q (molecular weight approximately 400000) consists of 18 polypeptide chains (6A, 6B, and 6C) each containing approximately 200 amino acids. Amino acid sequence analyses have shown that the three types of chains are similar and that each possesses a region of about 80 amino acids close to the N terminal with typically collagen-like sequences[23]. The triplet Gly-X-Y, which repeats itself in this region, often contains hydroxyproline or hydroxylysine in position Y. Similarly to collagen and the basal membrane, glucosylgalactosyl groups are bound to the hydroxy groups of this hydroxylysine; these groups account for about 2/3 of the total carbohydrate content (9.8%) of the C1q molecule.

The complement system can functionally follow one of two pathways[19,20]. The first or classical pathway is activated by type IgG or IgM complexes. The proteins involved can be divided into several functional units or complexes: the unit with recognition properties (C1q, C1r, C1s), the activation unit (C2, C3, C4) and the membrane attack complex which is finally responsible for membrane lysis (C5, C6, C7, C8 and C9). The alternative pathway or properdine pathway is activated by aggregated IgA and by naturally occurring polysaccharides and lipopolysaccharides. Six proteins are involved in this pathway, one of them (C3) also participates in the classical pathway. The unit with recognition properties is here formed together with the initiating factor from the components, C3, B and D, whilst the complex consisting of C3b, B, D and P (=properdin) shows activation properties and

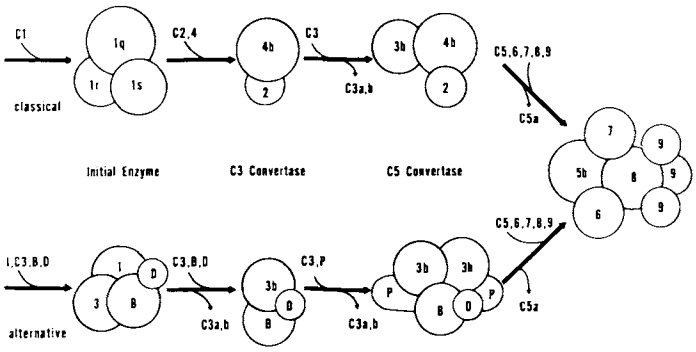


Fig. 3. Schematic representation of complement activation [20]. The circles symbolize different protein molecules. For details see text.

activation peptides (C3a and C5a) cause, for example, the liberation of histamine from mast cells, chemotactic attraction of polymorphonuclear leucocytes and contraction of smooth muscle.

3.3. The Proteinase Inhibitors

Whereas in the two preceding sections protein systems have been described in which the components react with one another, the proteinase inhibitors represent a group of human plasma proteins with similar functions. The proteinase inhibitors are closely connected with the blood clotting and complement systems. The inhibitors act in the cascade-like system of activating steps and are responsible for the regulation or inactivation of the activated enzymes. The special importance of the proteinase inhibitors lies in the fact that they maintain the equilibria of *several* multienzyme systems. This means, certain proteinase inhibitors are acting with a given priority in two or more multienzyme systems.

Eight proteinase inhibitors are so far known, seven of them have been purified and well characterized chemically (Table 6)[27,28].

Table 6. Properties of the proteinase inhibitors of human plasma.

	Inhibitors	Molecular weight	c [mg/100 ml] [a]	u_{rel} [b]	Carbohydrate [wt.-%]
α_1AT	α_1-Antitrypsin	54000	290.0	α_1	12.2
α_1X	α_1-Antichymotrypsin	69000	48.7	α_1	24.6
IαI	Inter-α-trypsin inhibitor	160000	50.0	α_1—α_2	8.4
ATIII	Antithrombin III	65000	23.5	α_1—α_2	13.4
C1-ina	C1 inactivator	104000	23.5	α_2	34.7
α_2M	α_2-Macroglobulin	725000	260.0	α_2	7.7
α_2AP	α_2-Antiplasmin	70000	7.0	α_2	14.0
	Inhibitors of plasminogen activation				

[a] Normal mean concentration in serum. [b] Relative electrophoretic mobility, pH 8.6.

acts on C5—C9 in an analogous fashion to the C5-convertase complex of the classical pathway (Fig. 3).

The biological consequences of activation of the complement system are:

1) irreversible structural and functional modification of biological membranes and subsequent cell death[24–26] and
2) activation of special cell functions triggered by the reaction products of complement components[19]. Two such

When compared with the proteins of the systems so far discussed, the concentrations of the proteinase inhibitors in human plasma are relatively high. They differ greatly in their molecular weights and, on the basis of their electrophoretic mobilities, they are all α-globulins. α_1-Antitrypsin, α_1-antichymotrypsin, antithrombin III, C1 inactivator, and α_2-antiplasmin each consist of a single polypeptide chain. α_2-Macroglobulin has a tetrameric structure[29,30]; the subunits (molecular weight 185000) are similar or identical. Two di-

sulfide dimers are held together by non-covalent bonds and form the native α_2-macroglobulin. One molecule of α_2-macroglobulin binds two zinc atoms[31]. The subunit structure of the inter-α-trypsin inhibitor is still unknown.

All proteinase inhibitors are glycoproteins. Little is yet known about their chemical composition. According to amino acid sequence analyses of the N-terminals of α_1-antitrypsin and α_1-antichymotrypsin, there is no sequence homology between their first amino acid residues. There is, however, a strong structural correlation of the two proteins between residues 33—45 of α_1-antitrypsin and residues 16—27 of α_1-antichymotrypsin[32,33]. There is no homology with the N-terminal moiety of antithrombin III. It is, however, remarkable that the unusual terminal arginine is found in both α_1-antichymotrypsin and inter-α-trypsin inhibitor.

All proteinase inhibitors with the exception of α_1-antichymotrypsin exhibit a wide spectrum of activities, *i.e.* they can neutralize several proteolytic enzymes (Table 7)[28].

inhibitor for each protease present in the plasma. Information about the real physiological function of an inhibitor cannot, however, be derived from its activity spectrum; this can only be achieved by determining the molar concentrations of the inhibitors and their relative affinities for the proteolytic enzymes in question.

The proteinase inhibitors can be classified into inhibitors of proenzyme activation, blood clotting, fibrinolysis, kinin liberation, and of endogenous and other proteases (cf. Table 8). In clinical diagnoses the inhibitors can be determined by functional and immunological methods.

3.4. The Immunoglobulins

The immunoglobulins represent a group of five proteins which have, in addition to functional similarity and structural homology, a common site of synthesis. Of all the plasma

Table 7. Spectrum of the action of proteinase inhibitors (see Table 6) of human plasma. + = strong, possibly stoichiometric inhibition, ? = not determined.

Proteinase Name	Function	Inhibitors α_1AT	α_1X	IαI	ATIII	C1-ina	α_2M	α_2AP
Factor IIa	clotting	–	–	–	+	–	+	+
Factor Xa	clotting	–	–	–	+	–	–	–
Factor XIa	clotting	–	–	–	weak	+	–	+
Factor XIIa	clotting	–	–	–	weak	+	–	+
Plasmin	fibrinolysis	+	–	–	weak	+	+	+
C1r	complement	–	–	?	–	+	–	–
C1s	complement	–	–	?	–	+	–	–
Prekallikrein activator	kallikrein activation	?	?	–	–	+	–	?
Plasma callikrein	kallikrein activation	+	–	–	weak	+	+	+
PF/Dil	permeability	–	–	?	–	+	?	?
Acrosin	fertilization	+	–	+	+	–	+	?
Trypsin	pancreatic hydrolysis	+	–	+	+	weak	+	+
Chymotrypsin	pancreatic hydrolysis	+	+	weak	–	weak	+	–
Elastase	phagocytosis	+	–	–	–	–	+	?
Collagenase	phagocytosis	+	–	–	–	–	+	?
Cathepsin D	phagocytosis	–	–	–	?	?	+	?
Cathepsin G	phagocytosis	?	+	?	?	?	?	?
Papain	metabolism	–	–	?	?	?	+	?
Bromelin	metabolism	–	–	?	?	?	+	?
Ficin	metabolism	–	–	?	?	?	+	?

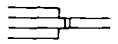
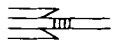
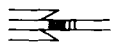
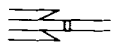
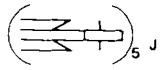
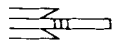
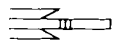
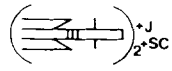
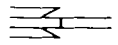
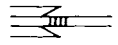
This is apparently a general feature of the inhibitory action and also of the specificity of proteinases. Most of them are serine proteinases. α_1-Antitrypsin, for example, thus inhibits a large number of enzymes regardless of their origin. A further consequence of this fact is that there is more than one

proteins the immunoglobulins have been investigated physicochemically and also functionally in the most detail. Since there are good review articles dealing with the immunoglobulins[34–37] we have only listed a few of their physicochemical properties (Table 9)[38].

Table 8. Physiological functions of some proteinase inhibitors of human plasma.

Inhibitor	Function	Pathology
C1 Inactivator	Activation and control of: blood clotting, fibrinolysis kallikrein, and complement	Hereditary angioneurotic edema: permeability disorders as a result of a deficiency or functional inactivity of the inhibitor
Antithrombin III	Local limitation of clotting	Hereditary antithrombin III deficiency: thromboembolic disorders
α_2-Macroglobulin	Local limitation of clotting	Consumption of antithrombin III: hypercoagulability
α_2-Macroglobulin	Limitation of fibrinolysis to pathological substrates	Consumption of α-macroglobulin during fibrinolytic therapy
C1 Inactivator	Limitation of fibrinolysis to pathological substrates	
α_1-Antitrypsin	Limitation of fibrinolysis to pathological substrates	
α_2-Macroglobulin	Control of infections and inflammations; prevention of autodigestive processes and side reactions in the clotting system	Hereditary α-antitrypsin deficiency: pulmonary emphysema
α_1-Antitrypsin	Control of infections and inflammations; prevention of autodigestive processes and side reactions in the clotting system	Local consumption of the inhibitors in: acute inflammations, infections of the nasal mucous membrane, rheumatic arthritis in the synovial fluid, in burns, leukemia, endotoxin shock
Inter-α-trypsin inhibitor	Control of infections and inflammations; prevention of autodigestive processes and side reactions in the clotting system	
α_2-Antiplasmin	Control of fibrinolysis	Hereditary α_2-antiplasmin deficiency: strong bleeding tendencies, hemarthrosis

Table 9. Properties of human immunoglobulins [38]. J indicates J-chaing, SC signifies secretory component.

Ig	Chain structure		Molecular weight	c [mg/100 ml] [a]	$\tau_{1/2}$ [b]	C-Fix. (C1q) [c]	Monocyt.-adhesion
IgG1			146000	900	21 ± 5	+	+
IgG2			146000	300	20 ± 2	±	−
IgG3		[d]	165000	100	7 ± 1	+	+
IgG4			146000	50	21 ± 2.5	a.p.	−
IgM			970000	150	5	+	−
IgA1		[e]	160000	300	6	a.p.	−
$A_2m(1)$ IgA2		[e]					
$A_2m(2)$		[e]	160000	50	6	a.p.	−
sIgA		[e]	380000—390000	0—5		−	
IgD			172000—200000	3	3	−	
IgE		[e]	188000—196000	0.03	2.3—4	a.p.	

[a] Normal mean concentration in serum. [b] Half-life (days). [c] Complement fixation; a.p. activation of complement *via* the alternative path by aggregated molecules. [d] Up to 15 disulfide bridges. [e] Number of interchain disulfide bridges uncertain.
m18,x

3.5. The Lipoproteins

The lipoproteins will be briefly described as the final example of the protein groups. Intensive studies on plasma lipoproteins have contributed considerably to the understanding of lipid metabolism and the diseases connected with it[39-41]. The lipoproteins are complex macromolecules whose lipid moieties are linked to the protein components by non-covalent bonds. The lipoproteins also have a small carbohydrate content. They are classified into four groups according to their physical characteristics and their chemical composition. Each of these groups can be further divided into subclasses by means of ultracentrifugation or gel filtration, the subclasses are however still heterogeneous with respect to their compositions and sizes (see Table 10).

Table 11. Distribution of polypeptide chains (apolipoproteins) within the lipoprotein classes. + = Detected in traces, − = not detected.

Apo-lipoprotein	Chylomicrons	VLDL	LDL	HDL
	[% of the apolipoprotein fraction]			
A-I	+	+	−	65—70
A-II	+	+	−	25—50
B	5—20?	40 [a]	>95	−
C-I	15	10 [a]	+	1—3
C-II	15	10 [a]	+	1—3
C-III	45	30 [a]	+	5—10
D [b]	−	+	−	+
E	+	[c]	−	+
F	−	−	+	[d]

[a] Varies within the VLDL subspecies, denser VLDL contain more B in relation to C. [b] Is also described as the "thin line protein" and Apo A-III. [c] Integral component of the apolipoprotein fraction of the VLDL. [d] Integral component of the apolipoprotein fraction of the HDL.

Table 10. Properties of the lipoproteins of human plasma. VLDL, LDL, and HDL indicate lipoproteins with very low, low, or high densities, respectively.

	Chylomicrons	VLDL	LDL	HDL
Density	0.95	0.95—1.006	1.006—1.063	1.063—1.210
Molecular weight		8×10^6—35×10^6	2×10^6—4×10^6	175000-360000
Diameter [Å]	750—10000	300—800	215—220	
Triglycerides [%]	80—95	60	10	5
Cholesterol [%]	5	12	50	20
Phospholipid [%]	3	18	15	25
Protein [%]	1—2	10	25	50

A series of proteins (apolipoproteins) is known to be involved in different concentrations in the construction of the lipoprotein classes (Table 11)[39]. Whereas the polypeptides A-I and A-II are found mainly in the HDL (high density lipoproteins), protein B is preferentially found in the LDL and VLDL (low and very low density lipoproteins respectively)[41a].

According to latest investigations[41], type A and B polypeptides have a "core" protein character and act as nuclei in the formation of all lipoprotein complexes apart from the chylomicrons. It is not known whether the Type C polypeptides have a corresponding function.

As the C proteins are readily transferred between the HDL and VLDL, it is not likely that they are tightly bound to the

core proteins A or B. Furthermore the stoichiometric ratio C-I:C-II:C-III is not the same in the HDL and VLDL. It can thus be concluded that at least one of the C peptides exchanges between these two lipoprotein classes. The peptide C-II has, in addition to lipid transport, another physiological function—it is a potent activator of the enzyme lipoprotein lipase.

4. Proteins with Known Functions (Carrier Proteins)

In this section proteins will be discussed which cannot be assigned to a protein system but whose function is known. This function is usually the transport or binding of substances in blood serum. The proteins can bring these substances to their sites of action or they prevent the body from losing important metabolic products or other compounds; they can, however, also remove metabolic products and thus have a detoxifying function. They do not carry out these functions in a systemic process as do the clotting or complement proteins, but act individually. In some cases, for example an inborn deficiency of one of these transport proteins, another protein can take over the function of the one that is lacking.

Some proteins with carrier functions are listed in Table 12.

Prealbumin[46] is a plasma protein with considerable biological importance; it transports a hormone and a vitamin. Whereas thyroxine is directly bound to the prealbumin molecule, retinol (vitamin A alcohol) is indirectly bound to prealbumin *via* its specific carrier protein—the retinol-binding protein[47]. Formation of this very loosely bound protein-protein complex prevents fast excretion of the relatively low molecular weight retinol-binding protein by the kidneys.

Scientists at the Laboratoire de Christallographie, CNRS, in Paris and the Laboratory of Molecular Biophysics in Oxford have performed structural studies in collaboration with our group on prealbumin at a resolution of 2.5 Å. According to these investigations, prealbumin consists of four identical subunits which are held together by non-covalent bonds. The subunits form a canal in the middle of the molecule which contains the two binding sites for thyroxine[48,49]. The complete complex of prealbumin and retinol-binding protein can bind one molecule of thyroxine and one of retinol.

Thyroxine-binding globulin[50]: the structure of this globulin which is found in serum in traces is also now well known. Its secondary and tertiary structures have been investigated by circular dichroism and fluorescence spectroscopy. The relaxation time shows that thyroxine-binding globulin is a compact, symmetrical molecule in which one half of the amino acid residues form α-helices and the other half β-pleated sheets. The molecule has only one polypeptide chain and is a

Table 12. Properties of the carrier proteins of human plasma.

Protein	Biological function	Molecular weight	c [mg/100 ml] [a]
Prealbumin	Binding of thyroxine and retinol binding protein	54980	25
Albumin	Transport of ions, pigments, *etc.*, osmotic function	66000	3500—5500
Transcortin	Binding and transport of cortisol	55700	4
Thyroxine binding globulin	Binding of thyroxine	54000	1—2
Retinol binding protein	Binding of retinol	21000	4.5
Gc-Globulin	Binding of vitamin D_3	50800	40
Transcobalamine I	Binding of vitamin B_{12}	60000	?
Transcobalamine II	Binding and transport of vitamin B_{12}	53900	Traces
Ceruloplasmin	Binding of copper; oxidase	132000	35
Transferrin	Binding and transport of iron	76500	295
Hemopexin	Binding of hemin	57000	80
Haptoglobin	Binding of hemoglobin	100000 (Typ 1-1)	170—235

[a] Normal mean concentration in serum.

The carrier proteins are synthesized at different sites; they differ in their molecular weights, and their concentrations in human serum range from 1 to over 1000 mg/ml (albumin). Of all the plasma proteins albumin has the most diverse binding properties. It is impossible to mention all the endogenous or exogenous substances which are transported by albumin. It should be mentioned here that the technique of electrophoresis provided the most important contribution in the discovery of the carrier proteins and in the recognition of the prime importance of albumin as a vehicle protein. The name of *Hans Bennhold*[42] is closely associated with these early studies.

The most important carrier proteins will be briefly dealt with in the following.

Albumin: a great deal of progress has been made as regards the elucidation of the biosynthesis of albumin, its structure and binding sites[43,44]. Bilirubin, for example, is bound with high affinity to the lysine residue at position 240[45].

glycoprotein. It is very stable in the alkaline range up to pH = 10.5, below pH = 5.0 it very readily loses its hormone-binding properties in an irreversible fashion[51,52].

Gc-globulin[53]: the group specific component discovered by *Hirschfeld*[54]—now called Gc-globulin—was recently shown to be identical with transcalciferin, a plasma carrier protein which transports vitamin D. Gc-globulin has a binding site for vitamin D_3 and its 25-hydroxyderivative, it may also transport other vitamin D metabolites[55,56].

Transcobalamin I and II[57-59]: at the present time, not very much is known about the structure and composition of the vitamin B_{12}-binding proteins. This is certainly closely connected with their very low concentrations in human serum. They can be chromatographically separated into two fractions—transcobalamin I and II. Transcobalamin I is a glycoprotein with a carbohydrate content of 33%, transcobalamin II is a pure polypeptide. The two proteins differ from each other immunologically. Transcobalamin II is apparently of

greater physiological importance than transcobalamin I; it is responsible for the transfer of vitamin B_{12} to tissue cells.

Hemopexin[60,61] is a heme-binding serum protein; it is a single-chain glycoprotein with a carbohydrate content of approximately 22%. It binds equimolar quantities of porphyrins and metallo-porphyrins and prevents the body from losing iron.

Haptoglobin[62], the hemoglobin-binding protein of the serum, exhibits genetic polymorphism. Haptoglobin from homozygote Hp 1-1 individuals only gives one band on molecular-sieve electrophoresis; haptoglobin of homozygote type Hp 2-2 and heterozygote type Hp 2-1 is, however, composed of a series of polymorphous proteins with increasing molecular weights[63,64]. Haptoglobin is composed of light (α) and heavy (β) chains. The heavy β chain (molecular weight 40000) is common to all types and contains the carbohydrate moiety. There are three forms of the lighter α chain—α_1F, α_1S, and α_2 chains (molecular weights 8900, 8900, and 16000 respectively). The α_2 chain is supposed to have originated from the α_1 chain by gene duplication. The complete amino acid sequence analyses of all the α chains are known. There is an evolutionary similarity between the α_2 chain of haptoglobin and the L chains of the immunoglobulins[65]. An α chain-like segment has also been found in the α_1-acid glycoprotein[66].

Transferrin[67,68] has, as a metal-binding protein, a true carrier function. It shows structural homology with lactoferrin and ovotransferrin in its N-terminal amino acid sequence[69]. Transferrin possesses two binding sites for iron which, contrary to earlier assumptions, show small but significant differences and can be identified by isoelectric focussing[70,71]. The mechanism of iron release at the reticulocytes has been well studied[72,73].

Ceruloplasmin[74] is not a true carrier protein, but possesses ferroxidase activity. It contains one peptide chain and six copper atoms which are bound differently[75,76]. Part of a 20000 dalton ceruloplasmin fragment has a structure similar to that of plant plastocyanins and bacterial azurines[77].

5. Human Plasma Proteins with Unknown Functions

Several α- and β-glycoproteins from human plasma have been purified and well characterized physicochemically without anything being known about their functions (Table 13).

Some more recent results concerning these proteins will be given in the following; the majority of these proteins were first purified and described by our laboratory.

The structure of the *α_1-acid glycoprotein*[78], which is found in human serum in relatively high concentrations, has been well studied thanks to the excellent work of *K. Schmid et al.*[79-81]. It consists of a single polypeptide chain whose asparagine residues in positions 15, 38, 54, 75 and 85 are *N*-glycosidically linked to polysaccharide units. Its carbohydrate content is almost 40%. There is a certain similarity between the amino acid sequences of α_1-acidic glycoprotein and the immunoglobulins. It is assumed that α_1-acidic glycoprotein originated from the same stem as the immunoglobulins but before the primitive L chain arose[80]. In connection with this fact it is interesting that α_1-acid glycoprotein is not only synthesized in the liver but also in lymphocytes, granulocytes, and monocytes[82]. α_1-Acidic glycoprotein binds several steroids and basic drugs such as aprenolol and imipramine[83] and exhibits striking inhibitory properties in platelet aggregation[84].

Table 13. Properties of human plasma proteins with unknown functions.

Protein	Molecular weight	Carbohydrate [wt.-%]	I.P. [a]	c [mg/100 ml] [b]
α_1-Acid glycoprotein	41000	37.9	2.7	90
α_1T-glycoprotein	60000	13.7		8
α_1B-glycoprotein	50000	13.3	4.4—4.6	22
9.5S-α_1-glycoprotein	308000	12.8	5.0	5.5
α_1-Microglobulin	26700	20		5.4
Zn-α_2-glycoprotein	41000	18.2	3.8	5
α_2HS-glycoprotein	49000	13.4	4.1	60
Histidine-rich 3,8S-α_2-glycoprotein	58500	14.3	5.6—6.5	9
Leucine-rich 3,1S-α_2-glycoprotein	49600	23	3.8—4.1	2.1
8S-α_3-glycoprotein	220000	31.4	4.2—4.6	4
4S-$\alpha_2\beta_1$-glycoprotein	60000	27.7	4.0	0.02
β_2-Microglobulin	11800	0	5.56	0.15
β_2-Glycoprotein I	40000	18.8	5.4—6.25	20
β_2-Glycoprotein III	35000	10	5.1—5.8	10
C-reactive protein	110000—140000	0		<0.1

[a] Isoelectric point. [b] Normal mean concentration in plasma.

Whereas there is no recent data for the *α_1T-*[85] and *α_1B-glycoproteins*[86], it has been shown that the *9.5Sα_1-glycoprotein*[87,88] is identical with the P component of human plasma and must be assigned to the "pentagonal structure" found on electron microscopical examination of organs with amyloid deposits[89]. The 9.5Sα_1-glycoprotein is also identical with the C1t protein described by *Painter et al.* which was erroneously considered to be a fourth subcomponent of the C1 complex of the complement system[90]. In reactions with galactans, the 9.5S-α_1-glycoprotein has lectin-like properties[91]. On the basis of the sequence analysis of the first 30 amino acids, there is extensive homology between the 9.5Sα_1-glycoprotein and the C-reactive protein[92,93].

There are no recent findings concerning the physiological functions of the *Zn-α_2-*[94], *8S α_3-*[95], *4S $\alpha_2\beta_1$-*[96] and leucine-rich *3.1S α_2-glycoproteins*[97]. 3.1S α_2-Glycoprotein was first discovered by us three years ago and is distinguished by the fact that about every fifth one of its amino acids is leucine.

According to more recent studies, *α_2-HS-glycoprotein*[98] is a component of bone matrix; it is supposed to have opsonizing properties (*i.e.* causes increased phagocytosis) and its level decreases in the serum of patients after major surgical operations[99,100].

According to *Morgan*, the histidine-rich *3.8S α_2-glycoprotein*[101] binds hemin, other organic compounds and some divalent metal ions[102,103]. It is, however, still not certain whether these properties are of physiological significance.

α_1-Microglobulin[104,105] is a glycoprotein and was first isolated from the urine of patients suffering from tubular proteinuria by a Swedish group of workers. It is also present in the serum and urine of healthy individuals. *Takagi et al.*[106] have recently examined its distribution in tissues. It is localized on the surface of T and B lymphocytes and is apparently synthesized there. It still has to be resolved whether α_1-microglobulin is identical with the α_1-microglycoprotein isolated by *Seon* and *Pressman*[107] from the urine of patients suffering from cancer.

Since the discovery of *β_2-microglobulin* more than ten years ago by *Berggård* and *Bearn*[108], many reports have been published about this protein. Here attention will therefore only be drawn to its structural and evolutionary relationship to the immunoglobulins, to its identification as a membrane protein and to the fact that it is a component of the histocompatibility antigens[109].

β_2-Glycoprotein I was already known in 1961[110]. It is a carbohydrate-rich, polymorphous glycoprotein which can be easily crystallized[111]. We were later able to find a family who suffered from an hereditary deficiency of β_2-glycoprotein I but without any recognizable ill effects[112]. On gel diffusion according to *Ouchterlony*, this protein is directly precipitated by dextran sulfate and heparin and transports heparin on agar gel electrophoresis[113]. *Burstein* and *Legmann*[114] have recently discovered that the precipitation of tryglyceride-rich lipoproteins with anionic detergents only succeeds in the presence of β_2-glycoprotein I. In connection with this, attention is drawn to a recent publication by *Polz et al.*[115] according to which β_2-glycoprotein is supposed to be an integral component of the very low density lipoproteins (VLDL). It is perhaps involved in triglyceride metabolism.

β_2-Glycoprotein III was also first described several years ago by our laboratory[116]; even now nothing more substantial is known about its physiological importance. *Chase* and *Prochaska*[117] showed by means of immunofluorescence that in several diseases it is deposited in the kidney where it is apparently associated with immunocomplexes.

The *C-reactive protein* is an example of the "acute phase reactants" whose serum levels rise rapidly in the acute phase of particularly inflammatory diseases. The C-reactive protein does not contain any carbohydrate; its amino acid sequence is known. It consists of five identical subunits (molecular weight 21 500) which are each composed of 187 amino acids[118]. According to electron microscopical studies, these subunits are assembled in the form of a ring so that a pentagonal structure[93] similar to that of the 9.5S-α_1-glycoprotein can be seen. The true physiological function of the C-reactive protein is still unknown despite these precise structural and chemical findings and although it has been found to perform a series of biological activities (such as immunoprecipitation[119] and -agglutination[120], complement activation[121,122], acceleration of phagocytosis[123,124], and inhibition of thrombocyte aggregation[125]).

6. Genetic Modifications in Human Plasma Proteins

All plasma proteins are genetically controlled. During the course of evolution the genes responsible for the synthesis of these proteins have been changed so much by mutations that the structures and activities of the proteins now differ considerably[126,127]. In human plasma proteins genetic defects must be distinguished from polymorphism. In the first case the structure of the proteins is modified with loss of the original biological activity or the proteins are completely lacking (*i.e.* they are not synthesized). In the case of loss of activity these proteins can still be detected by immunological techniques.

In the case of polymorphism, a change in the primary structure gives rise to separate phenotypes, the biological activity is not affected.

Hereditary deficiencies of more than 30 human plasma proteins are known. The lack or defective synthesis of these proteins is usually closely associated with a more or less serious disease (Table 14).

Table 14. Genetic deficiencies in human plasma proteins.

Protein	Clinical condition
α_1-Antitrypsin	Pulmonary emphysema; neonatal hepatitis
α_1-Lipoprotein	Tangiers disease; enlarged yellow tonsils; hepatosplenomegaly; lymphadenopathy
C1-Inactivator	Angioneurotic edema
Ceruloplasmin	Wilson's disease; actue hemolytic anemia
Transferrin	Hypochromic anemia
Transcobalamine II	Neonatal megaloblastic anemia, growth disorders, repeated infections
β-Lipoprotein	Steatorrhea, neuromuscular disorders
C1q	Hypogammaglobulinemia?
C1r	Kidney and skin disorders
C3, C5, C3b INA	Impaired bactericidal activity
IgG, IgA, IgM	Antibody-deficient diseases
Fibrinogen	Abnormal bleeding tendencies
Prothrombin	
Proaccelerin	
Proconvertin	
Antihemophilic globulin	
Christmas factor	
Stuart factor	
Fibrin-stabilizing factor	
Prekallikrein	
α_2-Antiplasmin	
Albumin	Healthy
Thyroxine-binding globulin	
Haptoglobin	
β-Glycoprotein I	
C2, C6, C7	

The plasma proteins which exhibit genetic polymorphism are compiled in Table 15. The phenotypes can be detected by electrophoretic or immunological techniques or, as in the case of cholinesterase, by enzymatic methods. In several cases it is known that polymorphism is due to the exchange of single amino acids or entire polypeptide chains.

Table 15. Human proteins with genetic variants or genetic polymorphism.

Protein	Variants
Albumin	So far 20 variants
α_1-Antitrypsin	Pi-system, so far 25 known alleles
α_1-Acid glycoprotein	Types FF, FS, SS
α_2-Macroglobulin	Xm-system
Gc-Globulin	Gc1-1, Gc2-1, Gc2-2 and rare variants
Ceruloplasmin	CpA, CpB, CpC, CpNH, CpBpt, CpTh
Haptoglobin	Hp1-1, Hp2-1, Hp2-2 and rare variants
Cholinesterase	So far 10 phenotypes
Transferrin	So far 20 variants
β-Lipoprotein	Ag-system, Lp(a)- and Ld-system
C3-Proactivator	Bf FF, Bf FS, Bf SS and others
C2-component	Types $C2^1$ and $C2^{2\text{-}1}$
C3-component	So far 16 variants
C4 component	So far 8 phenotypes
C6 component	Types A, B, AB and rare variants
Fibrinogen	Fibrinogen Baltimore, fibrinogen Detroit
IgG	Gm-allotypes of γ-chains
IgA	Am-allotypes of α-chains
IgM	Mm-allotypes of μ-chains

If the numerous polymorphisms of enzymes and other genetic characteristics of man are added to the genetic polymorphism of the plasma proteins, it is clear that each indi-

vidual has a unique combination of proteins and enzymes, *i. e.* is characterized by his pattern of polymorphism in the same way as by a fingerprint[128].

7. Function of Carbohydrates in Human Plasma Proteins

The majority of the human plasma proteins are glycoproteins, only a few such as albumin, the retinol-binding protein, or the C-reactive protein are free of carbohydrate.

Glycoproteins in the broadest sense of the word are proteins which contain carbohydrates as prosthetic groups. The carbohydrates which have so far been found in human glycoproteins are *N*-acetyl-D-glucosamine, *N*-acetyl-D-galactosamine, D-galactose, D-mannose, D-glucose, L-fucose, *N*-acetylneuraminic acid, and D-xylose.

The chemistry of the carbohydrates of the serum glycoproteins obeys the following rules: only asparagine, threonine, and serine—in rare cases also hydroxylysine—are linked to the oligosaccharide units. The oligosaccharides can be structurally divided into alkali-stable chains which are *N*-glycosidically bonded to asparagine or alkali-labile chains which are *O*-glycosidically bonded to serine or threonine. *N*-Acetyl-D-glucosamine always participates in the *N*-glycosidic bonds and only *N*-acetyl-D-galactosamine participates in the *O*-glycosidic bonds. In extremely rare cases, as is found in the C1q protein, a glucosyl-galactosyl disaccharide is *O*-glycosidically linked to hydroxylysine.

Of all the functions[129–131] performed by the carbohydrates of the glycoproteins, that of recognition is the most important. Positive recognition will be explained using ceruloplasmin as an example. As long as the terminal neuraminic acid molecule is still bound to ceruloplasmin it is not recognized by the parenchymal liver cells. After cleavage of this molecule however (asialoglycoprotein), the galactose residues exposed are immediately recognized by a lectin-like protein in the liver cell membrane and the protein is very quickly eliminated from the circulation[132]. An example of negative recognition is provided by the masking or covering of antigen determinants or of larger areas on the membrane surface[133].

Lectins are very important for the characterization and determination of glycoproteins. Lectins[134] are proteins or glycoproteins which, in a manner analogous to that of antibodies, react specifically with carbohydrates but they do not have an antibody structure. They are found in plants, invertebrates and vertebrates, and their property of recognizing specific carbohydrate structures is a valuable aid in the study and isolation of glycoproteins. We were recently able to show in collaboration with *Uhlenbruck* that some serum glycoproteins have lectin-like properties[91].

8. Clinical Importance of Plasma Proteins

8.1. Diagnoses

Many diseases are accompanied by changes in the plasma protein levels. The quantitative determination of one or more plasma proteins is thus of importance for diagnosing and monitoring the course of these diseases. In the first stages of this development the technique of electrophoresis[135–137] was most important but the plasma proteins are now mostly determined quantitatively by immunological methods[138,139]. The necessary precipitating antisera are chiefly obtained by immunizing animals with highly purified plasma proteins. More then 80 proteins can now be determined by these techniques.

8.2. Prophylaxis and Therapy

Since proteins with prophylactic and therapeutic actions were first obtained from human blood plasma, more than 20 protein preparations have been developed (Table 16).

Table 16. Prophylactically and therapeutically active "drugs" obtained from human plasma.

Year	Plasma protein	Indication
1942	Gammaglobulin (immunoglobulin)	Antibody deficiency
1942	Albumin	Volume substitute, plasma expander
1947	Fibrinogen	Fibrinogen-deficiency
1947	Antihemophilic globulin (AHG)	Hemophilia A
1948	Stabilized serum conserve	Volume substitute, plasma expander
1960	Cryoprecipitate (fibrinogen and AHG)	Fibrinogen deficiency and hemophilia A
1962	Intravenously administrable gamma globulin	Antibody deficiency
1965	Specific immunoglobulins	Antibody deficiency
1966	Anti-rhesus-D immunoglobulin	Hindrance of rhesus erythroblastosis
1968	Prothrombin concentrate	Prothrombin and factor-VII deficiency, hemophilia B
1969	Factor-IX concentrate	Hemophilia B
1969	IgA concentrate	Antibody deficiency
1969	IgM concentrate	Antibody deficiency
1969	Serum cholinesterase	In anesthesia with atypical cholinesterases
1970	Transferrin	Inborn deficiencies
1972	Fibrin-stabilizing factor (F XIII)	Deficiencies, wound-healing disorders
1973	C1 inactivator	Angioneurotic edema
1976	Plasminogen	Fibrinolysis therapy (in clinical trial)
1977	Antithrombin III	Deficiencies (high risk of thrombosis) (in clinical trial)
1979	Thyroxine-binding globulin	Hyperthyreosis (in clinical trial)

The immunoglobulins and albumin were the first proteins to be developed in this way. Blood clotting factors and several other biologically active proteins soon became available to hospitals for prophylactic or therapeutic use. Improved fractionation techniques and new findings concerning blood plasma proteins will certainly enable still more proteins from human blood to be developed as "drugs". In this way the limited quantities of blood plasma available can be better and more effectively utilized than is possible with blood plasma transfusion.

Received: November 19, 1979 [A 303]
German version: Angew. Chem. *92*, 83 (1980)
Translated by Dr. *Gail Schulz*, Darmstadt-Weiterstadt

[1] *H. E. Schultze*, Angew. Chem. *62*, 395 (1950).
[2a] *G. A. Jamieson, T. J. Greenwalt:* Trace Components of Plasma. Vol. V. Alan R. Liss, New York 1976.
[2b] *F. W. Putnam* in [2a], p. 1.
[3] *H. E. Schultze, H. G. Schwick*, Behringwerk-Mitt. *53*, 57 (1958).
[4] *F. Koch, H. E. Schultze, H. G. Schwick*, Klin. Wochenschr. *36*, 17 (1958).

[5] *O. Haferkamp, D. Schlettwein-Gsell, H. G. Schwick, K. Störiko,* Gerontologia *12*, 30 (1966).
[6] *O. Haferkamp, D. Schlettwein-Gsell, H. G. Schwick, K. Störiko,* Klin. Wochenschr. *44*, 725 (1966).
[7] *H. G. Schwick:* Alter und Blutgerinnung. Schattauer, Stuttgart 1970, pp. 85 ff.
[8] *B. Wecke, P. A. Krasilnikoff,* Acta Med. Scand. *192*, 149 (1972).
[9] *E. W. Davie, K. Fujikawa,* Annu. Rev. Biochem. *44*, 799 (1975).
[10a] *F. W. Putnam:* The Plasma Proteins. Academic Press, New York.
[10b] *E. W. Davie, D. J. Hanahan* in [10a], Vol. III, p. 422 (1977).
[11a] *D. H. Bing:* The Chemistry and Physiology of the Human Plasma Proteins. Pergamon Press, New York 1979.
[11b] *R. F. Doolittle, H. Bouma II, B. A. Cotrell, D. Strong, K. W. K. Wate* in [11a], p. 77.
[12] *O. D. Ratnoff,* Behring Inst. Mitt. *63*, 135 (1979).
[13] *J. W. Sutti, C. M. Jackson,* Physiol. Res. *57*, 1 (1977).
[14] *P. R. Morrison, J. T. Edsall, S. G. Miller,* J. Am. Chem. Soc. *70*, 3103 (1948).
[15] *A. Vaheri, D. F. Mosher,* Biochem. Biophys. Acta *516*, 1 (1978).
[16] *D. D. Wagner, R. O. Hynes,* J. Biol. Chem. *254*, 6746 (1979).
[17] *E. Engvall, E. Ruoslathi, E. J. Miller,* J. Exp. Med. *147*, 1584 (1978).
[18] *H. Hörmann, K. Kühn,* Fortschr. Med. *95*, 1299 (1977).
[19] *H. J. Müller-Eberhard* in [10a], Vol. I, p. 394 (1975).
[20] *H. J. Müller-Eberhard,* Behring Inst. Mitt. *61*, 1 (1977).
[21a] *M. Z. Atassi:* Immunochemistry of Proteins. Vol. III. Plenum Press, New York 1979.
[21b] *R. M. Stroud, J. E. Volanakis, S. Nagasawe, F. Lint* in [21a], p. 167.
[22] *P. J. Lachmann,* Behring Inst. Mitt. *63*, 25 (1979).
[23] *R. R. Proter, K. B. M. Reid,* Nature *275*, 699 (1978).
[24] *E. R. Podack, G. Biesecker, H. J. Müller-Eberhard,* Proc. Natl. Acad. Sci. USA *76*, 897 (1979).
[25] *S. Bhakdi, J. A. Tranum-Jensen,* Proc. Natl. Acad. Sci. USA *75*, 5655 (1978).
[26] *U. Rother,* Behring Inst. Mitt. *61*, 58 (1979).
[27] *C. B. Laurell, J.-O. Jeppsson* in [10a], Vol. I, p. 229 (1975).
[28] *N. Heimburger* in *E. Reich, D. Rifkin, E. Shaw:* Proteases in Biological Control. Cold Spring Harbor, New York 1975.
[29] *P. K. Hall, R. C. Roberts,* Biochem. J. *173*, 27 (1978).
[30] *R. P. Swenson, J. B. Howard,* J. Biol. Chem. *254*, 4452 (1979).
[31] *N. F. Adham, M. K. Song, H. Rinderknecht,* Biochem. Biophys. Acta *495*, 212 (1977).
[32] *J. Travis, J. Bowen, R. Baugh,* Biochemistry *17*, 5651 (1978).
[33] *J. Travis, D. Garner, J. Bowen,* Biochemistry *17*, 5647 (1978).
[34] *F. W. Putnam* in [10a], Vol. III, pp. 2, 156, 224 (1977).
[35] *N. J. Galvanico, T. B. Tomasi, Jr.* in [21a], p. 1.
[36] *J. M. Kehoe, R. Seide-Kehoe* in [21a], p. 87.
[37] *R. B. Weininger, F. F. Richards* in [21a], p. 123.
[38] *A. Nisonoff, J. E. Hopper, S. B. Spring:* The Antibody Molecule. Academic Press, New York 1975.
[39] *R. I. Levy* in [2a], pp. 25 ff.
[40] *A. M. Scanu, C. Edelstein, Ph. Keim* in [10a], Vol. I, p. 317 (1975).
[41] a) *Ch. Tanford, J. A. Reynolds* in [11a], p. 111; b) *H. J. Pownall, A. M. Gotto,* Jr. in [11a], p. 127.
[42] *H. Bennhold* in *H. Bennhold, E. Kylin, St. Rusznyak:* Die Eiweisskörper des Blutplasmas. Steinkopf, Dresden 1938, pp. 220 ff.
[43] *Th. Peters, Jr.* in [10a], Vol. I, p. 133 (1975).
[44] *G. Schreiber, J. Urban,* Rev. Physiol. Biochem. Exp. Pharmacol. *82*, 27 (1978).
[45] *Ch. Jacobsen,* Biochem. J. *171*, 453 (1978).
[46] *H. E. Schultze, M. Schönenberger, H. G. Schwick,* Biochem. Z. *328*, 267 (1956).
[47] *De Witt S. Goodman* in [2a], p. 313.
[48] *C. C. F. Blake, K. Heide, C. Rerat, J. D. A. Swan,* C. R. Acad. Sci. *272*, 195 (1971).
[49] *C. C. F. Blake, M. J. Geisow, J. D. A. Swan, C. Rerat, B. Rerat,* J. Mol. Biol. *88*, 1 (1974).
[50] *J. Robbins* in [2a], p. 331.
[51] *M. C. Gershengorn, S. Y. Cheng, R. S. Lord, J. Robbins,* J. Biol. Chem. *252*, 8713 (1977).
[52] *M. C. Gershengorn, R. E. Lippoldt, H. Edelhoch, J. Robbins,* J. Biol. Chem. *252*, 8719 (1977).
[53] *F. W. Putnam* in [10a], Vol. III, p. 334 (1977).
[54] *J. Hirschfeld,* Acta Pathol. Microbiol. Scand. *47*, 160 (1959).
[55] *S. P. Daiger, M. S. Schanfield, L. L. Cavalli-Sforza,* Proc. Natl. Acad. Sci. USA *72*, 2076 (1975).
[56] *J. Svasti, B. H. Bowman,* J. Biol. Chem. *253*, 3188 (1978).
[57] *R. H. Allen* in [2a], p. 537.
[58] *U. H. Stenman,* Scand. J. Haematol. *14*, 91 (1975).
[59] *S. N. Wickramasinghe, J. M. England, J. E. Saunders, M. C. Down,* Acta Haematol. *54*, 89 (1975).
[60] *K. Heide, H. Haupt, K. Störiko, H. E. Schultze,* Clin. Chim. Acta *10*, 460 (1964).
[61] *U. Müller-Eberhard, H. H. Liem,* La Riciera Clin. Lab. *5*, 275 (1975).
[62] *F. W. Putnam* in [10a], Vol. II, p. 1 (1975).
[63] *G. M. Fuller, M. A. Rasco, M. L. McCombs, D. R. Basset, B. H. Bowman,* Biochemistry *12*, 253 (1973).
[64] *J. V. Pastewka, A. T. Ness, A. C. Peacock,* Biochem. Biophys. Acta *386*, 530 (1975).
[65] *J. A. Black, G. H. Dixon,* Nature *218*, 736 (1968).
[66] *K. Schmid,* Chimia *26*, 405 (1972).
[67] *F. W. Putnam* in [10a], Vol. I, p. 266 (1975).
[68] *E. Regoeczi, K.-L. Wang, M. Ali, M. W. C. Hatton,* Int. J. Pept. Protein Res. *10*, 17 (1977).
[69] *G. Spik, J. Mazurier* in *E. B. Brown:* Proteins of Iron Metabolism. Grune and Stratton, New York 1977, p. 143.
[70] *E. H. Morgan, H. Huehers, C. A. Finch,* Blood *52*, 1219 (1978).
[71] *H. G. van Eijk, W. L. van Noort, M. J. Kroos, C. van der Heul,* J. Clin. Chem. Clin. Biochem. *16*, 557 (1978).
[72] *A. Leibman, Ph. Aisen,* Biochemistry *16*, 1268 (1977).
[73] *C. van der Heul, M. J. Kroos, H. G. van Eijk,* Biochem. Biophys. Acta *511*, 430 (1978).
[74] *M. D. Poulik, M. L. Weiss* in [10a], Vol. II, p. 52 (1975).
[75] *L. Rydin, J. Björk,* Biochemistry *15*, 3411 (1976).
[76] *V. Miskowski, S.-P. W. Tang, T. G. Spiro, E. Shapiro, T. H. Moss,* Biochemistry *14*, 1244 (1975).
[77] *J. B. Kingston, B. L. Kingston, F. W. Putnam,* Proc. Natl. Acad. Sci. USA *74*, 5377 (1977).
[78] *K. Schmid* in [10a], Vol. I, p. 184 (1975).
[79] *K. Schmid, R. B. Nimberg, A. Kimura, H. Yamaguchi, J. P. Binette,* Biochem. Biophys. Acta *492*, 291 (1977).
[80] *K. Schmid, J. Emura, M. F. Schmid, R. L. Stevens, R. B. Nimberg,* Int. J. Pept. Protein Res. *11*, 42 (1978).
[81] *K. Schmid, L. H. Chen, J. C. Occhino, J. A. Foster, K. Sperandio,* Biochemistry *15*, 2245 (1976).
[82] *C. G. Gahmberg, L. C. Andersson,* J. Exp. Med. *148*, 507 (1978).
[83] *K. M. Piafsky, O. Borgå,* Clin. Pharmacol. Ther. *22*, 545 (1978).
[84] *S. Snyder, E. L. Coodley,* Arch. Intern. Med. *136*, 778 (1976).
[85] *H. Haupt, K. Heide,* Clin. Chem. Acta *10*, 555 (1964).
[86] *H. E. Schultze, K. Heide, H. Haupt,* Nature *200*, 1103 (1963).
[87] *H. Haupt, N. Heimburger,* Hoppe-Seylers Z. Physiol. Chem. *353*, 1125 (1972).
[88] *H. Haupt, N. Heimburger, Th. Kranz, S. Baudner,* Hoppe-Seylers Z. Physiol. Chem. *353*, 1841 (1972).
[89] *P. Binette, M. Binette,* Biochem. J. *143*, 253 (1974).
[90] *L. Pinteric, S. N. Assimek, D. J. C. Kells, R. H. Painter,* J. Immunol. *117*, 79 (1976).
[91] *G. Uhlenbruck, D. Karduck, H. Haupt, H. G. Schwick,* Z. Immunitätsforsch. Allerg. klin. Immunolog. *155*, 262 (1979).
[92] *A. R. Thompson, D. L. Enfield,* Biochemistry *17*, 4304 (1978).
[93] *A. P. Osmand, B. Friedenson, H. Gewurz, R. H. Painter, Th. Hofman, E. Shelton,* Proc. Natl. Acad. Sci. USA *74*, 739 (1977).
[94] *W. Bürgi, K. Schmid,* J. Biol. Chem. *236*, 1066 (1961).
[95] *H. Haupt, S. Baudner, Th. Kranz, N. Heimburger,* Eur. J. Biochem. *23*, 242 (1971).
[96] *T. Iwasaki, K. Schmid,* J. Biol. Chem. *245*, 1814 (1970).
[97] *H. Haupt, S. Baudner,* Hoppe-Seylers Z. Physiol. Chem. *358*, 639 (1977).
[98] *H. E. Schultze, K. Heide, H. Haupt,* Naturwissenschaften *49*, 15 (1962).
[99] *J. R. Dickson, A. R. Poole, A. Veis,* Nature *256*, 430 (1975).
[100] *T. J. Triffitt, U. Gebauer, B. A. Ashton, M. E. Owen, J. J. Reynolds,* Nature *262*, 227 (1976).
[101] *N. Heimburger, H. Haupt, Th. Kranz, S. Baudner,* Hoppe-Seylers Z. Physiol. Chem. *353*, 1133 (1972).
[102] *W. T. Morgan,* Biochem. Biophys. Acta *533*, 319 (1978).
[103] *W. T. Morgan, P. Koskelo, H. Koenig, Th. P. Conway,* Proc. Soc. Exp. Biol. Med. *158*, 647 (1978).
[104] *L. Svensson, J. Ravenskov,* Clin. Chem. Acta *73*, 415 (1976).
[105] *B. Ekström, J. Berggård,* J. Biol. Chem. *252*, 8048 (1977).
[106] *K. Takagi, K. Kin, Y. Itok, T. Kawai, T. Kasahara, T. Shimoda, T. Shikata,* J. Clin. Invest. *63*, 318 (1979).
[107] *B. K. Seon, D. Pressman,* Biochemistry *17*, 2815 (1978).
[108] *J. Berggård, A. G. Bearn,* J. Biol. Chem. *243*, 4095 (1968).
[109] *M. D. Poulik* in [2a], p. 155; cf. *R. Henning,* Angew. Chem. *90*, 337 (1978); Angew. Chem. Int. Ed. Engl. *17*, 342 (1978).
[110] *H. E. Schultze, K. Heide, H. Haupt,* Naturwissenschaften *48*, 719 (1961).
[111] *H. Haupt, K. Heide,* Clin. Chem. Acta *14*, 418 (1966).
[112] *H. Haupt, H. G. Schwick, K. Störiko,* Humangenetik *5*, 291 (1968).
[113] *H. G. Schwick, H. Haupt,* unpublished.
[114] *M. Burstein, P. Legmann,* Protides Biol. Fluids Proc. Colloq. *25*, 407 (1977).
[115] *E. Polz, G. M. Kostner, A. Holasek,* Hoppe-Seylers Z. Physiol. Chem. *360*, 1061 (1979).
[116] *H. G. Schwick, H. Haupt, K. Heide,* Klin. Wochenschr. *46*, 981 (1968).
[117] *W. H. Chase, H. Prochaska,* Clin. Immunol. Immunopathol. *5*, 247 (1976).
[118] *E. B. Oliveira, E. C. Gotschlich, T.-Y. Lin,* J. Biol. Chem. *254*, 489 (1979).

[119] *J. E. Volanakis, M. H. Kaplan*, Proc. Soc. Exp. Biol. Med. *136*, 612 (1971).
[120] *K. Gal, M. Miltenye*, Acta Microbiol. Acad. Sci. Hung. *3*, 41 (1955).
[121] *M. H. Kaplan, J. E. Volanakis*, J. Immunol. *112*, 2135 (1974).
[122] *J. E. Volanakis, M. H. Kaplan*, J. Immunol. *113*, 9 (1974).
[123] *P. O. Ganrot, C.-O. Kindmark*, J. Clin. Invest. *24*, 215 (1969).
[124] *K. Heide, F. Seiler*, Arzneim.-Forsch. *21*, 1443 (1971).
[125] *B. A. Fiedel, R. M. Simpson, H. Gewurz*, J. Immunol. *119*, 877 (1977).
[126] *D. Gitlin, J. D. Gitlin* in [10a], Vol. II, p. 321 (1975).
[127] *E. R. Giblet:* Genetic Markers in Human Blood. Blackwell Science Publ., Oxford 1969.
[128] *H. Harris*, Can. J. Genet. Cytol. *13*, 381 (1971).
[129] *K. Heide, H. G. Schwick*, Angew. Chem. *85*, 803 (1973); Angew. Chem. Int. Ed. Engl. *12*, 721 (1973).
[130] *E. Köttgen, Ch. Bauer, W. Reuther, W. Gerok*, Klin. Wochenschr. *57*, 151 (1979).
[131] *E. Köttgen, Ch. Bauer, W. Reuther, W. Gerok*, Klin. Wochenschr. *57*, 199 (1979).
[132] *A. G. Morell, G. Gregoriadis, J. Scheinberg, J. Hickman, G. Ashwell*, J. Biol. Chem. *246*, 1461 (1971).
[133] *G. F. Springer, H. G. Schwick, M. A. Fletcher*, Proc. Natl. Acad. Sci. USA *64*, 634 (1969).
[134] *H. Lis, M. Sharon* in *M. Sela:* The Antigens. Vol. IV. Academic Press, New York 1977, p. 429.
[135] *G. Riva:* Das Serumeiweissbild. Verlag Hans Huber, Bern 1957.
[136] *W. Hitzig:* Die Plasmaproteine in der klinischen Medizin. Springer, Berlin 1963.
[137] *F. Wuhrmann, H. H. Märki:* Dysproteinämien und Paraproteinämien. Schwabe, Basel 1963.
[138] *W. Becker, W. Rapp, H. G. Schwick, K. Störiko*, Z. Klin. Chem. Klin. Biochem. *3*, 113 (1969).
[139] *L. Thomas, W. Opferkuch* in *L. Thomas:* Labor und Diagnose. Medizinische Verlagsgesellschaft, Marburg 1979, p. 585.

New Technologies for the Filmless Manufacture of Printing Forms[**]

By Hansjörg W. Vollmann[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

The economic reproduction of graphic information was first made possible in the western world by *Gutenberg*'s invention of movable type. In the printing methods of that time, mechanical transfer processes played the major role, while chemical processes were of secondary importance. When *Alois Senefelder* invented planographic printing (lithoprinting) at the end of the 18th century he called the new process "chemical printing". Since then, chemistry has attained great importance in the production of printing forms: Thus the manufacture of surface (litho-) printing forms with light required temporary storage materials and image reproduction processes based on chemical reactions. Since the advent of electronic processing of information, however, several former temporary storage media have become obsolete; newer, more sensitive image reproduction processes are increasingly making less use of chemical principles than of the electrical properties of materials.

1. Introduction

Printing, originally an art and later a craft, has today become a commercial process of great importance. In this paper we shall deal with some of the scientific aspects of printing.

1.1. Printing Processes

The four main commercial printing processes[1-4] are letterpress printing, gravure printing, planographic or offset printing, and screen printing. The various processes essentially differ from one another in the nature of the printing form or surface. The underlying principles of each of the processes are illustrated in Figure 1.

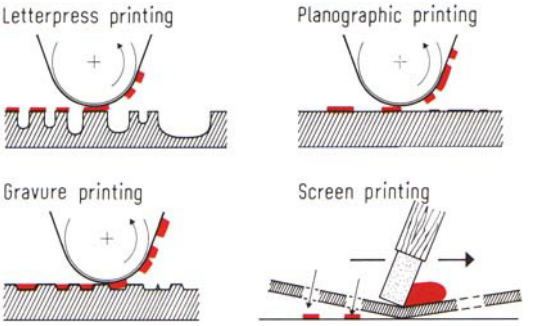


Fig. 1. Principles of the four main printing processes.

Whereas in letterpress printing, ink is transferred from raised areas of a printing form onto the material to be printed, in gravure printing the situation is exactly the converse: here the image areas of the printing form are recessed and a relatively low viscosity gravure ink is transferred from the recesses or cells of the printing form onto the material to be printed, for example paper.

In planographic or offset printing[5,6], the process with which we shall be primarily concerned here, the printing

[*] Dr. H. W. Vollmann
Kalle Niederlassung der Hoechst AG
Postfach 3540, D-6200 Wiesbaden 1 (Germany)

[**] Based on a GDCh lecture delivered at the Achema 1979 on June 20, 1979 in Frankfurt/Main.

form is without appreciable relief or depression, *i.e.* the image differentiation takes place virtually in one plane, and is effected physicochemically[7] by means of oleophilic and oleophobic areas on the printing form. The oleophobic areas consist of the decoated (ink-repelling) surfaces of the carrier material, usually aluminum, whilst the oleophilic, *i.e.* ink-receptive, areas normally consist of an organic resin coating.

In screen printing[8], the ink is forced through a stencil-like printing form, for example through the meshes of a screen—hence the name of the process.

Each of the above processes has its particular fields of application.

1.1.1. Economic Aspects

Figure 2 shows the forecast development of the three major printing processes up to 1990, both on a worldwide basis and for the Federal Republic of Germany: In 1980, planographic printing will overtake letterpress printing in the Federal Republic of Germany, and in 1984 will similarly overtake it world-wide. Letterpress printing, which in 1972 still accounted for a market share of 60%, will have dropped to 30% by 1990, whilst the market share for planographic printing will, over the same period, have risen from 25% to 50%.

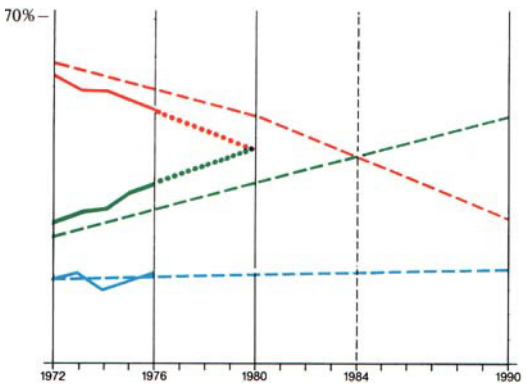


Fig. 2. Economic development of the major printing processes (excluding screen printing). Red: letterpress printing. Green: planographic or offset printing. Blue: gravure printing. ----: anticipated world-wide development; —— actual development in the Federal Republic of Germany; ····: anticipated development in the Federal Republic of Germany.

This forecast[9] is based on predictable trends of technological development. However, because of rapid changes in the graphic arts industry during the past few years no accurate statistics are available on a worldwide basis. If, for example, some revolutionary method made it possible to manufacture gravure printing forms much more cheaply, then the statistics could shift substantially in favor of gravure printing. At the present time, over 72% of all U.S. newspaper titles are already being printed by the planographic process[10a]; however, since those newspapers with the widest circulation are still being printed by the letterpress process, only 37% of the total newspaper output is accounted for by planographic printing.

1.1.2. Production of Printing Forms by means of Light Energy

In planographic printing, the production of printing forms by means of light energy has decades of tradition behind it, and is quite uncomplicated. It utilizes the change in solubility of a light-sensitive coating on exposure to light in order to produce an image-wise differentiation.

Photopolymer (wash-out) plates, which are produced photomechanically, are also of outstanding importance in letterpress printing, because of their compatibility with photocomposing[11–14]. However, owing to the degree of relief necessary in such plates, substantially higher energy is required for photohardening than in the case of planographic printing plates.

The term "photomechanical" is applied to all reproduction processes which are based on photochemical reactions and entail both photographic and etching type processes.

1.1.3. Areas of Application of the Various Printing Processes

Letterpress printing is used in particular for black-and-white printing, for example in the printing of newspapers and simple books. It is the oldest of the printing processes and, as already mentioned, still enjoys world-wide dominance. However, planographic printing is steadily attracting more attention because it gives prints of better quality, especially in color work, and allows simple and more rapid production of the printing form.

Gravure printing gives prints of particularly high quality. However, its rate of development and scope of application has so far been thwarted by the cost of producing the printing cylinder. Screen printing is a special type of printing, used for example in textile printing, in the advertising sector and, more recently, also in the field of electronics. In Germany, its share of the reprographic market is about 3% (see Fig. 3).

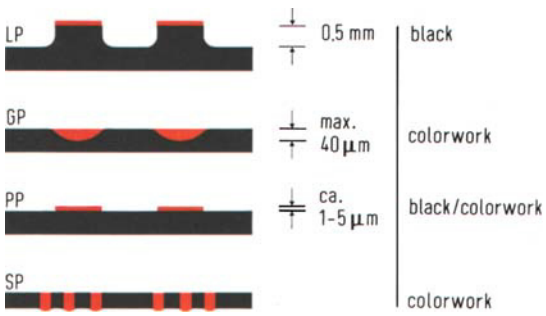


Fig. 3. Comparison of the four main printing processes. LP = letterpress printing (44%), GP = gravure printing (17%), PP = planographic printing (36%); SP = screen printing (estimated 3%). The figures refer to the market share in the Federal Republic of Germany (1977) [10b].

1.2. Photomechanical Production of Offset Printing Forms

Let us once again particularly compare the printing forms required for letterpress printing, gravure printing and offset printing. Whilst with a letterpress printing form a substantial relief, namely of about 0.5 mm, must be produced, and whilst considerable amounts of material, namely up to about 40 µm, must be etched from the surface of a gravure printing cylinder, the coatings constituting the image areas on a planographic printing form are only up to a few µm thick (Fig. 3). If we turn to the photochemical process or the etching

process, we see that undoubtedly the material which has to be converted or transferred to achieve image differentiation is least in the case of the photomechanical production of a planographic printing form.

Depending on whether the areas of a printing plate which have been exposed to light are more soluble or less soluble than initially, the system concerned is referred to as positive or negative, respectively. The process of producing a planographic printing form (*negative* system) is shown in Figure 4.

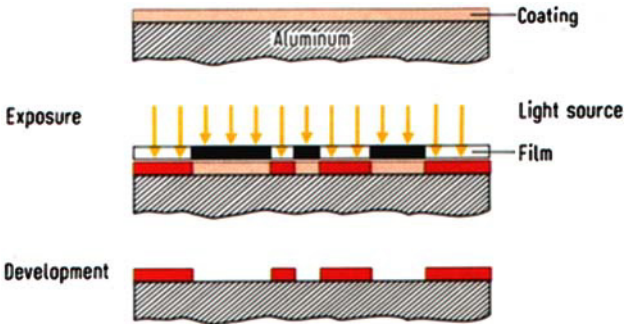


Fig. 4. Photomechanical manufacture of an offset printing form (negative plate).

A film original, generally a silver halide film negative, is placed on a printing plate consisting of an aluminum sheet, which is about 0.1—0.5 mm thick, and an organic light-sensitive coating, which is from less than 1 to 5 μm thick. The assembly of plate and negative is then held in contact by vacuum in a copying frame and exposed to the light of a metal halide-doped mercury vapor lamp, usually of 5 kW input power. After a typical exposure time of about 20 seconds to 1 minute, the coating is hardened, *i. e.* chemically cross-linked, in the exposed areas. After removing the non-cross-linked areas by means of a developer, the printing form is ready to use.

Positive planographic printing plates, on the other hand, are based on a chemical principle in which hydrophobic compounds, contained in a resin matrix of limited solubility in alkali, are converted photolytically to more hydrophilic compounds. The exposed areas of the coating are thus made accessible to the action of an aqueous alkaline developer, and are dissolved out. The image areas which remain on the aluminum carrier consist of chemically unchanged original coating material and correspond directly to the mask through which the exposure was carried out. These image areas transfer the ink during the printing process.

In both cases, the film is an intermediate "master" which has first to be produced from the actual original; this intermediate "master" is necessary for the conventional technique just described, but can be dispensed with in the filmless production of printing forms.

1.3. Filmless Production of Printing Forms

In small offset printing and duplicating, the production of printing forms without using a silver halide film as an intermediate master has long been known, and has proven its value over the years[15]. Examples which may be mentioned are the silver salt diffusion process and transfer process, photodirect films and electrophotographic films. These processes have proven successful for paper sizes of up to about DIN A2 and will retain their importance in the forseeable future.

On the other hand, the filmless production of planographic printing forms for medium and large paper sizes and for runs of up to about 100000 prints or even more, is novel[16–18]. It is a pioneer technology which essentially was first introduced to the public at the DRUPA printing and paper exhibition in Düsseldorf in 1977, and which is rapidly gaining favor, above all, but not exclusively, in newspaper printing.

This new technology was made feasible by the interdisciplinary co-operation of chemists, physicists, engineers and electronics experts.

Before dealing with the technology in more detail, we will first discuss the basic chemistry of the light-sensitive layers of some of the currently used planographic plates.

2. Printing Plates with Photochemically Active Coatings

The chemistry of a light-sensitive layer must be such that the absorption of the coating matches the emission of the light source if optimum energy utilization is to be achieved. As is shown in Figure 5, the sensitivity maxima of conventional light-sensitive systems are to be found in the near UV range or the short wavelength end of the visible range; an example of a light source which is particularly suitable for this sensitivity range is a gallium iodide-doped mercury vapor lamp[19], the emission spectrum of which is also shown in Figure 5. High power mercury vapor lamps have substantially superceded the previously used carbon arc lamps and xenon high pressure lamps.

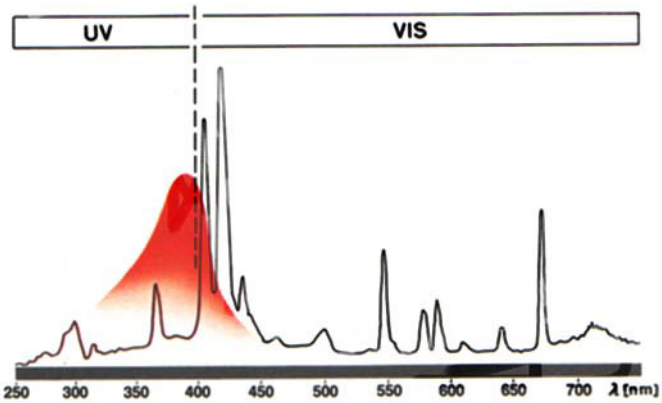


Fig. 5. Spectral sensitivity of an offset plate (red) and emission of a Ga-doped Hg high-pressure lamp.

From a chemical point of view, there is a great variety of possible ways of producing photoactive systems for reprographic applications. Correspondingly, such systems are well documented in the literature[20–25]. In practice, however, only a relatively small number of such chemical systems have found acceptance.

2.1. Positive Systems

Positively acting light-sensitive coatings are based virtually exclusively on "naphthoquinone diazides" (2-diazo-1(2*H*)-

naphthalinone derivatives)[26,27], which are mostly used in combination with phenolic resins. However, even today research work[28] is still being carried out on these light-sensitive compounds—30 years after their introduction.

Of the other positive lithographic systems which have been proposed, none has hitherto been able to gain a share of the market.

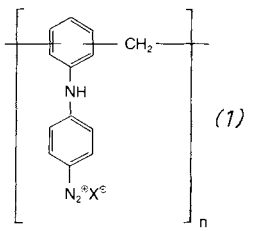
2.2. Negative Systems

Essentially four chemical principles are employed for negative photosensitive coatings which are to have a good shelf life.

2.2.1. Diazonium Salts and Azides

The oldest and even today the most widely used system employs diazo resins which are obtained by acid condensation of diphenylamine-4-diazonium (*p*-anilinophenyldiazonium) salts with formaldehyde[20,24,29].

The structure of these oligomeric "tanning diazo compounds" is shown in idealized form in Formula *(1)*. Suitable as anion $X^{\ominus}$ is, *e.g.* $1/2\ ZnCl_2^{\ominus}$; other suitable inorganic and organic anions $X^{\ominus}$ are to be found in the literature[30,31].



(1)

These soluble, and in most cases even water-soluble, polyfunctional diazonium salts lose their salt character as a consequence of nitrogen elimination on exposure to light. They become water-insoluble, and are at the same time able to crosslink the polymer matrix surrounding them. This well-proven principle forms the basis of most negative diazo planographic plates.

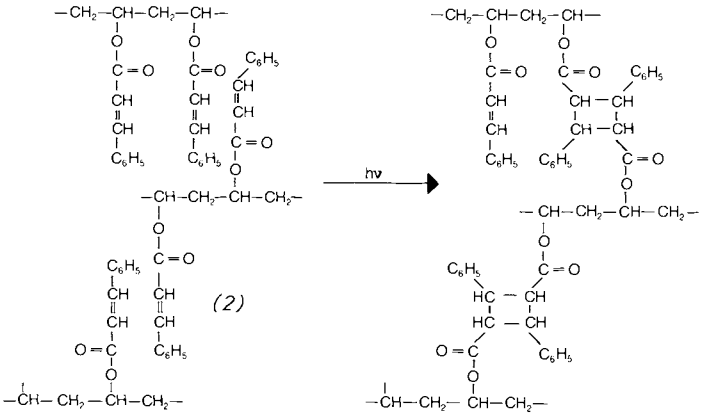
Light-sensitive coatings based on arylazides[20,22,23] are also employed. Arylazides can be spectrally sensitized.

Other systems which have attained considerable importance are coatings based on the principle of photodimerization[20,22,23] and on photoinitiated free radical polymerization[20–23].

2.2.2. Crosslinking by Photodimerization

The photodimerization of cinnamic acid derivatives is an example of the first of the crosslinking principles mentioned, in which the crosslinking of two molecules is brought about, *inter alia,* by light-induced cycloaddition of the activated double bonds to different kinds of cyclobutane structures[32]. For reprography, this chemistry is only of interest if a polymer chain carries many groups of this type. A typical example is the polyvinyl cinnamate shown in *(2)*.

A remarkable property of cinnamates is that they can be sensitized to light of relatively long wavelengths, up to about 500 nm[32], by triplet energy transfer; in the case of cinnamylidene derivatives, it is even possible to extend the sensitivity



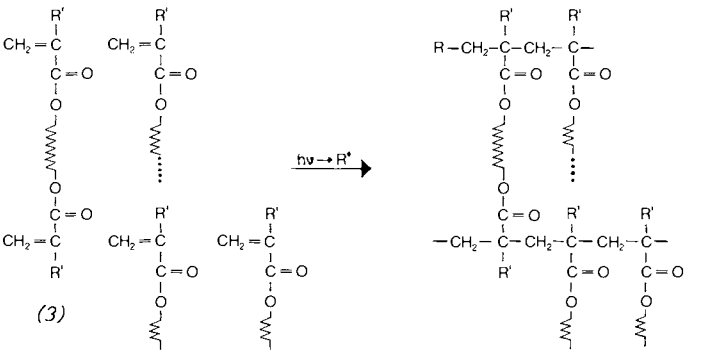
(2)

range beyond this wavelength[33]. It is true that spectral singlet sensitization of diazonium salts is feasible in solution[34,35], but it has hitherto not been possible to exploit this in practice for increasing the sensitivity in solid reprographic coatings; indeed for some fundamental reasons this is unlikely to be realized.

2.2.3. Photopolymerizing Systems

The additional and desirable increase in the light sensitivity of the systems hitherto discussed is limited so long as at best only one new linkage between two molecules can be produced per quantum of light.

This restriction also applies to photopolymerization in its narrower sense[36], where one photon is required per growth step, but not to photoinitiated polymerization, where light is merely required to activate an initiator. In industry, this latter process is generally also referred to as photopolymerization[37]; in the following text the term photopolymerization is to be understood only in this sense of photoinduced polymerization. The principle is illustrated for the example of acrylic acid derivatives *(3)*. Theoretically, one quantum of light can convert a large number of monomer molecules into high molecular weight polymers. However, termination reactions and the presence of inhibitors, especially atmospheric oxygen dissolved in the polymerizing layer, impose natural limits in such polymerizations.



(3)

As is shown for the example of reaction *(3)* it is however possible on this basis to devise planographic photopolymer plates which have somewhat higher light sensitivity than diazo layers or layers based on dimerizing compounds if suitable measures are taken to repress further diffusion of oxygen

into the layer during exposure. This can be achieved, for example, by applying an overcoat, of low permeability to oxygen, over the photopolymer coating[38].

2.3. Light Sensitivity

The sensitivity to light of even the best of these systems is, however, too low for them to be considered as ideal materials for the filmless production of planographic printing forms.

At the present time, the most sensitive formulations, based on diazo resins such as *(1)* or cinnamates such as *(2)*, require an energy of 5—10 mJ/cm^2 (50—100 J/m^2) for photohardening. This makes it possible to devise direct imaging systems without a film as intermediate master, but only when using very powerful light sources.

There are good reasons for employing such systems. On the one hand, all customers would like to have high-sensitivity materials, on the other they are used to daylight conditions, or at best to yellow safelight when processing the plates, *i.e.* when producing planographic printing forms. A change-over to darkroom conditions would be a major disadvantage to the user and incidentally, not least of all, also to the manufacturers of presensitized planographic printing plates, since these are currently produced under filtered light resembling daylight. "Presensitizing" means, in technical terms, the application of a light-sensitive coating.

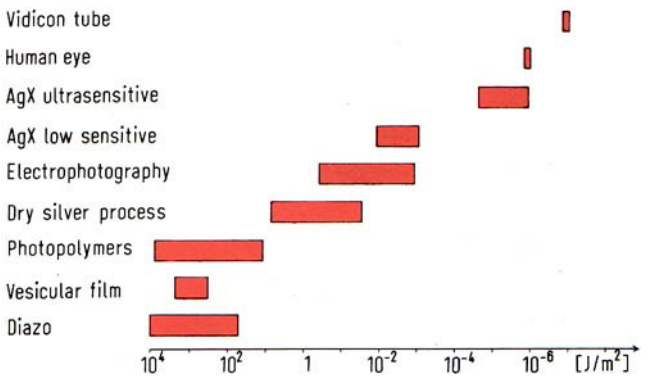


Fig. 6. Energy requirements of light-sensitive systems. (The photoactive layer of vesicular film consists of diazonium salts in a resin matrix. Bubbles of nitrogen liberated in the exposed areas give rise to opacity.)

A comparison of light-sensitive systems (see Fig. 6) shows that these highly sensitive photochemical systems are to be encountered at the lower end of the series, and their ranges partly overlap, whilst the silver halide film materials are to be found at the upper end of the series. This comparison encompasses different imaging mechanisms. However, quantitative comparison is subject to certain restrictions, since the read-out mechanism (physiological and electrical effects, and differences in optical density, conductivity and solubility) is, in practice, effected by a variety of methods.

3. Production of Printing Forms by Electrophotographic Processes

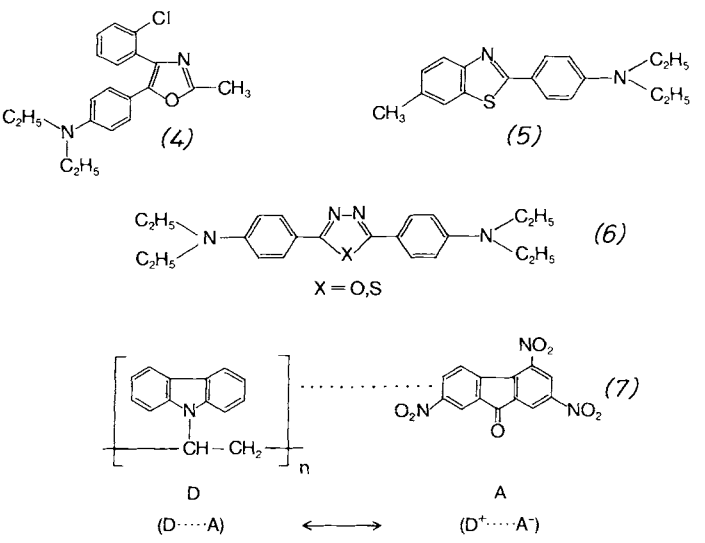
The electrophotographic materials shown in the middle of the series are ideal for the filmless production of printing forms, since their light sensitivity ranges from a few 100 to 1000 times greater than that of the diazo systems and photopolymer systems hitherto known. In order to be able to work with such photoconductive coatings under relatively bright darkroom illumination, materials whose exposure energies lie in the middle to upper range of the band shown in Figure 6 are preferred.

Suitable photoconductors for electrophotography have insulating properties in the dark and prevent the dissipation of charges applied by means of a corona discharge. The term corona discharge means a type of discharge which occurs at sharp edges, points or wires under atmospheric pressure at high voltage.

On exposure to light, the electrical conductivity of the photoconductors increases substantially. The charges are dissipated in the exposed areas and a latent charge image is formed. This can be rendered visible by means of colored liquids or powders, referred to as toners. Further details in this sector can be found in the standard work by *R. M. Schaffert*[39].

3.1. Photoconducting Systems

In the industrial filmless manufacture of printing forms, both inorganic and organic photoconductors[40-42] are used. The inorganic compounds include cadmium sulfide and zinc oxide. Examples of organic compounds which show photoconductivity, to a degree industrially utilizable in electrophotography, include various heterocyclic compounds, such as oxazoles, benzothiazoles, oxadiazoles and thiadiazoles[43]; *(4)*—*(6)* are examples. Certain charge transfer complexes are even more light-sensitive, but are not used in planographic printing plates. In these complexes, an ionic component is present even in the ground state, and becomes more pronounced as a result of photoexcitation. An extensively investigated example is the donor-acceptor complex *(7)* of polyvinylcarbazole and 2,4,7-trinitrofluorenone. Planographic printing forms can be readily produced electrophotographically by using organic photoconductors[44].



3.2. Manufacture of Printing Forms

The photoconductive coating on an aluminum carrier is negatively charged, as shown in Figure 7. On imagewise exposure, the charges on the areas exposed to light disappear, whilst those on the unexposed areas remain. Toner particles of the opposite charge—in the present instance positively charged particles—are attracted to the charge image areas

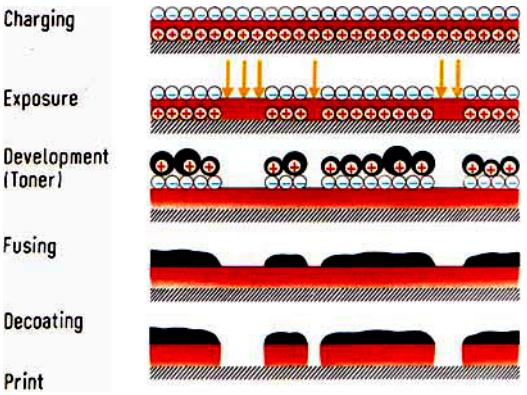


Fig. 7. Electrophotographic process for producing an offset printing form.

thus produced and are subsequently fixed to the surface of the coating by a heat treatment. The areas not protected by the toner stencil are removed by dissolving them in a decoating solution, so that in these areas the carrier surface is bared. After this treatment, the printing form is ready for the press and its application does not differ from that of a conventionally produced printing form.

4. Materials and Processing Lines for the Electrophotographic Manufacture of Printing Forms

Whilst electrophotographic printing plates based on zinc oxide have long been known[45] and are still being used industrially at the present time, for example as "Chemco-Newsplate"[15], an electrophotographic printing plate working on a different principle, namely the KC-crystal plate[9,46], was introduced at the IMPRINTA trade fair in Düsseldorf in February 1979; the heart of this plate is an inorganic cadmium sulfide photoconductor[47,48], as shown in idealized form in Figure 8. The cadmium sulfide, in a thickness of only

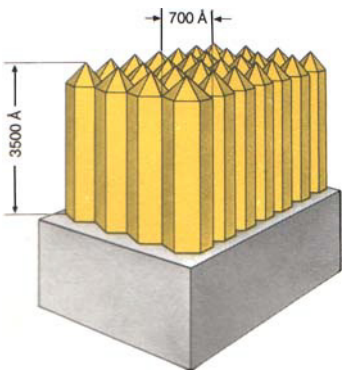


Fig. 8. Photoconductive cadmium sulfide crystals of the KC plate.

0.35 μm, is applied by cathode sputtering onto a metallic carrier. It grows onto the carrier in the form of very regular crystals. The crystal coating of this plate is then—exactly as described earlier for the case of an organic photoconductor—charged, exposed, developed with a special liquid toner and baked. In a further process step the unprotected cadmium sulfide coating must be rendered hydrophilic in the non-image areas before the plate can be used for printing; this is achieved by a chemical oxidation step. This novel printing plate, which has not yet found industrial acceptance and is very expensive, counts amongst the most sensitive of the electrophotographic systems known hitherto.

4.1. Methods of Exposure

The industrial processes for the electrophotographic filmless production of printing forms, explained below, in part use different exposure systems. Basically, there are two possibilities:

The first possibility is overall exposure in which the entire photosensitive coating is simultaneously exposed to light energy. Figure 9 (left) shows a copying process by transmitted light, on a 1:1 scale. Of course it is also possible, as,

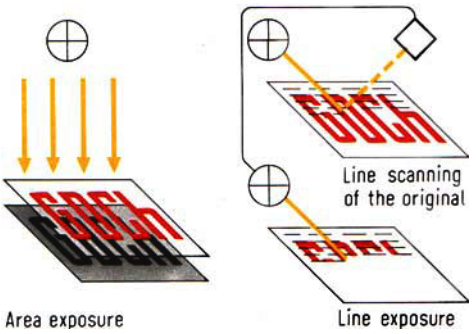


Fig. 9. Methods of exposure.

for example, in an episcope, to employ reflected light for copying or to magnify or reduce the original optically. When using an episcope, more light is lost in the reflecting rays during the copying process than when using a diascopic process, and therefore particularly light-sensitive printing plates are needed.

The alternative to overall exposure is line exposure, where it is possible to use the signals, received from an illuminated original, to control a second, independent light source. It is only the latter which transfers the information onto a light-sensitive coating.

4.2. Processing Lines

An automatic camera designed for newspaper production and already employed by many newspapers, namely the EA 692 Elfasol camera[49], employs an overall exposure system. Figure 10 illustrates the largely automated, photomechanical filmless production of a planographic printing form.

The operator introduces the original, in the present case the paste-up, into the copyholder and starts the machine. An electrophotographic plate is automatically taken from a plate stack, positioned in the exposure table, exposed, then treated

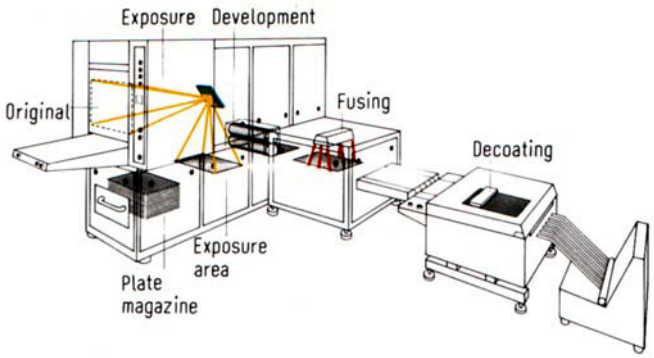


Fig. 10. Elfasol unit EA 692.

with toner, fixed by heating, stripped and placed, ready-to-print, on a stack. The first plate leaves the machine after four minutes and subsequent plates at intervals of one minute. In contrast, the exposure time alone of a conventionally processed planographic printing plate is up to one minute, with a total production time of 8—12 minutes[49], including the production of a silver halide film. In addition to the resulting reduction in labor costs, electrophotographic printing plates offer a cost saving due to film not being needed, and considerable time saving, which is particularly important in newspaper production.

A similar system—Pyrofax[15,17]—works on a somewhat modified principle (Fig. 11). The electrostatic charge image of an original, produced episcopically and by overall exposure on an electrophotographic zinc oxide film, is developed with a toner. A silicone rubber mat, the "transmat", takes the toner image from the film. In a separate, manual step the image is then transferred, in a fusion station, onto an uncoated planographic printing plate, and is burned into the latter. The procedure is not fully automatic. At the present time there are about 100 Pyrofax installations throughout the world.

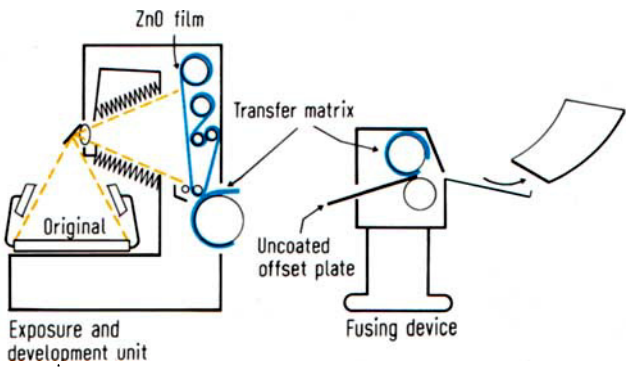


Fig. 11. Pyrofax system.

In the EPS system[50], in contrast to the above process, the toner image is transferred from a zinc oxide photoconductor coating directly onto the printing plate which is coated with a non-photoconductive resin. After the toner has been fused, the resin coating is removed from the non-image areas by dissolution in a decoating solution.

The printing plates with a cadmium sulfide photoconductive coating[47,48], already mentioned, are exposed by a modified slit exposure process, which can be regarded as an intermediate stage between pure overall exposure and line exposure.

In the apparatus used for exposure of the plate, namely the KC-Camera-Platemaker (Fig. 12), the image of the original is optically transferred, a strip at a time, onto a cadmium sulfide crystal plate by means of transmitted light or reflected light.

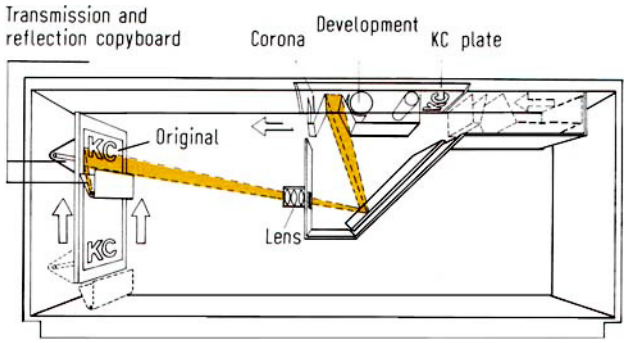


Fig. 12. Exposure device KC camera plate maker.

Table 1 once again compares the various systems. In the KC system and the Chemco-system[15], in contrast to conventional planographic printing forms and to the remaining systems, the function of the non-image areas is not fulfilled by the surface of the carrier but by the photoconductive coating which has been made hydrophilic.

Table 1. Comparison of electrophotographic printing plate systems.

System	KC	Chemco	Pyrofax	EPS	Elfasol
Photoconductor	CdS	ZnO	ZnO	ZnO	organic
Binder in photoconductive coating	−	+	+	+	+
Toner	liquid	liquid	dry	dry	dry
Image differentiation	hydrophilation	hydrophilation	transfer	transfer and decoating	decoating
Printing layer	toner and photoconductive coating	toner and photoconductive coating	toner	toner and resin coating	toner and photoconductive coating

5. Lasers as Sources of Modulatable Radiation

In recent times, line-imaging, which has long been known and extensively used, particularly in television technology—has found increasing application. The reason for its increasing use in reprography is the development of lasers of sufficient stability, which can also be employed on a production scale.

Laser light[51] has various properties, which predestine it for use in reprography: first, in contrast to light from conventional sources which radiate in all directions, it is emitted in one direction only, possesses good parallelity and is mono-

chromatic; second, it has a high energy density, can be modulated and responds to control signals with virtually no delay. Even making optimistic assumptions in favor of the most powerful currently available doped gas discharge lamps, the energy densities achievable with these in the 300—450 nm region are lower by at least a factor of 1000 than the energy density of an argon ion laser with 2—3 W UV output power, such as is used industrially in printing form production.

Because of their high energy density and also because of the position of their emission lines in the ultraviolet and visible region, argon ion lasers, in particular, are used in reprography (Fig. 13). This is true both for the exposure of conventional printing plates and of electrophotographic printing plates[52]. Figure 13 also shows the principal emission lines of the krypton ion laser, which for many conventional systems would be an even better choice. Unfortunately its stability, *i.e.* the life of the laser tube, is at present still inadequate when compared with the stability of the argon ion laser.

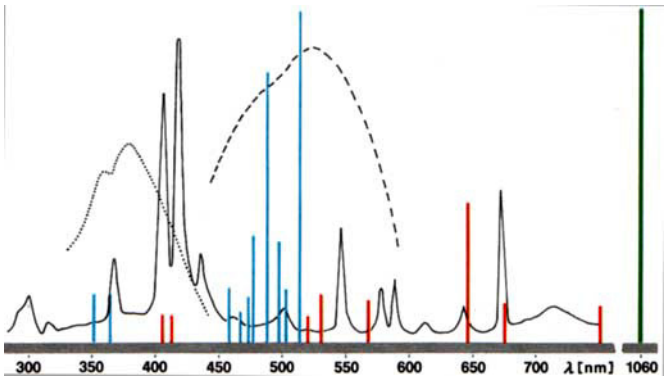


Fig. 13. Spectral sensitivity of different types of printing plates and principal emission of various radiation sources; —: Ga-doped Hg high-pressure lamp; ·····: diazo laser printing plate; ----: electrophotographic laser printing plate; blue: argon ion laser; red: Krypton ion laser; green: yttrium-aluminum-garnet (YAG) laser.

The height of the argon and krypton laser lines shown in Figure 13 indicates their relative intensity under specific operating conditions. The emission spectrum of a gallium-doped mercury high pressure lamp, the intensity of the yttrium aluminum garnet (YAG) laser line and the curves of the spectral sensitivities of the two types of printing plate are based on different, arbitrarily chosen scales.

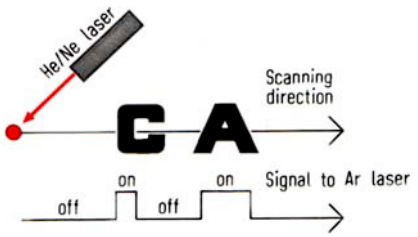


Fig. 14. Laser scanning mode.

The principle of how an image is sensed and built up linewise with the aid of lasers is shown in Figure 14. The light beam of a helium-neon laser, which emits with comparatively low power at 633 nm, scans the original which is to be reproduced. The light is reflected at the non-image areas whilst it is absorbed at the image areas. The local image information thus becomes a time sequence of light/dark information, which can be converted into electrical signals. These control another laser, for example a high-output argon ion laser, which is used to expose the light-sensitive material.

6. Lasers in Printing Form Production

6.1. The Laserite System

Industrially, this principle is put into operation in, for example, the Laserite system[53,54] (Fig. 15). The beams of the helium-neon read laser and of the argon ion write laser are combined, and again separated, in this equipment with the aid of dichroic mirrors. The linewise deflection of the light is effected by a pyramidal mirror which rotates at about 5000 revolutions per minute and travels, on a carriage, over the original and the plate. By superposing line scanning and forward travel of the optics on the carriage, the whole surface is scanned. The beams of the read laser which are deflected by the pyramidal mirror pass through the optics, and through the dichroic mirror—which transmits the red light of the He/Ne laser—onto the original, where they are absorbed by the image areas and reflected by the nonimage areas. This produces a sequence of light/dark information, which is picked up by a glass fiber optics bundle and fed to a photomultiplier. The latter converts the optical signals into electrical signals and passes them, as control pulses, to the modulator of the argon ion write laser. Thus, the sequence of light/dark information from the original is imprinted on the light beam of the write laser. This light now travels by the same optical path as the light of the read laser, *via* the pyramidal mirror and the optics, to the dichroic mirror, where it is reflected onto the plate.

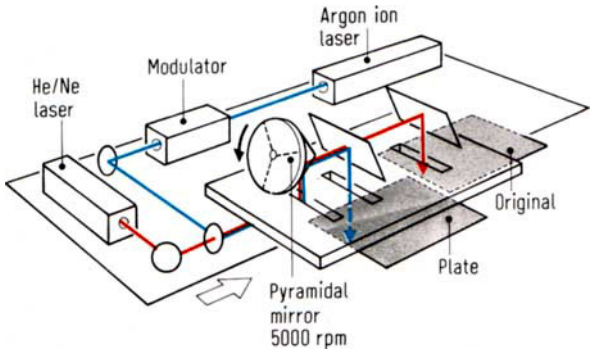


Fig. 15. Laserite system, schematic.

Using a high-energy argon ion laser it is possible, in such imaging units, to expose highly light-sensitive diazo plates or photopolymer plates with an energy of 5—10 mJ/cm^2 (50—100 J/m^2). Alternatively, using a substantially weaker—and correspondingly less expensive and more robust—argon ion laser, electrophotographic printing plates can be exposed with an energy of 10^{-2} to several 10^{-3} mJ/cm^2 (10^{-1}—10^{-2} J/m^2), *i.e.* with an energy expenditure which is less by about a factor of 1000[55]. In Laserite installations it is possible, during the relatively short and hence hectic produc-

tion state of a newspaper just before starting the press, to automatically produce one ready-to-print newspaper printing form about every minute.

6.2. The LogEscan System

The LogEscan system[15,56] also employs laser radiation in the filmless production of planographic printing forms. However, it operates on a different principle (Fig. 16):

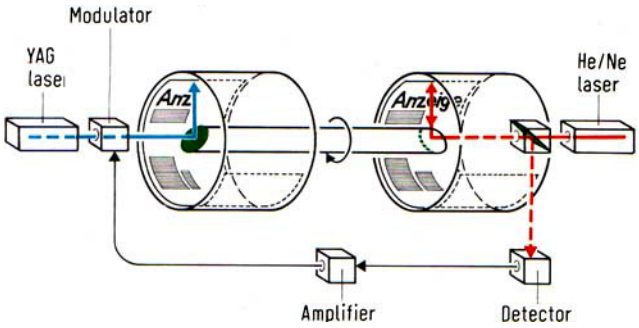


Fig. 16. LogEscan system, schematic.

The apparatus consists of two stationary, transparent drums, of which the drum shown on the right in Figure 16 is fed with the original whilst the other carries a black transfer film[57]—referred to as a "laser mask"—in contact with an uncoated aluminum plate. The "laser mask" consists of a film which is essentially coated with nitrocellulose and carbon black. A rotating He/Ne laser beam in the axis of one drum scans the original and controls, *via* the modulator, the write laser beam running in the other drum. This beam originates from a neodymium-doped YAG laser, which emits in the infrared. Where the beam of the YAG laser strikes the black transfer film, an oleophilic composition which accepts printing ink is thermally transferred onto the uncoated aluminum plate. After a fusing step, the planographic printing form is ready for use in the press. The transferred resin composition leaves transparent areas on the transfer film, which accordingly has simultaneously been converted into a negative image and can be used for the conventional production of additional plates, or for archive storage.

6.3. Use of Lasers for the Production of Printing Forms for Letterpress and Gravure Printing

There has been no lack of attempts at filmless production of printing forms for letterpress printing and gravure printing using imaging equipment which employs lasers. Whilst the LGS process[15,58] for the production of letterpress printing plates, which was developed at the beginning of the 1970's, did not prove right for the market, the Crosfield system[59], introduced in 1979, may be able to reduce the production costs of gravure printing cylinders (Fig. 17): A 0.75 mm-thick plastic tube is first shrunk onto a metal cylinder which is then rotated rapidly in the imaging unit, and, in one and the same process step is first turned by means of a diamond until exactly circular in shape and immediately afterwards "engraved" image-wise by means of a modulated CO_2 laser beam. This produces a groove of variable depth, running spirally round the cylinder, in the plastic; in the printing process, the groove takes up the printing ink and transfers it onto the paper.

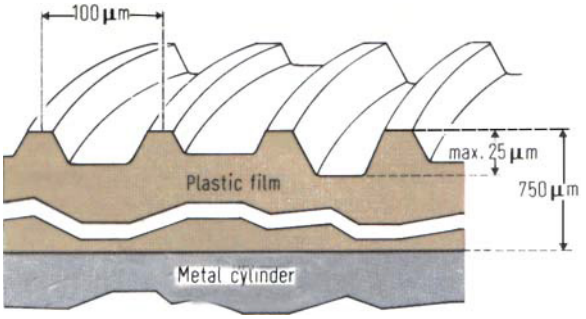


Fig. 17. Gravure cylinder manufactured by means of a laser beam.

7. Long-distance Transmission and Data Compression

The processes which have just been described show the diverse ways in which laser radiation can be employed in the production of printing forms if the image information is to be scanned directly from the original without an intermediate film. However, as already described, this can also be achieved with overall exposure of electrophotographic printing plates. Accordingly, the exposure equipment fitted with lasers would be nothing more than an expensive camera if the system employed were not to offer additional capabilities.

A factor of vital importance is that the high energy density of the laser radiation permits linewise exposure of reprographic coatings. The light/dark information, converted for this purpose, can easily be transmitted as an electrical signal from one location to another, so that image sensing—*i. e.* reading—and image reproduction—*i. e.* writing—can take place at separate locations.

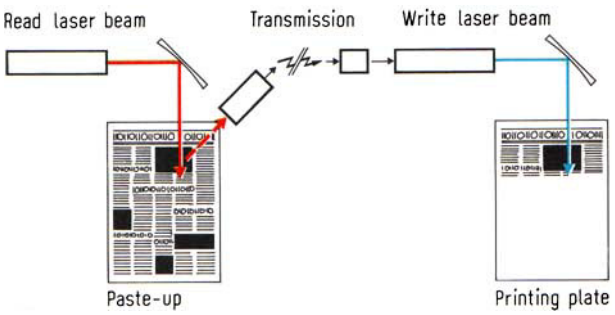


Fig. 18. Fascimile transmission, schematic.

Figure 18 illustrates the principle: The read beam scans the image which is to be reproduced; the electrical information ultimately obtained from this scanning is transmitted *via* a conventional communication channel to the location where the write laser exposes light-sensitive material, either synchronously or after intermediate storage of the data. Depending on the energy of the write laser, electrophotographic or highly sensitive conventional planographic printing plates can be exposed in this way, thereby surpassing the previous state of the art which only allowed exposure of highly sensitive silver halide film materials.

The frequency required for the transmission follows from the information density, the speed of travel of the scanning spot, its size and the line spacing. Normally, the frequency is of the order of 5 megahertz, so that transmission channels similar to those for television are needed.

In principle, the analog image signal produced from the converted light/dark information could be transmitted amplitude-modulated or frequency-modulated (Fig. 19)[60].

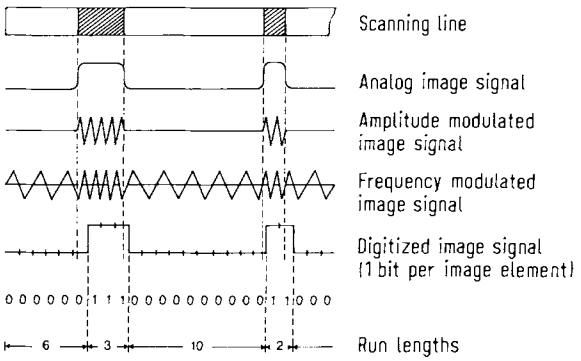


Fig. 19. Types of signals.

Because of the short transmission times needed in the newspaper industry, with its particular production sequence—one page should as rule require not longer than one minute for transmission—a digitized signal instead of the analog signal is transmitted if a video channel is not available. This has the advantage that data compression becomes possible. The extent of the information to be processed is thereby reduced; for example, all that is transmitted is that the first white signal is six units long, the first black signal is three units long, and so on. It is only this data compression which ensures rapid yet nevertheless economical long-distance transmission. Digitization results in strictly rectangular signals; these at the same time make it possible to modulate the write laser unambiguously, *i.e.* to direct the beam onto the information carrier which is to be imaged, or to deflect it. Furthermore, threshold value suppression becomes possible, in that, for example, up to a certain optical density gray shades are not accepted as signals. By this method, the contrast of the copy on the printing form can be made higher than the contrast in the original.

8. Electronics on the Advance

This cooperation of reprography and electronics produces a variety of possibilities. Thus, filmless printing form production in the newspaper sector is being greatly assisted by rapid development in the field of electronic information processing systems. The individual stages have, even today, already been mapped out[61,62].

At the present time (Table 2) the text is generally fed out from the phototype setter as galley proofs in the form of photopaper prints (pulls). Photographs are brought to the form required for the "print original" by means of a line scanner. For example, the images are screened, the tonal values are corrected, and changes in format are effected.

The text columns and the screened positive prints (pulls) are assembled, in accordance with the layout, to produce the paste-up of a page, which then serves as the original, either in a camera (overall exposure) or in a laser unit (line exposure), for the direct production of a printing form.

At the present time it is also already possible (Table 2) to produce the makeup of the text electronically and to obtain the text portion of a complete newspaper page, set ready-to-print, from the phototype setter. By inserting the screened positive prints of the pictures, the paste-up can then be quickly completed and used to produce the printing form in a camera or a laser unit.

The next stage of development of filmless printing form production will dispense with feed-out of text matter in a material form (Table 2). The text information will be fed into the central processing unit, where it will be stored. Pictorial information—which, particularly for colored reproduction, requires a higher store capacity—is supplied by a scanner in the form of a screened positive image and, correctly positioned, is fed, on an otherwise empty original sheet into a

Table 2. Simplification of printing form production by increasing use of electronics. a)—d) see text.

a)		b)		c)		d)	
Text	Image	Text	Image	Text	Image	Text	Image
Central processing unit	Scanner	Central processing unit	Scanner	Central processing unit	Scanner	Central processing unit	← Scanner
↓	↓	↓	↓	↓	↓	↓	
Phototype setter		Phototype setter					
↓		↓					
Galley	Screened positive proof	Full page pagination	Screened positive proof		Screened positive proof		
↓	↓	↓	↓		↓		
Paste up		Paste up			Paste-up		
↓		↓		↓		↓	
Area or line exposure *e.g.* Elfasol camera or Laserite		Area or line exposure *e.g.* Elfasol camera or Laserite		Line exposure *e.g.* Laserite		Line exposure *e.g.* Laserite	
↓		↓		↓		↓	
Printing form		Printing form		Printing form		Printing form	

laser unit for producing the printing form. On exposure of the printing plate, the beam of the write laser is directly controlled by the central processing unit in those areas which are to contain text information. When, on the other hand, the write laser beam reaches an area where a picture is to be imaged onto the plate, the modulation of the write laser is taken over by signals which are read off a paste-up. The information on the newspaper page is thus only collated on the printing form, and is not already collated on the paste-up. This form of newspaper production is likely, for economic reasons, to be ultimately the most advantageous in many cases.

Fully integrated picture scanning and text scanning by electronic methods (Table 2 and Figure 20) furthermore means an additional simplification, which, however, at the present time cannot yet be achieved at commercially justifiable expense.

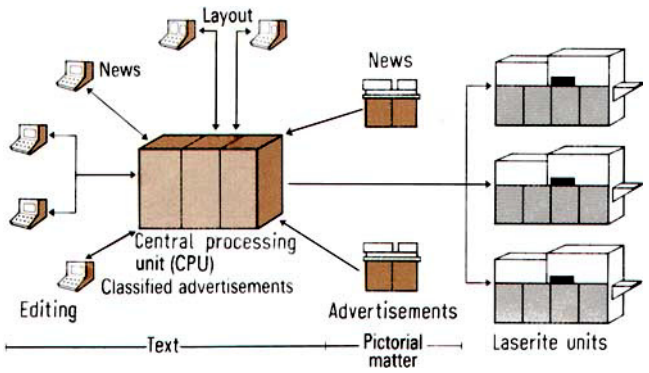


Fig. 20. Combination of full page pagination and direct plate making.

Not only do the individual editors write their contributions *via* terminals into the store of the central processing unit, where previously received and stored news and advertisements are deposited, but the processed pictures are also fed into this store. The makeup is then produced fully electronically by rearrangement of the information which has thus been stored. After approval of this non-material makeup on the screen, the entire page is directly written by laser imaging units onto printing plates.

This approach could most easily be realized in the case of the production of newspaper printing forms, because the format always remains the same, the number of pictures to be reproduced is small and is mainly black-and-white, and the print quality is of a relatively simple standard.

Where, however, four-color work of high quality, and in large amounts, is to be electronically processed and stored, store capacities which are a hundred or a thousand times greater than those for text areas of the same size would be needed. Even this already appears technically feasible at the present time, especially if it is borne in mind that store capacity will in future become progressively less expensive. Of course, stores of the conventional type will not be able to grow indefinitely, since the storage density and the read-out mechanism will not permit this. In the problem of economical storage of colored pictures, we at present come up against the limits of data processing.

9. Outlook

The innovatory leap forward which electronics have triggered will, within a forseeable time, force numerous traditional reprographic processes to give way to novel electronic methods[63]. This demands rethinking not only by the user of such complex systems but also by the chemical industry, regarding the role it plays in the processing of optical information. Even more versatility and flexibility will be expected of those newly entering this field of research—attributes which are not only equatable with personal endeavor but which are to a large extent dependent upon internal and external motivation. *Bunsen*'s dictum "Ein Chemiker, der kein Physiker ist, ist gar nichts"[64] aptly underscores the situation regarding those engaged in research in the sector of reprography, not forgetting that electronics and engineering also belong to this interdisciplinary field of activity.

Discussion with colleagues have prompted the submission of this paper for publication; valuable information accruing from such discussions have greatly helped in its planning and composition. Special thanks are due to Dr. G. Buhr and Dr. W. Frass for their enthusiastic assistance with the drafting of the manuscript and the diagrams.

Received: November 22, 1979 [A 304 IE]
German version: Angew. Chem. *92*, 95 (1980)

[1] Ullmanns Encyklopädie der technischen Chemie. 3rd Edit. Urban and Schwarzenberg, München 1963, Vol. 14, pp. 658—675.
[2] Lexikon der graphischen Technik. 4th Edit. Verlag Dokumentation, München 1977, pp. 162—163.
[3] Pocket Pal, A Graphic Arts Production Handbook. 11th Edit. International Paper Company, New York 1974, pp. 28—36.
[4] *G. A. Stevenson* in: Graphic Arts Encyclopedia. McGraw-Hill, San Francisco 1968, pp. 303—307.
[5] *C. Shapiro:* The Lithographers Manual. Graphic Arts Technical Foundation, Pittsburgh 1974.
[6] *E. D. Stiebner:* Bruckmann's Handbuch der Drucktechnik. Verlag F. Bruckmann KG, München 1976, pp. 162—188.
[7] *A. Senefelder:* Vollständiges Lehrbuch der Steindruckerey. Bey Karl Thienemann, München, and bey Karl Gerold, Wien 1818, p. 137.
[8] *O. Zeman*, Polygraph *30*, 1213, 1601 (1977).
[9] *K. Eingärtner*, Deutscher Drucker *15*, No. S1, p. 46 (1979); *14*, No. 31, p. 24 (1978); *15*, No. S2, p. XII (1979).
[10] a) Deutscher Drucker *15*, No. 31, p. VI (1979); b) Deutscher Drucker *14*, No. 29, p. 29 (1978).
[11] *H. E. Crawford*, Photo-Engravers Bull., Nov. 1964, p. 83.
[12] *D. Reger*, Hauszeitschrift "Die BASF", No. 4, p. 4 (1967); *A. Wasserrab*, Druckspiegel *31*, 498 (1976); *31*, 878 (1976).
[13] *G. Beiner*, Druckspiegel *33*, 365 (1978).
[14] Deutscher Drucker *13*, No. 24, pp. 8, 13 (1977); *R. V. Cannon, ibid. 14*, No. 31, p. 11; No. 37, p. 26 (1978).
[15] *K. Eingärtner*, Deutscher Drucker *13*, No. 19/20, p. 82 (1977).
[16] *F. Uhlig*, Referate des 3. Kongress-Halbtages, IMPRINTA, Düsseldorf, February 17, 1979, pp. 31—38.
[17] *J. Mare*, Lithoprinter *22*, p. 36, Aug. 1979.
[18] Druckwelt *29*, 897 (1979).
[19] *A. Dobrusskin, H. Leyendecker, G. Schmid*, Fachreferate, 4. Internationaler Kongreß für Reprographie und Information, Hannover 1975, pp. 9—14.
[20] *J. Kosar:* Light-Sensitive Systems. Wiley, New York 1965.
[21] *P. Walker, V. J. Webers, G. A. Thommes*, J. Photogr. Sci. *18*, 150 (1970).
[22] *H. Steppan*, Kongressband, 4. Internationaler Kongress für Reprographie und Information, Hannover 1975, pp. 147—162.
[23] *K. I. Jacobson, R. E. Jacobson* in: Imaging Systems. Focal Press, London 1976, pp. 173—180; 181—222.
[24] *O. Süs, J. Munder, H. Steppan*, Angew. Chem. *74*, 985 (1962).
[25] *P. Ziegler*, Polygraph *32*, 1102, 1600 (1979).
[26] *O. Süs*, Justus Liebigs Ann. Chem. *556*, 65 (1944).
[27] See [20], pp. 339—352.
[28] *J. Pacansky, J. R. Lyerla*, IBM J. Res. Dev. *23*, 42 (1979).
[29] *M. P. Schmidt, R. Zahn*, DRP 596731 (1931), Kalle.
[30] *M. S. Dinaburg* in: Photosensitive Diazo Compounds and their Uses. Focal Press, London 1967, pp. 91—94.
[31] *H. Steppan, R. Dietrich*, Angew. Makromol. Chem., in press.

[32] *J. L. R. Williams*, Fortschr. Chem. Forsch. *13*, 227 (1969).
[33] *G. W. Leubner, C. C. Unruh*, US-Pat. 3257664 (1966), Eastman Kodak.
[34] *H. G. O. Becker*, J. Signalaufzeichnungsmaterialien *5*, 381 (1975).
[35] *H. G. O. Becker*, Papers from the International Congress of Photographic Science, Rochester 1978, p. 173.
[36] *F. C. De Schryver, N. Boens, J. Huybrechts, J. Daemen, M. De Brackeleire*, Pure Appl. Chem. *49*, 237 (1977).
[37] *H. Barzynski, K. Penzien, O. Volkert*, Chem.-Ztg. *96*, 545 (1972).
[38] *F. P. Alles*, DOS 1572153 (1967), E. I. du Pont de Nemours.
[39] *R. M. Schaffert:* Electrophotography. Enlarged and Revised Edition. Focal Press, London 1975; see also *J. W. Weigl*, Angew. Chem. *89*, 386 (1977); Angew. Chem. Int. Ed. Engl. *16*, 374 (1977).
[40] Winnacker-Küchler: Chemische Technologie. 3rd Edit. Hanser, München 1972, Vol. 5, p. 640.
[41] *D. Winkelmann*, Kongressband, 4. Internationaler Kongress für Reprographie und Information, Hannover 1975, pp. 81—88.
[42] *E. Lind*, lecture, IARIGAI-Symposium Lichtempfindliche Materialien, Wien, November 21—23, 1979.
[43] *D. Winkelmann*, J. Appl. Phot. Eng. *4*, 187 (1978).
[44] *F. Uhlig*, DAS 1117391 (1959), Kalle.
[45] *M. L. Sugarman, Jr.*, DBP 974162 (1955), Radio Corp. of America.
[46] Techn. Fortschr. Nr. 760, May 10, 1979 (Verlag Handelsblatt, Düsseldorf).
[47] *M. R. Kuehnle*, J. Appl. Photogr. Eng. *4*, 155 (1978).
[48] Offsetpraxis *20*, No. 9, p. 50 (1978).
[49] *H. Martschina*, lecture, IFRA-Symposium über Ganzseitentechnik und Plattenherstellung, Amsterdam, January 24 and 25, 1978.
[50] Informations on Newspaper Technology *11*, No. 15, August 1, 1979.
[51] *K. Tradowsky:* Laser. 3rd Edit. Vogel-Verlag, Würzburg 1977.
[52] *R. E. Gillespie, S. J. Lee*, Proc. Soc. Photo-Opt. Instrum. Eng. *169*, 116 (1979).
[53] *T. S. Dunn*, Lasers and Newspaper Platemaking, lecture by *R. E. Amtower*, PIRA-Seminar, Surrey (England) 1975.
[54] *R. E. Amtower*, lecture, Electro-Optics/Laser '76, Conference and Exhibition, New York 1976.
[55] *H.-W. Fraß*, ZV+ZV, Zeitschrift für Presse und Werbung *1977*, 1514.
[56] Druckspiegel *32*, 780 (1977).
[57] *J. O. H. Peterson*, DOS 2500905 (1975), Scott Paper.
[58] Deutscher Drucker *10*, No. 36, p. 24 (1974).
[59] Deutscher Drucker *15*, No. 21, p. VII (1979).
[60] *P. Grupen, H. Karius, H. W. Peters, R. Sommer, K. Maier, D. Preuß, E.-H. Rittberg* in: Stand und Entwicklung der Faksimiletechnik. Forschungsbericht T 77—33, Bundesministerium für Forschung und Technologie, Bonn 1977, pp. 25 ff.
[61] *L. G. Larson*, lecture, PIRA-Institut, London, September 14 and 15, 1977.
[62] *L. G. Larson*, Proc. Soc. Photo-Opt. Instrum. Eng. *169*, 22 (1979).
[63] *F. W. Burkhardt*, ZV+ZV, Zeitschrift für Presse und Werbung *1979*, 1660.
[64] *F. A. Henglein:* Grundriß der Chemischen Technik. 8th Edit. Verlag Chemie, Weinheim 1954, p. 22.

On the Symbolic Language of the Chemist

By Rudolf Hoppe[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Körper und Stimme verleiht die Schrift dem stummen Gedanken;
Durch der Jahrhunderte Strom trägt ihn das redende Blatt.
(Friedrich von Schiller)

1. Introduction

In a stroke of genius, *Jöns Jacob Berzelius* created the formula language of chemistry still in use today. Few changes have been made to that language in the intervening 160 years. New methods and materials, entirely different concepts and modern theories have meanwhile drastically modified our discipline. Has its formula language become outmoded? Can it be altered? Is it still capable, particularly in the case of inorganic solid state chemistry, of describing what we know, believe to know, or want to know?

Unlike the other exact sciences, chemistry utilizes not only mathematical symbols but its own formulae, *e.g.* C_6H_6 or NaCl, which can be combined in equations (*e.g.*: $2KInO_2 + Na_2O = 2NaInO_2 + K_2O$[1]). Such formulae and equations qualitatively and quantitatively encode experience, often in facile manner. Moreover, they stimulate the expert to undertake new experiments if everyday experience (*e.g.*: noble gases are inert[2]) is combined with a portion of critical doubt (SnF_4, SbF_5, TeF_6, IF_7, Xe/F?[3]) and suitably formulated (here: $Xe + F_2 = XeF_2$[4]).

As *Homo sapiens*, and hence *ξῶον πολιτικόν*, we differ from other anthropoids, and possibly even from other hominoids, by our ability to transmit not only feelings and moods but also experience, knowledge, and cognition in a well-defined phonetic language to other members of our species. However, it is only the written word, an early discovery in some cultures and a late one in others, in many cases simply copied, which permits flow of essentially error-free information between past and future. Since language was (at least formerly) subject to spatial and temporal limitations, in times of tempestuous cultural development the written word became a new tool also of the enquiring mind.

Unlike language *per se*, the written word can, as a huge clamp, hold together entities which would otherwise fall apart all too readily (*e.g.* such a gigantic empire as China with so many different languages, dialects, and ethnic groups). It is the written word which enables someone "in the know" to communicate intellectual activities (and other matters) from one generation to the next with hitherto unknown accuracy. There are of course various kinds of writing. Pictograms (Figs. 1 and 2) are important precursors of

[*] Prof. Dr. R. Hoppe
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring, D-6300 Giessen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0110 $ 02.50/0

any kind of script intended to transmit as much information as possible to as many people as possible (see also Fig. 3).



Fig. 1. Offer to barter. The cross means crossed hands, no weapons, gesture for trading/bartering. Offer (right): bison, otter, and weasel skins; wanted (left): gun and 30 beaver skins. Based on *G. Mallery*, Annu. Rep. Bureau Ethnol. (Washington) Vol. *4* (1882/83), Vol. *10* (1888/89).

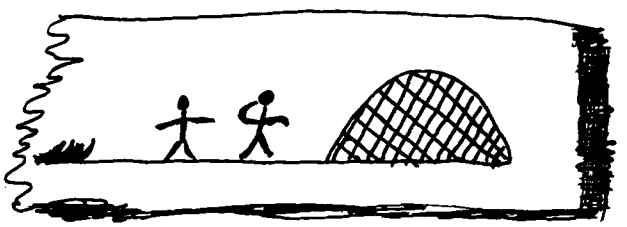


Fig. 2. "There is nothing to eat in this hut, we are hunting". Left-hand figure: gesture for negation. Right-hand figure: gesture for eating, with indication of hut. Left: suggestion of hunting (??). Based on: The Graphic Art of the Eskimos, Annu. Rep. Board Regents Smithsonian Inst. 1895. Hoffmann, Washington 1897.

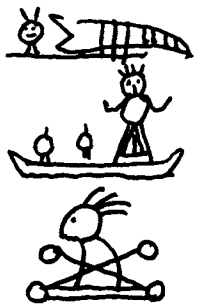


Fig. 3. From Walam Olum of the Delaware Indians dating form pre-European times. Cf. *H. Jensen:* Die Schrift in Vergangenheit und Gegenwart. Verlag der Wissenschaften, Berlin 1958. [Aid to memory for the following text: "The great fish, the many, they ate some, the moon-woman with the boat, she helped come! She came, she came, helped all, Nanabusch (God of awakening life) is the grandfather of all, the grandfather of the creatures, the grandfather of mankind, the grandfather of the tortoise tribe" (totem animal of the Delaware: tortoise).]

The example from the notebook of an East Frisian messenger woman unable to read and write (Fig. 4) nevertheless shows that there are simple possibilities of storing information in such a way that it is, sometimes intentionally, incomprehensible to most people (except herself in this case). This also applies, *e.g.*, to hobo signs (cf. Fig. 5) and modern coded texts of political intelligence departments[5].

The symbols used by alchemists undoubtedly number among those methods of recording experience such that it is accessible only to the initiated. It is quite conceivable—as reported—that the same author used different signs depending upon whether he wished to inform just his own circle of associates or friends or also his "competitors". Formerly inexplicable differences in chemical behavior (*e.g.* of tin when it is comparatively pure or contains relatively large amounts of lead) were indicated by different names (*i.e.* al quasḍīr or al kal'ī)[6] ("kalaitic lead").

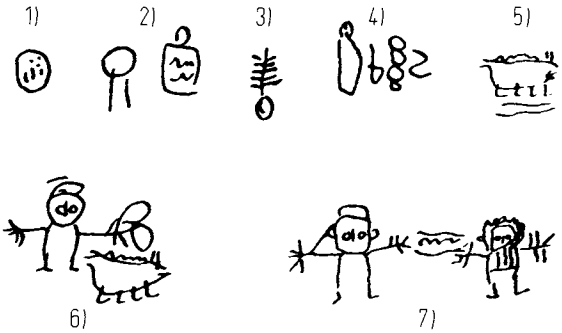


Fig. 4. From the notebook of an East Frisian messenger woman. Cf. Kosmos, Handweiser für Naturfreunde, 1914, p. 225. [Meaning: 1) rice; 2) slate and sponge; 3) leeks; 4) wine; 5) bacon, pork, lard; 6) a man should come to slaughter a pig and bring two additional pigs' bladders; 7) hand over letter from village smith to his lover in the town.]

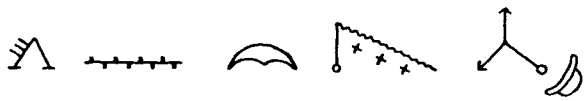


Fig. 5. From "Der Mordbrenner Zeichen und Losungen, etwa bey Dreiyhundert und viertzig ausgeschickt". Nürnberg 1540. [Content: imprisoned (under a roof, thrice questioned), for highway robbery, at night, help requested, quickly (don't run around, but straight here and take me under your protection(?).]

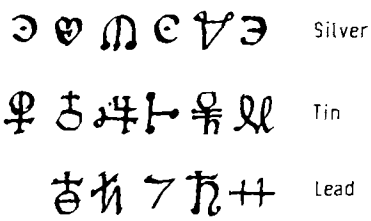


Fig. 6. Examples of alchemical symbols (Ag, Sn, Pb).

The advent of the balance, and thus of the principle of quantitative measurement in chemistry, compelled investigators to symbolically express the composition of substances "additively" according to analytical findings. The proposals of *Hassenfratz* and of *Adet*, and also of *Dalton*[7] were too arbitrary and cumbersome. Moreover, *Dalton*'s "formulae" (*e.g.* the highly modern formulation of CO_2 as ⊕○⊕) appeared to overtax the printer's art.

It is to the everlasting credit of *Berzelius*[8] that he laid the foundation stone of present day chemical formulation in 1813. He proposed that the elements should be represented by *one* (typical nonmetals) or *two* Roman characters—*e.g.* S, Sb, Se, Si, Sm, Sn, Sr—of which the first, upper case one is the first letter of the scientific name, and the second, lower-case one provides supplementary information. If several atoms of the same kind are present in a molecule, the composition was initially indicated by superscripts—*e.g.* CH^4. *Berzelius* also introduced shorthand forms (*e.g.* Cy for cyanide or A for acetate) strongly suggestive of modern practice, and

denoted oxygen, which he considered so very important from his atomic weight determinations by analysis of oxides, by dots (*e.g.* S̈ instead of SO^2). This did not help his contemporaries to immediately appreciate the inestimable advantages of his system.

This way of describing something new by combination of individual characters is strongly reminiscent of the creation of various signs of Chinese script (Fig. 7). Duplication, *e.g.* ClCl for the chlorine molecule as against Cl for the atom, leads to something so entirely different as does the doubling of the old Chinese sign for woman 女 to give that for quarrel 奸 (modern form: 女女).

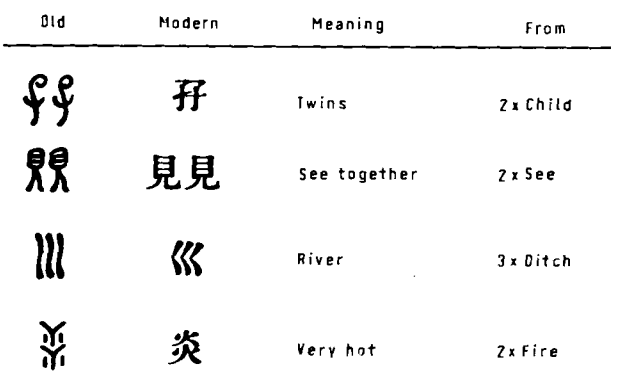


Fig. 7. Examples of Chinese characters.

After the known corrections had been made to *Berzelius'* original notation, we now write SO_2 and $K_3[Fe(CN)_6]$, *etc.*, his formulae have decisively influenced chemistry ever since. *Kekulé*'s benzene formula[9] and the discovery of the "asymmetric carbon atom"[10] introduced pronounced steric aspects which were subsequently also introduced into inorganic chemistry by *Werner*[11]. Since then, structural formulae supplement molecular or empirical formulae according to *Berzelius*.

Nevertheless, the wealth of information about the structure of chemical compounds and their reactions available from a simple molecular formula such as β-$C_{10}H_7SO_3H$ or $C_6H_{12}O_6$ is enormous and largely accessible even to the novice!

2. Problems of Inorganic Solid State Chemistry

To this day, the conceptual world of many chemists is to some extent colored by the overwhelming endorsement of *Berzelius'* sign language in connection with the dispute with *Berthollet* concerning the composition of chemical compounds. Contrary to the opinion of *Dalton* and *Berzelius*, *Berthollet* had maintained that the laws of constant and multiple proportions—*i.e.* the prerequisites for the representation of analytical results by simple formulae such as Cu_2O and CuO—do not always apply.

Today we know just how right he was. Even simple metal oxides can "only just" (*e.g.* Fe_2O_3) or "hardly" (Nb_2O_5) be characterized by these simplifying formulae, as demonstrated by the classical example of "FeO"[12]. In $NbO_{2.500-\delta}$, the value of δ *may be*, but *is not necessarily* distinct from zero, and the extent of maximum deviation also differs in the various modifications, of which 25 are known to date[13]; *e.g.* $0 \leq \delta \leq 0.011$ in H-Nb_2O_5[14]. Other oxides, which like "PbO_2" may be of great industrial importance, are known as materials but have not (yet) been prepared as "pure substances" or even as single crystals having a composition corresponding to the formula[15].

Inorganic solid state chemistry is a decidedly *young* science. It was only about 1930 that X-ray structures were first undertaken in conjunction with preparative work on the production of new substances in chemical laboratories like those of *E. Zintl* and *W. Klemm*; modern methods of structural solution employing single crystals have only been used during the past twenty years or so. Yet solid-state chemistry proper starts from a knowledge of crystal structure.

This is probably connected with the notable absence, or inadequate treatment, in most textbooks of facts peculiar to compounds whose characteristic properties are associated with the solid state: compounds made up of molecules such as benzene can usually be prepared in very different ways. The products of varying quality can be subsequently purified, however, and the final samples are all "identical" within the present limits of analytical accuracy.

In the case of solids, however, the formula (*e.g.* CsOH) primarily represents the "compound *per se*", almost in the sense of an idea of *Plato*. Again, one can attempt to prepare samples of "CsOH" by entirely different methods (*e.g.* dehydration of $CsOH \cdot H_2O$, reaction of metallic Cs or of Cs_2O with the properly calculated amount of H_2O, reaction of Cs_2O_2 with H_2). The procedure adopted also plays a role (Cs_2O_2 can be heated in a current of H_2 or annealed in sealed Ag tubes under H_2, reacting in the latter case only with H_2 that has diffused through the wall, and thus undergone further purification[16]). Subsequent purification is hardly possible. Not even samples obtained by the same synthetic pathway are necessarily "identical" (*e.g.* because of differences in quality of the starting material Cs_2O or Cs_2O_2). Recent findings with KCo_2O_4[17] have shown that practically every single crystal belongs to one of two superstructures, and yet exhibits a further individual "super-superstructure"[18].

Only in the light of modern studies with high-resolution electron microscopes did the incredible complexity of the structure of individual single crystals became evident, as regards structural defects and hence composition (cf. Fig. 8)[19]. Thus it becomes understandable that many a simple compound generally considered to be known is still awaiting preparation. Sb_2O_5, known as a metal oxide since the publication of the "*Triumphwagen des Antimonii*"[20], has only recently been prepared pure by *Jansen*[21]; he also obtained the first sample of "pure" As_2O_5[22]. Not only could the structure be elucidated with the aid of previously unavailable single crystals, but, even more remarkably, there are striking differences in behavior: thus according to former reports[23] As_2O_5 melts with decomposition at 330 °C, whereas *Jansen*'s samples melt without decomposing at 760 °C.

Long known as a titration product of KOH with H_3PO_4 in solution, K_3PO_4 was only recently prepared in the pure anhydrous state in our laboratory[24]; the industrial product Na_3PO_4 has likewise only recently been prepared as single crystals[25]; no "pure" samples of the powder have yet been obtained.

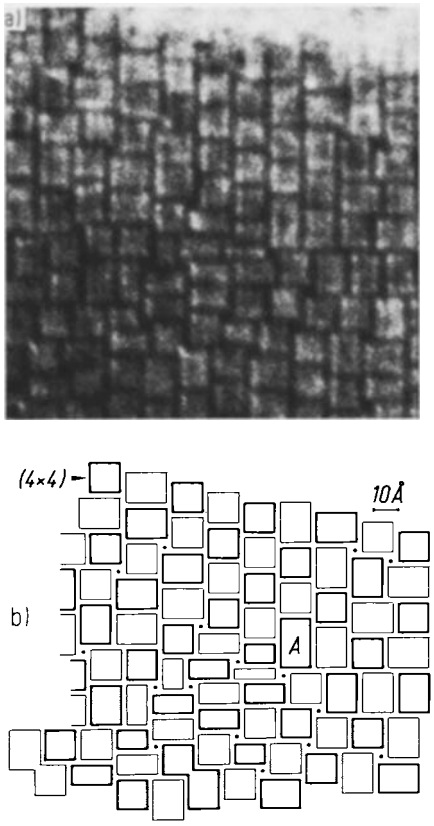


Fig. 8. a) Transmission electron micrograph shows disorder in a WO_3-containing preparation of niobium pentoxide deposited at 780 °C from the gas phase; incorporation of WO_3 leads to $O/\sum M = 2.53$ (M = Nb, W).—b) As shown by the interpretation of the transmission electron micrograph both the linkage and the size of the structural units ["block" consisting of $(n \times m)$ M O octahedra] are irregular. Unusual block sizes, such as the (6×4)-block (A) with $O/M = 2.584$ and the neighboring (5×2) block with $O/M = 2.381$ are characteristic of the metastable preparation. Worthy of note are the unusual edge linking in the (4×5)-blocks and the (4×4)-blocks which are to be regarded as a typical structural unit of the N-Nb_2O_5 modification.

Only few methods—*e.g.* chemical transport, zone melting, recrystallization from the flux—are presently available which permit subsequent purification of typical solids in special cases. This difficult problem still requires experimental solution.

3. Shortcomings of the Berzelius Notation

After just a few semesters of study, any chemistry student can appreciate the wealth of information about structure, symmetry, spectra, chemical behavior, and reaction pathways of "smaller" molecules, which is transmitted by the simple Berzelius notation, and the extent to which the properties of such molecular compounds are established thereby.

A formula such as NaCl, CdS, or CuI reveals neither the thermodynamically stable crystal structure nor whether (and if so how many) other modifications occur and what their structural characteristics may be. It may even claim to give false information, a fact which has received far too little attention. CuS, the characteristic sulfide of copper in group analysis, is certainly not to be formulated as $Cu^{2+}S^{2-}$ but according to $Cu^{2+}Cu_2^{1+}(S_2)^{2-}S^{2-}$, in every respect a "mixed-valence" sulfide[26].

In the case of nonmetallic elements such as P_4[27], S_8, S_{12}[28], and Cl_2, a certain amount of structural information is provided by the formula, but none is forthcoming in the case of metals such as Fe or Mn. One must *know* what transformations occur on heating α-iron, and while the hypothesis that all metals melt from the cubic space-centered form[29], provided they can exist in this form, provides an "explanation" why δ-Fe (like α-Fe) forms cubic space-centered crystals, there is still no real understanding in this matter or with regard to the structural capers of α- and β-manganese[30].

4. Chemical Nomenclature of Solid State Compounds

International rules for the notation of chemical names and formulae are indispensable for coding and for the compilation of thesauri. They are a welcome aid in the standardization of curricula for the teaching of beginners. They hinder progress if instead of $K_2[PtCl_6]$ (or more consistently: $[PtCl_6]K_2$) the formula $KCl_3(Pt_{1/2})$ is not permitted: the first, and, even more so, the second formulation emphasizes that a complex is present with Pt^{4+} as the central ion and Cl as ligand. It is almost irrelevant whether electroneutrality is achieved by K^+ or any other ion, *e.g.* Cs^+: the chemical behavior will be modified at most by the difference in solubility. However, neither formulation says why K^+ has a coordination number (C.N.) of 12 towards Cl^- instead of 6 as in KCl. The reason can be deduced (cf. Section 8) from the notation $KCl_3(Pt_{1/2}) = KCl_{12/4}(Pt_{1/2}) = ClK_{4/12}Pt_{1/6}$ with C.N. 5 for Cl^-.

Why do we write Al_2O_3? In memory of Daltonian concepts which are fundamentally inapplicable here? Why do we convey to the beginner the impression that NaCl is a compound made up of molecules like HCl? Why don't we write $Al_{0.4}O_{0.6}$? Or $AlO_{3/2}$? Or $OAl_{2/3}$? Why not Al_6O_9?

Chemistry is an empirical science. Without one's own experience and that of others it is impossible to pursue the study of chemistry. Experience, however, particularly when it is encoded in formulae and equations, can resemble a chitin shell, and the stronger it becomes the more difficult it will be to shed in order to permit further growth, *i.e.* to recognize and experience something new for what it is. But it is precisely this ability which the young science of solid-state chemistry constantly needs, particularly from the most experienced chemists. More than elsewhere, it is necessary not only to look for what is new but to question what is known (or more precisely: what is believed to be known). To this end it is useful to shock oneself and, where possible, others too by use of new notations, *e.g.* $ClPt_{1/6}K_{4/12}$.

We shall therefore not adhere to canonical formula and nomenclature rules such as those laid down by IUPAC.

5. The Notation of *Niggli*

Many have tried to adapt Berzelius formulae to solids. A particularly impressive and comprehensible notation is that proposed by *Niggli*. He was the first[31] to write $SiO_{4/2}$ instead of SiO_2 and thereby discovered what is termed the *motif of functionality*, and sometimes *motif of mutual adjunction* in what follows. He employed his notation only descriptively. Perhaps *Niggli* himself, like so many others who were less

gifted, fell to the enchantment of structural elucidation as a result of the fascinating aspects and results of X-ray structure analysis.

6. Motif of Coordination

All of the (*ca.* 20) known crystalline forms of SiO_2 except stishovite[32] exhibit Si^{4+} in a tetrahedral environment of $4O^{2-}$. We designate SiO_4 as the motif of coordination (Mo.C.) of Si^{4+}, and OSi_2 analogously as the Mo.C. of O^{2-} in SiO_2.

The corresponding motifs for stishovite are SiO_6 and OSi_3 respectively. We find the same Mo.C. in SiP_2O_7[33]. This becomes understandable when we employ the unconventional formulation $SiO_6(POP)$, ascribe the bridging O-entity a special status, and require that all "terminal" O-entities of the P_2O_7 groups be equivalent towards Si. A series of questions arises, *e.g.* whether or when SiO_5 also plays a role instead of the Mo.C. SiO_4 on glass formation, or which oxides of silicon $SiO_n(Y)$ with suitably chosen Y (in place of POP) permit the case of $n=5$ and thus possibly the hitherto unknown C.N. of 5 for Si towards O? Does this Mo.C. possibly even occur in SiO_2 itself? Table 1 lists possible data for such a hypothetical form of SiO_2, and Figure 9 shows the proposed structure.

Table 1. Coordination number 5 in $SiO_2=Si(O1)_{3/3}(O2)_{2/2}$, a hypothetical form (cf. Fig. 9) with $a=b=3.043$, $c=3.220$ Å, $\gamma=120°$.

Madelung part of lattice energy (MAPLE) in kcal/mol			
	$Si(O1)_{3/3}(O2)_{2/2}$	α-Quartz	β-Quartz
Si^{4+}	2277.6	2219	2209
$O(1)^{2-}$	688.8	710 × 2	703 × 2
$O(2)^{2-}$	643.7		
Σ	3610	3639	3615

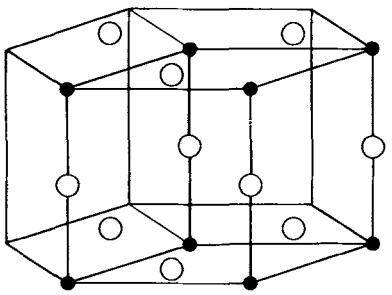


Fig. 9. Hypothetical form of SiO_2 with C.N. 5 for Si towards O (cf. Table 1). Si^{4+}: 0, 0, 0; $(O1)^{2-}$: 2/3, 1/3, 0; $(O2)^{2-}$: 0, 0, 1/2.

The search for the Mo.C. SiO_3, *e.g.* in the form of a "carbonate-analogous" silicate also belongs to this genus of questions.

Thus formulated, compounds appearing inconspicuous in the classical notation often offer stimulating starting points for new studies. $Mn(IO_3)_2$ and $Fe(IO_3)_3$ having the isoelectronic ions Mn^{2+} and Fe^{3+} appear to be "harmless" iodates. On formulation as $MnO_6(I_2)$ and $FeO_9(I_3)$, it is immediately seen that $FeO_6(IO)_3$ appears far more likely than $FeO_9(I_3)$ owing to preference of C.N. 6 by Fe^{3+} towards O^{2-}, and that the different O^{2-} of the IO_3 groups act nonequivalently towards Fe^{3+}, as confirmed by the structure determination[34]; hence pecularities are possible in the physical behavior of $Fe(IO_3)_3$.

In view of the variety of known forms of Al_2O_3, the question arises whether AlO_6 is always the Mo.C. as in corundum.

7. Motifs of Functionality

The motifs of coordination (Mo.C.) in inorganic chemistry are almost invariably "fictive" quantities. Even in "island silicates" such as Mg_2SiO_4 there are no truely "isolated" SiO_4 groups—rather they are linked *via* shared Mg^{2+} (the ionic charges are given as indicators of oxidation states or sums thereof) to form three-dimensional networks. In the following we shall call formulations such as $SiO_{4/2}$ motifs of functionality (Mo.F.). In the case of our example, the formulation means that all O in the forms of SiO_2 (except stishovite) bridge two $2Si^{4+}$ each. Owing to the expected C.N. of 4 (valid for all oxosilicates known so far) the Mo.F. in, *e.g.*, Na_2SiO_3 is surely $Si(O1)_{2/1}(O2)_{2/2}$.

The simpler the composition of a solid, the less informative is the Mo.F. The same Mo.F. of $ClNa_{6/6}$ applies to NaCl as to NiAs ($NiAs_{6/6}$) although the two structures are entirely different. In contrast, if functional differences of chemically equivalent particles are to be expected in binary compounds, then such differences are soon recognized in the Mo.F.

For a variety of reasons, partly because of its relatively high melting point, SnF_4[35] is not expected to have a molecular structure but instead the C.N. of Sn^{4+} for F^- is expected to be 6. This leads directly to $Sn(F1)_{4/2}(F2)_{2/1}$ as the Mo.F. of Sn^{4+}; the (F1) are seen to act as bridges according to $(F1)Sn_{2/4}$ and the (F2) are terminal.

In silicates such as Na_2SiO_3 or $MgSiO_3$, $Si(O1)_{2/1}(O2)_{2/2}$ is expected as Mo.F. of Si^{4+}; bridges and terminal anions are again present.

8. Motifs of Mutual Adjunction

Only the motifs of mutual adjunction (Mo.A.) clearly reveal structural details or peculiarities.

It has so far remained unanswered what reasons are actually responsible for the way in which a given motif of functionality (Mo.F.) is crystallographically solved in a real case.

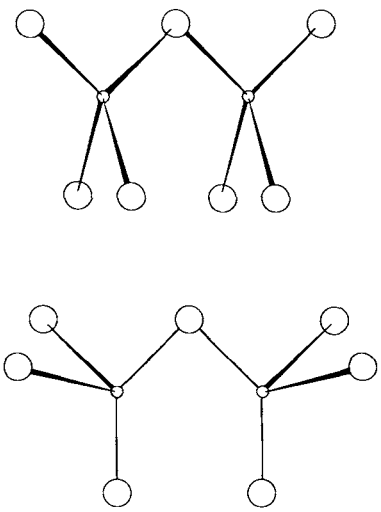


Fig. 10. Conformations of the Cr_2O_7 group in $Sr[Cr_2O_7]$.

One must bear in mind that many simple concepts, even though frequently substantiated, need not always apply.

For example, not all the groups $[Cr_2O_7]$ have to have the same conformation in the crystal of a dichromate like $K_2[Cr_2O_7]$; *e.g.* in $Sr[Cr_2O_7]$ it has been shown[36] that the conformations given in Figure 10 occur in the ratio of 1:1.

Thus the crystallographic description of mutual adjunction for a given Mo.F. can vary widely even for related compounds. For example, according to the occupation of different point sites in Na_2SiO_3[37] corresponding to $Na_2Si(O1)_{2/1}(O2)_{2/2}$, the starting situation is completely different from that of $MgSiO_3$ in which, according to (Mg1)(Mg2)(Si1)(Si2)(O1)...(O6)[38], a far more complicated crystallographic situation prevails. The Mo.A. of these two "metasilicates" are given in Table 2.

Table 2. Motifs of mutual adjunction in Na_2SiO_3 and $MgSiO_3$.

a) $Na_2Si(O1)_{2/1}(O2)_{2/2}$

	2(O1)	(O2)	C.N.
Si	2/1	2/2	4
2 Na	4/4	1/2	5
C.N.	5	4	

b) (Mg1)(Mg2)(Si1)(Si2)(O1)...(O6)

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	C.N.
(Si1)	1/1	1/1	2/2				4
(Si2)				1/1	1/1	2/2	4
(Mg1)	2/1	1/1		2/2	1/1		6
(Mg2)	1/1	1/1	1/1	1/1	1/1	1/1	6
C.N.	3	3	3	4	3	3	

c) $MgSi(O1)_{2/1}(O2)_{2/2}$ (hypothetical)

	2(O1)	(O2)	C.N.
Si	2/1	2/2	4
Mg	4/2	2/2	6
C.N.	3	4	

or

	2(O1)	(O2)	C.N.
Si	2/1	2/2	4
Mg	6/3		6
C.N.	4	2	

d) MgSi(O1)(O2)(O3) (hypothetical)

	(O1)	(O2)	(O3)	C.N.
Si	1/1	1/1	2/2	4
Mg	3/3	2/2	1/1	6
C.N.	4	3	3	

e) Diopside, $CaMgSi_2(O1)_2(O2)_2(O3)_2$; distances [Å] are given in addition to the Mo.A.

	2(O1)	2(O2)	2(O3)	C.N.	E.C.N. [a]
Ca	2/1 2.44	2/1 2.34	2/1 2.52 (2/1 2.87)	6 (+2)	6.7
Mg	2/1 2.07, 2/1 2.12	2/1 2.11		6	6.0
2 Si	1/1 1.54	1/1 1.59	1/1 1.64, 1/1 1.76!	4	3.6!
C.N.	4	3	3 (+1)		

[a] E.C.N. = effective coordination number (ECoN: *R. Hoppe*, Z. Kristallogr., in press).

Hence, in the case of $MgSiO_3$, it follows for the formulation of $MgSiO_{2/2}O_{2/1}$ (Table 2c) either that the coordination number of the terminal O^{2-} is smaller than that of the bridging moieties or that it is two units greater at C.N. 4 as against C.N. 2 (for bridging O^{2-})—experience shows both alternatives to be unlikely. It is thus appreciated why the equality of Mo.F. and Mo.A. found for Na_2SiO_3 does not hold for $MgSiO_3$, with the terminal O^{2-} being present in two different forms. It is not clear, however, why two crystallographically distinct Mg positions are necessary. The differences between these positions become more obvious in derivatives such as diopside ($MgCaSi_2O_6$)[39], although it can be reasonably doubted whether Ca^{2+} can be assigned C.N. 8 towards O^{2-} in the case of diopside (cf. Table 2e); we shall refrain from discussing such misgivings in this article.

Of interest in this context is $BaSiO_3$[40] for which the Mo.A. (cf. Table 3) show that the functionally equivalent terminal O^{2-} are now also equal with regard to their C.N. towards all cations. Owing to the formal agreement in composition with $MgSiO_3$, this requires that the C.N. of Ba^{2+} is now 7 instead of 6.

Table 3. Motifs of mutual adjunction in $BaSiO_3 = BaSi(O1)(O2)(O3)$.

	(O1)	(O2)	(O3)	C.N.
Si	2/2	1/1	1/1	4
Ba	1/1	3/3	3/3	7
C.N.	3	4	4	

Not only do the Mo.A. quickly provide a simple and readily understood description of relatively complicated crystallochemical situations; what is even more important, they promote new syntheses and provide some indication of their probable chances of success. Let us consider two examples:

8.1. Oxoniccolates(II) of Alkali Metals

Numerous attempts to prepare oxoniccolates(III) such as $KNiO_2$[41] have so far proved unsuccessful; the products obtained could not be identified. On the basis of preparative considerations we first attempted the synthesis of Li_2NiO_2, and were successful[42]. Table 4 lists the Mo.A. and shows that C.N. 4 for Li^+ must necessarily lead to C.N. 4 for Ni^{2+}, a value otherwise not encountered in oxides, if it is assumed that a maximum of six cations can be assigned to O^{2-}. This assumption has been frequently confirmed, even though isolated exceptions are found, *e.g.* in $K_6[Fe_2O_6]$[43] and $K_6[Mn_2O_6]$[44], two oxides with discrete anions having a structure analogous to Al_2Cl_6. Table 5 shows that, under these premisses, "isolated" structural units $^0_\infty[NiO_{2/1}]$ may occur in $K_2[NiO_2]$ if K^+ is allowed to have C.N. 5 instead of the expected value of 6.

Table 4. Motifs of mutual adjunction in Li_2NiO_2.

	O	C.N.
Li	4/4	4
Ni	4/2	4
C.N.	6	

Table 5. Motifs of mutual adjunction in K_2NiO_2.

	O	C.N.
K	5/5	5
Ni	2/1	2
C.N.	6	

In the experimentally difficult synthesis we first consciously exploited the "wall reaction" (Ni tubes), otherwise regarded as the bane of solid state reactions, in order to rule out partial oxidation by residual traces of O_2. Structural analysis[45] revealed a "filled" molecular structure of XeF_2 type[46], *i.e.* a structure isotypic with $K_2[HgO_2]$[47] and the presence of linear CO_2-analogous dumbbells with a surprisingly short distance $d(Ni\text{--}O) = 1.68$ Å (knight's move relationship between Ni and Hg in the Periodic Table!).

The related highly interesting question of the crystal structure of Na_2NiO_2[48] was only recently answered, and then for only one of the two modifications: α-Na_2NiO_2 exists as a further variant of the Li_2NiO_2 principle ($PdCl_{4/2}$-analogous chains $^1_\infty[NiO_{4/2}]$)[49], with one of the two O^{2-} showing C.N. 7 towards the cations (cf. Table 6). Surprisingly, therefore, the premise for the "understanding" of the occurrence of C.N. 2 of Ni towards O in K_2NiO_2 is not fulfilled. Despite considerable effort, the crystal structure of β-Na_2NiO_2 is still unknown.

Table 6. Motifs of mutual adjunction in Na_2NiO_2.

	(O1)	(O2)	C.N.
(Na1)	2/2	3/3	5
(Na2)	2/2	2/2	4
Ni	2/2	2/2	4
C.N.	6	7	

8.2. Oxocobaltates(II) of Alkali Metals

It came as a surprise when we found that the first oxoferrate(II), $Na_4[FeO_3]$, again obtained by "reaction with the wall" (the Fe inlet of the tube), unexpectedly exhibited carbonate-analogous discrete groups $[FeO_3]$[50]. Table 7a shows why the unusually low C.N. of 3 towards O^{2-} occurs for Fe^{2+}. Viewed in this light, the tremendous effort involved in the syntheses of alkali metal oxocobaltates(II) as single crystals appeared well worthwhile. The synthesis was successful and we also found CO_3^{2-}-analogous "anions" in $Na_4[CoO_3]$[51] (cf. Table 7b). If such experiments give other

Table 7a. Motifs of mutual adjunction in $Na_4[FeO_3]$.

	(O1)	(O2)	(O3)	C.N.
(Na1)	1/1	2/2	1/1	4
(Na2)	2/2	1/1	1/1	4
(Na3)	1/1	1/1	1/1	3
(Na4)	1/1	1/1	2/2	4
Fe	1/1	1/1	1/1	3
C.N.	6	6	6	

Table 7b. Motifs of mutual adjunction in $Na_4[CoO_3]$ [a].

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	C.N.
(Co1)	1/1			1/1		1/1	3
(Co2)		1/1	1/1		1/1		3
(Na1)	1/1	1/1	1/1		1/1		4
(Na2)	1/1		1/1	1/1	1/1 (2.79)		3 (+1)
(Na3)		1/1	1/1	1/1		1/1 (2.80)	3 (+1)
(Na4)	1/1	1/1		1/1		1/1	4
(Na5)		1/1	1/1		1/1	1/1	4
(Na6)	1/1		1/1		1/1		3
(Na7)	1/1			1/1	1/1	1/1	4
(Na8)		1/1		1/1		1/1	3
C.N.	6	6	6	6	5 (+1)	5 (+1)	

[a] "Long" Na O distances [Å] given in parentheses.

Table 8a. Motifs of mutual adjunction in $Na_{10}[Co_4H_9]$ (proposed model).

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	(O7)	(O8)	(O9)	C.N.
(Co1)					1/1	1/1	1/1			3
(Co2)	1/1							1/1	1/1	3
(Co3)		1/1	1/1	1/1						3
(Co4)					1/1	1/1	1/1			3
(Na1)	1/1	1/1	1/1	1/1						4
(Na2)					1/1	1/1	1/1	1/1		4
(Na3)	1/1	1/1	1/1						1/1	4
(Na4)				1/1	1/1	1/1	1/1			4
(Na5)	1/1	1/1						1/1	1/1	4
(Na6)			1/1	1/1	1/1	1/1				4
(Na7)	1/1						1/1	1/1	1/1	4
(Na8)		1/1	1/1	1/1	1/1					4
(Na9)						1/1	1/1	1/1	1/1	4
(Na10)	1/1	1/1	1/1	1/1						4
C.N.	6	6	6	6	6	6	6	⑤	⑤	

Table 8b. Motifs of mutual adjunction in $Na_{10}[Co_4O_9]$ (real structure).

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	(O7)	(O8)	(O9)	C.N.
(Co1)					1/1	1/1			1/1	3
(Co2)							1/1	1/1	1/1	3
(Co3)			1/1	1/1			1/1			3
(Co4)	1/1	1/1	1/1							3
(Na1)	1/1			1/1		1/1	1/1			4
(Na2)	1/1	1/1					1/1		1/1	4
(Na3)		1/1			2/2			1/1		4
(Na4)		1/1		2/2		1/1				4
(Na5)		1/1	1/1 (2.67 Å)		1/1			1/1	1/1	4+1
(Na6)			1/1		1/1		1/1	1/1		4
(Na7)	1/1		1/1			1/1			1/1	4
(Na8)		1/1			1/1	1/1	1/1			4
(Na9)	2/2			1/1					1/1	4
(Na10)			1/1			1/1		2/2		4
C.N.	6	6	5+1	5	6	6	6	6	6	

Table 9. Motifs of mutual adjunction in $Na_{14}[Al_4O_{13}]$; distances [Å] are also given in addition to the Mo.A.

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	(O7)	C.N.
(Al1)	1/1 1.78	1/1 1.74			1/2 1.74		1/2 1.78	4
(Al2)	1/1 1.80		1/1 1.76	1/1 1.76		1/1 1.76		4
(Na1)		1/1 (1/1) 2.27 (2.66)			1/1 (1/1) 2.28 (2.64)		1/2 2.43	3+2
(Na2)	1/1 2.44	(1/1) (2.58)	1/1 2.27	(1/1) (2.66)	1/1 2.30			3+2
(Na3)			1/1 2.43	1/1 2.23		1/1 1/1 2.23 2.36		4
(Na4)	1/1 2.37	1/1 2.44			1/1 2.44		(1/2) (2.55)	3+1
(Na5)	(1/1) (2.80)		1/1 2.38	1/1 2.47		1/1 2.26		3+1
(Na6)			1/1 2.32	(1/1) (2.52)		1/1 (1/1) 2.37 (2.54)		2+2
(Na7)	1/1 2.44	1/1 2.25	(1/1) (2.75)	1/1 2.30	(1/1) (2.52)			3+2
C.N.	5+1	4+2	5+1	4+2	4+2	5+1	4+2	

oxides, as sometimes happens, such as $Na_{10}Co_4O_9$, the simplest possible Mo.A. (Table 8a) shows that either not all O^{2-} or not all Na^+ are coordinationally equivalent if Co^{2+} is assumed to have C.N. 3 towards O^{2-} as in $Na_4[CoO_3]$. Structural elucidation[52] revealed that a compromise is reached between the two limiting cases. We have just obtained another oligooxometalate, *viz.* the first tetraaluminate $Na_{14}[Al_4O_{13}]$[53] (cf. Table 9). In this connection, mention should also be made of the "island oxometalates" $Na_5[FeO_4]$[54], $Na_5[NiO_4]$[55], and the recently prepared intermediate member $Na_5[CoO_4]$[56] (cf. Table 10).

Table 10. Motifs of mutual adjunction in $Na_5[CoO_4]$.

	(O1)	(O2)	(O3)	(O4)	C.N.
(Na1)	2/2	1/1		1/1	4
(Na2)	1/1		2/2	1/1	4
(Na3)	1/1	2/2		1/1	4
(Na4)	1/1		2/2	1/1	4
(Na5)		2/2	1/1	1/1	4
Co	1/1	1/1	1/1	1/1	4
C.N.	6	6	6	6	

9. Motifs of Mutual Linkage (Knotting)

α-Ga_2O_3 is isotypic with corundum. In discussing the structure of possible other forms of gallium oxide it appears justifiable to query whether Ga^{3+} has C.N. 4 towards O^{2-} in Ga_2O_3, as is present in oxogallates such as $KGaO_2$[57]. A possible Mo.A. would be, *e.g.* $GaO_{3/3}O_{1/2}$. However, this would imply that part of O^{2-} serve as a bridge between two Ga^{3+} which is highly unlikely in view of the structure of α-Ga_2O_3. While such oxides are indeed known, *e.g.* $Na_8Ga_2O_7$[58], the bridging position of O^{2-} in the Cr_2O_7-analogous group Ga_2O_7 is enforced by the numerous Na^+ partners of this "cation-rich oxide"[59]. Accomplishment of C.N. 4 in Ga_2O_3 is possible only when Ga^{3+} partly retains C.N. 6 of the corundum type, or a least adopts C.N. 5.

Let us consider the argumentation for the simplest possible such case with only two kinds of Ga particles of different coordination in the ratio (Ga1):(Ga2) = 1:1 (in the case of the ratio 1:3 our discussion would lead to the spinel type). Corresponding to the Mo.A.

$$(Ga1)(O1)_{(4-x)/4}(O2)_{x/3}, \quad (Ga2)\ldots$$

there are five distinct possibilities ($x = 0, 1, \ldots 4$) for (Ga1), of which we rule out that with $x = 0$: given a tetrahedral environment of (Ga1) then $(Ga1)(O1)_{4/4}$ leads either to layers consisting only of (Ga1) and (O1) strictly isolated from the (Ga2) part of the structure, or to the ZnS type for this part of the structure which would then no longer have room for (Ga2) and its O fraction. Conversely, for $x = 0$ the formulation $(Ga2)(O2)_{6/3}$ would apply to (Ga2), again leading to "strictly isolated" layers as in CdI_2 or to three-dimensional linkage *e.g.* of rutile type leaving no room for (Ga1) and its O fraction.

Among the other possibilities, which can be analogously assessed on the basis of the Mo.A., that with $x = 3$ is realized in β-Ga_2O_3:

$$(Ga1)(O1)_{1/4}(O2)_{3/3}, \ (Ga2)(O1)_{3/4}(O3)_{3/3}$$

$(Ga2)(O1)_{3/4}(O3)_{2/2}$ would lead to C.N. 5 for (Ga2); however, we have definitively excluded the possibility of such bridges as in $Na_8Ga_2O_7$.

These Mo.A. imply that (O1) necessarily links (Ga1) and (Ga2) together. By analogy, (O2) and (O3) may also be expected to link both kinds of Ga entities. This expectation finds expression in the *motif of knotting* (Mo.K.)

$$(Ga1)(O1)_{1/4}(O2)_{2/3}(O3)_{1/3}, \ (Ga2)(O1)_{3/4}(O2)_{1/3}(O3)_{2/3}$$

or in greater detail

$$(Ga1)(O1)_{1/(1+3)}(O2)_{2/(2+1)}(O3)_{1/(1+2)},$$
$$(Ga2)(O1)_{3/(1+3)}(O2)_{1/(2+1)}(O3)_{2/(1+2)}$$

where, *e.g.* $(Ga1)(O1)_{1/(1+3)}\ldots$ means that (Ga1) has one (O1) as neighbor which in turn links one (Ga1) and three (Ga2) together. The Mo.A. is seen in Table 11.

It is the Mo.K. which can predict in specific cases whether a given Mo.A. is geometrically realistic.

Table 11. Motifs of mutual adjunction in β-Ga_2O_3.

	(O1)	(O2)	(O3)	C.N.
(Ga1)	1/1	2/2	1/1	4
(Ga2)	3/3	1/1	2/3	6
C.N.	4	3	3	

At the present state of knowledge we cannot say why the formulation

$(Ga1)(O1)_{2/(2+2)}(O2)_{1/(1+2)}(O3)_{1/(1+2)}$,
$(Ga2)(O1)_{2/(2+2)}(O2)_{2/(1+2)}(O3)_{2/(1+2)}$

has not yet been found or cannot be realized.

10. A Critical Incidental Remark

Sections 6 to 9 introduced four concepts, of which the Mo.C. does not correspond entirely to the conventional coordination number. In practice, any statement about the number of "bonding partners", *e.g.* for SiO_5, is very difficult to divorce from the question of their geometric arrangement. In view of the difficult "real" aspects of a more general discussion of crystal structures, even of simple compounds, we have not mentioned this before. However, the very mention of the existence of an unknown form of SiO_2 (according to $SiO_{2/2}O_{3/3}$) underlines the close relationship between the Mo.C. and the Mo.A. The Mo.K. permits consideration of the fundamental likelihood of the structures found if one is not merely content to accept them at face value. The price to be paid for the relative ease with which the Mo.F. can frequently (but by no means always) be given is that they often fail to provide definite indication of specific structural characteristics.

It might therefore be suspected that these concepts are essentially formal in nature. That is not the case, as we shall see on considering an appropriate example.

Before proceding further, however, the reader is reminded that the concept of atomic, ionic, or "covalent" radius is over 50 years old. Since the early days of structure determinations, however, it has been known that an additivity of radii or volumes[60] does not strictly apply, even for alkali metal halides. This is underscored by the structure of $ZrCl_4$[61] (cf. Table 12). Just how differently chemically equivalent entities may act within the same compound is demonstrated by the example of UF_3[62] (Fig. 11 and 12).

Our example is taken from the chemistry of thorium and embraces the fluorides $KNaThF_6$[63], $(NH_4)_3ThF_7$[64], $(NH_4)_4ThF_8$[65], K_5ThF_9[66], and $K_7Th_6F_{31}$[67] (which actually belongs at the beginning of the series of increasing F:Th ratio). The Mo.A. are given in Tables 13—17.

Table 12. Concerning the structure of $ZrCl_4$ [61].

$ZrCl_4 = Zr(Cl1)_{2/1}(Cl2)_{4/2}$
d(Zr Cl) = 2.42 Å; thus it follows for an octahedron:
d(Cl Cl) = 3.41 Å; hence:
$R(Cl^-) \leq 1.70$ Å (according to *Shannon* [92]: 1.81 Å)

For the shortest distances d_k, it holds that:

d_k[(Cl1) (Cl1)] = 3.30 Å; → R(Cl1) = 1.65 Å
d_k[(Cl1) (Cl2)] = 3.49 Å; → R(Cl2) = 1.84 Å
d_k[(Cl2) (Cl2)] = 3.55 Å; → R(Cl2) = 1.78 Å

Yielding:

a) R(Cl1) < R(Cl2)

For the Zr Cl distances:

d_k[Zr (Cl1)] = 2.50 Å
d_k[Zr (Cl2)] = 2.31 Å

b) R(Cl1) > R(Cl2)

a) contradicts b)

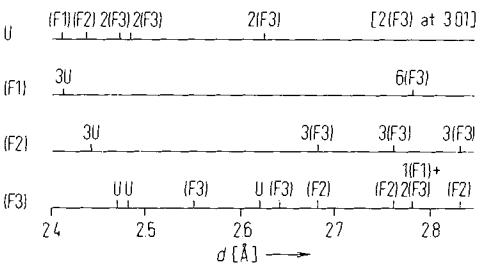


Fig. 11. Interatomic distances in UF_3.

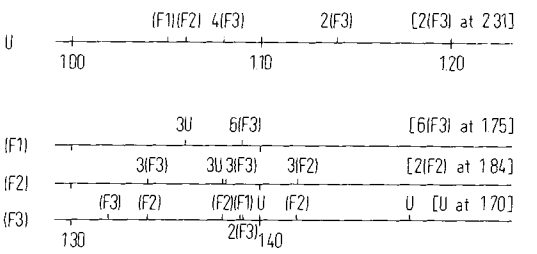


Fig. 12. Reduced distances in UF_3.

$$d(U-F)_{red} = d(U-F) \cdot \frac{R(U^{3+})}{R(U^{3+}) + R(F^-)}$$

$$d(F-U)_{red} = d(F-U) \cdot \frac{R(F^-)}{R(U^{3+}) + R(F^-)}$$

Table 13. Motifs of mutual adjunction in $KNaThF_6 = KNaTh(F1)_3(F2)_3$; distances [Å] are also given in addition to the Mo.A.

	(F1)	(F2)	C.N.
K	3/1 3/1 2.7 2.8	3/1 2.9	9
Na	3/1 2.3	3/1 2.5	6
Th	3/1 2.3	3/1 3/1 2.4 2.4	9
C.N.	4	3 + 1	

Table 14. Motifs of mutual adjunction in $(NH_4)_3ThF_7 = (N1)(N2)_2Th(F1)_1(F2)_1(F3)_1(F4)_2(F5)_2$; distances [Å] are also given in addition to the Mo.A.

	(F1)	(F2)	(F3)	(F4)	(F5)	C.N.
Th	1/1 2.3	1/1 2.3	1/1 2.4	2/1 2.3	2/1 2/1 2.4 2.6	9
(N1)	1/1 3.0	1/1 2.7	1/1 3.2	2/1 2/1 2.9 3.0	2/1 2.9	9
(N2)	1/2 2.7	1/2 3.0	1/2 1/2 2.7 3.2	1/1 1/1 2.8 3.0	1/1 2.8	7
C.N.	4	4	6	5	4	

Table 15. Motifs of mutual adjunction in $(NH_4)_4ThF_8$ = (N1)(N2)(N3)(N4)Th(F1)(F2)(F3)(F4)(F5)(F6)(F7)(F8); distances [Å] are also given in addition to the Mo.A.

	(F1)	(F2)	(F3)	(F4)	(F5)	(F6)	(F7)	(F8)	C.N.
(N1)	1/1 1/1 2.7 2.9	1/1 2.9				1/1 2.7	1/1 3.1	1/1 1/1 2.8 2.9	7
(N2)	1/1 2.7		1/1 (1/1) 2.7 (3.3)	1/1 3.1		1/1 2.7		1/1 2.7	5+1
(N3)		1/1 (1/1) 2.8 (3.3)	(1/1) (3.2)		1/1 1/1 2.7 2.9	1/1 3.1	1/1 2.9	1/1 2.6	6+2
(N4)		1/1 3.0	1/1 2.7	1/1 2.8	1/1 2.7			1/1 2.7	5
Th	1/1 2.4	1/1 2.3	1/1 2.3	1/1 1/1 2.4 2.4	1/1 2.3	1/1 2.4	1/1 1/1 2.4 2.4		9
C.N.	4	4+1	4+1	4	4	4	4	5	

F(4) F(4) = 2.48 Å! F(7) F(7) = 2.54 Å

Table 16. Motifs of mutual adjunction: β-K_5ThF_9 = (K1)(K2)$_2$(K3)$_2$Th(F1)(F2)(F3)(F4)(F5)(F6)$_2$(F7)$_2$; distances [Å] are also given in addition to the Mo.A.

	(F1)	(F2)	(F3)	(F4)	(F5)	(F6)	(F7)	C.N.
(K1)			1/1 2.9		1/1 1/1 2.8 3.0	2/1 2.6	2/1 2.6	7
(K2)	1/2 2.9	1/2 2.8	1/2 2.7	1/2 2.7	1/2 2.6	1/1 2.6	(1/1) (1/1) 3.0 (3.2)	6+1 (+1)
(K3)	1/2 2.7	1/2 2.8	1/2 2.8	1/2 2.8	1/2 2.6	(1/1) (1/1) 3.0 (3.2)	1/2 2.6	6+1 (+1)
Th	1/1 2.3	1/1 2.3	1/1 2.3	1/1 2.4		2/1 2.3	2/1 2.3	8
C.N.	5	5	6	5	6	3 (1+1)	4+1 (+1)	

Table 17. Motifs of mutual adjunction in $K_7Th_6F_{31}$ = (K1)$_6$(K2)$_1$(Th1)$_6$(F1)$_6$(F2)$_6$(F3)$_6$(F4)$_6$(F5)$_6$(F6)$_1$; distances [Å] are also given in addition to the Mo.A.

	(F1)	(F2)	(F3)	(F4)	(F5)	(F6)	C.N.
(K1)	1/1 1/1 2.8 2.8	1/1 1/1 2.6 2.7	1/1 1/1 1/1 2.7 2.7 2.7	(1/1) (1/1) (3.3) (3.3)	(1/1) (3.2)		7 (+3)
(K2)		6/1 2.7		(6/1) (3.4)			6 (+6)
Th	1/1 1/1 2.4 2.4	1/1 2.2	1/1 2.2	1/1 1/1 2.3 2.4	1/1 1/1 2.3 2.3	(1(6) 3.0)	8 (+1)
C.N.	4	4	4	2+3	2+1	0	

In spite of the relatively small quotients F: Th = 6, Th^{4+} undoubtedly has C.N. 9 towards F^- in $KNaThF_6$. The Mo.A. lead to C.N. 4 towards the cations for all F^-. Th^{4+} has the same C.N. of 9 in $(NH_4)_3ThF_7$; however the two NH_4 show distinctly different coordination; such differences also apply to the C.N. of F^- which for $(NH_4)_4ThF_8$ (also with C.N. 8 for Th^{4+}) are again somewhat better balanced. Unexpectedly, the fluorine-richest member K_5ThF_9 exhibits only C.N. 8 for Th^{4+} and "without any compelling necessity" 4+1+1 K^+ are assigned to (F7).

Even more surprising is the C.N. 8 for Th^{4+} also in the fluorine-poorest compound $K_7Th_6F_{31}$ (F: Th = 5.17) and the unexplained failure of (F6) to contribute to the C.N. of Th^{4+} or of K^+ in spite of the "dearth of fluorine"; as in solid solutions of CaF_2 and fluorides MF_3, and in BiF_3[68], it is present as "lone ion".

In view of these inexplicable contradictions for comparable fluorides of very simple composition, it can hardly be expected that theory will soon dispel the darkness of the reasons which determine crystal structure. It might be thought that the structure analyses of these thorium fluorides are not of compatible accuracy. In such cases, calculations of the Madelung part of the lattice energy (MAPLE)[69] permit scrutenization without the need for new experiments. We have calculated the MAPLE values and thence, by subtraction (with NH_4F as N^+F^- since the H positions of $(NH_4)_3ThF_7$ and $(NH_4)_4ThF_8$ are still unknown), *e.g.* according to MAPLE($KNaThF_6$) − MAPLE(KF) − MAPLE(NaF), obtained MAPLE(ThF_4). Now while the crystal structure of ThF_4 itself is still unknown, the agreement between the values of MAPLE(ThF_4) is so good that the available structure determinations should be of comparable quality (cf. Table 18).

Table 18. Madelung part of lattice energy (MAPLE) of ThF_4 [kcal/mol].

	MAPLE (ThF_4)
$KNaThF_6$	2095
$(NH_4)_3ThF_7$	2107
$(NH_4)_4ThF_8$	2109
β-K_5ThF_9	2095
$K_7Th_6F_{31}$	2104
Mean value	2102

11. Motifs of Spatial Arrangement

The varying size of various entities raises questions that have not yet been considered. The example of the series NiO(d(Ni—O) = 1.98 Å), Li_2NiO_2 (1.84 Å), and K_2NiO_2 (1.68 Å)—cf. Section 8.1—shows how large changes in distances (and thus of "radii") can be on changing coordination numbers, and therefore how difficult it is to build up structural arguments on the basis of radii—whatever kind they may be (unless nothing better were available: "A poor estimate is better than none at all").

We shall therefore only apply such arguments "implicitly" in this paper.

These questions, still largely uninvestigated, will first be illustrated by one example and then will undergo the most detailed treatment presently possible in the case of another example.

11.1. Cs_2PbO_3

Whether strictly cubic[70], which appears questionable, or not[71], $BaPbO_3$ undoubtedly belongs to the perovskite family[72]. The parent type (ReO_3 type, cf. Fig. 13) is characterized by the motif $^3_\infty[PbO_{6/3}]$ and exhibits *one* large vacancy per Pb^{4+} which can be occupied by correspondingly large cations, Ba^{2+} in this case. In the case of Cs_2PbO_3[73], the presence of *two* such large cations can lead either to a layer structure $^2_\infty[PbO_{6/3}]$, which we know to be most unlikely and hardly possible geometrically, or to a drastic change of the C.N. of Pb^{4+}. The latter occurs. Formation of $PdCl_2$-type chains is found according to $^1_\infty[PbO_{4/2}O_{1/1}]$, where an additional O per Pb *alternately* (electrostatically "favorably") enlarges their environment to a tetragonal pyramid (cf. Fig. 14a).

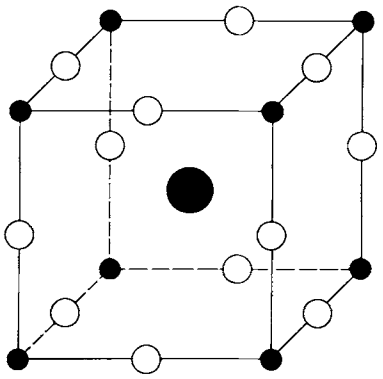


Fig. 13. ReO_3 type (•:Re^{6+}, ○:O^{2-}) with the "large" vacancy (●) occupied in representatives of the perovskite type.

This principle not only solves these structural difficulties but also extends to thiotitanates(IV) such as Cs_2TiS_3[74] (Fig. 14b).

11.2. Ba_2HgS_3

It has long been known that HgS dissolves in solutions of alkali metal sulfides and, *e.g.* after precipitation as metacinnabarite can be transformed by repeated "cooking" into cinnabar as the more stable form. In contrast to thiozincates like Ba_2ZnS_3[75] or thiocadmates like $BaCdS_2$[76], thiomercurates long remained uninvestigated. After earlier attempts[77], we again turned our attention to the preparation and study of such materials and obtained first $A_6[HgX_4]$ with A = K, Rb, Cs and X = S, Se[78] and more recently barium thiomercurates, *viz.* Ba_2HgS_3[79] and $BaHgS_2$[80], and elucidated their structure.

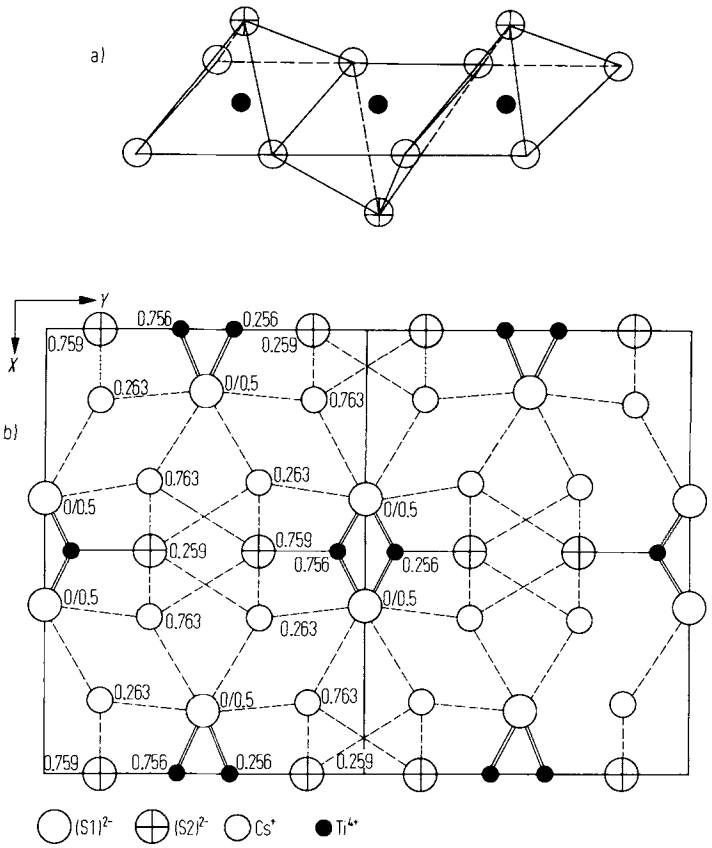


Fig. 14. Crystal structure of Cs_2TiS_3 (Cs_2PbO_3 type). a) Motif of the chain. b) Projection onto [001], heights in z/c.

Owing the possibility of comparison with Ba_2ZnS_3 we select Ba_2HgS_3 as example here.

Preliminary note: All the concepts introduced so far will be employed in the following disussion. An attempt will be made to show how the motifs of structural arrangement "necessarily" result on applying assumptions soundly based on experience. Opportunity will be taken to show where decisive switching or branching points are to be found.

1st Assumption: The structural situation is represented by the notation (Ba1)(Ba2)Hg(Si)(S2)(S3), simpler [*e.g.* $Ba_2Hg(S1)(S2)(S3)$] or more complicated forms [*e.g.* $(Ba1)_2(Ba2)_2(Hg1)(Hg2)(S1)_2(S2)_2(S3)(S4)$] are excluded.

2nd Assumption: The C.N. of Hg^{2+} towards S^{2-} is 4 and the Mo.C. is a tetrahedron. Reasoning: HgS is known to exist in two modifications, in which C.N. of Hg is 2 and 4, respectively. Since $BaHgS_3$ is a comparatively sulfur-rich compound this assumption appears plausible.

3rd Assumption: All S^{2-} have C.N. 6 towards the cations. Reasoning: In accord with $Ba_2S_3(Hg)$ a BaS derivative is almost present; BaS has an NaCl structure.

4th Assumption: The Mo.C. of S^{2-} is a (distorted) octahedron, not a trigonal prism. This rules out (cf. Table 19) nu-

merous other possibilities. Reasoning: It is "less common" for an anion to be surrounded by six cations in the form of a trigonal prism.

Table 19. Possible combinations of the coordination polyhedra octahedron (O) and trigonal prism (TP) around sulfur in Ba_2HgS_3.

(S1)	(S2)	(S3)
O	O	O
TP	O	O
O	TP	O
O	O	TP
TP	TP	O
TP	O	TP
O	TP	TP
TP	TP	TP

5th Assumption: C.N. (Ba1) should be equal to C.N. (Ba2). Simplicity is the sole justification for this assumption. It is also satisfied for $BaHgS_2$.

1st Conclusion: As shown by Table 20 there are a total of 90 possibilities for the corresponding Mo.A.

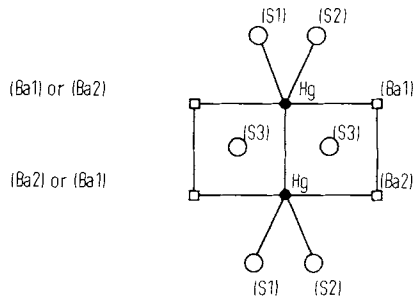


Fig. 15. Double group $(Ba1)_2(Ba2)_2Hg_2(S1)_2(S2)_2(S3)_2$.

4th Conclusion: Owing to $Hg(S3)_{2/2}$ and $(S3)Hg_{2/2}$, only a double group (Fig. 15) or a one-dimensional chain of octahedra (Fig. 16) can be present.

5th Conclusion: The double group in Figure 15 already has the composition Ba_2HgS_3 and no further Ba is available for constructing the undoubtedly three-dimensional network. It therefore offers no possibility of a reasonable arrangement (cf. Fig. 17).

Table 20. Motifs of mutual adjunction in Ba_2HgS_3.

	(S1)			(S2)						(S3)				
	a	b	c	a	b	c	d	e	f	a	b	c	d	e
(Ba1) [a]	5/5	4/4	3/3	5/5	4/4	3/3	2/2	1/1	0/0	4/4	3/3	2/2	1/1	0/0
(Ba2) [a]	0/0	1/1	2/2	0/0	1/1	2/2	3/3	4/4	5/5	0/0	1/1	2/2	3/3	4/4
Hg	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	2/2	2/2	2/2	2/2	2/2
C.N.	6	6	6	6	6	6	6	6	6	6	6	6	6	6

[a] The combinations (Ba1) 0/0, 1/1, 2/2 and (Ba2) 5/5, 4/4, 3/3 only mean renumbering of Ba.

2nd Conclusion: Of the motif of coordination of (Ba1) is $(Ba1)(S1)_m(S2)_n(S3)_p$, then there follows $(Ba2)(S1)_{5-m}(S2)_{5-n}(S3)_{4-p}$.

6th Assumption: m, n, p $\neq 0$. Reasoning: It is plausible that for a sulfide with the $\sum$ cation: $\sum$ anion ratio of 1, each S^{2-} will have at least one of each kind of cation as neighbor. The example of the thorium fluorides (Section 10) shows how uncertain this conclusion is.

3rd Conclusion: Accordingly, C.N. (Ba1) = C.N. (Ba2) = 7.

There remain only the possibilities given in Table 21. Of these, (a) is identical with (e) [simultaneous renumbering of (Ba1) and (Ba2) and of (S1) and (S2)].

Table 21. Remaining motifs of mutual adjunction for Ba in Ba_2HgS_3; C.N. (Ba1) = C.N.(Ba2) = 7.

	(Ba1):			(Ba2):		
	(S1)	(S2)	(S3)	(S1)	(S2)	(S3)
(a)	4/4	2/2	1/1	1/1	3/3	3/3
(b)	4/4	1/1	2/2	1/1	4/4	2/2
(c)	3/3	3/3	1/1	2/2	2/2	3/3
(d)	3/3	2/2	2/2	2/2	3/3	3/3
(e)	3/3	1/1	3/3	2/2	4/4	1/1

7th Assumption: In the approximately octahedral coordination polyhedron around (S3) the two Hg occupy *cis* positions.

Reasoning: Both modifications of HgS show HgSHg valence angles of about 100°. In contrast to the S—Ba bond, the Hg—S bond has more covalent character.

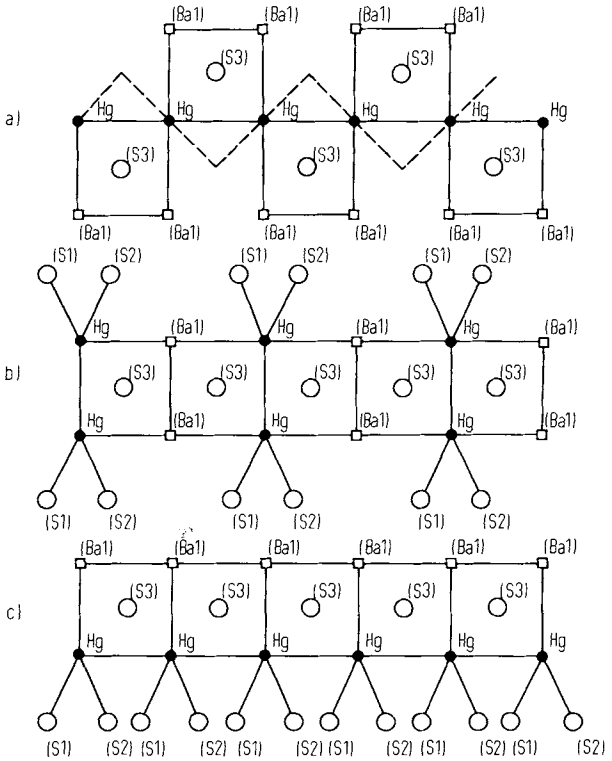


Fig. 16. Possible chains of octahedra as structural unit of Ba_2HgS_3.

Observation: As immediately seen with a model, a chain of the kind shown in Figure 16a or 16b cannot lead to a three-

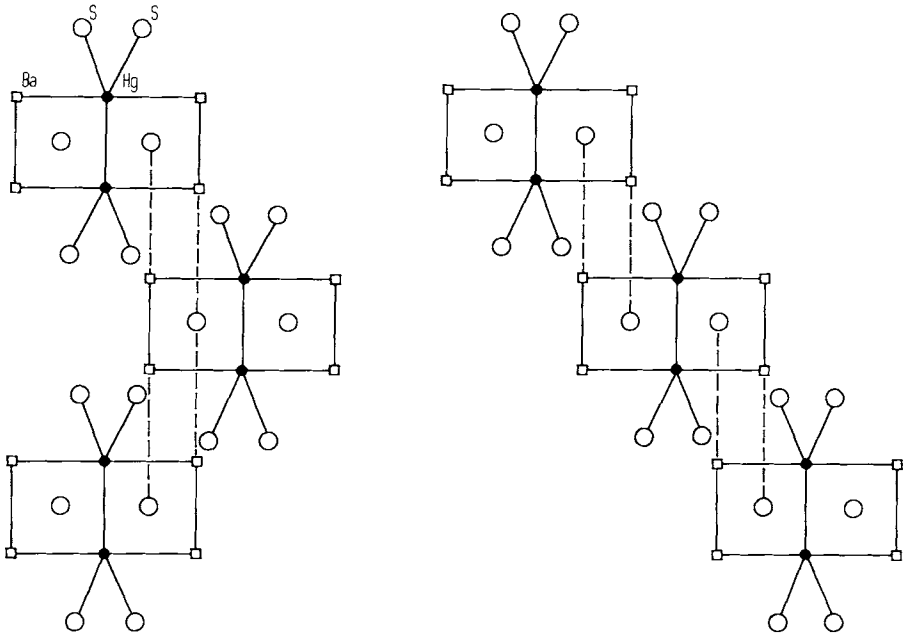


Fig. 17. Attempts to stack the unit $(Ba1)_2(Ba2)_2Hg(S1)_2(S2)_2(S3)_2$ (topological relationships).

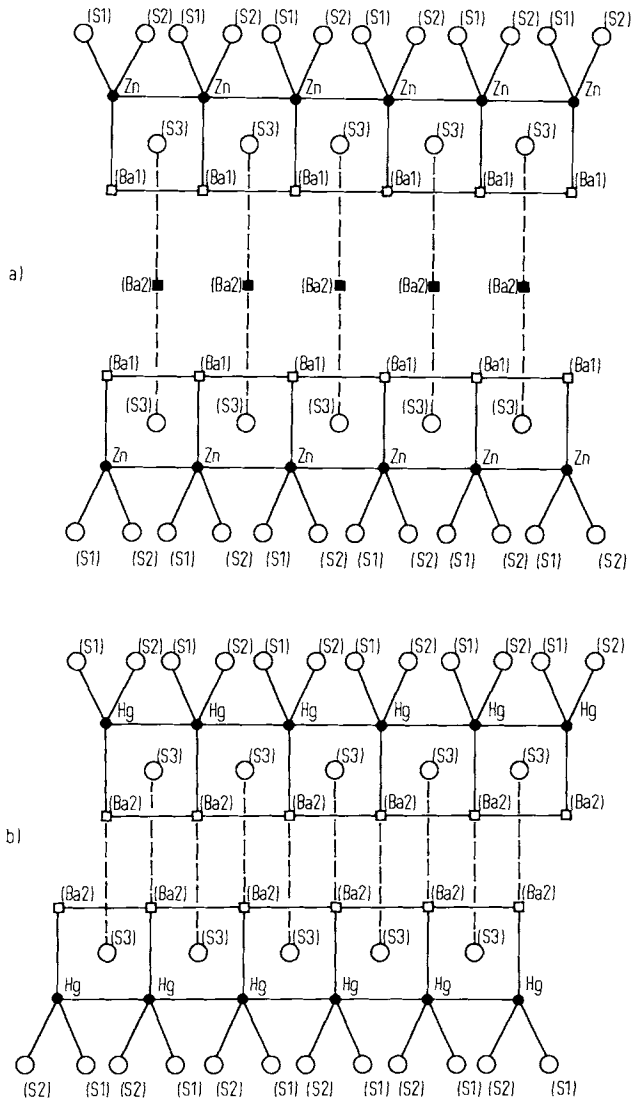


Fig. 18. a) Double chain in Ba_2ZnS_3. b) Double chain in Ba_2HgS_3.

dimensional network since (S1) and (S2) of such chains will be subject to hindrance.

6th Conclusion: There accordingly remain only the two possibilities corresponding to Figure 18:

a) either the Ba entities expanding the coordination polyhedron around (S3) to a distorted octahedron are *equivalent*—and thus necessarily distinct from the Ba present in the chain which contribute to the base of the octahedron (this case is encountered in Ba_2ZnS_3, cf. Fig. 18a)

b) or they are *nonequivalent*—then one will be necessarily identical with that present in the chain and stacking of the chain as shown in Figure 18b must occur (this is the case with Ba_2HgS_3).

Incidental comment: All the assumptions listed, which are plausible if not necessarily valid, lead to a *structural predisposition.* That one alternative is encountered in Ba_2ZnS_3 and the other in Ba_2HgS_3 depends, at our present state of knowledge, on the ratio of ionic radii [in this case $R(M_a^{2+})/R(M_b^{2+})$ where M_a = Ba and M_b = Zn, Hg] (cf. Table 22 which contains further examples).

Table 22. Ionic radii (in Å according to [92]) and ratios of ionic radii of compounds crystallizing in the Ba_2HgS_3 and Ba_2ZnS_3 types.

A_2BX_3	A	B	X	A/B	A/X	B/X	Ref.
Ba_2HgS_3	1.38	0.96	1.84	1.43	0.75	0.52	[79]
Ba_2CdS_3	1.38	0.78	1.76	1.76	0.75	0.52	[76]
K_2AgI_3	1.46	0.79	2.20	1.84	0.65	0.35	[89]
$(NH_4)_2AgI_3$	1.46	0.76	2.20	1.84	0.65	0.35	[89]
Rb_2AgI_3	1.56	0.79	2.20	1.97	0.65	0.35	[89]
Ba_2ZnS_3	1.38	0.78	1.84	2.30	0.75	0.32	[75]
K_2CuCl_3	1.46	0.57	1.81	2.56	0.80	0.30	[90]
$(NH_4)_2CuBr_3$	1.46	0.57	1.96	2.56	0.74	0.29	[91]
Cs_2AgCl_3	1.67	0.79	1.81	2.10	0.92	0.43	[90]
Cs_2AgI_3	1.67	0.79	2.20	2.10	0.75	0.36	[90]

7th Conclusion: The spatial arrangement derived so far is shown as a projection in Figure 19a and in perspective in Figure 19b. It necessarily follows: If the Ba entity located in

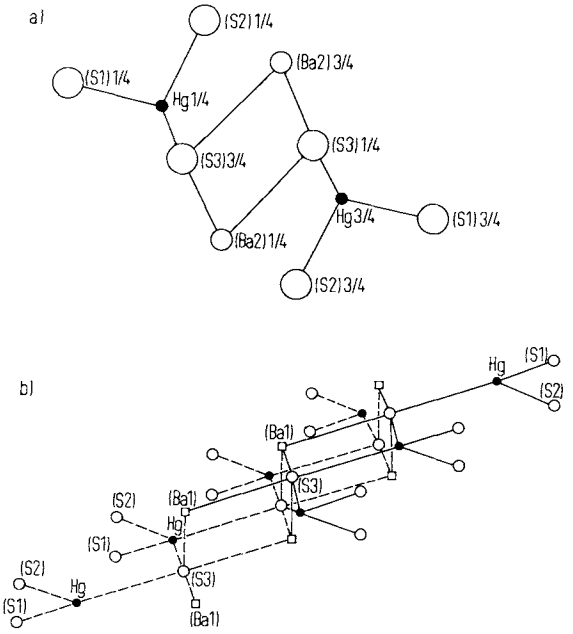


Fig. 19. a) Projection of double chain of Ba_2HgS_3 along [010]. b) $(Ba)_1Hg(S1)_1(S2)_1(S3)_1$, shown in perspective.

the "chain" is designated as (Ba2) then (Ba1) must complete the "octahedron" around (S3) which therefore contains one (S3) and two (S1) from the double chain as ligands. Since the double chain with the additional two (Ba1) expanding the octahedron by (S3) already has the composition $(Ba1)_2(Ba2)_2Hg_2(S1)_1(S2)_2(S3)_2$, completion of the coordination polyhedron around (Ba1) can only occur by joining of such supplemented double chains. Since (S3) does not contribute to completion of the coordination polyhedron around Ba, only (S1) and (S2) can serve this purpose, necessarily to equal extents. Thus the crystal structure of Ba_2HgS_3 shown as projection in Figure 20 is logically established. It corresponds to the alternative (a) in Table 21—the structure of Ba_2ZnS_3 corresponds to alternative (d).

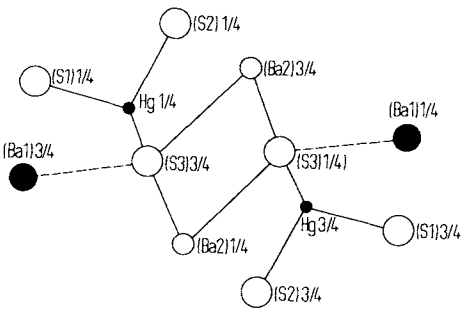


Fig. 20. Ba_2HgS_3: Enlargement of the coordination polyhedron around (S3) by (Ba1), heights in y/b.

Supplementing the coordination polyhedron by (Ba1) can then only take place as shown in Figure 21, thus establishing the structure of Ba_2HgS_3.

Summary: On the basis of seven plausible but not absolutely necessarily valid assumptions, the variety of possible motifs of coordination, functionality, adjuncture, and knotting can be restricted such that a structural predisposition is established, branching into two alternatives: this leads on the

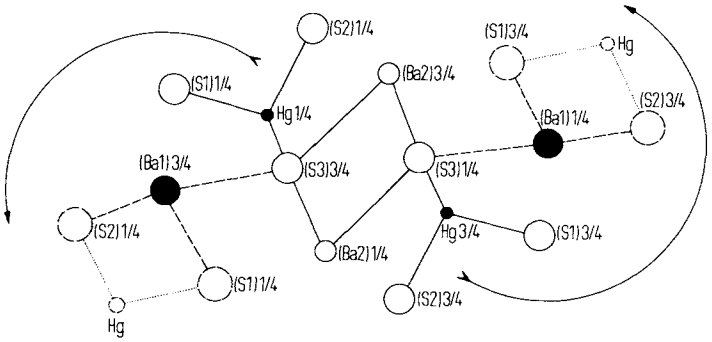


Fig. 21. Ba_2HgS_3: Enlargement of the coordination polyhedron by (Ba1), heights g/b.

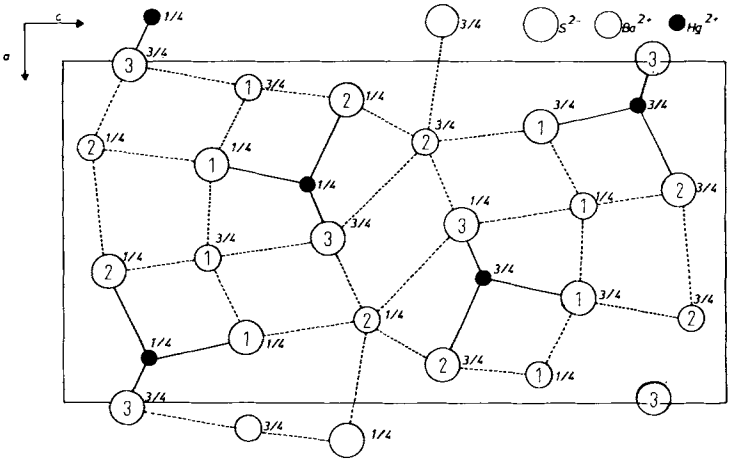


Fig. 22. Crystal structure of Ba_2HgS_3, projection along [010].

one hand, as already shown in detail, to the motif of structural arrangement of the Ba_2HgS_3 type, and on the other hand, not shown here, with similar logic to that of the Ba_2ZnS_3 type. In both cases the principal axis of the "capped trigonal prisms" around (Ba1) and (Ba2) are mutually perpendicular. The situation is different in $SrZnO_2$[81], $BaCdO_2$[82], $BaCdS_2$[76], and $BaHgS_2$[80], where the axes are all parallel.

12. Closing Comments

1) The conclusions presented in Section 11.2 for Ba_2HgS_3 still lead to an almost infinite range of variants having the same fundamental topology. The gap separating this situation and the real crystal structure with given space group and occupied sites appears unbridgeable. Even for the simplest composition it is incredibly difficult to enumerate the possibilities open—as demonstrated by *Hahn*[83] for tetrahedral structures.
2) The avoidance of any direct reference to radii is intentional. It does not mean (cf. [73]) that the author underestimates their influence.
3) The overall result remains unsatisfactory. The general situation is even less clear than these attempts at a systematic discussion of $Ba_2HgS_3/(Ba_2ZnS_3)$ would indicate. In particular, crystal structures such as that of C_6H_6, CCl_4, *etc.* reveal our almost breathtaking inability to imbue structural knowledge with understanding. The example of $Cs_3Ta_5O_{14}$[84], an oxotantalate(v), which we discovered

and elucidated structurally during a search for $CsTaO_3$, which is still unknown in contrast to $LiTaO_3$[85], $NaTaO_3$[86], $KTaO_3$[87], and $RbTaO_3$[88] may serve to illustrate the (still almost hopeless) position of the preparative solid-state chemist.

When will the new *Berzelius* arrive?

Table 23. Motifs of mutual adjunction in $Cs_3Ta_5O_{14}$ = (Cs1)(Cs2)(Cs3)(Ta1)(Ta2)(Ta3)(Ta4)$_2$(O1)...(O6)(O7)$_2$...(O10)$_2$.

	(O1)	(O2)	(O3)	(O4)	(O5)	(O6)	(O7)	(O8)	(O9)	(O10)	C.N.
(Cs1)	—	—	2/2 (1/1)	1/1	—	2/2	4/2	4/2	(2/1)	(2/1)	13 (+5)
(Cs2)	2/2	(2/2)	—	—	1/1	—	—	—	2/1	2/1 (2/1)	7 (+4)
(Cs3)	—	—	—	(2/2)	1/1 (1/1)	1/1	2/1	2/1	2/1	2/1	10 (+3)
(Ta1)	2/2	1/1	—	1/1	—	—	—	—	2/1	—	6
(Ta2)	—	2/2	—	1/1	—	—	—	—	—	2/1	5
(Ta3)	—	—	—	—	—	2/2	2/1	2/1	—	—	6
(Ta4)	—	—	1/2	—	1/2	—	1/1	1/1	1/1	1/1	6
C.N.	4	3 (+2)	4 (+1)	3 (+2)	4o(+1)	5	5	5	4 (+1)	4 (+2)	

Thanks are due to my industrious co-workers, especially Dipl.-Chem. M. Serafin, who patiently evaluated the various kinds of motifs considered in this article for numerous examples, including many unmentioned ones. Support of projects related to the concepts presented above by the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

Received: December 4, 1979 [A 309]
German version: Angew. Chem. *92*, 106 (1980)

[1] *R. Hoppe, K.-P. Martens,* to be published; cf. Diplomarbeit *K.-P. Martens,* Universität Giessen 1973.
[2] *W. Ramsay, G. Rudolf* "Die Edelgase" in *W. Ostwald, C. Drucker:* Handbuch der allgemeinen Chemie. Akademische Verlagsgesellschaft Leipzig 1918.
[3] *R. Hoppe,* unpublished (1948/49).
[4] *R. Hoppe, H. Mattauch, K. M. Rödder, W. Dähne,* Z. Anorg. Allg. Chem. *324*, 214 (1963).
[5] *M. E. Hellman,* Sci. Am. *241*, No. 2, 130 (1979).
[6] The present-day Serbian word for tin is Kalaj.
[7] Cf. *G. Bugge:* Das Buch der großen Chemiker, Vol. 1. Verlag Chemie, Weinheim 1955, p. 447.
[8] *J. J. Berzelius,* Thomsons Ann. Philos. *1* (1813).
[9] *A. Kekulé,* Bull. Soc. Chim. Fr. [2] *3*, 98 (1865).
[10] *J. H. van't Hoff,* Arch. Neerl. Sci. Exactes Nat. *9*, 445 (1874); *J. A. Le Bel,* Bull. Soc. Chim. Fr. [2] *22*, 337 (1874).
[11] *A. Werner,* Z. Anorg. Chem. *3*, 267 (1893).
[12] Cf. *M. Hansen:* Constitution of Binary Alloys, 2nd Ed. McGraw-Hill, New York 1958, p. 686.
[13] *H. Hibst, R. Gruehn,* Z. Anorg. Allg. Chem. *442*, 49 (1978).
[14] *R. Gruehn,* Nat. Bur. Stand. (U. S.) Spec. Publ. 364, Solid State Chem. Proc. 5th Mater. Res. Symp. 1972.
[15] *J. Leciejewicz, I. Padlo,* Naturwissenschaften *49*, 373 (1962); cf. also *R. Hoppe, H. D. Stöver,* Z. Anorg. Allg. Chem. *437*, 123 (1977).
[16] *R. Hoppe, H. Sommer,* to be published; cf. Dissertation *H. Sommer,* Universität Giessen 1976.
[17] *K. Wahl, W. Klemm, G. Wehrmeyer,* Z. Anorg. Allg. Chem. *285*, 322 (1956).
[18] *M. Jansen, R. Hoppe,* Z. Anorg. Allg. Chem. *408*, 97 (1974).
[19] Cf. *e.g. G. Heurung, R. Gruehn,* unpublished; cf. Dissertation *G. Heurung,* Universität Giessen 1980.
[20] *Basilius Valentinus:* Der Triumphwagen des Antimonii. Leipzig 1604.
[21] *M. Jansen,* Acta Crystallogr. *B 35*, 539 (1979).
[22] *M. Jansen,* Z. Anorg. Allg. Chem. *441*, 5 (1978).
[23] Handbook of Chemistry and Physics, 55th Ed. The Chemical Rubber Co., Cleveland, Ohio 1974.
[24] *R. Hoppe, H. M. Seyfert,* Z. Naturforsch. *B 28*, 507 (1973).
[25] *D. Wiench, M. Jansen,* Z. Anorg. Allg. Chem., in press.
[26] *S. Djurle,* Acta Chem. Scand. *12*, 1415 (1958).
[27] *H. G. von Schnering* in *A. L. Rheingold:* Homoatomic Rings. Chains and Macromolecules of Main Group Elements. Elsevier, New York 1976.
[28] *M. Schmidt, E. Wilhelm,* Angew. Chem. *78*, 1020 (1966); Angew. Chem. Int. Ed. Engl. *5*, 964 (1966).
[29] *R. Hoppe,* Lecture, 1. Nachkriegstagung Dtsch. Ges. Metallkunde, Clausthal-Zellerfeld 1947.
[30] *J. A. Oberteuffer, J. A. Ibers,* Acta Crystallogr. *B 26*, 1499 (1970); *J. S. Kasper, B. W. Roberts,* Phys. Rev. *101*, 537 (1956).
[31] *P. Niggli:* Grundlagen der Stereochemie. Birkhäuser, Basel 1945, pp. 122ff.
[32] *W. H. Baur, A. A. Kahn,* Acta Crystallogr. *B 27*, 2133 (1971).
[33] *F. Liebau, K. F. Hesse,* Z. Kristallogr. *133*, 213 (1971).
[34] *M. Jansen,* J. Solid State Chem. *17*, 1 (1976).
[35] *R. Hoppe, W. Dähne,* Naturwissenschaften *49*, 254 (1962).
[36] *K. A. Wilhelmi,* Ark. Kemi *26*, 149 (1967).
[37] *W. S. McDonald, D. W. J. Cruickshank,* Acta Crystallogr. *22*, 37 (1967).
[38] *F. C. Hawthorne, J. Ito,* Can. Mineral. *15*, 321 (1977); *W. Lindemann,* Neues Jahrb. Mineral. Monatsh. *10*, 226 (1961).
[39] Strukturbericht, Vol. 2, p. 130 (Leipzig 1937).
[40] *H.-P. Gross, E. Tilmanns,* Cryst. Struct. Commun. *3*, 603 (1974).
[41] *H. Bade, W. Bronger, W. Klemm,* Bull. Soc. Chim. Fr. *1965*, 1124.
[42] *H. Rieck, R. Hoppe,* Z. Anorg. Allg. Chem. *392*, 193 (1972).
[43] *H. Rieck, R. Hoppe,* Z. Anorg. Allg. Chem. *408*, 151 (1974).
[44] *G. Brachtel, R. Hoppe,* Naturwissenschaften *63*, 339 (1976).
[45] *H. Rieck, R. Hoppe,* Z. Anorg. Allg. Chem. *400*, 311 (1973).
[46] *S. Siegel, E. Gebert,* J. Am. Chem. Soc. *85*, 240 (1963).
[47] *R. Hoppe, H. J. Röhrborn,* Z. Anorg. Allg. Chem. *329*, 110 (1964).
[48] *R. Hoppe, H. Rieck,* unpublished; cf. Dissertation *H. Rieck,* Universität Giessen 1974.
[49] *H. Zentgraf, R. Hoppe,* Z. Anorg. Allg. Chem., in press.
[50] *H. Rieck, R. Hoppe,* Z. Anorg. Allg. Chem. *437*, 95 (1977).
[51] *W. Burow, R. Hoppe,* Angew. Chem. *91*, 577 (1979); Angew. Chem. Int. Ed. Engl. *18*, 542 (1979).
[52] *W. Burow, R. Hoppe,* Angew. Chem. *91*, 71 (1979); Angew. Chem. Int. Ed. Engl. *18*, 61 (1979).
[53] *R. Hoppe, F. Griesfeller,* unpublished; cf. Dissertation *F. Griesfeller,* Universität Giessen 1980.
[54] *G. Brachtel, R. Hoppe,* Z. Anorg. Allg. Chem. *446*, 77 (1978).
[55] *H. Zentgraf, R. Hoppe,* Naturwissenschaften *65*, 154 (1978).
[56] *W. Burow, R. Hoppe,* to be published.
[57] *E. Vielhaber, R. Hoppe,* Z. Anorg. Allg. Chem. *369*, 14 (1969).
[58] *D. Fink, R. Hoppe,* Z. Anorg. Allg. Chem. *422*, 1 (1976).
[59] *R. Hoppe,* The Alkali Metals, Spec. Publ. Chem. Soc. No. 22, 452 (1967).
[60] *W. Biltz:* Raumchemie der festen Stoffe. L. Voss, Leipzig 1934.
[61] *B. Krebs,* Z. Anorg. Allg. Chem. *378*, 263 (1970).
[62] *J. Laveissiere,* Bull. Soc. Fr. Mineral. Cristallogr. *90*, 304 (1974).
[63] *G. Brunton,* Acta Crystallogr. *B 26*, 1185 (1970).
[64] *R. A. Penneman, R. R. Ryan, I. K. Kressin,* Acta Crystallogr. *B 27*, 2279 (1971).
[65] *R. R. Ryan, R. A. Penneman, A. Rosenzweig,* Acta Crystallogr. *B 25*, 1958 (1969).
[66] *R. R. Ryan, R. A. Penneman,* Acta Crystallogr. *B 27*, 829 (1971).
[67] *G. Brunton,* Acta Crystallogr. *B 27*, 2290 (1971).
[68] *B. Aurivillus, T. Lindquist,* Acta Chem. Scand. *9*, 1209 (1955).
[69] *R. Hoppe,* Angew. Chem. *78*, 52 (1966); *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *5*, 95 (1966); *9*, 25 (1970); Adv. Fluorine Chem. *6*, 387 (1970); Izvj. Yugoslav. Centr. Krist. (Zagreb) *8*, 21 (1973); in *C. J. M. Rooymans, A. Rabenau:* Crystal Structure and Chemical Bonding in Inorganic Chemistry. Elsevier, Amsterdam 1975, p. 127.
[70] *R. Hoppe, K. Blinne,* Z. Anorg. Allg. Chem. *293*, 135 (1958).
[71] *G. Thornton, A. J. Jacobsen,* Mater. Res. Bull. *11*, 837 (1976).
[72] Calculations of the Madelung part of the lattice energy (MAPLE) show, on comparison with MAPLE values for other oxoplumbates, that both proposed structures require revision: *R. Hoppe,* unpublished (1979).
[73] *P. Panek, R. Hoppe,* Z. Anorg. Allg. Chem. *393*, 13 (1972).

[74] *H. D. Rad, R. Hoppe,* Z. Naturforsch. *B 33*, 1184 (1978).
[75] *H. G. von Schnering, R. Hoppe,* Z. Anorg. Allg. Chem. *312*, 99 (1961).
[76] *J. E. Iglesias, K. E. Pachali, H. Steinfink,* J. Solid State Chem. *9*, 6 (1974).
[77] *R. Hoppe, H. J. Röhrborn, H. G. von Schnering,* unpublished (1964).
[78] *H. Sommer, R. Hoppe,* Z. Anorg. Allg. Chem. *443*, 201 (1978).
[79] *H. Rad, R. Hoppe,* 6. Int. Conf. Solid Compounds of Transition Elements, Stuttgart 1979.
[80] *R. Hoppe, H. Rad,* unpublished; cf. Dissertation *H. Rad,* Universität Giessen 1980.
[81] *H. G. von Schnering, R. Hoppe,* Z. Anorg. Allg. Chem. *312*, 89 (1961).
[82] *H. G. von Schnering,* Z. Anorg. Allg. Chem. *314*, 144 (1962).
[83] *S. J. Chung, Th. Hahn,* Acta Crystallogr. *A 31*, Suppl. 1 (1975).
[84] *R. Hoppe, M. Serafin,* unpublished; cf. Dissertation *M. Serafin,* Universität Giessen 1980.
[85] *S. C. Abrahams, J. L. Bernstein,* J. Phys. Chem. Solids *28*, 1685 (1967).
[86] *H. F. Kay, J. L. Miles,* Acta Crystallogr. *10*, 213 (1957).
[87] *P. Vousden,* Acta Crystallogr. *4*, 373 (1951).
[88] *M. Serafin, R. Hoppe,* Angew. Chem. *90*, 387 (1978); Angew. Chem. Int. Ed. Engl. *17*, 354 (1978).
[89] *C. Brink, H. A. Stenfert Kroese,* Acta Crystallogr. *5*, 433 (1952).
[90] *C. Brink, C. H. McGillavry,* Acta Crystallogr. *2*, 158 (1949).
[91] *C. Brink, A. E. van Arkel,* Acta Crystallogr. *5*, 505 (1952).
[92] *R. D. Shannon,* Acta Crystallogr. *A 32*, 751 (1976).

COMMUNICATIONS

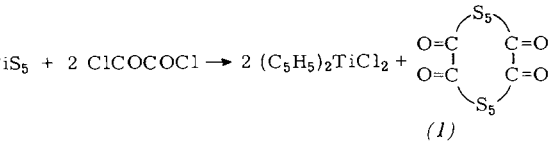
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Synthesis and Crystal Structure Analysis of Decathiacyclotetradecane-6,7,13,14-tetraone, $S_{10}(CO)_4$[**]

By *Herbert W. Roesky, Hamid Zamankhan, Jan Willem Bats,* and *Hartmut Fuess*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

So far the structures of the following sulfur homocyclic systems have been reported: S_6, S_7, S_8, S_{10}, S_{12}, and S_{20}[1]; some of them are stable for any length of time only at low temperature. They should be stabilized by incorporation of heteroatoms into the ring systems—numerous cases of such stabilization are known from sulfur-nitrogen chemistry[2]—and novel systems should thus become accessible. For example, on condensation of Cp_2TiS_5[3] with oxalyl chloride in carbon disulfide we obtained a fourteen-membered ring, *viz.* the title compound *(1)*, for the first time.



(1)

Precession photographs of crystals of *(1)* revealed monoclinic symmetry, space group $P2_1/n$, $Z=4$, $a=781.2(2)$, $b=727.3(2)$, $c=1257.0(7)$ pm, $\beta=91.33(4)°$, $V=714.0\times10^6$ pm^3. Using an automatic Syntex $P2_1$ diffractometer ($Mo_{K\alpha}$ radiation), 2194 reflections (942 non-equivalent ones) were recorded. The standard reflections, recorded at intervals of 50 reflections, indicated considerable radiation damage and resulting intensity losses of between 30 and 60%. After corresponding correction of the data ($\mu=1.48$ mm^{-1}) and solution of the structure with the Multan program (positions of C and O by Fourier syntheses), refinement led to $R(F)=0.104$ and $R_w(F)=0.065$.

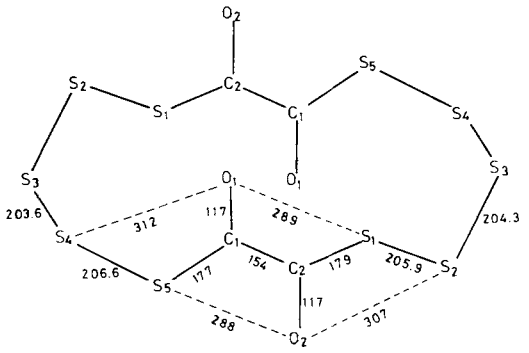


Fig. 1. Molecular shape and interatomic distances [pm] of $S_{10}(CO)_4$ in crystal (standard deviations: S—S, 0.5; S—C, S—O, C—O, 1.0; C—C, 2 pm).

The conformation of the heterocyclic tetraone *(1)* corresponds to expectation. The mean value of the SS bond lengths of 205.1 pm is comparable with that for S_{12} (205.3 pm)[4a]. The SS bonds adjacent to the long SS bonds are shortened, as in S_7O[4b], by bond interaction (the shortest one is located next to the longest SS bond, and the latter in turn next to the shortest SC bond, cf. Fig. 1). The torsional angle between the planes S1–C2–O2–C1 and S5–C1–O1–C2 is 15°. The compound is not volatile without decomposition; only fragments are observed in the mass spectrum of *(1)*. On the basis of our results we assume that the readily soluble species $S_5(CO)_2$ occurs as "monomeric" intermediate during the formation of *(1)*.

[*] Prof. Dr. H. W. Roesky, Dr. H. Zamankhan
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. H. Fuess, Dr. J. W. Bats
Institut für Kristallographie der Universität
Senckenberganlage 30, D-6000 Frankfurt am Main 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Federal Ministry of research and Technology.

Experimental

Oxalyl chloride (1.5 g, 11.8 mmol) is added at room temperature to a suspension of Cp_2TiS_5[3] (4 g, 11.8 mmol) in CS_2 (250 ml) under a nitrogen atmosphere. On heating under reflux for 5 h, the color of the solution changes from dark violet to yellow, and red Cp_2TiCl_2 precipitates. After filtration, evaporation, and repetition of these separation steps, the yellow product *(1)* crystallizes on cooling to $-20\,^{\circ}C$; yield 1.2 g (48%), dec. 110 °C.

Received: April 27, 1979;
supplemented: May 14, 1979 [Z 295a IE]
German version: Angew. Chem. *91*, 122 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 71582-55-3; Cp_2TiS_5, 12116-82-4; oxalyl chloride, 79-37-8

[1] *R. Reinhardt, R. Steudel, F. Schuster*, Angew. Chem. *90*, 55 (1978); Angew. Chem. Int. Ed. Engl. *17*, 57 (1978); *M. Schmidt, E. Wilhelm, T. Debaerdemaeker, E. Hellner, A. Kutoglu*, Z. Anorg. Allg. Chem. *405*, 153 (1974).
[2] *H. W. Roesky*, Angew. Chem. *91*, 112 (1979); Angew. Chem. Int. Ed. Engl. *18*, 91 (1979).
[3] *M. Schmidt, B. Block, H. D. Block, H. Köpf, E. Wilhelm*, Angew. Chem. *80*, 660 (1968); Angew. Chem. Int. Ed. Engl. *7*, 632 (1968).
[4] a) *R. Steudel*, Angew. Chem. *87*, 683 (1975); Angew. Chem. Int. Ed. Engl. *14*, 655 (1975); b) *R. Steudel, R. Reinhardt, T. Sandow, ibid. 89*, 757 (1977) and *16*, 716 (1977), respectively.

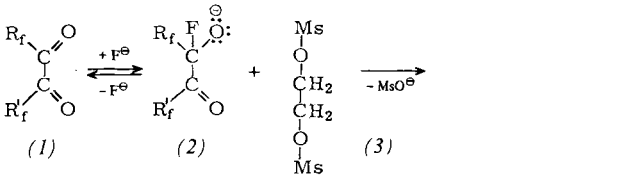
1,4-Dioxanes with Four Fluorine and/or Trifluoromethyl Substituents on C^2 and C^3 from Vicinal Perfluorodicarbonyl Compounds[**]

By *Werner Schwertfeger* and *Günter Siegemund*[*]

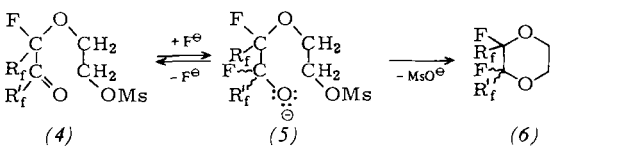
Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

So far, two reactions have been reported in the literature for the preparation of 1,4-dioxanes perfluorinated at C^2 and C^3. Thus, 2,2,3,3-tetrafluoro-1,4-dioxane *(6a)* was obtained in *ca.* 3% yield on catalytic hydrogenation of the difficultly accessible perfluoro-2,3-dihydro-1,4-dioxane[1]. In contrast, reaction of perfluoropinacol and 1,4-dioxane affords 2,2,3,3-tetrakis(trifluoromethyl)-1,4-dioxane in quantitative yield[2].

In the search for general synthetic routes for the preparation of fluorinated 1,4-dioxanes *(6)* we found that these ethers are formed on reaction of perfluorinated vicinal dicarbonyl compounds *(1)* with ethylene dimesylate *(3)* (mesyl = methanesulfonyl) and potassium fluoride and/or cesium fluoride in the molar ratio 1:1:2.



(1) *(2)* *(3)*



(4) *(5)* *(6)*

(a), $R_f = R'_f = F$; *(b)*, $R_f = F$, $R'_f = CF_3$ or $R_f = CF_3$, $R'_f = F$; *(c)*, $R_f = R'_f = CF_3$

Scheme 1. Proposed reaction mechanism. The simultaneous addition of two fluoride ions to *(1)* has not been considered.

From hexafluorobiacetyl *(1c)*[3] the diastereomeric 1,4-dioxanes *(6c)* are obtained in the ratio 10:1. Hitherto, the mixture could not be separated, either by distillation or by preparative gas-chromatography. The proposed reaction mechanism (Scheme 1) suggests that the sterically more favorable *trans* product is the main component.

Experimental

The dry alkali-metal fluoride and dried solvent are transferred to a previously dried flask fitted with a mechanical stirrer, thermometer, and reflux condenser. After addition of *(1)* and *(3)*, the mixture is slowly warmed to the reaction temperature. The reaction mixture is steam distilled and the organic phase recovered is dried over sodium sulfate and distilled.

(6a) 0.5 mol *(1a)*[4], 0.5 mol *(3)*, 1.1 mol KF, 0.05 mol CsF, 500 ml diethylene glycol dimethyl ether; 8 h at 85 °C, 14% yield, b.p. 119—121 °C/750 torr. ^{1}H-NMR[5]: $\delta = 4.20$ (s); ^{19}F-NMR[5]: $\delta = -93.73$ (s).

(6b): 0.25 mol *(1b)*[6] (as dimer), 0.25 mol *(3)*, 0.75 mol KF, 200 ml tetraethyleneglycol dimethyl ether; 24 h at 110 °C, 4.4% yield, b.p. 74.5—76.5 °C/100 torr. ^{1}H-NMR[5]: $\delta = 3.25$—4.80 (m); ^{19}F-NMR[5]: $\delta = -81.27$ (m, 3F, CF_3), -85.46 (dm, $J_{gem} = 156$ Hz, 1F, CF_2), -87.37 (dm, $J_{gem} = 156$ Hz, 1F, CF_2), -139.26 (m, 1F, CF).

(6c): 0.3 mol *(1c)*[3], 0.3 mol *(3)*, 0.625 mol CsF, 200 ml tetraethylene glycol dimethyl ether; 14 h at 100—105 °C, 46% yield, b.p. 75—90 °C/100 torr. ^{1}H-NMR[5]: $\delta = 3.65$—4.75 (m); ^{19}F-NMR[5] "α-form": $\delta = -79.76$ (m, CF_3), -125.35 (m, CF); "β-form": $\delta = -79.98$ (m, CF_3), -133.37 (m, CF); intensity ratio of signals at -125.35 and $-133.37 \approx 1:10$.

Received: November 23, 1979 [Z 376 IE]
German version: Angew. Chem. *92*, 123 (1980)

CAS Registry numbers:
(1a), 359-40-0; *(1b)*, 7309-82-2; *(1c)*, 685-24-5; *(3)*, 4672-49-5; *(6a)*, 56625-47-9; *(6b)*, 72749-36-1; *(6c)*, 72749-37-2

[1] *P. L. Coe, P. Dodman, J. C. Tatlow*, J. Fluorine Chem. *6*, 115 (1975).
[2] *A. F. Eleev, S. J. Pletnev, G. A. Sokol'skii, V. F. Cherstkov, I. L. Knunyants*, Izv. Akad. Nauk SSSR, Ser. Khim. *1978*, 509.
[3] *L. O. Moore*, J. Org. Chem. *35*, 3999 (1970).
[4] *C. W. Tullock, D. D. Coffman*, J. Org. Chem. *25*, 2016 (1960).
[5] ^{1}H-NMR: Varian T 60, solvent $CDCl_3$, TMS as internal standard; ^{19}F-NMR: Varian XL 100; solvent $CDCl_3$, $CFCl_3$ as internal standard.
[6] *Th. Martini*, DOS 2623089 (1976), Hoechst; Chem. Abstr. *88*, 89652b (1978).

A Selective Pathway from Methanol to Ethylene and Propene[**]

By *Friedrich August Wunder* and *Ernst Ingo Leupold*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Increasing scarcity of crude oil compels us to look for alternative entries to the feedstocks of the chemical industry.

Apart from hydrogenation of coal and the Fischer-Tropsch synthesis[1] increasing attention is being focused on

[*] Dr. W. Schwertfeger, Dr. G. Siegemund
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

[**] Cyclization with Participation of Fluoride Ions, Part 1.

[*] Dr. F. A. Wunder, Dr. E. I. Leupold
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

[**] This work was supported by the Federal German Ministry of Research and Technology (grant designation: 01 VM 399-ZK/NT/NTS 2036).

the catalytic synthesis of ethylene and propene from methanol[2] which is readily accessible, in principle, from all carbonaceous raw materials[3]. Most of the known catalysts[4] transform methanol into a wide range of products with a considerable proportion of higher aliphatic and aromatic hydrocarbons[5].

$$n\ CH_3OH \xrightarrow{cat.} \text{Hydrocarbons} + n\ H_2O \qquad (a)$$

More selective catalysts are accessible by doping zeolites with lanthanoids[6].

Use of manganese-doped aluminosilicates[7] has now given a surprisingly narrow product spectrum with a high proportion of ethylene and propene.

For instance, if a methanol/water mixture (30 vol. % water) is passed at 400 °C and normal pressure over a mixture of chabasite and erionite whose exchangeable cations have been replaced by manganese, then only C_1 to C_4 hydrocarbons are formed. The conversion is over 90%. After condensation of the water of reaction, the gas compositions given in Table 1 are obtained.

Table 1. Composition of the gas obtained [eg. (a)] after condensation of the water of reaction.

Products	Amount [vol. %]	
Ethylene	37.1	66.3 C_2- to C_4-olefins
Propene	26.5	
Butenes	2.7	
Methane	12.6	21.8 C_1- to C_4-alkanes
Ethane	1.3	
Propane	6.6	
Butanes	1.3	
C_5- and higher hydrocarbons	<0.1	
Aromatics	<0.1	
CO	0.5	
H_2	5.2	
H_2O	≈2	
Dimethyl ether	4.7	

Dimethyl ether can be recycled as an intermediate[8]. Table 2 shows the selectivities in this case.

Table 2. Selectivity of reaction (a) on recycling of dimethyl ether. The selectivity refers to the gaseous products.

Products	Selectivity [%]	
Ethylene	36.3	80.3 C_2- to C_4-olefins
Propene	38.8	
Butenes	5.2	
C_1- to C_4-alkanes	19.5	

The high concentration of the C_2 to C_4 olefins in the reaction gas suggests a future industrial exploitation of this reaction. The relatively narrow product spectrum facilitates distillative work-up. Thus the procedure opens a route to these important feedstocks of industrial synthesis which is independent of the availability of individual raw materials.

Received: November 23, 1979 [Z 377 IE]
German version: Angew. Chem. 92, 125 (1980)

[1] *W. Peters, H.-D. Schilling,* Erdöl Kohle, Erdgas, Petrochemie Brennst.-Chem. *30*, 552 (1977).
[2] Chem. Eng., August 13, 86C (1979).
[3] *K. Weissermel, H.-J. Arpe:* Industrielle Organische Chemie. Verlag Chemie, Weinheim 1978.
[4] *N. Y. Chen, W. E. Garwood,* J. Catal. *52*, 453 (1978); *D. C. Hargis, L. J. Kehoe,* US-Pat. 4072732 (1978).
[5] *C. D. Chang, W. H. Lang, R. L. Smith,* J. Catal. *56*, 170 (1979); *C. D. Chang et al.,* Ind. Eng. Chem. Process Des. Dev. *17*, 257 (1978).
[6] *F. N. Lin, J. C. Chao, R. G. Anthony,* Coal Process Technol. *1978*, 72.
[7] *F. A. Wunder, H.-J. Arpe, H. Hachenberg, E. I. Leupold,* DOS 2755229 (1979), Hoechst.
[8] *N. Y. Chen, W. J. Reagan,* J. Catal. *59*, 123 (1979).

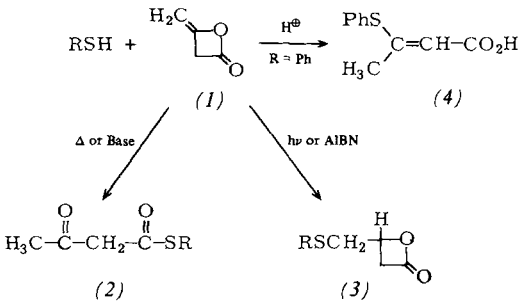
Addition of Alkanethiols to Diketene

By *Ulrich Hertenstein*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

The course taken by an acid-catalyzed addition of alkanethiols to diketene *(1)* could not be predicted from the reactions known so far.

Thermal and base-catalyzed additions of thiols to diketene *(1)* give thioesters *(2)*[1]; on irradiation or in the presence of azodiisobutyronitrile (AIBN), however, β-(alkylthiomethyl)-β-propiolactones *(3)* are formed[2]. This addition proceeds in anti-Markownikoff fashion.



In the same way, thiols add to vinyl esters. This reaction is subject to both radical-[3] and acid catalysis[4].

In contrast, the likewise acid-catalyzed addition of thiophenol to diketene[5] proceeds according to the Markownikoff rule to give β-phenylthiocrotonic acid *(4)*.

We found that alkanethiols undergo anti-Markownikoff H_2SO_4-catalyzed addition to diketene *(1)*. The adducts *(3)* were isolated and identified by ^{1}H-NMR spectroscopy (Table 1).

$$RSH + (1) \xrightarrow{H_2SO_4/Et_2O} (3)$$

Table 1. Data for β-(alkylthiomethyl)-β-lactones *(3)*.

	R	B.p. [°C/torr]	Yield [%]	IR [cm^{-1}] νC=O	^{1}H-NMR (δ values)
(3a)	*n*-C_4H_9	111—115/ 0.06	72	1780	0.95 (d, 3H); 1.10—1.75 (m, 4H); 2.25—3.00 (m, 4H); 3.55 (quin, 1H); 4.25 (J_{AB}=12.3 Hz, 1H); 4.26 (J_{AB}=12.3 Hz, 1H)
(3b)	*i*-C_4H_9	90—93 0.15	68	1780	1.05 (d, 6H); 1.76 (m, 1H); 2.48 (d, 2H); 2.55—2.80 (m, 2H); 3.60 (quin., 1H); 4.30 (J_{AB}=12.3 Hz, 1H); 4.40 (J_{AB}=12.3 Hz, 1H)
(3c)	C_2H_5	75—80/ 0.2	59	1780	

[*] Dr. U. Hertenstein
Hoechst Aktiengesellschaft, Werk Gersthofen
D-6230 Frankfurt am Main 80 (Germany)

γ-Substituted crotonic esters *(5)* can be obtained without isolation of *(3)* by addition of an alcohol and increasing the temperature.

$$n\text{BuSH} + (1) \xrightarrow[2)\ \text{ROH}]{1)\ H_2SO_4} n\text{BuS}{-}CH_2{-}CH{=}CH{-}CO_2R$$
(5)

Table 2. Data of γ-(*n*-butylthio)crotonic esters *(5)*.

	R	B.p. [°C/torr]	IR [cm^{-1}] $\nu_{C=O}$	IR [cm^{-1}] $\nu_{C=C}$	Yield [%]
(5a)	CH_3	92—95/0.15	1715	1595	51
(5b)	C_2H_5	70—75/0.001	1720	1600	53
(5c)	n-C_3H_7	76—79/0.001	1720	1600	53
(5d)	n-C_4H_9	83—93/0.001	1720	1600	50

Procedure

(3): Diketene *(1)* (0.5 mol) is added between 0 and 3 °C to a solution of thiol (0.5 mol) in anhydrous ether (200 ml) cooled to 0 °C. Concentrated H_2SO_4 (49.0 g, 0.5 mol) is then added dropwise between 0 and 5 °C to the cooled (ice/salt) reaction mixture. Stirring is continued for 2 h at room temperature, the two phases are separated, the organic phase washed with water, dried over Na_2SO_4 and distilled.

(5): The procedure is as above but without work-up. After addition of alcohol (2 mol), the ether is distilled off. The mixture is heated to 70 °C for 1.5 h, poured on to 1 l of crushed ice, extracted with ethyl acetate, dried over Na_2SO_4, and distilled.

Received: November 23, 1979 [Z 378 IE]
German version: Angew. Chem. *92*, 123 (1980)

CAS Registry numbers:
(1), 674-82-8; *(3a)*, 72749-29-2; *(3b)*, 72749-30-5; *(3c)*, 72749-21-6; *(5a)*, 72749-32-7; *(5b)*, 72749-33-8; *(5c)*, 72749-34-9; *(5d)*, 72749-35-0; 1-butanethiol, 109-79-5; isobutanethiol, 513-44-0; ethanethiol, 75-08-1; methanol, 67-56-1; ethanol, 64-17-5; 1-propanol, 71-23-8; 1-butanol, 71-36-3

[1] *F. Lynen, O. Wieland,* Meth. Enzymol. *1*, 567 (1955); *F. Duus, P. Jakobsen, S.-O. Lawesson,* Tetrahedron *24*, 5323 (1968); *S. Motaki, Te Sato,* Bull. Chem. Soc. Jpn. *42*, 1322 (1969); *F. J. Pohl, W. Schmidt,* DRP 717652 (1971); *B. V. Kurgane, A. K. Grinwalde, Ya. P. Stradyn, M. D. Brakmane, S. A. Giller,* Zh. Org. Khim. *10*, 2321 (1974); *H. White, W. P. Jencks,* J. Biol. Chem. *251*, 1688 (1976).
[2] *C. W. Theobald,* US-Pat. 2675392 (1954); Chem. Abstr. *49*, 4722a (1955); *G. A. Hüll, F. A. Daniker, T. F. Conway,* J. Org. Chem. *37*, 1837 (1972).
[3] *A. Schöberl, A. Wagner* in Houben-Weyl: Methoden der organischen Chemie. Thieme, Stuttgart 1955, Vol. 9, p. 128.
[4] *G. Baumeyer, G. Dittus, E. Müller* in Houben-Weyl: Methoden der organischen Chemie. Thieme, Stuttgart 1966, Vol. 6/4, p. 376.
[5] *N. F. Yaggi, K. T. Douglas,* J. Chem. Soc. Chem. Commun. *1977*, 609.

Direct Synthesis of the Perfluoroalkanesulfinates of Iron(II), Cobalt(II), and Nickel(II): SO_2-Assisted Addition of Alkyl Halides to Transition Metals

By *Konrad von Werner* and *Hermann Blank*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Typical transition metals normally react with alkyl halides only when they have been transformed into a particularly energetic state by physical (metal atom technique[1]) or chemical methods (reduction of metal salts[2]).

We have now found that commercial grade iron, cobalt, and nickel powder react under mild conditions with 1-iodoperfluoroalkanes *(1)* in the presence of sulfur dioxide and strongly polar aprotic solvents (dimethylformamide, dimethyl sulfoxide, hexamethylphosphoric triamide). Use of DMF gave products shown by elemental analysis, IR data, and magnetic moments to be cationic di-μ-iododimetal(II) complexes *(2)* (see Table 1).

$$2\ M + 2\ R{-}I + 2\ SO_2 \xrightarrow[20\,^\circ C]{DMF}$$
(1)

$$\left[(Me_2N{-}CH{=}O)_4M\begin{smallmatrix}I\\I\end{smallmatrix}M(O{=}HC{-}NMe_2)_4\right]^{2\oplus}\ \left[RSO_2^{\ominus}\right]_2$$
(2)

M = Fe, Co, Ni; R = $CF_3(CF_2)_n$, n = 1-9

Table 1. Characteristic data of some complexes *(2)*, R = n-C_6F_{13}.

	M	IR (Nujol) [cm^{-1}] $\nu(CF)+\nu_{as}(SO_2)$	IR (Nujol) [cm^{-1}] $\nu_s(SO_2)$	Magn. moment [BM] exp.	Magn. moment [BM] calc. [a]	Color	Dec. [°C]	Yield [%]
(2a)	Fe	1241 s, 1203 s, 1174 w, 1148 s, 1130 w	1018 m	4.88	4.90	ocher-yellow	>42	88
(2b)	Co	1240 s, 1204 s, 1172 w, 1147 s, 1127 w	1018 m-s	3.65	3.87	violet	>47	67
(2c)	Ni	1241 s, 1205 s, 1168 w, 1147 s	1018 m-s, 1005 sh	—	2.83	green	>45	43

[a] "Spin only" values.

The complexes *(2)* can be isolated as paramagnetic crystals which are highly sensitive to oxidation and moisture. The IR spectra indicate the DMF ligands to be coordinated *via* oxygen ($\nu(C{=}O) = 1645\ cm^{-1}$) and the very weakly nucleophilic RSO_2 groups to be present only as counterions. In their chemical behavior, the complexes *(2)* resemble the structurally analogous compounds of type $[L_2MCl_2ML_2][CF_3SO_2]_2$ (M = Fe, Ni; L = bpy, phen) described by *Lindner et al.*[3].

On warming in DMF solution, *(2)* already decomposes at 40 °C into $M(DMF)_4(I)_2$ and $[M(DMF)_6][RSO_2]_2$. Nor is SO_2 liberated at higher temperatures.

No reaction occurred with very finely divided metal powders after prolonged exposure to air. In these cases, a dense oxide layer was expectedly found on the metal surface by ESCA.

Activation of the metal by chemisorption of SO_2 as a $(M{\rightarrow}SO_2)$-adduct is assumed to occur during formation of *(2)*. This is supported (i) by the slow reaction of the metals with *(1)* in DMF only above 100 °C in the absence of SO_2,

[*] Dr. K. von Werner, H. Blank
Werk Gendorf, Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0128 $ 02.50/0

and (ii) by the absence of any shift of the ^{19}F-NMR signal of the terminal CF_2I group of *(1)* in DMF solution after saturation with SO_2, ruling out activation of *(1)*. Complexes *(2)* are most probably formed by oxidative addition of *(1)* to an initially formed $M^0(SO_2)$ complex, to give a solvated (RMI) species and insertion of SO_2 into the M—C bond.

The postulated insertion reaction of SO_2 into a perfluoroalkyl-transition metal bond appears unusual[4]. However, it could be accomplished with the model compound *(3)*[5] which can be readily transformed by SO_2 and DMF into *(2a)*.

$$\underset{(3)}{cis\text{-}(CO)_4Fe(C_6F_{13})I} + SO_2 \xrightarrow[-4CO]{DMF,\ 20\,^\circ C} \underset{90\%\ \text{yield}}{(2a)}$$

The synthesis of sulfinato complexes is not limited to *(1)* but is also possible with other halides. The products are sometimes highly labile and could not all be characterized. The following reaction series was found for M=Fe: $C_6F_{13}I$ > CH_2=CH—CH_2Br > C_6H_5—CH_2Cl > $C_6F_{13}Br$ > $C_6F_{13}CH_2CH_2I$ > $C_8H_{17}I$.

The compound C_6H_5-NSO also reacts at 20 °C with Fe and *(1)*, albeit slower than SO_2. The resulting $[C_6H_5\text{--}N\text{--}S(=O)R]^{\ominus}$ anion was detected by methylation with CH_3I[6] to give *N*-methyl-*N*-phenylperfluoroalkanesulfinamides.

Procedure

(All operations performed under dry N_2)!

(2a): $C_6F_{13}I$ (231.9 g, 0.52 mol) is added dropwise to a stirred suspension of Fe powder[7] (27.9 g, 0.5 mol) in DMF (750 ml) over 3 h with simultaneous introduction of SO_2 (64 g, 1.0 mol). The mixture is kept below 25 °C, and first turns green and then yellowish-brown. After stirring for 48 h, it is filtered and as much DMF removed as is possible at 0.1 torr and a maximum temperature of 30 °C. The distillate contains *ca.* 5 g of $C_6F_{13}H$. The residue is cooled to −20 °C for several days; the crystal slurry is filtered under suction and the crystals dried *in vacuo* (yield 378 g). *(2b, c)* can be prepared similarly.

Received: November 23, 1979 [Z 380 IE]
German version: Angew. Chem. *92*, 124 (1980)

CAS Registry numbers:
(1), *n*=5, 355-43-1; *(2a)*, 72778-97-3; *(2b)*, 72778-95-1; *(2c)*, 72778-93-9

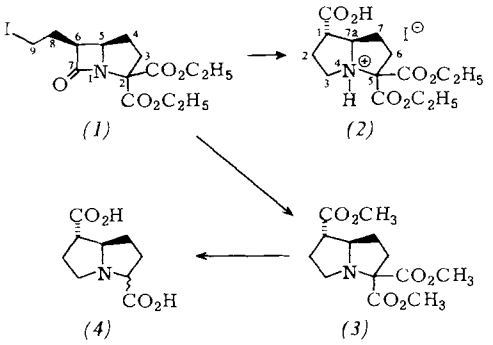
[1] *K. J. Klabunde*, Angew. Chem. *87*, 309 (1975); Angew. Chem. Int. Ed. Engl. *14*, 287 (1975).
[2] *R. D. Rieke*, Acc. Chem. Res. *10*, 301 (1977).
[3] *E. Lindner, G. Vitzthum*, Chem. Ber. *102*, 4053 (1969); Angew. Chem. *83*, 315 (1971); Angew. Chem. Int. Ed. Engl. *10*, 315 (1971).

Pyrrolizidines by Rearrangement of β-Lactams

By *Friedrich Cavagna, Adolf Linkies, Hartmut Pietsch*, and *Dieter Reuschling*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

During attempts to synthesize compounds with thienamycin-like structure we obtained the racemic 6-(2-iodoethyl)-7-oxo-1-azabicyclo[3.2.0]heptane-2,2-dicarboxylic acid diethyl ester *(1)*, which on reaction with acids or bases surprisingly undergoes rearrangement with ring expansion. Thus, on treatment with glacial acetic acid, *(1)* is slowly, with trifluoroacetic acid rapidly, converted into the pyrrolizidium salt *(2)*. On reaction with bases such as sodium methoxide or sodium cyanide in methanol, *(1)* undergoes transesterification, giving the pyrrolizidine *(3)*.



The intramolecular reaction of *(1)* with bases can be explained in terms of the increased reactivity of the nitrogen by the annelated five-membered ring and the consequently enforced perturbation of the amide mesomerism[1]. The spatial proximity of the two reactive groups leads to additional entropic promotion of the reaction. No racemization occurs, either in the acidic or in the basic conversion, *i.e.* the steric arrangement at C-5 and C-6 of *(1)* remains intact at C-7a and C-1, respectively, of *(2)* and *(3)*.

This reaction opens an entry to 1,5-disubstituted pyrrolizidines. On hydrolysis with KOH, *(3)* is decarboxylated to the sterically homogeneous 1,5-pyrrolizidinedicarboxylic acid *(4)*. The configuration at C-5, however, is still unclear.

The rearrangements have been established by the ^{1}H-NMR spectra (270 MHz, INDOR technique). Diagnostically decisive for the structures are the parameters of H-3 [*(2)* (in D_2O): ^2J=11.0 Hz, δ=3.82, ^3J=0 and 6.5 Hz, δ=3.18, ^3J=7.2 and 9.0 Hz; *(3)* (in [D_6]-DMSO): ^2J=−11.0 Hz, δ=3.01, ^3J=2.2 and 10.1 Hz, δ=2.80, ^3J=7.2 and 11.0 Hz] and H-7a; instead of J_{cis}(H-5, H-6)=5.5 Hz in *(1)* we find in *(3)* J(H-1, H-7a)=9 Hz. In contrast to the β-lactam spec-

Table 1. ^{13}C-NMR data of *(1)*, *(2)*, and *(3)*.

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	Ester-CO
(1) [a]	—	72.3	39.7 [b]	25.4 [b]	57.3	50.8	174.4	29.0 [b]	2.5	166.7, 168.4
(2) [c]	51.6	31.2 [d]	55.5	—	81.6	31.6 [d]	29.5 [d]	73.1	—	165.5, 168.1, 175.9 [e]
(3) [f]	49.6	32.6 [b]	47.5	—	74.9	37.1 [b]	28.7 [b]	68.6	—	170.5, 171.7, 173.4

[a] In $CDCl_3$, δ values referred to TMS. [b] Assignment by correlation of the ^{13}C- with the ^{1}H-NMR shifts. [c] In D_2O, δ values referred to $Me_3SiCH_2CH_2CH_2COONa$. [d] Alternative assignments. [e] Carboxylic CO. [f] In [D_6]-DMSO, δ values referred to TMS.

[4] *A. Wojcicki*, Adv. Organomet. Chem. *12*, 31 (1974).
[5] Prepared according to *R. B. King, S. L. Stafford, P. M. Treichel, F. G. A. Stone*, J. Am. Chem. Soc. *83*, 3604 (1961).
[6] *K. v. Werner*, J. Fluorine Chem. *8*, 451 (1976).
[7] Riedel-de Haën Catalog 1978, article number 12310.

[*] Dr. F. Cavagna, Dr. A. Linkies [+], Dr. H. Pietsch, Dr. D. Reuschling
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)
[+] Author to whom correspondence should be addressed.

trum, the pyrolizidine spectra are strongly pH-dependent. In acid medium the spectrum of *(3)* is almost identical to that of *(2)*. In *(3)* the signals of H-7a appear at higher field ($\delta = 3.68$), in *(2)* at lower field ($\delta = 4.20$), than the signals of H-5 in *(1)* ($\delta = 4.03$). The anisochronism of the aminomethylene protons (H-3) becomes greater on protonation of the nitrogen atom.

Also the ^{13}C-NMR spectra allow an unequivocal assignment to the two structural types (Table 1).

Experimental

(2): A solution of *(1)* (10 g, 24 mmol) in CH_3CO_2H (50 ml) and CF_3CO_2H is stirred for 45 minutes. After removal of solvent *in vacuo*, the residue is stirred in ethyl acetate until it becomes completely crystalline. Yield 6.2 g (60%), m.p. 126 °C (acetone).

(3): A mixture of *(1)* (10 g, 24 mmol) and NaCN (2.8 g, 54 mmol) in methanol (50 ml) is heated to boiling for 12 h. After evaporating down, the reaction product is isolated by passage through silica gel (ethyl acetate/hexane 1/2; $R_f = 0.36$) and distilled; b.p. 120 °C/0.05 torr; yield 4.2 g (62%). With $NaOCH_3$ instead of NaCN (6 days at room temperature), *(3)* is obtained in 95% yield.

(4): To a solution of *(3)* (16.5 g, 61.3 mmol) in methanol (20 ml) is added 100 ml of methanolic KOH and the mixture heated at 60 °C for 12 h. After dilution with 400 ml methanol the mixture is treated dropwise with 200 ml 70% $HClO_4$, filtered and the filtrate evaporated down; the residue, dissolved in 10 ml H_2O, crystallizes out on addition of acetone. Yield 8.5 g (64%); m.p. above 290 °C, dark coloration.

Received: November 23, 1979 [Z 381 IE]
German version: Angew. Chem. 92, 126 (1980)

[1] *R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Laraguina, W. B. Scanton, S. L. Andrews*, J. Am. Chem. Soc. *91*, 1401 (1969).

Syntheses with Cyanogen—A Simple Route to 4,5-Dichloroimidazoles

By *Dieter Günther* and *Dieter Bosse*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Bromine and iodine derivatives of imidazoles not substituted on nitrogen can be prepared easily and in good yields by halogenation[1]. The corresponding chlorine derivatives, on the other hand, are virtually unknown. Thus imidazole reacts with bromine in chloroform or ether to give 2,4,5-tribromoimidazole[2,3], while chlorination with elemental chlorine affords 2,2,4,5-tetrachloro-2*H*-imidazole[4]. Some imidazoles can be converted into the 4,5-Dichloroderivatives by reaction with *N*-chlorosuccinimide[5] or sodium hypochlorite[6].

We have now found that 4,5-dichloro-2-phenylimidazole *(1a)* ($R = C_6H_5$) is formed in good yields on reaction of benzaldehyde with cyanogen and hydrogen chloride in diethyl ether. The sole by-product formed in the reaction is oxamide, which is only sparingly soluble in most common solvents and can easily be separated.

To illustrate the scope of this reaction we report here on the reaction of some aliphatic, aromatic, and heteroaromatic

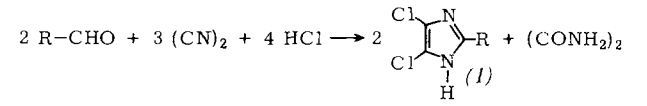


Table 1. Synthesis of 2-substituted 4,5-dichloroimidazoles *(1)*.

	R [a]	Solvent [b]	Yield [%]	M.p. [°C]
(1a)	C_6H_5	DME	67	165
(1b)	*p*-Cl C_6H_4	DEE	71	176
(1c)	*m*-$C_6H_5OC_6H_4$	DEE	72	175
(1d)	*p*-O_2N C_6H_4	Dioxane	46	235
(1e)	2-Benzo[*b*]furyl	Dioxane	70	195
(1f)	2-Thienyl	DEE	36	216
(1g)	$(CH_3)_3C$	Dioxane	45	236

[a] The composition and structure of the compounds are also confirmed by ^{1}H- and/or ^{13}C-NMR, IR and mass spectra. [b] DME = dimethoxyethane. DEE = diethyl ether.

aldehydes with cyanogen and hydrogen chloride (see Table 1). Aromatic aldehydes and aliphatic aldehydes with a tertiary α-C atom afford compounds *(1)* in good yields. In the case of enolizable aliphatic aldehydes and basic heteroaromatic aldehydes side reactions such as catalyzed aldol reactions and salt formation drastically reduce the yields. The 2-aryl-4,5-dichloroimidazoles *(1)* are crystalline, stable substances having the properties of weak acids. Only treatment with concentrated mineral acids leads to formation of salts, which completely hydrolyze on dilution.

While reaction of *(1)* with dimethyl sulfate or methyl iodide under phase-transfer catalysis conditions (NaOH/toluene) led smoothly to the 1-methyl derivatives *(2)*, attempted acylations with acid chlorides or isocyanates were unsuccessful. The salt *(4)*, formed on reaction with sodium methoxide, however, could be acylated to *(5)* in the usual way (see Table 2).

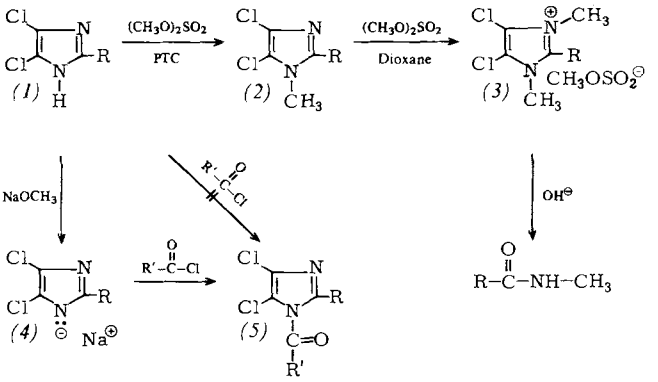


Table 2. Synthesis of derivatives of the 4,5-dichloroimidazoles *(1)*.

	R	R'	M.p. [°C]
(2a)	*p*-Cl C_6H_4	—	92–93
(2b)	*p*-O_2N C_6H_4	—	126–128
(2c)	*p*-CH_3OCO C_6H_4	—	116
(5d)	2-Benzo[b]furyl	—	138–139
(3a)	*p*-Cl C_6H_4	—	168
(5a)	*p*-Cl C_6H_4	C_2H_5O	110–111
(5b)	*o*-F C_6H_4	C_6H_5O	93–95

Quaternated 4,5-dichloroimidazoles *(3)* are extremely sensitive to bases; even on treatment with dilute alkali-metal hy-

[*] Dr. D. Günther, Dr. D. Bosse
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0130 $ 02.50/0

droxides at room temperature they spontaneously decompose to *N*-methylbenzamides.

Received: November 23, 1979 [Z 382 IE]
German version: Angew. Chem. *92*, 138 (1980)

CAS Registry numbers:
(1a), 72796-33-9; *(1b)*, 72796-34-0; *(1c)*, 72796-35-1; *(1d)*, 72796-56-7; *(1e)*, 72796-57-7; *(1f)*, 72796-58-8; *(1g)*, 72796-59-9; *(2a)*, 72796-60-2; *(2b)*, 72796-61-3; *(2c)*, 72796-62-4; *(2d)*, 72796-63-5; *(3a)*, 72796-65-7; *(5a)*, 72796-66-8; *(5b)*, 72796-67-9; benzaldehyde, 100-52-7; *p*-chlorobenzaldehyde, 104-88-1; *m*-phenoxybenzaldehyde, 67-36-7; *p*-nitrobenzaldehyde, 555-16-8; 2-benzofurancarboxaldehyde, 4265-16-1; 2-thiophenecarboxaldehyde, 98-03-3; 2,2-dimethylpropanal, 630-19-3; cyanogen, 460-19-5

[1] *K. Hofmann* in *A. Weissberger:* The Chemistry of Heterocyclic Compounds. Wiley, New York 1953, Vol. 6, p. 111 ff.
[2] *G. Wyss*, Ber. Dtsch. Chem. Ges. *10*, 1365 (1877).
[3] *J. E. Balaban, F. L. Pyman*, J. Chem. Soc. *121*, 947 (1922).
[4] *K. H. Büchel, H. Erdmann*, Chem. Ber. *109*, 1625 (1976).
[5] *J. J. Baldwin, P. K. Lumma, F. C. Novello, G. S. Ponticello, J. M. Sprague, D. E. Duggan*, J. Med. Chem. *20*, 1189 (1977).
[6] *A. W. Lutz, S. DeLorenzo*, J. Heterocycl. Chem. *4*, 399 (1967).

Functionalization of α-Methylene Ketones

By *Jürgen Sander* and *Karl Clauss*[*]

Dedicated to Professor Rolf Sammett on the occasion of his 60th birthday

Chlorosulfonyl isocyanate (CSI) and fluorosulfonyl isocyanate (FSI) are well-investigated, highly reactive compounds[1]. α-Methylene ketones *(1)* can be transformed by CSI into β-oxonitriles[2]. On reaction with FSI, α-methylene ketones *(1)* form *N*-fluorosulfonyl-β-oxocarboxamides *(2)*, which cyclize to 1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxides *(3)*[3].

We have now found that the products *(3)* react with phosphorus pentachloride to give 4-chloro-1,2,3-oxathiazine 2,2-dioxides *(4)* which in turn undergo a novel reaction with nucleophiles NuH *via* ring opening and SO_3 elimination to form β-substituted acrylonitriles *(5)* and/or *(6)*. Suitable choice of reaction conditions largely suppresses or avoids formation of substitution products *(7)*.

Table 1 lists examples for steps *(3)*→*(4)* and *(4)*→*(5)* and/or *(6)*.

Procedure

(4): A mixture of *(3)*[3] (0.50 mol), CCl_4 (400 ml), and PCl_5 (0.53 mol) is heated and stirred until a solution arises and evolution of HCl ceases. After cooling, the solvent and phosphorus oxide chloride are removed by vacuum distillation. The residue *(4)* is purified by vacuum distillation in a thin-layer evaporator or by crystallization from diisopropyl ether.

(5) and/or *(6):* A solution of *(4)* (30 mmol) in CH_2Cl_2 (25 ml) is added dropwise at 20 °C to a solution of NuH (30 mmol) in CH_2Cl_2 (50 ml) and triethylamine (90 mmol) [in the case of *(j)—(l)*] or triethylamine (60 mmol) and 4-dimethylaminopyridine (30 mmol) [in the case of *(a)—(i)*]. After 12 hours' stirring at room temperature, the organic phase is washed with water and dried over sodium sulfate. The solvent is evaporated *in vacuo* and the residue chromatographed on a silica gel column (70—230 mesh, cyclohexane : ethyl acetate, 1:1). The products *(5)* and/or *(6)* are distilled or recrystallized from diisopropyl ether or acetonitrile.

Received: November 23, 1979 [Z 383 IE]
German version: Angew. Chem. *92*, 138 (1980)

[1] *R. Graf*, Angew. Chem. *80*, 179 (1968); Angew. Chem. Int. Ed. Engl. *7*, 172 (1968); *H. Bestian*, Pure Appl. Chem. *27*, 611 (1971); *J. K. Rasmussen, A. Hassner*, Chem. Rev. *76*, 389 (1976).
[2] *G. Lohaus*, Chem. Ber. *100*, 2719 (1967); *J. K. Rasmussen, A. Hassner*, Synthesis *1973*, 682.
[3] *K. Clauß, H. Jensen*, Angew. Chem. *85*, 965 (1973); Angew. Chem. Int. Ed. Engl. *12*, 869 (1973); DBP 2001017 (1970), Hoechst.

Table 1. Chlorooxathiazine dioxides *(4)* from oxathiazinone dioxides *(3)* and acrylonitriles *(5)* and/or *(6)* from chlorooxathiazine dioxides *(4)*. The compounds gave correct elemental analyses. Yields are not optimized.

				(4)		*(5)* and/or *(6)*				
	R^1	R^2	Nu	Yield [%]	M.p. [°C]	Yield [%]	M.p. [°C] [a]	*(5)*	*(6)*	*(1)*
a	CH_3	H	NHC_6H_5	90	24	58	112—114	90	10	Acetone [c]
b	CH_3	CH_3	NHC_6H_5	80	Oil	46	122—124	1	99	2-Butanone
c	CH_3	C_6H_5	NHC_6H_5	73	85	48	98—99	95	5	Phenylacetone
d	C_6H_5	CH_3	NHC_6H_5	82	77	27	144—146	65	35	Propiophenone
e	C_6H_5	H	NHC_6H_5	76	126	29	128—130	60	40	Acetophenone [c]
f	CH_3	Cl	NHC_6H_5	87	36	38	134—136	—	100	Chloroacetone
g	$(CH_2)_4$		NHC_6H_5	75	53	60	95—98	—	100	Cyclohexanone
h	$(CH_2)_2$	*o*-C_6H_4	NHC_6H_5	30	172	31	147—148	—	100	β-Tetralone
i	*o*-C_6H_4	$(CH_2)_2$	NHC_6H_5	89	100	20	158—159	—	100	α-Tetralone
j	CH_3	H	OC_6H_5			38	Oil	95	5	Acetone [c]
k	CH_3	H	SC_6H_5			40	Oil	90	10	Acetone [c]
l	CH_3	H	SC_2H_5			38	Oil	50	50	Acetone [c]

[a] Based on the isomer ratio given. [b] Determination of the isomer ratio and assignment of configurational isomers by NMR spectroscopy [4]. [c] Use of the acetylated ketones *(1)*, $R^2 = COCH_3$, is recommended for the synthesis of *(3)*.

[*] Dr. J. Sander, Dr. K. Clauss
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main (Germany)

[4] *F. Théron, R. Vessière*, Bull. Soc. Chim. Fr. *1968*, 2994; *J. C. Chalchat, F. Théron, ibid. 1974*, 953; *S. Deswarte, C. Bellec, P. Souchay*, Bull. Soc. Chim. Belg. *84*, 321 (1975); *J. Dedina, J. Kuthan, J. Palecek, J. Schraml*, Collect. Czech. Chem. Commun. *40*, 3476 (1975).

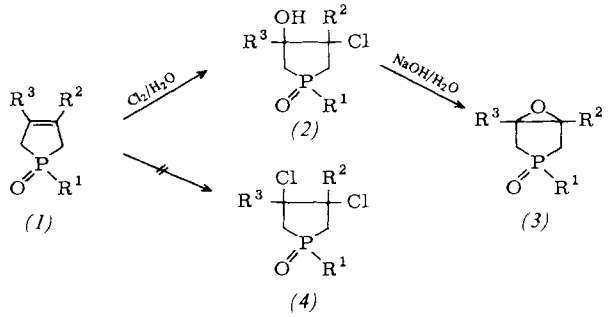
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0202-0131 $ 02.50/0*

Synthesis and Structure of 3-Chloro-4-hydroxy- and 3,4-epoxyphospholane 1-Oxides

By *Friedrich Cavagna, Utz-Hellmuth Felcht,* and *Erich F. Paulus*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

1-Alkyl(alkoxy,aryl)-3-phospholene 1-oxides *(1)* add cleanly at the C=C double bond with hypochlorous acid formed *in situ* from chlorine and water to give 1-alkyl(alkoxy,aryl)-3-chloro-4-hydroxyphospholane 1-oxides *(2)* (Table 1), which, apart from the derivative with $R^1 = C_6H_5$, R^2, $R^3 = CH_3$[1a], were hitherto unknown. Alkaline cleavage of the chlorohydrins *(2)* affords the 3,4-epoxyphospholane 1-oxides *(3)* (Table 1) in almost quantitative yield and is thus



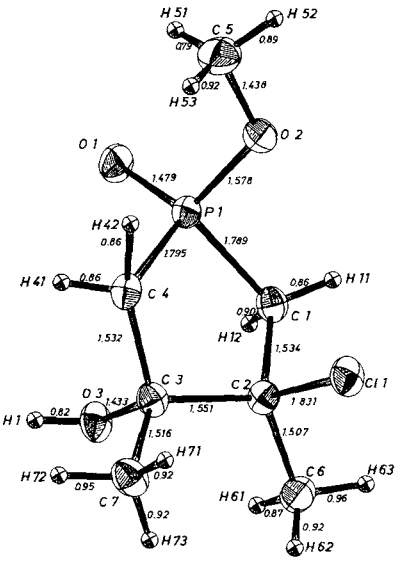


Fig. 1. ORTEP diagram of the molecular structure of (1*SR*, 3*SR*, 4*RS*)-3-chloro-4-hydroxy-3,4-dimethyl-1-methoxyphospholane 1-oxide *(2f$_1$)* in the crystal. Standard deviations Cl C, P O: 0.002 Å, O C, C C: 0.003 Å, C H: 0.02 Å.

Table 1. Some data on 3-chloro-4-hydroxy- *(2)* [a] and 3,4-epoxyphospholane 1-oxides *(3)* [b]. Coupling constants J_{PH} in Hz.

Cpd.	R^1	R^2	R^3	Yield [%]	B.p. [°C/bar] M.p. [°C] (Solvent)	IR [c] $\nu_{P=O}$ [cm^{-1}]	^{1}H-NMR (TMS int., δ-values) *(2):* in [D$_6$]-DMSO; *(3):* in CDCl$_3$
(2a) [d]	CH_3	H	H	98	134 (acetone)	1190	1.70 (d, ^2J = 15, CH_3), 1.9—2.9 (m, H-2, 5), 4.1—4.7 (m, H-3, 4), 5.90 (s, OH)
(2b) [d]	CH_3	CH_3	H	97	126—127 (ethyl acetate)	1150, 1180	1.50 (s, CH_3-3), 1.70—1.71 (dd, ^2J = 14, CH_3-1), 1.9—2.9 (H-2, 5), 4.1–4.7 (m, H-4), 5.10 (s, broad, OH)
(2c)	C_6H_5	H	H	86	138 (acetonitrile)	1175	2.0—2.9 (m, H-2, 5), 4.3—4.9 (m, H-3, 4), 6.15 (s, broad, OH), 7.5—8.1 (m, H-arom.)
(2d$_1$) [e]	C_6H_5	CH_3	H	96	174—175 (2-propanol)	1150	1.60 (s, CH_3-3), 2.1—3.1 (m, H-2, 5), 4.3—4.8 (m, H-4), 5.81 (s, OH), 7.5—8.2 (m, H-arom.)
(2d$_2$) [e]	C_6H_5	CH_3	H	96	134 (ethyl acetate/ ether 1:2)	1185	1.51 (s, CH_3-3), 2.2—3.2 (m, H-2, 5), 4.4—4.9 (m, H-4), 5.85 (s, OH), 7.5—8.2 (m, H-arom.)
(2e)	OCH_3	H	H	99	82 (ethyl acetate)	1195	1.6—2.8 (m, H-2, 5), 3.71 (d, ^3J = 11, OCH_3), 4.0—4.7 (m, H-3, 4), 5.40 (s, broad, OH)
(2f$_1$) [e]	OCH_3	CH_3	CH_3	95	183 (2-propanol)	1205	1.57 (d, ^4J = 2, CH_3-3), 1.79 (d, ^4J = 2, CH_3-4), 2.1—2.8 (m, H-2, 5), 3.75 (d, ^3J = 11, OCH_3), 5.4 (s, broad, OH)
(2f$_2$) [e]	OCH_3	CH_3	CH_3	95	159 (acetonitrile)	1195	1.55 (d, ^4J = 2, CH_3-3), 1.76 (d, ^4J = 2, CH_3-4), 2.1—2.8 (m, H-2, 5), 3.72 (d, ^3J = 11, OCH_3), 5.4 (s, broad, OH)
(3a$_1$) [f,g]	CH_3	H	H	99	120/1.3 × 10^{-5} [h] (82/6 × 10^{-5} [2b])	1150	1.65 (d, ^2J = 14, CH_3), 2.1—2.4 (m, H-2, 5), 3.67 (d, ^3J = 26, H-3, 4)
(3a$_2$) [f]	CH_3	H	H	99	120/1.3 × 10^{-5} [h]	1160	1.67 (d, ^2J = 14, CH_3), 2.1—2.5 (m, H-2, 5), 3.65 (d, ^3J = 25, H-3, 4)
(3b)	CH_3	CH_3	H	98	104—106/1.3 × 10^{-4}	1150	1.50 (s, CH_3-3), 1.61 (d, ^2J = 14, CH_3-1), 1.8—3.0 (m, H-2, 5), 3.40 (d, ^3J = 26, H-4)
(3c)	C_6H_5	H	H	98	109 (ethyl acetate)	1180	2.2—2.8 (m, H-2, 5), 3.80 (d, ^3J = 25, H-3, 4), 7.4—8.0 (m, H-arom.)
(3d$_1$)	C_6H_5	CH_3	H	97	143 (ethyl acetate)	1150, 1155	1.60 (s, CH_3), 2.1—2.8 (m, H-2, 5), 3.55 (d, ^3J = 26, H-4), 7.3—7.9 (m, H-arom.)
(3d$_2$)	C_6H_5	CH_3	H	98	89 (ether, −70 °C)	1150	1.60 (s, CH_3), 2.1—2.9 (m, H-2, 5), 3.60 (d, ^3J = 28, H-4), 7.4—8.1 (m, H-arom.)
(3e)	OCH_3	H	H	91	78/1.3 × 10^{-4}	1250	2.0—2.4 (m, H-2, 5), 3.65 (d, ^3J = 30, H-3, 4), 3.75 (d, ^3J = 11, OCH_3)
(3f$_1$) [g]	OCH_3	CH_3	CH_3	97	128/1.3 × 10^{-5}	1255	1.50 (d, ^4J = 1, CH_3-3, 4), 1.9—2.4 (m, H-2, 5), 3.70 (d, ^3J = 11, OCH_3)
(3f$_2$) [g]	OCH_3	CH_3	CH_3	93	130/1.3 × 10^{-5}	1250	1.46 (d, ^4J = 2, CH_3-3, 4), 1.9—2.6 (m, H-2, 5), 3.70 (d, ^3J = 11, OCH_3)

[a] Correct elemental analyses (C, H, Cl, P). [b] Correct elemental analyses (C, H, P). [c] *(2), (3c), (3d$_1$), (3d$_2$):* KBr pellet; *(3a$_1$), (3a$_2$), (3b), (3f$_1$), (3f$_2$):* nujol; *(3e):* film (NaCl). [d] Isomeric mixture. [e] Diastereomers separated by fractional crystallization; overall yields. [f] Isomers separated by preparative layer chromatography; overall yields. [g] Hygroscopic crystals after distillation. [h] Oven temperature on bulb-to-bulb distillation.

[*] Dr. F. Cavagna, Dr. U.-H. Felcht [+], Dr. E. F. Paulus
Hauptlaboratorium, Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

[+] Author to whom correspondence should be addressed.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0132 $ 02.50/0

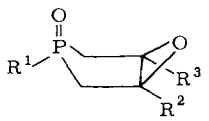
superior to previously known syntheses of such compounds[1b,2].

If during the chlorination of *(1)* in aqueous solution the pH is kept between 3 and 7 (see Experimental) then a maximum yield of the chlorohydrins *(2)* is obtained without formation of *(4)* being observed.

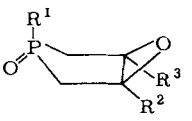
The arrangement of the substituents on C-3 and C-4 relative to the P=O group in the chlorohydrins *(2)* is decisive for the position of the epoxide ring in the epoxides *(3)*. Hence, an X-ray structure analysis was carried out on *(2f$_1$)*[3]. As shown in Figure 1 the hydroxy- and oxo groups are situated on the same side of the ring plane.

Diastereomeric mixtures of *(2)* lead also to diastereomeric mixtures of *(3)*, whereas use of the individual diastereomers [*(2d$_1$), (2d$_2$), (2f$_1$), (2f$_2$)*] affords in each case only one isomer of *(3)*[4]. In the case of *(3a)* the isomers could be separated by preparative layer chromatography[5]. Basically, two configurational isomers (A and B) are conceivable[6].

Isomer A



Isomer B



The structural assignment of the two pairs of isomers *(3a$_1$)/(3a$_2$)* and *(3d$_1$)/(3d$_2$)* must however still remain open[7], whereas in the case of the epoxides *(3f$_1$)/(3f$_2$)* an assignment of conformation is possible by X-ray structure analysis of *(2f$_1$)*; *(2f$_1$)* ought to afford *(3f$_1$)* as isomer A, while *(2f$_2$)* ought to give *(3f$_2$)* as isomer B[6].

Experimental

(2): Chlorine (0.5 mol) is passed into a stirred solution of *(1)* (0.5 mol) in water (180 ml) at 20—25 °C with external cooling and with simultaneous dropwise addition of a solution of sodium carbonate (0.25 mol) in water (100 ml) such that the pH of the mixture is kept between 3 and 7. The mixture is then neutralized, water removed at 40 °C/1.6 × 10^{-2} bar, and the residue stirred with 100 ml CH_2Cl_2. Filtration followed by removal of solvent at 30 °C/1.0 × 10^{-2} bar affords *(2)* as colorless crystals.

(3)[8]: A solution of sodium hydroxide (0.5 mol) in water (50 ml) is added dropwise to a stirred and externally cooled solution of *(2)* (0.5 mol) in water 150 ml. After 15 min the mixture is neutralized and worked-up as in the case of *(2)*. Thin-layer chromatographically homogeneous *(3)* is obtained as a colorless oil or crystals.

Received: November 23, 1979 [Z 379 IE]
German version: Angew. Chem. 92, 127 (1980)

[1] a) *B. A. Arbuzov, A. P. Rakov, A. O. Vizel, L. A. Shapshinskaya, N. P. Kulikova*, Izv. Akad. Nauk SSSR (Engl.) *1968*, 2079; b) *ibid. 1968*, 1237.

[2] a) *D. G. Smith, D. J. H. Smith*, Tetrahedron Lett. *1973*, 1249; b) *C. Symmes, L. D. Quin, ibid. 1976*, 1853; c) *B. A. Arbuzov, L. A. Shapshinskaya, A. P. Rakov, A. O. Vizel, N. P. Kulikova*, USSR-Pat. 212258 (1968).

[3] On crystallization from 2-propanol, *(2f$_1$)* forms triclinic crystals; space group P$\bar{1}$, $a = 10.247(2)$, $b = 8.423(2)$, $c = 5.846(2)$ Å, $\alpha = 82.56(2)$, $\beta = 89.37(2)$, $\gamma = 79.93(2)°$; $Z = 2$; the cell constants were determined fully automatically (*D. Kobelt, E. F. Paulus*, Siemens Power Eng. 1, 269 (1979); 1914 independent reflections (computer-controlled Siemens single-crystal diffractometer, $\theta_{max} = 28°$, $Mo_{K\alpha}$), refinement to $R_1 = 0.0412$, $R_2 = 0.0278$ (*D. Kobelt, E. F. Paulus:* Sexray, Program system for single crystal X-ray structure analysis, Hoechst AG (1970); *P. Main, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq, M. M. Woolfson:* Multan '78. University of York 1978).

[4] In the epoxidation of *(1)* with peroxy acids, however, apart from in the case of *(3)*, $R^1 = OC_6H_5$, R^2, $R^3 = CH_3$, only the isomer is obtained [1b].

[5] PLC plates (Merck 60 F 254), fivefold development with ethanol/ethyl acetate 1:9, extraction of the solid phase with CH_2Cl_2. Charge 400 mg/plate (20 × 40 cm).

[6] Without taking into account all possible conformations.

[7] Though the ^{1}H- and ^{13}C-NMR data of *(3a$_1$)* and *(3a$_2$)* agree with those quoted in *(2b)* their assignment would seem to us to remain uncertain without considering all the possible conformations.

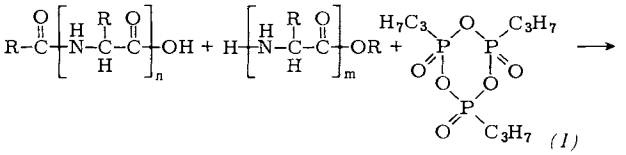
[8] *(2)* does not need to be isolated in the synthesis of *(3)* from *(1)*.

New Peptide Synthesis

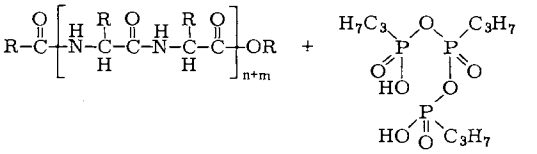
By *Hans Wissmann* and *Hanss-Jerg Kleiner*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

We wish to report on a novel peptide synthesis using alkylphosphonic anhydrides such as *(1)* as condensation agents. In contrast to the analogous phosphorus compounds used previously[1], the alkylphosphonic anhydrides have the following advantages: simple preparation, long shelf-stability at room temperature, very good solubility in all solvents employed in peptide synthesis, little tendency to racemization.



(1)



One advantage over the convenient and stable dicyclohexylcarbodiimide lies in the fact that no difficultly soluble secondary products of the new condensation agent occur; the resulting alkylphosphonic acid derivative is also soluble in water. Moreover, the well-known allergenicity of dicyclohexylcarbodiimide should not be forgotten[2].

With regard to the yield and degree of racemization the new method has so far proven just as good as, and in certain cases superior to, the improved dicyclohexylcarbodiimide technique (see Table 1). Of the alkylphosphonic anhydrides it would seem that propylphosphonic anhydride[3] is especially suitable owing to its favorable solubility properties and also because of its ready accessibility from commercially available starting materials. The alkylphosphonic anhydrides can be prepared by well-established methods[4]. Thermal dehydration of the alkylphosphonic acids also leads to the anhydrides[5] in good yields. Propylphosphonic anhydride is up to more than 50-wt.% soluble in dichloromethane, dioxane, tetrahydrofuran, and dimethylformamide. The lipophilicity of the alkylphosphonic anhydrides increases with increasing length of the alkyl chain. While crystalline methylphosphonic anhydride shows satisfactory solubility only in dimethylformamide and dimethyl sulfoxide, the non-crystalline higher homologs are also soluble in much less polar solvents. Thus, *n*-hexylphosphonic anhydride is even soluble in *n*-hexane.

[*] Dr. H. Wissmann, Dr. H.-J. Kleiner
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

According to experimental observations made thus far, propylphosphonic anhydride is at least a "trimer". During the course of peptide synthesis anhydride bonds are opened, yielding alkylpyrophosphonic acid groups. Further cleavage apparently proceeds very slowly under the conditions of peptide synthesis. For peptide synthesis, the reagent is best used in twofold excess with respect to the reactive anhydride bonds. Moreover, the excess of alkylphosphonic anhydride has a good solvating action. During the synthesis, free acid groups are buffered with a tertiary base, *e.g. N*-ethylmorpholine. The components used in the peptide synthesis should be adequately cooled (0—5 °C) during mixing; as a rule the reaction time amounts to 24 h at room temperature (see Experimental).

Table 1. Examples of syntheses. The arrow in the tripeptides and higher peptides indicates the coupling site. DMF = dimethylformamide. Eoc = ethoxycarbonyl

Peptide derivative	M.p. [°C]	$[\alpha]_D$ [°] $c=1$	Yield [%]
Z-Gly-Gly-OEt	82	—	80
Z-Asp-(OBu^t)-Phe-NH_2	162	−33.9 (EtOH)	85
	158.5—159 [6]	−30.7 (EtOH) [6]	94 [6]
Boc-Met-Gly-OEt	55	−15.4 (DMF)	93
Boc-Trp-Met-OMe	62	−24.8 (DMF)	96
Z-Phe-Gly-OEt	109	−17 (EtOH) [a]	86
	109—110 [7]	−16 (EtOH) [a] [7]	53 [7]
Z-Trp-Ser-OMe	71	− 9.9 (MeOH)	96
		−20.5 (DMF)	
Z-Gly-Phe↓-Gly-OEt	118—119	−11.9 (EtOH) [a]	99
	119 [8]	−11.6 (EtOH) [a] [8]	76 [8]
Z-Val-Tyr(Bu^t)↓-His-OMe	189—190	− 8.2 (DMF)	76
Z-(D)-Phe↓-Phe-His-OMe	214	−20.9 (DMF)	71
Z-Gly↓-Thr(Bu^t)-Phe-OMe	95	+26.2 (DMF)	78
Boc-Tyr(Eoc)↓-Met-Gly-OEt	137	−10.6 (DMF)	84
Z-Pro-Ala↓-Lys(Boc)-Phe-NH_2	163	−27 (DMF)	87
Z-Ala-Tyr(Bu^t)-Gly↓-Val-Tyr(Bu^t)-OMe	182	−18.2 (DMF)	93

[a] $c=2$.

Table 1 shows the results comparable with those cited in the literature and the, in part, considerably improved yields. The racemization model peptide described by *Anderson et al.*[8] was isolated in good yield and in higher optical purity. No DL-peptide could be obtained on recrystallization from ethanol.

Experimental

Propylphosphonic anhydride: Distilled water (85 g) is added dropwise with stirring to 760 g (588 ml) of *n*-propylphosphonic dichloride. At first the temperature rapidly increases to 40 °C. The water is then so added that the temperature remains constant. Complete addition of the water requires about 2.5 h. At the same time hydrogen chloride escapes *via* a highly-efficient condenser. After addition of water is complete a tube of calcium chloride is attached to the condenser and stirring is continued for 1 h, then 3 h at 80 °C/17 torr, and 3 h at 80 °C/5 torr. There remains 500 g of propylphosphonic anhydride (100%); b.p. 200 °C/0.3 torr, chlorine content < 0.1%. The colorless, water-clear, syrupy anhydride can be distilled in a high vacuum, but is also sufficiently pure for use in peptide synthesis without distillation. A 50% solution of the anhydride can be stored in a brown bottle for several months.

Peptide synthesis: *N*-Ethylmorpholine (60 ml) is added at 0 °C to a solution or suspension of 0.1 mol each of amino component (*e.g.* amino acid or peptide ester hydrochloride) and carboxyl component (*e.g.* benzyloxycarbonylamino acid or -peptide) in dimethylformamide. A 50 wt-% solution (88 g) of propylphosphonic anhydride in dichloromethane is then added with stirring to the cooled (0—20 °C) mixture. After one hours' further stirring the mixture is allowed to stand at room temperature for 24 h before the solvent is removed by distillation in a vacuum at or just above room temperature. For isolation of the peptide derivative the reaction product is digested with saturated sodium hydrogen carbonate solution, filtered and the product washed thoroughly with water and 10% citric acid solution or taken up in ethyl acetate and washed several times with water, sodium hydrogen carbonate solution and 5% potassium hydrogen sulfate. Finally, the ethyl acetate solution is dried over magnesium sulfate and the peptide derivative isolated by concentration of the solution and precipitation with ether or petroleum ether.

Received: November 23, 1979 [Z 385 IE]
German version: Angew. Chem. *92*, 129 (1980)

[1] *E. Wünsch* in Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit. Thieme, Stuttgart 1974, Vol. XV/2, p. 226ff.
[2] *J. M. Stewart, J. D. Young* in: Solid Phase Peptide Synthesis. Freeman, San Francisco 1969, p. 24/25, p. 39.
[3] Riedel-de-Haën AG, Article No. 65183.
[4] *K. Sasse* in Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit. Thieme, Stuttgart 1973, Vol. 12/1, p. 612/613.
[5] *H. J. Kleiner, W. Dürsch*, DOS 2811628 (1979), Hoechst.
[6] *E. Wünsch, K. H. Deimer*, Hoppe Seylers Z. Physiol. Chem. *353*, 1246 (1972).
[7] *G. W. Anderson, R. W. Young*, J. Am. Chem. Soc. *74*, 5307 (1952).
[8] *G. W. Anderson, F. M. Callahan*, J. Am. Chem. Soc. *80*, 2902 (1958).

Stereocontrolled Intramolecular Diels-Alder Reaction of Heterodienes; Studies on the Synthesis of Cannabinoids[**]

By *Lutz-F. Tietze, Günter von Kiedrowski, Klaus Harms, William Clegg,* and *George Sheldrick*[*]

In recent years the intramolecular Diels-Alder reaction of 1,3-dienes has been most successfully applied to the stereoselective synthesis of natural products[1]. To our knowledge, however, the heteroanalogous variant[2] using α,β-unsaturated carbonyl compounds has not yet been described, although the intermolecular reaction has long been used in the preparation of dihydropyran derivatives[3].

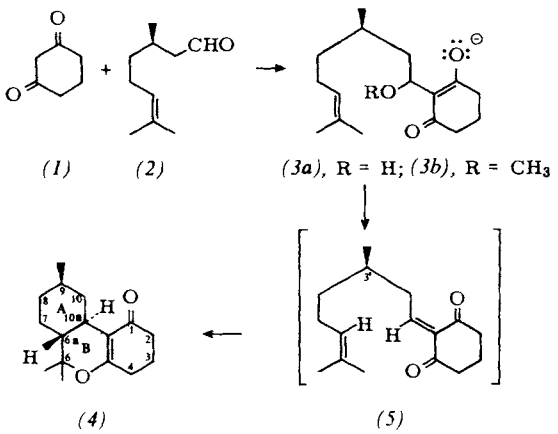
We now wish to describe the synthesis of the tricyclic dihydropyran *(4)*, in which a 100% stereocontrolled intramolecular Diels-Alder reaction of the intermediate α,β-unsaturated ketone *(5)* can be assumed as key step. Having the (*R*)-configuration at C-6a and *trans* linkage of rings A and B, compound *(4)* corresponds to the parent skeleton of tetrahydrocannabinol[4].

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. G. von Kiedrowski
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)
Prof. Dr. G. Sheldrick, Dr. W. Clegg, K. Harms
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We wish to thank Prof. Dr. *D. Leibfritz* and Dr. *M. Feigl*, Universität Bremen, for recording the 360-MHz ^{1}H-NMR spectrum and the Dragoco Company, Holzminden, for supplying citronellal.

In order to synthesize *(4)*, 1,3-cyclohexanedione *(1)* was transformed by sodium methoxide into the enolate and treated as such with (*R*)-citronellal *(2)* ($[\alpha]_D^{20} = 14.9°$ ($c = 1$, $CHCl_3$)) according to the method of *Polansky et al.*[5].

Initial formation of the enolate *(3a)* can be assumed; it does not react further under these conditions. Formation of a methyl ether *(3b)* as is observed in similar systems[5] could not be detected by NMR spectroscopy. Acid work-up led, after chromatography on silica gel, distillation, and recrystallization, to a 33% yield of *(4)* (m.p. 90 °C, $[\alpha]_D^{20} = 291.5°$ ($c = 1$, $CHCl_3$)).



(1) *(2)* *(3a)*, R = H; *(3b)*, R = CH_3

(4) *(5)*

Isolation of the ketone *(5)* was impossible. This accords with an estimate of the energies of the LUMO and the HOMO of the heterodiene and the dienophile, which suggests the occurrence of a fast reaction corresponding to a Diels-Alder reaction with inverse electron demand[6].

In addition to *(4)*, condensation products of citronellal *(2)* could also be isolated. However, no diastereomers of *(4)* were detected. It can thus be deduced that complete control by the chiral center of the reactant citronellal *(2)* is operative in the transition state of cycloaddition of *(5)*. Owing to the *trans* linkage of the rings A and B in *(4)*, it must also be assumed that the *exo* transition state is energetically more favorable than the *endo* transition state[7]. Thus molecular models show that minimum steric interaction is to be expected in the *exo* transition state with pseudo-chair-shaped arrangement of the carbon chain and pseudo-equatorial orientation of the methyl group on C-3'.

The structure and configuration of *(4)* were established by analysis of a 360-MHz ^{1}H-NMR spectrum[8] and by X-ray structure analysis[9] (Fig. 1).

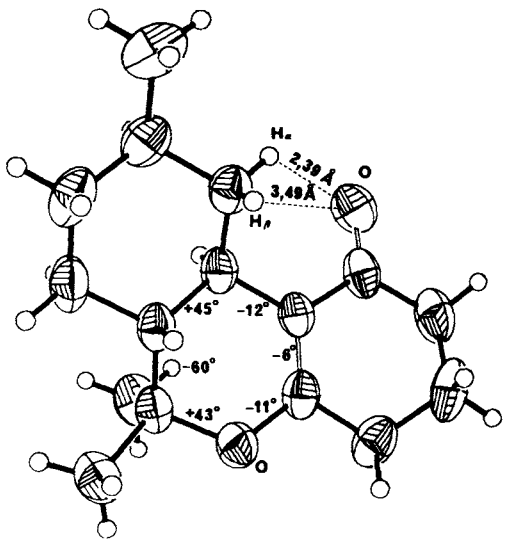


Fig. 1. Structure of compound *(4)* with thermal ellipsoids (50% probability) for C and O. *(4)* crystallizes in the monoclinic space group $P2_1/n$, $a = 11.907(3)$, $b = 8.094(2)$, $c = 14.868(5)$ Å, $\beta = 90.03(5)°$, $V = 1432.9$ Å^3, $Z = 4$, $\rho_{calc.} = 1.152$ g cm^{-3}, $\mu = 0.7$ cm^{-1} ($Mo_{K\alpha}$). Structure solved from diffractometer data by direct methods, refinement (C and O anisotropic, H isotropic, fixed C H bond lengths) gave $R = 0.063$ for 1487 reflections with $F > 4\sigma(F)$. The torsion angles in ring B and the distances from the carbonyl oxygen to 10α-H and 10β-H are shown.

Procedure

(4): A solution of *(1)* (2.00 g, 17.9 mmol) and freshly prepared sodium methoxide (997 mg, 17.9 mmol) in anhydrous methanol (70 ml) was added dropwise over 30 min at 0 °C to (*R*)-citronellal *(2)* (10 ml, 8.59 g, 50.5 mmol) in anhydrous methanol (70 ml). The mixture was then stirred for 1 h at 20 °C, evaporated down *in vacuo*, and the residue extracted with dichloromethane (30 ml) to remove excess *(2)*. The remaining slime (sodium salt) was shaken with dichloromethane (150 ml) and 1 N HCl, the organic phase washed with water, dried, and after evaporation of the solvent chromatographed on silica gel (light petroleum/ether (1:1)). Bulb-to-bulb distillation (150 °C) of the major fraction ($R_F = 0.40$) and recrystallization from diisopropyl ether/light petroleum gave 1.47 g (33%) of colorless platelets.

Received: October 8, 1979 [Z 386 IE]
German version: Angew. Chem. 92, 130 (1980)

CAS Registry numbers:
(1), 504-02-4; *(2)*, 2385-77-5; *(4)*, 72785-03-6

[1] *W. Oppolzer*, Angew. Chem. *89*, 10 (1977); Angew. Chem. Int. Ed. Engl. *16*, 10 (1977).

[2] An intramolecular Diels-Alder reaction with 4,6-dihydroxypyrimidine as heterodiene has already been described: *P. G. Sommer, R. A. Watt*, J. Chem. Soc. Chem. Commun. *1975*, 502.

[3] *J. Sauer*, Angew. Chem. *79*, 76 (1967); Angew. Chem. Int. Ed. Engl. *6*, 16 (1967); *L.-F. Tietze*, Chem. Ber. *107*, 2491 (1974), and references cited therein.

[4] *R. Mechoulam, N. K. McCallum, S. Burstein*, Chem. Rev. *76*, 75 (1976).

[5] *P. Margaretha, O. E. Polansky*, Monatsh. Chem. *101*, 824 (1970).

[6] *R. Sustmann*, Pure Appl. Chem. *40*, 569 (1975); *K. N. Houk, R. W. Strozier*, J. Am. Chem. Soc. *95*, 4094 (1973); cf. also *I. Fleming:* Grenzorbitale und Reaktionen organischer Verbindungen. Verlag Chemie, Weinheim 1979.

[7] Cf. *R. L. Funk, K. P. C. Vollhardt*, J. Am. Chem. Soc. *99*, 5483 (1977), and references cited therein.

[8] The 100-MHz ^{1}H-NMR spectrum does not provide information about the configuration of the centers of chirality in *(4)*.—^{1}H-NMR (360 MHz, $CDCl_3$): $\delta = 2.79$ (ddt, $J_{10\alpha,10\beta} = 11.5$ Hz, $J_{10\alpha,9} = J_{10\alpha,10a} = 3.0$ Hz, $J_{10\alpha,8\alpha} = 1.7$ Hz, 10α-H), 2.43—2.16 (m, 2α, 2β, 4α, 4β-H), 2.09 (tdd, $J_{10a,10\beta} = J_{10a,6a} = 11.5$ Hz, $J_{10a,10\alpha} = 3.0$ Hz, $J_{10a,4\alpha} = 2.0$ Hz, 10a-H), 1.94—1.84 (m, 3α, 3β-H), 1.84—1.76 (m, 8α-H), 1.76—1.70 (m, 7β-H), 1.60—1.50 (m, 9-H), 1.33 (s, 6-CH_3), 1.26 (dt, $J_{6a,7\alpha} = J_{6a,10a} = 11.5$ Hz, $J_{6a,7\beta} = 2.5$ Hz, 6a-H), 1.04 (s, 6-CH_3), 0.94—1.13 (m, 7α, 8β-H), 0.90 (d, $J = 6.5$ Hz, 9-CH_3), 0.49 (q, $J_{10\beta,10\alpha} = J_{10\beta,9} = J_{10\beta,10a} = 11.5$ Hz, 10β-H).

[9] X-ray structure analysis was performed on (±)-*(4)*, prepared from (±)-citronellal and *(1)*. The absolute configuration of *(4)* follows from the chirality in reactant *(2)*.—We have deposited the atomic coordinates and other crystallographic data at the Cambridge Data Centre (England).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0202-0135 $ 02.50/0*

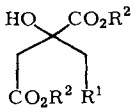
(3*R,S*)-3,4-Dicarboxy-3-hydroxybutyl Coenzyme A, an Inhibitor of the Citrate Synthase Reaction

By *Hermann Eggerer, Walter Giesemann,* and *Horst Aigner*[*]

The enzyme citrate synthase of the tricarboxylic acid cycle catalyzes the formation of citrate and coenzyme A from acetyl CoA and oxalacetate[1]. It also catalyzes the hydrolysis of (3*S*)-citryl CoA to the products and the cleavage of (3*S*)-citryl CoA to the reactants of the overall reaction[2], as well as the methyl-activation of acetyl CoA[3]. However, the question whether (3*S*)-citryl CoA is formed as genuine intermediate on the synthase, as has been demonstrated for the enzyme citrate lyase[4], is still unclear. Also unclear is the nature of the active centers of the identical subunits of the dimeric enzyme[5].

In order to contribute to the solution of these ambiguities, we have synthesized the title compound *(5)* as an intermediate analog suitable for enzymological and crystallographic investigations. In *(5)* the carbonyl group of citryl CoA attached to sulfur is replaced by a methylene group, so that besides chemical stability also high affinity to the enzyme can be expected.

The alkylating agent (*RS*)-2-(2-bromomethyl)-2-hydroxybutane required for formation of the alkyl thioether *(5)* was obtained from (*R,S*)-*S*-citryl-*N*-octanoylcysteamine *(1)*[6] by reduction with $NaBH_4$ to (*R,S*)-2-hydroxy-2-(2-hydroxyethyl)butanedioic acid *(2)*, esterification, and subsequent bromination. Reaction of *(3)* with coenzyme A afforded the dimethyl ester *(4)*, which on mild alkaline hydrolysis gave *(5)*. The structure of the compounds *(2)*—*(5)* is confirmed by elemental analysis and by spectroscopic and chromatographic data.



(1), $R^1 = CO{-}S(CH_2)_2NHCO(CH_2)_6CH_3$, $R^2 = H$
(2), $R^1 = CH_2OH$, $R^2 = H$
(3), $R^1 = CH_2Br$, $R^2 = CH_3$
(4), $R^1 = CH_2SCoA$, $R^2 = CH_3$
(5), $R^1 = CH_2SCoA$, $R^2 = H$

Simple alkylthio CoA compounds[7], *inter alia* the ethylthio-CoA first described[8] after completion of our work, have been prepared in order to check the influence of the substituents in *(5)* on the interaction with the enzyme. Further alkyl thioethers analogous to acetyl CoA have recently been reported[9].

According to kinetic measurements *(5)* is a strong noncompetitive inhibitor of the overall reaction between acetyl CoA and oxalacetate and a strong competitive inhibitor of the cleavage and hydrolysis of (3*S*)-citryl CoA. An X-ray structure analysis of the complex of *(5)* with the monoclinic form of the citrate synthase[5] is in progress[10].

Received: October 15, 1979 [Z 389 IE]
German version: Angew. Chem. *92*, 133 (1980)

[*] Prof. Dr. H. Eggerer, Dipl.-Chem. W. Giesemann, H. Aigner
Physiologisch-Chemisches Institut der Technischen Universität
Biedersteiner Str. 29, D-8000 München 40 (Germany)

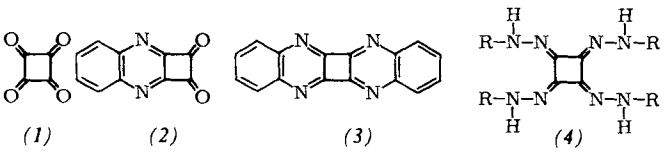
[1] *J. R. Stern, S. Ochoa, F. Lynen*, J. Biol. Chem. *198*, 313 (1952).
[2] *H. Eggerer, U. Remberger*, Biochem. Z. *337*, 202 (1963).
[3] *H. Eggerer*, Biochem. Z. *334*, 111 (1965).
[4] *W. Buckel, K. Ziegert, H. Eggerer*, Eur. J. Biochem. *37*, 295 (1973); *P. Dimroth, H. Eggerer*, Proc. Nat. Acad. Sci. USA *72*, 3458 (1975).
[5] *G. Wiegand, D. Kukla, H. Scholze, T. A. Jones, R. Huber*, Eur. J. Biochem. *93*, 41 (1979).
[6] *H. Eggerer*, Justus Liebigs Ann. Chem. *666*, 192 (1963).
[7] *E. Bayer*, planned Dissertation, Technische Universität München, 1980.
[8] *H. P. Blaschkowski, J. Knappe, Th. Wieland*, FEBS Lett. *98*, 81 (1979).
[9] *M. S. Owens, R. E. Barden*, Arch. Biochem. Biophys. *187*, 875 (1978); *K. K. Yabusaki, C. E. Ballou*, Biochemistry *17*, 875 (1978).
[10] *G. Wiegand, R. Huber*, private communication.

Tetrakis(phenylimino)cyclobutane (Tetrameric Phenyl Isocyanide)

By *Hans Jürgen Bestmann, Günter Schmid,* and *Eberhard Wilhelm*[*]

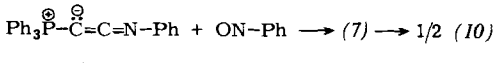
Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

All previous attempts to prepare cyclobutanetetraone *(1)* (tetrameric carbon monoxide) have so far failed; only its tetrahydrate could be isolated[1]. *Hünig et al.* succeeded in synthesizing the bis- and tetrakis-imino compounds *(2)* and *(3)*[2], while *Seitz et al.* have reported the preparation of the tetrahydrazones *(4)*[3].



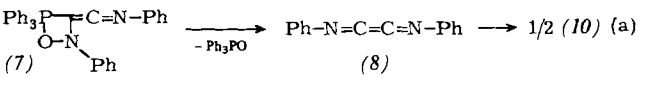
(1) *(2)* *(3)* *(4)*

We have now found a simple entry to tetrakis(phenylimino)cyclobutane *(10)* (tetrameric phenyl isocyanide). Reaction of equimolar amounts of (phenyliminovinylidene)triphenylphosphorane *(5)*[4] and nitrosobenzene *(6)* in benzene at room temperature affords red-violet crystals of *(10)*, m.p. 181 °C, in 53% yield.

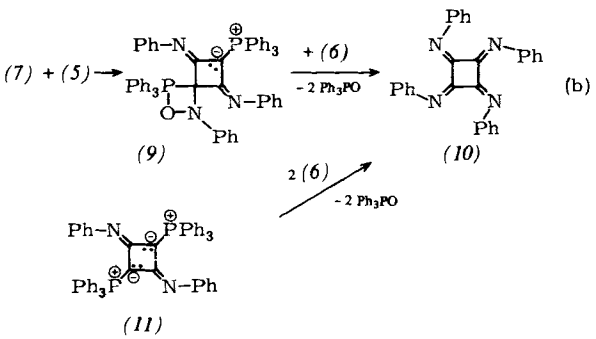


(5) *(6)*

We propose two possible reaction paths (a and b), but as yet we are unable to distinguish between the pair of them. Path a: *(5)* and *(6)* unite to form the cyclic phosphorane *(7)*, which on elimination of triphenylphosphane oxide is converted into the "dimeric isocyanide" *(8)*. *(8)* dimerizes to



(7) *(8)* (a)



(9) *(10)* (b)

(11)

[*] Prof. Dr. H. J. Bestmann, Dr. G. Schmid, Dr. E. Wilhelm
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0136 $ 02.50/0

(10). Path b: *(7)* undergoes cycloaddition with *(5)* to give *(9)*, which on reaction with *(6)* loses phosphane oxide with formation of *(10)*. We could also prepare *(10)* by reaction of the "dimer" of *(5)*, namely *(11)*[5], with *(6)*.

X-ray structure analysis provides proof of the structure of *(10)* (cf. Fig. 1). Several geometric isomers of *(10)* are possible having variously arranged phenyl groups. However, only the isomer with substituents oriented in the same direction crystallizes[6]. From the bond lengths, the exocyclic bonds can be regarded as pure C=N double bonds; other than in *(3)*, there is no double bond component in the ring[8]. N2 deviates by +21.3 pm, N1 by only +4.7 pm, from the plane of the four-membered ring; the phenyl C-atoms C9 and C3, on the other hand, deviate by +29.6 and −14.9 pm, respectively, from the plane of the ring. The sum of the angles at C1 is 360°, and at C2 358.4°. The two phenyl groups are inclined to the plane of the four-membered ring; the phenyl ring I at 59°, and phenyl ring II at 46°.

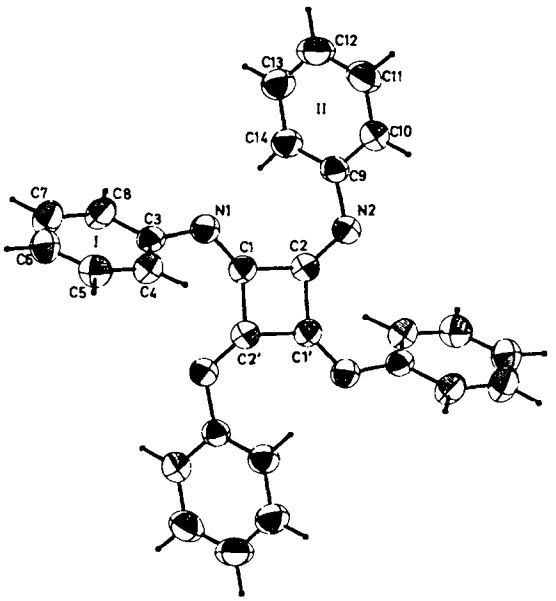
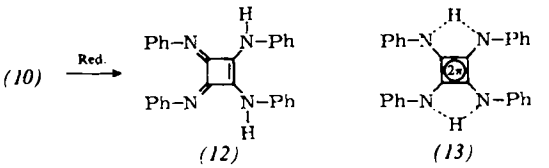


Fig. 1. Molecular structure of *(10)* in the crystal [6, 7]. Selected bond lengths [pm] and angles [°]: C1 C2 150.5, C2 C1' 150.6, C1 N1 127.0, C2 N2 127.7, N1 C3 141.6, N2 C9 141.7; C2' C1 C2 90, C1 C2 C1' 90, C2' C1 N1 131.4, C1' C2 N2 138.3, C2 C1 N1 138.6, C1 C2 N2 130.1, C1 N1 C3 122.0, C2 N2 C9 120.4.

The ^{13}C-NMR spectrum (in CD_3NO_2, TMS internal) of *(10)* shows five signals [δ = 148.18 (C=N), 130.02, 129.42, 124.50, 121.41 (arom. C)], which appear as sharp lines at 70 °C but considerably broaden on cooling. A splitting could not be achieved below 0 °C owing to sparing solubility. We attribute the temperature-dependence to a to-and-fro vibration of the phenyl groups.— In the EI mass spectrum a stepwise fragmentation of phenyl isocyanide is observed [*m/e* = 412 (M^+), 309 ($M^+ - 103$), 206 ($M^+ - 206$), 103].— UV (CH_2Cl_2): $\lambda_1 = 244$ ($\varepsilon = 3.1 \times 10^4$), $\lambda_2 = 433$ nm (1.7×10^4).

Compound *(10)* proves to be a strong oxidizing agent; for example it oxidizes hydroquinone to quinone and primary alcohols to the corresponding aldehydes. *(10)* is thereby reduced to *(12)*. Reaction of *(10)* with phenylhydrazine also leads *via* elimination of nitrogen to *(12)* (yellow crystals, m.p. 100 °C). *(12)* is the first squaric acid amidine in which the four N atoms are not ring members[2]. IR and Raman spectra[9] are consistent with the amidine structure *(12)* in the crystal. *(12)* forms intra- and intermolecular hydrogen bridges; its ^{13}C-NMR is therefore solvent-dependent. In $CDCl_3$ a spectrum very rich in lines is obtained, indicating the presence of several geometric isomers and tautomeric forms. In nitromethane, however, only five signals are observed (δ = 153.83, 145.53, 129.93, 124.37, 121.63) (TMS internal). This finding indicates the equivalence of all four C···N C_6H_5 units, as would arise by complete delocalization of the NH protons by intra- or intermolecular hydrogen bonding. Formula *(13)* represents one possibility.



The phenylamino groups in *(12)* can be replaced by phenylhydrazine. In contrast to the extremely stable *(12)* the reaction products, so far unobtainable in pure form, undergo autoxidation and form structural analogues of *(3)* and *(4)*.

Received: November 2, 1979 [Z 387 IE]
German version: Angew. Chem. *92*, 134 (1980)

CAS Registry numbers:
(5) charged form, 64448-06-2; *(5)* uncharged form, 21385-80-8; *(6)*, 586-96-9; *(7)*, 72784-69-1; *(8)*, 72784-70-4; *(9)*, charged form, 72784-71-5; *(9)* uncharged form, 72784-72-6; *(10)*, 72784-73-7; *(11)* charged form, 72784-74-8; *(11)* uncharged form, 62085-97-6; *(12)*, 72784-75-9

[1] *S. Skujins, J. Delderfield, G. A. Webb*, Tetrahedron *24*, 4805 (1968); *R. West, H. Y. Niu, M. Ito*, J. Am. Chem. Soc. *85*, 2584 (1963).
[2] *S. Hünig, H. Putter*, Angew. Chem. *84*, 481 (1972); *85*, 143 (1973); Angew. Chem. Int. Ed. Engl. *11*, 431 (1972); *12*, 149 (1973); Chem. Ber. *110*, 2524, 2532 (1977).
[3] *E. Seitz, R. Matusch, K. Mann*, Chem.-Ztg. *101*, 557 (1977).
[4] *H. J. Bestmann, G. Schmid*, Angew. Chem. *86*, 274 (1974); Angew. Chem. Int. Ed. Engl. *13*, 273 (1974).
[5] *H. J. Bestmann, G. Schmid, D. Sandmeier, L. Kisielowski*, Angew. Chem. *89*, 275 (1977); Angew. Chem. Int. Ed. Engl. *16*, 268 (1977).
[6] *(10)*, orthorhombic crystals from *tert*-butanol/acetone, space group Pbca-D_{2h}^{15}, $a = 1163.1$, $b = 887.7$, $c = 2052.8$ pm, $Z = 4$, $\rho_{calc} = 1.29$ g/cm^3, 1309 independent reflections from 5581 measurements. From $Z = 4$ it follows that each molecule in the unit cell occupies a special position and thus must be centrosymmetric. The structure was solved and refined to $R = 0.043$ using the program system "CRYSTAN" [7].
[7] *H. Burzlaff, R. Bohme, M. Gomm*: CRYSTAN, a crystallographic programme system for minicomputers (1977). Institut für Angew. Physik, Lehrstuhl für Kristallographie, Loewenichstr. 22, D-8520 Erlangen, Germany. We thank Prof. Dr. *H. Burzlaff* for placing the program and computer PDP 11/45 at our disposal.
[8] *R. Allmann*, Crystal Struct. Commun. *3*, 47 (1974).
[9] IR (KBr): broad band between 3600 and 2800 cm^{-1} with distinguishable absorptions at 3130 and 3360 cm^{-1}; strong bands in the amidine region at 1640, 1590 and 1500 cm^{-1}. Raman spectrum (solid): 1619, 1558 (C=N), 1601 cm^{-1} (C=C); MS: *m/e* = 414 (M^+), 311 (M^+ − PhNC), 310 (M^+ − PhNHC), 208, 207.

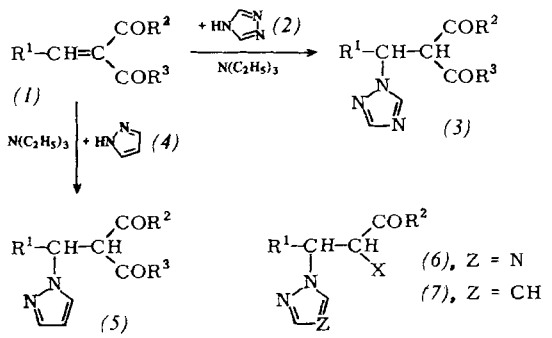
β-Azolyl-α,α-dicarbonyl Compounds

By *Thomas Maier* and *Hilmar Mildenberger*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

1,2,4-Triazole *(2)* and pyrazole *(4)* add with surprising ease to α,β-unsaturated α,α-dicarbonyl compounds *(1)*. Spontaneous, weakly exothermal reaction affords the hitherto unknown stable β-azolyl-α,α-dicarbonyl compounds *(3)* and *(5)* which precipitate from the reaction mixture in generally quantitative yield and high purity. A basic catalyst such as triethylamine is of advantage. The "heteroderivatives" *(6)* and *(7)* are accessible in similar manner.

[*] Dr. Th. Maier [*], Dr. H. Mildenberger
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)
[*] To whom correspondence should be addressed.



Tetrachlorovinylcarbene from Tetrachlorocyclopropene; Facile Synthesis of Vinylcyclopropanes[**]

By *Walter Weber* and *Armin de Meijere*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

The Diels-Alder reactivity of tetrachlorocyclopropene *(1)* with 1,3-dienes is sufficiently well known[1]. However, apparently no investigations have hitherto been carried out to check whether *(1)* is also capable of undergoing cycloadditions with monoolefins analogously to the highly fluorinated and chlorinated ethylenes[2]. We report here on a series of such experiments and their unexpected results.

Table 1. Compounds *(3)* and *(5)*, as well as *(6)* and *(7)*, synthesized. Correct elemental analyses and appropriate NMR spectra were obtained for all compounds [a].

	R^1	R^2	R^3	Solvent	*(3)* M.p. [°C]	*(5)* M.p. [°C]
a	n-C_3H_7	CH_3O	CH_3O	Methanol	75—78	43—44
b	2-Thienyl	CH_3O	CH_3O	Methanol	125—127	95—97
c	C_6H_5	C_2H_5O	C_2H_5O	Ethanol	79—82	59—60
d	C_6H_5	CH_3O	4-Cl C_6H_4	Triethylamine	114—116	—
e	4-Cl C_6H_4	CH_3O	$(CH_3)_2N$	Trichloromethane	144—146	—
f	4-Cl C_6H_4	C_2H_5O	CH_3	Ethanol	87—90	70—72
g	C_6H_5	CH_3	CH_3	Triethylamine	90—92	97
h	CH_3O CO	CH_3O	CH_3	Methanol	114—118	—
	R^1	R^2	X	Solvent	*(6)* M.p. [°C]	*(7)* M.p. [°C]
a	4-CH_3 C_6H_4	C_2H_5O	$(C_2H_5O)_2PO$	Triethylamine	75—77	—
b	4-Cl C_6H_4	CH_3O	4-CH_3 $C_6H_4SO_2$	Trichloromethane	125—128	172—174
c	4-Cl C_6H_4	CH_3	4-CH_3 $C_6H_4SO_2$	Dichloromethane	148—151	—

[a] ^{1}H-NMR ($CDCl_3$): *(3a)*: δ = 8.15 (s, 1 H, triazole 5-H), 7.95 (s, 1 H, triazole 3-H), 4.9 (ddd, J = 10 and 10 and 4 Hz; 1 H, CH-β), 4.05 (d, J = 10 Hz, 1 H, CH-α), 3.8 (s, 3 H, OCH_3), 3.55 (s, 3 H, OCH_3), 2.5—1.35 (m, 2 H, CH_2), 1.35—0.75 (m, 5 H, C_2H_5). *(5a)*: δ = 7.55—7.4 (m, 2 H, pyrazole 3- and 5-H), 6.15 (t, J = 2.3 Hz, 1 H, pyrazole 4-H), 4.8 (ddd, J = 10 and 10 and 4 Hz, 1 H, CH-β), 4.1 (d, J = 10 Hz, 1 H, CH-α), 3.75 (s, 1 H, OCH_3), 3.5 (s, 1 H, OCH_3), 2.4—1.4 (m, 2 H, CH_2), 1.35—0.75 (m, 5 H, C_2H_5). *(3g)*: δ = 8.05 (s, 1 H, triazole 5-H), 7.9 (s, 1 H, triazole 3-H), 7.35 (mc, 5 H, aromatic H), 6.1 (d, J = 11.5 Hz, 1 H, CH-β), 5.25 (d, J = 11.5 Hz, 1 H, CH-α), 2.2 (s, 3 H, CH_3), 2.0 (s, 3 H, CH_3). *(5g)*: δ = 7.5—7.2 (m, 7 H, aromatic H and pyrazole 3- and 5-H), 6.15 (t, J = 2.3 Hz, 1 H, pyrazole 4-H), 6.0 (d, J = 10.5 Hz, 1 H, CH-β), 5.25 (d, J = 10.5 Hz, 1 H, CH-α), 2.2 (s, 3 H, CH_3), 2.0 (s, 3 H, CH_3).

Alcohols should be avoided as solvents for addition of *(2)* to α,β-unsaturated diketones such as *(1g)* because an acyl group can be eliminated under mild conditions.

Numerous triazole derivatives *(3)* and *(6)*, expecially *(3c)* and *(3g)*, have excellent fungicidal activity towards various mildews, while the pyrazole derivatives *(5)* and *(7)* are ineffective.

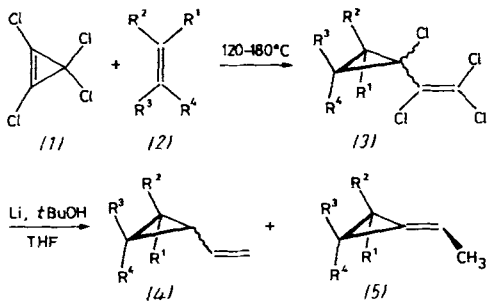
The imidazole derivatives corresponding to compounds *(3)* and *(5)* can be isolated as sparingly soluble components from the reaction mixtures but decompose upon dissolution in the solvents examined. Thus the half-life of a 6% (2%) solution of *(3g)*, imidazolyl in place of triazolyl, in chloroform is 7 min (40 min); the equilibrium lies 70% (90%) on the side of the reactants.

Procedure

(3c): A mixture of *(1c)* (74.4 g, 0.3 mol), 1,2,4-triazole *(2)* (20.7 g, 0.3 mol), triethylamine (40 ml), and ethanol (20 ml) is stirred for 20 h at room temperature. Crystallization occurs on scratching with a glass rod. The crystals are filtered off, washed with diisopropyl ether, and dried; yield 82 g, m.p. 79—82 °C. The concentrated mother liquor affords a further crop of 8.2 g, m.p. 79 °C. Overall yield: 90.2 g (95%).

Received: November 23, 1979 [Z 384 IE]
German version: Angew. Chem. 92, 128 (1980)

The first indication that *(1)* is capable of reacting with a monoolefin was provided by its reaction with bicyclopropylidene at 80 °C, in which it behaves formally as trichlorocyclopropenylium chloride to give a product of electrophilic addition[3]. Normal olefins *(2)*, however, were only attacked at 150—180 °C, and then in a completely different fashion. Thus, reaction of 2,3-dimethyl-2-butene *(2a)* with *(1)* for 12 h at 180 °C afforded 1-chloro-2,2,3,3-tetramethyl-



[*] Prof. Dr. A. de Meijere, Dipl.-Chem. W. Weber
Institut für Organische Chemie und Biochemie
der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13

[**] This work was supported by the Fonds der Chemischen Industrie, Hoechst AG, and the Hermann-Schlosser-Stiftung.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0138 $ 02.50/0

Table 1. Reaction of tetrachlorocyclopropene *(1)* with olefins *(2)* and reductive dehalogenation of the primary adducts *(3)* [4] to *(4)* and *(5)*. Yields referred to isolated compounds.

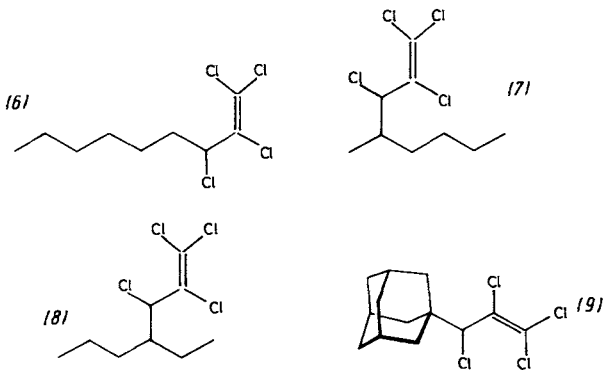
	Olefins *(2)*				Reaction conditions		Yield of *(3)*	Yield [%]	
	R^1	R^2	R^3	R^4	*t* [h]	*T* [°C]	[%] (*E*:*Z*)	*(4)*	*(5)*
a	Me	Me	Me	Me	12	180	82 (—)	43	8
b	Me	Me	Me	H	14	180	88 (1:4)	18 (*E*); 16 (*Z*)	7
c	Me	Me	H	H	8	180	24 (—)	— [a]	—
d	H	Me	Me	H	18	180	11 (*E*), 67 (*Z*)	22 (*E*); 18 (*Z*)	0 [b]
e	H	Me	H	Me	18	180	76 (—)	0 [c]	24
f	Et	Me	H	H	14	170	46 (?)	— [a]	—
g	H	Et	Et	H	16	180	61 (1:17)	42 (*E*); 15 (*Z*)	11
h	H	Et	H	Et	16	180	52 (—)	51	0
i	H	*n*Pr	H	H	18	180	79 (?)	16 (*E*); 17 (*Z*)	0 [b]
j	$(CH_2)_2$		H	H	168	120	21 (—)	— [a]	—
k	H	$(CH_2)_4$		H	72	150	66 (?)	17 (*E*); 17 (*Z*)	6
l	H	$(CH_2)_5$		H	12	180	64 (2:3)	24 (*E*); 20 (*Z*)	0
m	H	$(CH_2)_6$		H	12	180	73 (1:3)	34 (*E*); 18 (*Z*)	0 [b]
n	Me	$(CH_2)_4$		H	12	180	69 (1:3)	43 (*E*/*Z*)	17
o	Me	Me	H	CN	36	160	18 (?)	— [a]	—
p	Me	Me	H	CO_2Et	92	150	61 (?)	— [a]	—
q	Me	Me	H	CO_2tBu	24	170	64 [d] (1:6)	— [a]	—
r	H	Me	H	CO_2Et	10	180	66 (4:1)	— [a]	—
s	H	Me	H	CO_2tBu	12	180	64 [d] (4:1)	— [a]	—
t	H	Ph	H	CO_2Et	12	180	37 (4:9)	— [a]	—

[a] Reductive dehalogenation not investigated. [b] A further product was isolated but could not be unequivocally characterized. [c] For reasons still unclear only *(5e)* could be isolated. [d] The free vinylcyclopropanecarboxylic acids are formed from *tert*-butyl esters by acid-catalyzed elimination of isobutylene.

1-(trichlorovinyl)cyclopropane *(3a)* in 82% yield. Numerous examples show that this is a generalizable type of reaction (see Table 1). The method is also suitable for the preparation of substituted 2-(trichlorovinyl)cyclopropanecarboxylates and carboxylic acids[4] which are of interest as potential components in pyrethroid insecticides[5] [see Table 1, *(3p)*—*(3t)*]. The ^1H- and ^{13}C-NMR spectroscopic assignment of configuration was confirmed by an X-ray structure analysis[6] on *(Z)-(3q)*.

The ^1H-NMR spectra of the esters of *(3q)* show double signals at room temperature for most kinds of protons, which coalesce at higher temperatures (+40 to +90 °C in the case of the (*Z*)- and (*E*)-configurated methyl and benzyl esters). This phenomenon is indicative of an equilibrium between two conformers with an unusually high torsional barrier for vinylcyclopropanes[7]; from the coalescence temperatures, $\Delta G^{\neq}$ values of 77 kJ/mol and 74 kJ/mol, respectively, could be estimated for the (*E*)- and (*Z*)-configurated esters.

The finding that the configuration of the olefin moiety is retained in all adducts of *cis*- *(2d)* and *trans*-2-butene and of *cis*- *(2g)* and *trans*-3-hexene *(2h)* suggests that a vinylcarbene intermediate is first formed from *(1)*[8]; the high efficiency with which this intermediate can be intercepted intermolecularly to give vinylcyclopropanes[9] is most surprising. The formation of the by-product 1,1,2,3,3-pentachloropropene, which was found in varying relative amounts (2—20%) in almost all reactions of *(1)*, can also be explained in terms of intermediary tetrachlorovinylcarbene. Further conclusive evidence for the occurrence of this carbene is the observation that *(1)*, like dichlorocarbene[10], forms C—H insertion products with saturated hydrocarbons. Thus, reaction of *(1)* with *n*-hexane at 180 °C afforded the isomeric tetrachloroolefins *(6)*, *(7)*, and *(8)*[4] (yield 23%, ratio 14:43:43) and with adamantane the bridgehead derivative *(9)*[4] (28%) and the 1,3-bisadduct (5%). Whether tetrachlorovinylcarbene is formed by simple ring opening of *(1)*, or ionically[3] *via* the pentachlorocyclopropyl- and the pentachloroallyl anion, is still unknown.



The thermal addition of *(1)* to olefins *(2)* provides a generally useful method for the synthesis of chloro(trichlorovinyl)cyclopropanes *(3)*[4] and also of vinylcyclopropanes *(4)*[4], since the derivatives *(3)* can be conveniently dehalogenated (see Table 1). With lithium/*tert*-butyl alcohol in tetrahydrofuran, ethylidenecyclopropanes *(5)*[4] are formed as by-products, which, however, can also be converted into the vinylcyclopropanes *(4)* without isolation with potassium *tert*-butoxide. In this way *(4a)* and *(4k)* were isolated in total yields of 67 and 63%, respectively, from *(3a)* and *(3k)*.

Experimental

(3): A mixture of *(2)* and *(1)* (molar ratio 1:1) in a sealed, thick-walled glass ampule (dimensions according to amount of mixture, wall thickness 2.5 mm) and protected by a 2-mm thick steel cylinder is heated in a hot-air oven (see Table 1). The viscous reaction mixture, which is usually black, is taken up in a minimum of dichloromethane; *(3)* is purified by short-path distillation *in vacuo*. Where appropriate, stereoisomers are isolated by preparative gas chromatography.

(4) and *(5):* A mixture of *(3)* (4 mmol) in anhydrous tetrahydrofuran, finely divided lithium (100 mmol), *tert*-butyl alcohol (50 mmol) and water (4 mmol) is allowed to boil under reflux for 3 h. The mixture is then poured into 100 ml H_2O and extracted with pentane (3 × 50 ml). The organic phase is washed with saturated sodium chloride solution (5 × 50 ml), dried over sodium sulfate and concentrated to *ca.* 3—5 ml on a 30-cm packed column. *(4)* and *(5)* are isolated from the residue by gas chromatography (see Table 1).

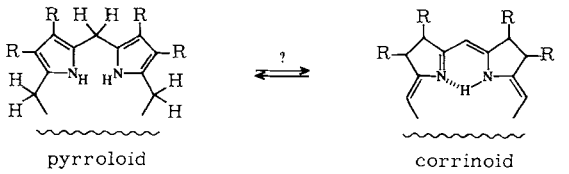
Received: December 17, 1979 [Z 390 IE]
German version: Angew. Chem. 92, 135 (1980)

[1] *D. C. F. Law, S. W. Tobey*, J. Am. Chem. Soc. *90*, 2376 (1968).
[2] *P. D. Bartlett, J. J.-B. Mallet*, J. Am. Chem. Soc. *98*, 143 (1976), and references cited therein.
[3] *W. Weber, U. Behrens, A. de Meijere*, unpublished results.
[4] All the new compounds were unequivocally characterized by ^{1}H-NMR (in part also by ^{13}C-NMR), mass spectra and elemental analyses.
[5] Cf. *E. Elliott, N. F. Janes*, Chem. Rev. *78*, 473 (1978).
[6] We are grateful to Dr. *U. Behrens*, Institut für Anorganische Chemie der Universität Hamburg, for the X-ray structure analysis.
[7] Cf. *A. de Meijere, W. Lüttke*, Tetrahedron *25*, 2047 (1969); *H. Günther, H. Klose, D. Wendisch, ibid. 25*, 1531 (1969).
[8] Cf. *H. D. Hartzler* in *M. Jones, Jr., R. A. Moss:* Carbenes. Wiley-Interscience, New York 1973, 1975, Vol. 2, p. 43.
[9] In the few known cases of intermolecular reactions of thermally or photochemically generated vinylcarbenes the yields are markedly lower: cf. *M. Franck-Neumann, J.-J. Lohmann*, Angew. Chem. *89*, 331 (1977); Angew. Chem. Int. Ed. Engl. *16*, 323 (1977); Tetrahedron Lett. *1979*, 2397; and references cited therein.
[10] Cf. *I. Tabushi, Z. Yoshida, N. Takahashi*, J. Am. Chem. Soc. *92*, 6670 (1970); *A. de Meijere, O. Schallner, C. Weitemeyer*, Angew. Chem. *84*, 63 (1972); Angew. Chem. Int. Ed. Engl. *11*, 56 (1972).

Mutual Interconversion of the Chromophoric Systems of Porphyrinogen and Isobacteriochlorin[**]

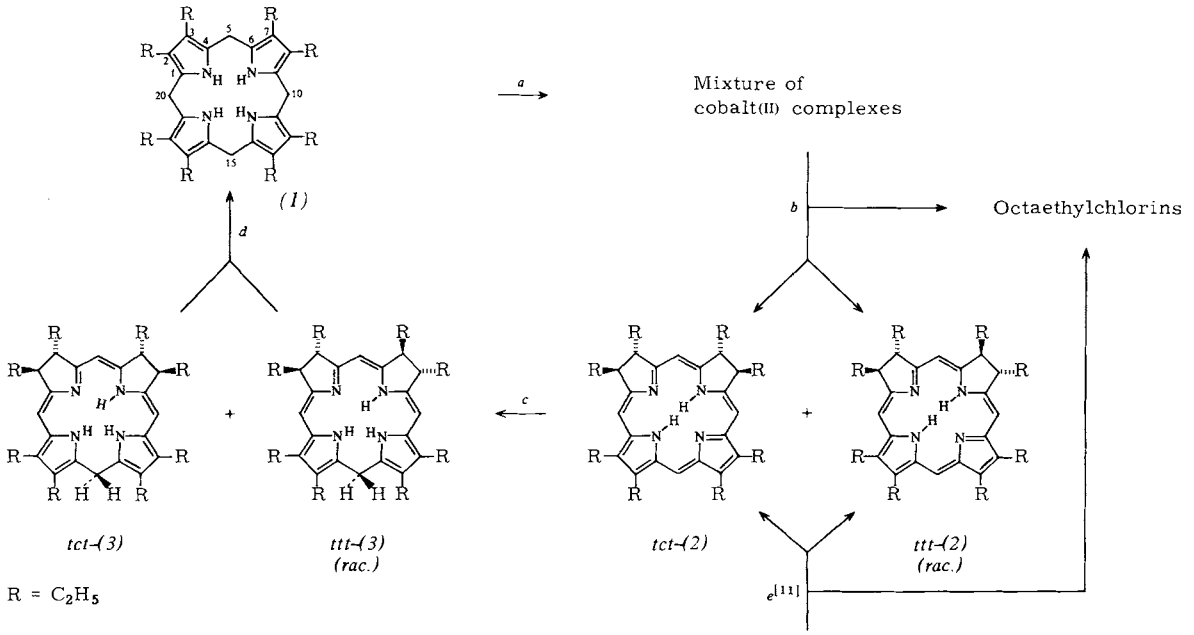
By *Christof Angst, Masahiro Kajiwara, Engelbert Zass*, and *Albert Eschenmoser*[*]

Recently raised questions concerning the origin and ancestral forms of the corrin structure[1] as well as present knowledge of vitamin B_{12} biosynthesis[2] demand an extension of our understanding of the anaerobic chemistry of hexahydroporphyrins. In this and the following publication[3] we report experimental results concerning the position and establishment of equilibria between hydroporphinoid ligands with pyrroloid and corrinoid chromophores (see Scheme 1) as well as the dependence of such equilibria upon metal ions.



Scheme 1

Heating highly diluted solutions of octaethylporphyrinogen *(1)*[4] in xylene and in the presence of $CoCl_2$, acetic acid, and triethylamine in a sealed tube (exclusion of light) under the best possible exclusion of oxygen[5] leads to a mixture of hydroporphinoid cobalt(II) complexes. According to VIS spectroscopic analysis[6], this mixture consists predominantly of chlorin- and isobacteriochlorin complexes in about equal proportions (see Scheme 2). Decomplexation by trifluoroacetic acid at room temperature produced, besides 19% *trans*- and 10% *cis*-octaethylchlorin[8], a mixture of diastereomeric octaethyl-isobacteriochlorins (recognized by UV/VIS and ^{1}H-NMR spectra) in *ca.* 30% yield. The main components of this latter mixture were the diastereomers *ttt-(2)* and *tct-(2)* (*ca.* 60%) in a ratio of about 2:1. Column chroma-



Scheme 2 [12]. *a*: 1.0 *(1)* [4] (2.7×10^{-3} M) in xylene + 1.2 $CoCl_2$ (anhydrous) + 4 CH_3COOH + 1.0 $(C_2H_5)_3N$, evacuated tube, 145 °C, 6 days.—*b*: CF_3COOH, *ca.* 0.5 h, *ca.* 20 °C, under N_2.—*c*: H_2/Pt on carbon (5%), ethyl acetate, *ca.* 20 °C (yield 70%).—*d*: in pyridine-acetic acid (1:1), 60 °C, 40 h, evacuated tube.—*e*: sodium in isopentyl alcohol, 160 °C, under argon, decomplexation of the product with conc. HCl under argon [11].

tography on silica gel, followed by HPLC separation[9], gave the pair of isomers *ttt-(2)* and *tct-(2)* crystallizing as a (*ca.*) 1:1-mixture[10]. These crystals were spectroscopically identified (UV/VIS, ^{1}H-NMR, MS; see Table) by comparison with crystalline "octaethylisobacteriochlorin", prepared according to the literature[11] by reduction of iron(III) octaethylporphyrinate with sodium in isopentyl alcohol.

Catalytic hydrogenation of binary *ttt/tct-(2)* mixtures produced corresponding mixtures of the extremely oxygen-sen-

[*] Prof. Dr. A. Eschenmoser, dipl. Naturwiss. ETH Ch. Angst, Dr. E. Zass
Laboratorium für organische Chemie,
Eidgenössische Technische Hochschule
ETH-Zentrum
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dr. M. Kajiwara
Shiseido Laboratories
1050 Nippa-cho, Kohoku-ku, Yokohama 223 (Japan)

[**] The Chemistry of Hexahydroporphyrins, Part 1. This work was supported by the Swiss National Science Foundation.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0202-0140 $ 02.50/0*

sitive dipyrroloid octaethyl-hexahydroporphyrins *ttt-(3)* and *tct-(3)* which are clearly distinguishable in the ^{1}H-NMR spectrum (see Table 1). The C-15 methylene protons of the

Table 1. Spectroscopic data of the pairs of compounds *ttt-(2)/tct-(2)* and *ttt-(3)/tct-(3)* [12]. *tct* = *trans* (R on C-2/C-3), *cis* (C-3/C-7), *trans* (C-7/C-8).

ttt/tct-(2): ttt:*tct* = 56:44 (^{1}H-NMR), dark violet needles from ether/methanol, m.p. 146—147 °C.—UV/VIS ($CHCl_3$, red): λ_{max} = 360 sh (log ε = 4.75), 373 (4.96), 380 sh (4.90), 403 (4.64), 484 (3.76), 513 (3.95), 548 (4.21), 590 (4.46), 635 (3.89) nm.—MS: *m/e* = 538 (100%, M$^+$), 509 (15%, M$^+ - C_2H_5$), *etc.*—^{1}H-NMR [a] ($CDCl_3$): δ = 1.00 (t/J = 4 Hz/2CH$_3$), 1.03 (t/J = 4 Hz/2CH$_3$), 1.47 (t/J = 4 Hz/2CH$_3$), 1.52 (t/J = 4 Hz/2CH$_3$), 1.7—2.3 (m/4CH$_2$), 2.95 (s/broad/2 NH), 3.26 (q/J = 4 Hz/2CH$_2$), 3.40 (q/J = 4 Hz/2CH$_2$), 3.5—3.8 (m/4CH), 6.82 (s/HC-5 of *tct*), 6.84 (s/HC-5 of *ttt*), 7.43 (s/HC-10 and HC-20 of *tct*), 7.45 (s/HC-10 and HC-20 of *ttt*), 8.48 (s/HC-15 of *tct*), 8.50 (s/HC-15 of *ttt*).—^{13}C-NMR [a] ($CDCl_3$): δ = 10.81 (q/4CH$_3$), 17.42 (q/2CH$_3$), 18.06 (q/2CH$_3$), 18.65 (t/2CH$_2$), 18.95 (t/2CH$_2$), 29.09 (t/2CH$_2$ of *tct*), 29.29 (t/2CH$_2$ of *ttt*), 30.27 (t/2CH$_2$), 50.10 (d/2CH of *ttt*), 50.48 (d/2CH of *tct*), 53.66 (d/2CH), 90.92 (d/C-5), 93.53 (d/C-10 and C-20 of *ttt*), 93.76 (d/C-10 and C-20 of *tct*), 104.26 (d/C-15 of *ttt*), 104.50 (d/C-15 of *tct*), 131.64 (s/2C), 134.32 (s/2C of *ttt*?), 134.46 (s/2C of *tct*?), 139.54 (s/2C), 144.75 (s/2C of *ttt*), 144.89 (s/2C of *tct*), 157.21 (s/2C of *tct*), 157.46 (s/2C of *ttt*), 165.11 (s/2C of *tct*), 165.37 (s/2C of *ttt*)

ttt/tct-(3): ttt:*tct* = 45:55 (^{1}H-NMR), not crystalline.— UV/VIS (hexane, yellow): λ_{max} = 281 sh (ε relative = 1.09), 288 (1.11), 302 sh (0.84) broad absorption 350—550 nm (0.30 [b]).—MS: *m/e* = 540 (100%, M$^+$), 511 (10%, M$^+ - C_2H_5$), *etc.*—^{1}H-NMR [a] ($CDCl_3$): δ = 0.8—1.2 (superimposed m/8CH$_3$), 1.3—1.8 (m/4CH$_2$), 2.47 (q/J = 4 Hz/2CH$_2$), 2.49 (q/J = 4 Hz/2CH$_2$), obviously superimposed by signals of 4CH, 3.51/4.07 (AB-system, J_{AB} = 8 Hz/H$_2$C-15 of *tct*), 3.79 (s/H$_2$C-15 of *ttt*), 5.00 (s/HC-5 of *ttt*), 5.05 (s/HC-5 of *tct*), 5.61 (s/HC-10 and HC-20 of *ttt*), 5.64 (s/HC-10 and HC-20 of *tct*), 7.92 (s/broad/3 NH).—^{13}C-NMR [a] ($CDCl_3$): δ = 10.66/10.91/11.05/11.45 (4q/2× each 2CH$_3$ of *ttt* and *tct*), 16.64 (q/2CH$_3$), 16.70 (q/2CH$_3$), 17.57 (t/2CH$_2$), 17.71 (t/2CH$_2$), 22.40 (t/C-15), 27.18 (t/2CH$_2$ of *ttt*?), 27.42 (t/2CH$_2$ of *tct*?), 28.94 (t/2CH$_2$), 47.07/52.15 (2d/2× 2CH of *ttt*), 48.07/53.07 (2d/2× 2CH of *tct*), 87.91 (d/C-5 of *ttt*), 88.46 (d/C-5 of *tct*), 96.16 (d/C-10 and C-20 of *ttt*), 96.64 (d/C-10 and C-20 of *tct*), 120.26 (s/2C), 121.10/121.39 (2s/2C each of *ttt/tct*), 123.39 (s/2C), 125.20 (s/2C), 148.18 (s/2C of *tct*), 148.43 (s/2C of *ttt*), 167.50 (s/2C).

[a] If the designations "*ttt*" or "*tct*" are absent then the NMR signals of the two isomers are identical. [b] The UV/VIS spectrum shows additional weak bands of about 1 mol-% *(2)*; cf. the spectrum of *(10)* in [7]. The assignment of NMR-signals of *(2)* and *(3)* to *ttt* and *tct* respectively is derived from the relative intensities of the singlet/double doublet signal pair originating from the H_2C-15 in the ^{1}H-NMR of a (1:2)-mixture of *ttt/tct-(3)*.

ttt-isomer are homotopic and appear in the spectrum as a singlet (δ = 3.79), while those of the *tct*-isomer are diastereotopic and give rise to a clearly discernible AB-system (δ = 3.51 and 4.07, J_{AB} = 8 Hz). The ^{1}H- and ^{13}C-NMR spectra of both components show the presence of a twofold simple and an alternating axis of symmetry, respectively. This symmetry argument does not exclude the structures *ctc* and *ccc*; however, these are ruled out by the results of *Inhoffen et al.*[11a], who observed *trans*-octaethylchlorin as the exclusive autoxidation product of their "octaethylisobacteriochlorin"[13].

Tautomerization of the binary mixture of dipyrroloid hexahydroporphyrins *ttt/tct-(3)* in pyridine/acetic acid 1:1 at 60 °C for 40 hours under exclusion of oxygen led, after strict anaerobic work-up, to a product consisting of more than 98% octaethylporphyrinogen *(1)* according to the ^{1}H-NMR spectrum. From one such experiment, we have preparatively isolated in good yield the highly oxygen-sensitive product *(1)* in crystalline, spectroscopically pure form.

Our results show that the equilibrium between the tetrapyrroloid chromophore of 5,10,15,20,21,23-hexahydroporphyrins ("porphyrinogens") and the hemicorrinoid-dipyrroloid structure of the tautomeric 2,3,7,8,15,23-hexahydroporphyrins can lie on the side of the porphyrinogen[14] and that metal ions reverse the trend of this equilibrium. The earlier observation of *Eisner*[11b] and *Shul'ga et al.*[15] on the formation of isobacteriochlorins (among other products) in the tetramerization of 2-(dimethylaminomethyl)pyrroles by Grignard reagents bears an important relationship to the porphyrinogen → isobacteriochlorin interconversion[16] described here.

Received: October 29, 1979 [Z 388a IE]
German version: Angew. Chem. *92*, 139 (1980)

[1] *A. Eschenmoser*, Chem. Soc. Rev. *5*, 377 (1976); Recordings Leermaker Symposium April *1977*, Wesleyan University; Jahrb. Akad. der Wiss. Göttingen *1977*, 29; cf. *K. Decker, K. Jungermann, R. K. Thauer*, Angew. Chem. *82*, 153 (1970); Angew. Chem. Int. Ed. Engl. *9*, 138 (1970); *N. H. Georgopapadakou, A. I. Scott*, J. Theor. Biol. *69*, 381 (1977); *A. Eschenmoser* in [2], pp. 89—117.

[2] Cf., the lectures of *G. Müller, A. R. Battersby, A. I. Scott* in *B. J. Zagalak*: Vitamin B_{12} and Intrinsic Factor; Proceedings of the 3rd European Symposium, Zürich. De Gruyter, Berlin 1979, pp. 280, 217, 247.

[3] *J. E. Johansen, Ch. Angst, Ch. Kratky, A. Eschenmoser*, Angew. Chem. *92*, 141 (1980); Angew. Chem. Int. Ed. Engl. *19*, 141 (1980).

[4] Prepared by catalytic hydrogenation of octaethylporphyrin with platinum in acetic acid; cf. *H. Fischer, W. Zerweck*, Hoppe-Seylers Z. Physiol. Chemie *137*, 242 (1924); *H. Budzikiewicz, R. Pesch*, Org. Mass Spectrom. *11*, 821 (1976). We thank Prof. *H. Inhoffen* (TU Braunschweig) for a generous gift of octaethylporphyrin.

[5] All reactions (including work-up and chromatography) were performed under nitrogen in a dry-box (O_2 content *ca.* 5 ppm; DriLab DL 001-S-P/Dri-Train HE-493, Vacuum Atmospheres Corporation, Hawthorne, Calif., USA).

[6] VIS spectrum in benzene of such a mixture: λ_{max} (ε relative) = 611 (0.62) (chlorinate), 586 (0.92) (isobacteriochlorinate), 550 (0.31), 518 (0.22), 490 nm (0.23). UV/VIS spectra of cobalt(II) isobacteriochlorinate (cf. [7]) and cobalt(II) chlorinate; cf. *A. W. Johnson, I. T. Kay*, J. Chem. Soc. *1960*, 2979.

[7] *P. Naab, R. Lattmann, Ch. Angst, A. Eschenmoser*, Angew. Chem. *92*, 143 (1980); Angew. Chem. Int. Ed. Engl. *19*, 143 (1980).

[8] The chlorin mixture, only sparingly soluble in ether/methanol, was isolated by crystallization and separated into homogeneous diastereomers by HPLC (neutral alumina, pentane/dimethoxyethane/triethylamine 1000:30:15, no exclusion of oxygen). These diastereomers were identified by comparison of the UV/VIS, ^{1}H/^{13}C-NMR, MS, and IR spectra with those of reference material prepared according to [11a].

[9] Neutral alumina, pentane/dimethoxyethane/triethylamine 2000:30:15.

[10] The less soluble *tct*-isomer can be enriched by repeated crystallizations of the *ttt/tct*-mixture from ether/methanol; the corresponding nickel(II) complexes are easily separable by HPLC (results of *J. E. Johansen* with material prepared according to [11a], cf. [3]).

[11] a) *H. H. Inhoffen, J. W. Buchler, R. Thomas*, Tetrahedron Letters *1969*, 1141, 1145; *R. Thomas*, Dissertation, TU Braunschweig 1967; b) *U. Eisner*, J. Chem. Soc. *1957*, 3461; c) *R. Bonnett, I. A. D. Gale, G. F. Stephenson, ibid. C 1967*, 1168.

[12] For experimental details, see *Ch. Angst*, Diss. ETH Zürich (planned for 1980).

[13] This proves that the crystalline "octaethyl-isobacteriochlorin" described in the literature [11] also consists of an approximately 1:1-mixture of *ttt*- and *tct*-diastereomers. The assignment of configuration is indirectly supported by X-ray structural analyses [3].

[14] Cf. *Whitlock*'s facile deuteration of the *meso*-methylene groups in *(1)* by CH_3COOD without concomitant changes in structure: *H. H. Whitlock Jr., D. H. Buchanan*, Tetrahedron Letters *1969*, 3711.

[15] *G. D. Egorova, K. N. Solov'ev, A. M. Shul'ga*, Zh. Obshch. Khim. *37*, 357 (1967); J. Gen. Chem. USSR *37*, 333 (1967).

[16] The accompanying bis-dehydrogenation presumably occurs *via* disproportionation, cf. [7].

1,2,3,7,8,20-Hexahydroporphyrin, an Easily Formed Ligand System Isomeric to Porphyrinogens[**]

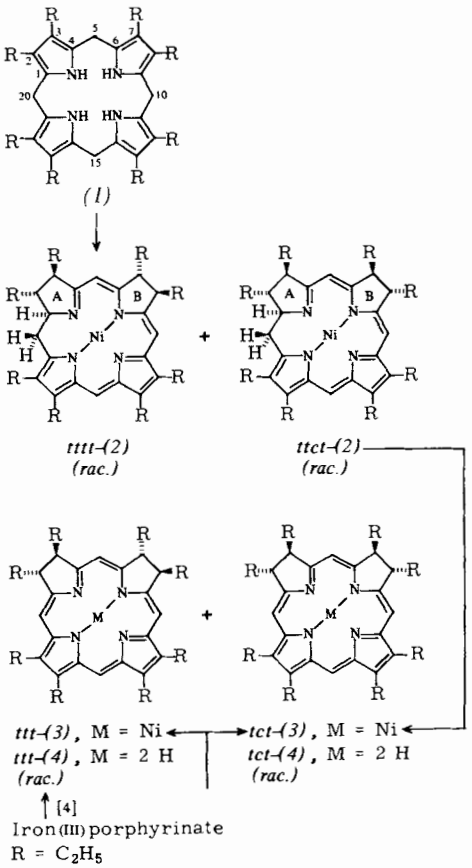
By *Jon Eigill Johansen, Christof Angst, Christoph Kratky*, and *Albert Eschenmoser*[*]

The tautomerization of octaethylporphyrinogen *(1)* in nonpolar media in the presence of nickel(II) salts with exclu-

[*] Prof. Dr. A. Eschenmoser, Dr. J. E. Johansen,
dipl.-Naturwiss. ETH Ch. Angst
Laboratorium für organische Chemie,
Eidgenössische Technische Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dr. Ch. Kratky
Institut für physikalische Chemie der Universität,
Heinrichstrasse 28,
A-8010 Graz (Austria)

[**] The Chemistry of Hexahydroporphyrins, Part 2. This work was supported by the Swiss National Science Foundation. *Ch. K.* gratefully acknowledges financial support by the Austrian National Science Foundation (project no. 3763) and the Austrian Academy of Sciences.—Part 1: [1].

sion of oxygen leads to a different pattern of reactions than the analogous treatment of porphyrinogen *(1)* in the presence of cobalt(II) salts[1]. The major reaction products formed at high dilution are diastereomeric nickel(II) complexes *(2)* of a previously unknown hemicorrinoid-pyrromethenic ligand system, octaethyl-1,2,3,7,8,20-hexahydroporphyrin, which is a protomer of octaethyl-porphyrinogen (yields up to 90%, see Scheme 1). If the reaction is conducted at higher concentrations of starting material (10^{-3} instead of 10^{-4} M), the product contains about 45% each of *(2)* and of a fraction of (diastereomeric) nickel(II) isobacteriochlorinates *(3)*, in addition to small amounts of nickel(II) chlorinates (*ca.* 5%) and traces of nickel(II) octaethylbacteriochlorinates (*ca.* 1%)[2] (Scheme 1). After removal of side products by column chromatography, mixtures of the stereoisomeric nickel(II) hexahydroporphyrinates can be separated into the crystalline major components *tttt-(2)* and *ttct-(2)* by HPLC[3]. On dehydrogenation with DDQ in hexane/ether, the faster moving (HPLC) isomer *ttct-(2)* gives crystalline nickel(II) isobacteriochlorinate *tct-(3)*, the configurational assignment of which can be deduced from the results reported in [1]. In contrast to the free ligands *(4)* the corresponding mixture of nickel(II) complexes *ttt/tct-(3)* (cf. [1,4b]) is easily separable by HPLC. The faster moving nickel(II) complex has the configuration *tct*[5] and is identical with the dehydrogenation product of *ttct-(2)* (HPLC, ^{1}H-NMR, UV/VIS, MS).



Scheme 1. For experimental details, see [6]. *(1)→(2):* 1.0 *(1)* (*ca.* 10^{-4} M), 7.3 $Ni(OAc)_2 \cdot 4H_2O$ in *p*-xylene, 2 vol.-% $AcOH/(CH_3CH_2)_3N$ (4:1), 140 °C in evacuated tube, 15—21 h; cf. [2].—*(2)→(3):* *ttct-(2)* in hexane, DDQ in diethyl ether, *ca.* −10 °C, reaction followed by UV/VIS [yield 60% *tct-(3)* plus 20% starting material and 6% chlorinate].—*(4)→(3):* 1.0 *ttt/tct-(3)* (3:2) [4b, 1], 3.7 $Ni(OAc)_2 \cdot 4H_2O$, in ethanol, 70 °C, evacuated tube (yield 96%), HPLC separation [3] of *ttt-(3)* and *tct-(3)*.

X-ray structural analyses of *tttt-(2)* and *ttct-(2)* carried out in the Graz laboratory (Fig. 1) confirm the constitution deduced from spectroscopic data[7] and provide the complete configurational assignment for both isomers[8]. In addition, they reveal the remarkable phenomenon of a conformational coupling between rings A and B (presumably *via* the coordinated nickel(II) ion). Both ethyl groups at ring B of the *tttt*-isomer are in a quasi-diaxial conformation. If ring A were not conformationally coupled with ring B, the ring B ethyl groups of *tttt-(2)* would be expected to prefer a quasi-diequatorial conformation, or otherwise the ring B ethyl groups of the *ttct*-isomer would show up in a quasi-diaxial conformation[9].

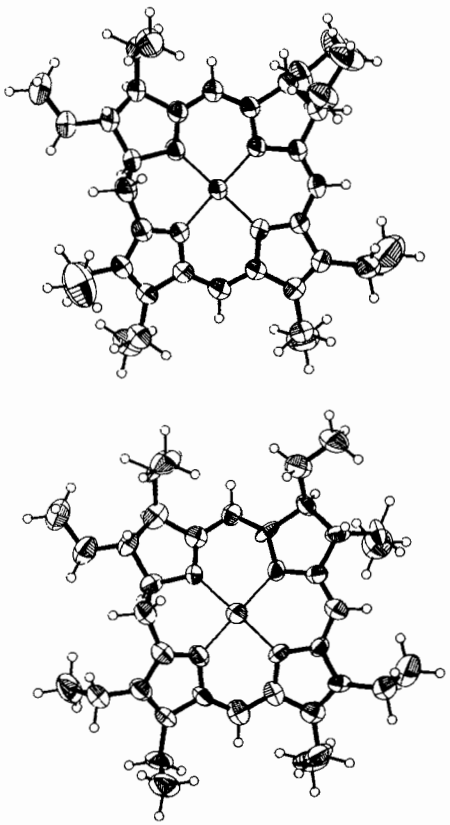
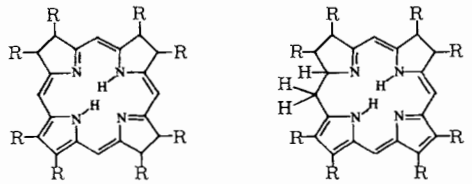


Fig. 1. ORTEP drawings of molecules *tttt-(2)* (top) and *ttct-(2)* (bottom). *tttt-(2):* triclinic, $P\bar{1}$, $a = 11.485$, $b = 11.702$, $c = 13.376$ Å, $\alpha = 72.06$, $\beta = 76.92$, $\gamma = 73.28°$, $Z = 2$, $d_x = 1.23$ g cm^{-3}; 4234 reflections refined, $R = 0.08$; *ttct-(2):* triclinic, $P\bar{1}$, $a = 11.853$, $b = 12.856$, $c = 13.021$ Å, $\alpha = 118.81$, $\beta = 98.5$, $\gamma = 100.44°$, $Z = 2$, $d_x = 1.21$ g cm^{-3}; 4869 reflections refined, $R = 0.058$. A complete description of the crystal structure analyses will be published separately (*Ch. Kratky*, Mh. Chem., in press).

On repeating the classical experiments of *Eisner*[4a] on the reduction of iron(III) octaethylchlorinate to hydroporphyrins with sodium and isopentyl alcohol, the ^{1}H-NMR spectrum of the product showed clearly[6] that the reported "hexahydro derivative" is not of structural type *(5)* (cf. Scheme 2) as had previously been assumed[4a], but a mixture of four diastereomeric hexahydroporphyrins of the structural type *(6)*[10].



Scheme 2 *(5)* R = C_2H_5 *(6)*

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0202-0142 $ 02.50/0

The chemical conversion of the porphyrinogen-structure [cf. *(1)*] *via* a tautomerization-complexation-disproportionation pathway leads preferentially, as does the reduction of porphyrins[4, 11], to those chromophoric systems found in biologically active hydroporphinoid cofactors. The particular ease with which the isobacteriochlorin-chromophore forms chemically[11] on the tetrahydroporphyrin oxidation level is of special interest in relation to the recent discovery of sirohydrochlorin[12]. On the other hand, the ligand system of 1,2,3,7,8,20-hexahydroporphyrin which seems to be a thermodynamically and kinetically favored type of structure, is not known to occur in nature, and the ligand system of natural corrinoids still has to be shown to form by transformation of porphyrinogens *via* simple tautomerization and complexation processes.

Table 1. Spectroscopic data of compounds *tttt-(2)*, *ttct-(2)*, *ttt-(3)* and *tct-(3)*. For experimental details, see [6]. *ttct*: methylene group C-20 at C-1 and R at C-2 in *trans* position, *etc.*

ttct-(2): dark green cubes (contains 3% *tct-(3)*, HPLC [3]).—UV/VIS (hexane, green): λ_{max} = 264 (log ε = 4.24), 300 (4.18), 370 sh (4.18), 381 (4.43), 407 sh (4.16), 440 (4.10), 465 sh (3.76), 550 sh (3.65), 591 (4.15), 642 nm (4.54).—MS: *m/e* = 596 (100%, M^+, ^{58}Ni) + isotope peaks, 581 (4%, $M^+ - CH_3$), *etc.*—^{1}H-NMR ($CDCl_3$): δ = 0.8—2.0 (32 H/8 CH_3 + 4 CH_2), 2.15—2.75 (10 H/4 CH_2 + H_2C-20), 4.12 (m/HC-1?), 5.13 (s/HC-5), 5.69 (s/HC-10), 6.68 (s/HC-15).—^{13}C-NMR ($CDCl_3$): δ = 11.28/11.38/12.65 (3 q/4 CH_3), 15.82 (q/4 CH_3), 17.21/17.67/17.99/18.06 (4 t/4 CH_2), 25.90/28.27/28.55/28.65 (4 t/4 CH_2), 36.31 (t/C-20), 47.73/50.01/51.65/55.73 (4 d/4 CH), 69.74 (d/C-1), 92.33/93.14 (2 d/C-5, 10), 113.46 (d/C-15), 126.53/130.01/130.65/133.83/136.22/143.29/149.13/152.62/157.97/167.07/167.37 (11 s/11 C)

The spectroscopic data of *tttt-(2)* (dark green platelets, contains 6% *ttt-(3)* (HPLC) [3]) show the following characteristic deviations from those of *ttct-(2):* UV (hexane): λ_{max} = 634 (log ε = 4.45).—^{1}H-NMR ($CDCl_3$): δ = 3.0—3.3 (m/HC-20?), 3.4—3.7 (m/HC-1), 5.18 (s/HC-5), 5.80 (s/HC-10), 6.83 (s/HC-15).—^{13}C-NMR ($CDCl_3$): 33.93 (t/C-20), 89.74/93.81 (2 d/C-5, 10)

tct-(3): dark blue needles.—UV/VIS (CH_2Cl_2, violet-blue): λ_{max} = 281 (log ε = 4.14), 293 sh (4.09), 365 sh (4.55), 386 (4.71), 518 (3.22), 548 (4.03), 593 nm (4.75).—MS: *m/e* = 594 (100%, M^+, ^{58}Ni) + isotope peaks, *etc.*—^{1}H-NMR ($CDCl_3$): δ = 0.86 (t/*J* = 4 Hz/2 CH_3), 0.91 (t/*J* = 4 Hz/2 CH_3), 1.37/1.45 (2 t/*J* = 4 Hz each/4 CH_3, partly superimposed by signals of 4 CH_2), 3.26 (q/*J* = 4 Hz/4 CH_2, partly superimposed by signals of 4 CH), 6.58 (s/HC-5), 7.30 (2 s/HC-10, 20), 8.34 (s/HC-15).—^{13}C-NMR ($CDCl_3$): δ = 10.78/11.50 (2 q/4 CH_3), 17.26/18.00 (2 q/4 CH_3), 18.63/18.93 (2 t/4 CH_2), 27.13/28.57 (2 t/4 CH_2), 52.37/54.82 (2 d/4 CH), 91.24 (d/C-5), 95.61 (d/C-10, 20), 106.11 (d/C-15), 132.37 (s/4C), 139.99/142.42/150.49/161.55 (4 s/8 C)

Characteristic deviations of *ttt-(3)* compared to *tct-(3):* ^{1}H-NMR ($CDCl_3$): δ = 1.7—2.1 (m/4 QCH_2), 3.13/3.25 (2 q/*J* = 4 Hz each/4 CH_2), 2.3—2.6 (m/4 CH).—^{13}C-NMR ($CDCl_3$): δ = 27.27/27.10 (2 t/4 CH_2), 50.12/52.95 (2 d/4 CH)

Received: October 29, 1979 [Z 388 b IE]
German version: Angew. Chem. *92*, 141 (1980)

[1] *Ch. Angst, M. Kajiwara, E. Zass, A. Eschenmoser*, Angew. Chem. *92*, 139 (1980); Angew. Chem. Int. Ed. Engl. *19*, 140 (1980).

[2] The percentages of Ni^{II} isobacteriochlorinates, -bacteriochlorinates, and -chlorinates were determined by UV/VIS spectroscopy after chromatographic separation from *(2)*. Characterization of the main fraction of Ni^{II} 7,8,17,18-tetrahydroporphyrinate (= Ni^{II} bacteriochlorinate) (after separation by column chromatography (silica gel, hexane/benzene/triethylamine 140:20:3.2) and HPLC separation [3] in 3 fractions, *ca.* 6:3:1): UV/VIS (pentane/triethylamine, 1000:1): λ_{max} = 743 (ε relative = 100), 707 (12), 680 (6), 508 (4), 520 (4), 390 (74), 327 nm (48); MS: *m/e* = 597 (19%), 596 (44), 595 (43), 594 (100, M^+), 592 (28). A UV/VIS controlled experiment (before HPLC) with 2-chloro-5,6-dicyano-1,4-quinone led within seconds to the spectrum of a Ni^{II} chlorinate and within minutes to that of a Ni^{II} porphyrinate.

[3] Stationary phase: Merck alumina T, 12 μm; mobile phase: pentane/triethylamine 1000:1; see *E. Walter, J. Schreiber, E. Zass, A. Eschenmoser*, Helv. Chim. Acta *62*, 899 (1979).

[4] a) *U. Eisner*, J. Chem. Soc. *1957*, 3461; b) *H. H. Inhoffen, J. W. Buchler, R. Thomas*, Tetrahedron Lett. *1969*, 1141.

[5] *tct-(4)* [1, 4] was enriched by up to 97% by 11 recrystallizations from ether/methanol and converted into the nickel(II) complex, which was shown by UV/VIS spectrum and HPLC [3] to be identical with the faster moving isomer of *(3)*.

[6] *Ch. Angst*, Diss. ETH Zürich (planned for 1980).

[7] Cf. *P. Naab, R. Lattmann, Ch. Angst, A. Eschenmoser*, Angew. Chem. *92*, 143 (1980); Angew. Chem. Int. Ed. Engl. *19*, 143 (1980).

[8] The diastereomers *tttt-(2)* and *ttct-(2)* are presumably the thermodynamically most stable of the 16 possible isomers (cf. [9]). A third isomer (?) (about 1%) was detected during HPLC of the isomer mixture *(2)* resulting from the reaction *(1)* → *(2)*.

[9] According to preliminary experiments, *tttt-(2)* can be epimerized to *ttct-(2)* to an extent greater than 50%; the latter isomer hardly reacts under the same conditions (potassium *tert*-butoxide in THF, RT).

[10] A non-crystalline fraction of *Eisner*'s "hexahydroporphyrin", prepared according to [4a] with a modified work-up and isolated by HPLC (silica gel, hexane/triethylamine/dimethoxyethane 200:1:1) in 20% yield, showed the following data: MS and FD-MS: M^+ at 540 (100%); UV/VIS (hexane): λ_{max} = 340 sh (ε relative = 1.10), 355 (1.43), 374 (1.21), 444 (0.15), 486 sh (0.27), 520 (0.51), 553 (0.68), 630 (0.21), 667 nm sh (0.17); ^{1}H-NMR (360 MHz, $CDCl_3$): three signal groups of vinylic protons at 4.75/5.30/6.55 ppm with four signals each (unchanged by decoupling), corresponding to four diastereomers. The UV/VIS spectrum after incorporation of Ni^{II} ($Ni(OAc)_2$ in ethanol, 60 °C) corresponded very closely to the spectrum of pure *ttct-(2)* (cf. Table 1).

[11] *G. R. Seely, K. Talmadge*, Photochem. Photobiol. *3*, 195 (1964); *A. N. Sidorov*, Biofizika *10*, 226 (1965); Biophysics *10*, 250 (1965); *A. M. Shul'ga, G. P. Gurinovich, ibid. 13*, 42 (1968) and *13*, 46 (1968); *H. W. Whitlock Jr., R. Hanauer, M. Y. Oester, B. K. Bower*, J. Am. Chem. Soc. *91*, 7485 (1969); *D. G. Whitten, J. C. Yau, F. A. Caroll, ibid. 93*, 2291 (1971); *J. W. Buchler, H. H. Schneehage*, Tetrahedron Lett. *1972*, 3803; *Y. Harel, J. Manassen*, J. Am. Chem. Soc. *100*, 6228 (1978).

[12] *M. J. Murphy, L. M. Siegel, H. Kamin, D. Rosenthal*, J. Biol. Chem. *248*, 2801 (1973); *A. R. Battersby, E. McDonald, H.-R. Morris, D. C. Williams, V. Ya. Bykhovsky, N. I. Zaitseva, V. N. Bukin*, Tetrahedron Lett. *1977*, 2217; *A. I. Scott, A. J. Irwin, L. M. Siegel, J. N. Shoolery*, J. Am. Chem. Soc. *100*, 316, 7987 (1978); *K. H. Bergmann, R. Deeg, K. D. Gneuss, H. P. Kriemler, G. Müller*, Hoppe-Seylers Z. physiol. Chem. *358*, 339 (1977).

Synthesis and Transformations of 5-Cyano-2,2,8,8,12,13,17,18-octamethylisobacteriochlorin[**]

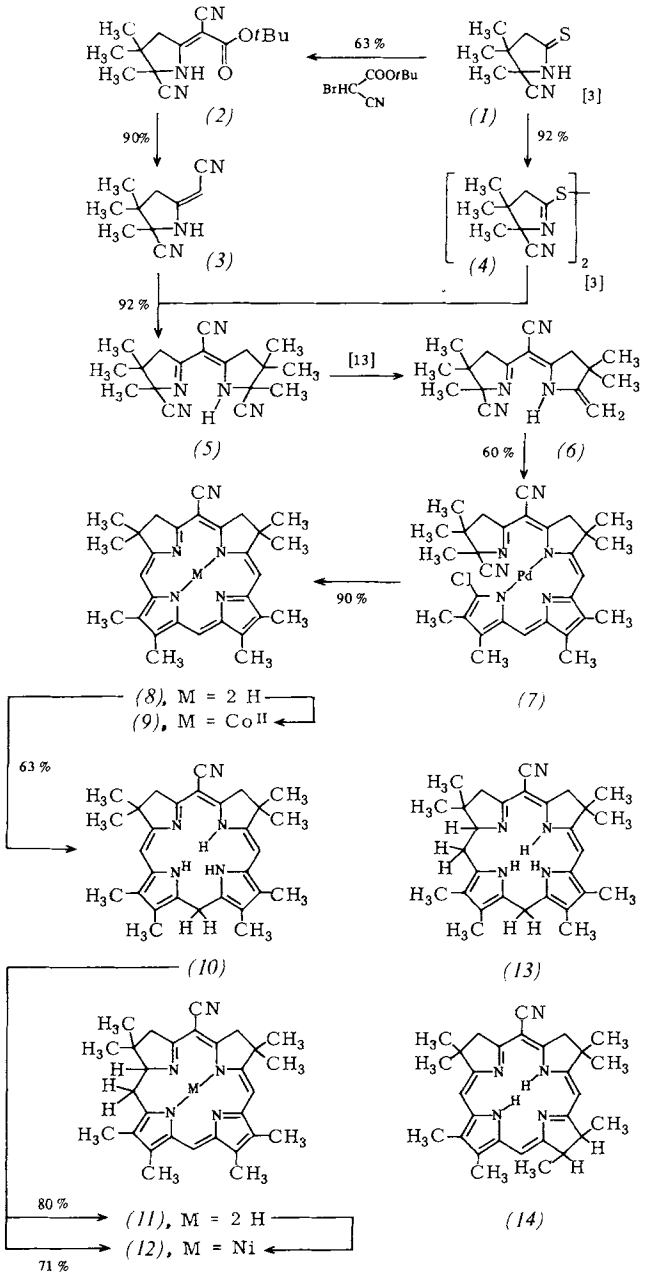
By *Paul Naab, René Lattmann, Christof Angst,* and *Albert Eschenmoser*[*]

The title compound *(8)*, possessing C_{2v} symmetry, is one of the model substrates in our studies on the anaerobic chemistry of hexahydroporphyrins. We describe here the synthesis and transformations of *(8)*, which are of relevance to the two preceding communications[1a, b].

The preparation of *(8)* (Scheme 1) follows the concept of the *de novo* synthesis of isobacteriochlorins recently published together with *Battersby et al.*[1c]. The condensation of the hemicorrinoid A/B-component *(6)* with 5,5'-dichloro-3,3',4,4'-tetramethylpyrromethene[2] to give *(7)*, requiring the template effect of palladium(II)[1d], and the cyclization of the intermediate zinc(II) 19,20-*seco*-isobacteriochlorinate to *(8)* proceed in this series in good yields. The preparation of the new compound *(6)* starts from the thiolactam *(1)*[3], using previously established procedures for corrin syntheses[3, 4]. Both C,C-bond formation steps in this sequence [*(1)* → *(2)* and *(3)* + *(4)* → *(5)*] are accomplished *via* the sulfide contraction method. Direct C,C-bond formation *via* intermolecular iminoester condensations[5] is sterically hindered in this series[6].

[*] Prof. Dr. A. Eschenmoser, dipl.-Chem. ETH R. Lattmann, dipl.-Naturwiss. ETH Ch. Angst
Laboratorium für organische Chemie,
Eidgenössische Technische Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dr. P. Naab
Chemisch-wissenschaftliches Laboratorium Bayer AG
D-5600 Wuppertal 1 (Germany)

[**] The Chemistry of Hexahydroporphyrins, Part 3. This work was supported by the Swiss National Science Foundation. *P. N.* (postdoctoral fellow at the ETH 1977/1978) gratefully acknowledges a scholarship from the German Science Foundation.—Part 2: [1b].



Scheme 1 [11]. *(1)→(2):* 1.0 *(1)* [3] + 1.5 *tert*-butyl bromocyanoacetate + 1.2 DBU [12] in CH_2Cl_2, RT (removal of elemental S with Hg).—*(2)→(3):* a) CF_3COOH, 0 °C; b) melting the carboxylic acid, 180 °C.—*(3)→(5):* 1.0 *(3)* + 1.0 DBU [15] + 1.0 *(4)* [3] in DMF, RT; then $(C_2H_5O)_3P$ in xylene, 130 °C.—*(5)→(6):* K-salt of *(5)* in toluene/acetonitrile (15:1), 80 °C [13].—*(6)→(7):* 1.0 *(6)* + 1.4 $Pd(OAc)_2$ + 2.65 DBU + 1.6 5,5'-dichloro-3,3',4,4'-tetramethyl-pyrromethene [2] in CH_3CN, 80 °C, HV, sealed tube.—*(7)→(8):* a) 10 KCN in CH_3OH/CH_2Cl_2, RT, then + 20 $Zn(OAc)_2 \cdot 2H_2O$; b) 4 *t*-BuOK in *t*-BuOH, 140 °C, HV, sealed tube, then CF_3COOH under N_2.—*(8)→(9):* 5 $Co(OAc)_2 \cdot 4H_2O$ in $CH_3OH/CHCl_3$ (1:1), 60 °C, HV, sealed tube (work-up with benzene/H_2O under N_2).—*(8)→(10):* 3 times Pt/C by weight (5%), H_2, in $CH_3COOC_2H_5$, RT.—*(10)→(11):* in HCOOH (degassed), HV, sealed tube, 70 °C, 50 h.—*(10)→(12):* *ca.* 7 $Ni(OAc)_2 \cdot 4H_2O$ in benzene + 1 Vol.-% $CH_3COOH/(CH_3CH_2)_3N$ (4:1), 100 °C, HV, sealed tube.—*(11)→(12):* *ca.* 5 $Ni(OAc)_2 \cdot 4H_2O$, in $CH_3OH/CHCl_3$ (1:1), 60 °C, HV, sealed tube.—*(10)→(8)+(13):* 110 °C in xylene + 4 Vol.-% pyridine/HCOOH (1:1.3), 110 °C, HV, sealed tube.

The symmetry of the substitution pattern in *(8)* facilitates the study of the transformations of the isobacteriochlorin chromophore. The extremely oxygen-sensitive[7] hexahydroporphyrin *(10)*, for example, produced from *(8)* by catalytic hydrogenation with platinum in ethyl acetate, is a crystalline compound with a symmetrical dipyrroloid constitution easily recognizable by the NMR spectra (cf. Table 1). We originally assumed that the monopyrroloid ligand system *(14)*, a tautomer of *(10)*, might be fixed by complexation with suitable metal ions. This could not be confirmed experimentally. Under reaction conditions sufficiently vigorous for the incorporation of metal ions such as nickel(II) and zinc(II), complexes of the isomeric hemicorrinoid-pyrromethenic chromophore *(11)* are formed instead. The free ligand *(11)* can be isolated in crystalline form by acidolysis of the zinc complex[8]. Remarkably, *(11)* is also formed in good yield by heating *(10)* in formic acid in the absence of metal ions. The thermodynamic and kinetic lability of the hemicorrinoid-dipyrroloid structure also manifests itself in the fact that *(10)* disproportionates to a mixture of *(8)* (52%) and *(13)* (39%)[9] on heating with pyridine/formic acid (1:1.3) in xylene at 110 °C with exclusion of air[10]. This lability can be rationalized by regarding the conjugative destabilization between all three (NH)-lone pairs in *(10)*.

Table 1. Spectroscopic data of compounds *(8)*—*(11)* [11].

(8): violet needles from CH_2Cl_2/hexane, m.p. >250 °C.—UV/VIS (CH_2Cl_2): λ_{max} = 363 sh (log ε = 4.90), 369 (4.95), 380 (4.71), 402 (5.21), 483 (4.03), 508 (4.09), 541 (3.82), 585 (4.25), 629 nm (4.63).—MS: *m/e* = 453 (6%), 452 (33), 451 (100, *M'*). *etc.*—^{1}H-NMR ($CDCl_3$): δ = 1.78 (s/4CH_3), 1.86 (broad s/2NH), 2.92/3.01 (2s/2CH_3 each), 4.25 (s/2CH_2), 7.68 (s/2CH), 8.70 (s/1CH)

(9): red-violet crystals from CH_2Cl_2/methanol, m.p. >300 °C.—UV/VIS (hexane): λ_{max} = 345 sh (log ε = 4.45), 372 (4.68), 405 sh (4.20), 515 (3.78), 550 (4.12), 587 (4.71).—MS: *m/e* = 538 (4%), 509 (34), 508 (100, *M'*), *etc.* presumably no fifth ligand; paramagnetic (NMR) *(10):* red rhombohedra from CH_2Cl_2/hexane, m.p. >200 °C.—UV/VIS (CH_2Cl_2): λ_{max} = 294 (log ε = 4.57), 420 nm (4.06) [a, b].—MS: *m/e* = 456 (16%), 455 (49), 454 (37), 453 (100, *M'*), 452 (38), 451 (96), *etc.*—^{1}H-NMR ($CDCl_3$): δ = 1.28 (s/4CH_3), 1.98/2.02 (2s/2CH_3 each), 2.92 (s/2CH_2), 3.78 (s/CH_2), 5.73 (s/2CH), 7.82 (broad s/2NH), 9.47 (broad s/1 NH).—^{13}C-NMR ($CDCl_3$): δ = 9.0/9.4 (2q/4CH_3), 22.1 (t/CH_2), 28.7 (q/4CH_3), 40.3 (s/2C), 49.4 (t/2CH_2), 75.6 (s/C), 98.4 (d/2CH), 121.2 (s/CN), 114.4/119.0/122.6/124.4/152.1/164.0 (6s/2C each)

(11): blue crystals from CH_2Cl_2/hexane, m.p. >200 °C.—UV/VIS [b] (CH_2Cl_2): λ_{max} = 271 (log ε = 4.45), 280 sh (4.41), 335 sh (4.45), 354 (4.59), 370 sh (4.35), 402 (3.88), 432 (3.84), 465 (3.74), 523 sh (3.96), 562 (4.14), 588 (4.13), 618 sh (4.02).—MS: *m/e* = 455 (9%), 454 (35), 453 (100, *M'*), *etc.*—^{1}H-NMR (360 MHz, $CDCl_3$): δ = 1.17/1.20/1.26/1.28 (4s/1CH_3 each), 1.97/2.04/2.15/2.17 (4s/1CH_3 each), 2.66—2.76 (m/H_2C-20), 2.72/2.89 (AB system/*J* = 16.5 Hz/H_2C-3), 2.85 (s/H_2C-7), 3.76—3.87 (m/HC-1) [c], 5.60 (s/CH), 6.73 (s/CH), 11.05 (broad s/2NH).—^{13}C-NMR ($CDCl_3$): 29 signals in accordance with structure *(11)* [11].

(12) and *(13):* the spectroscopic data (UV/VIS, ^{1}H-NMR, MS) are in agreement with the given structural formulas [11]. For data of nickel complexes of type *(12)*, see [1b]

[a] Superimposed by (weak) signals of *ca.* 1 mol-% *(8)*. [b] *A. Eschenmoser* in *B. J. Zagalak:* Vitamin B_{12} and Intrinsic Factor. Proceedings of the 3rd European Symposium, Zürich, de Gruyter, Berlin 1979, pp. 89—117; cf. Figure on p. 112. [c] Decoupling experiments (90 MHz, $CDCl_3$): irradiation at δ = 2.67: m→d 2.83 (*J* = 10 Hz), irradiation at δ = 2.77: m→d 2.83 (*J* = 5 Hz).

Received: October 29, 1979 [Z 388c IE]
German version: Angew. Chem. *92*, 143 (1980)

[1] a) *Ch. Angst, M. Kajiwara, E. Zass, A. Eschenmoser*, Angew. Chem. *92*, 139 (1980); Angew. Chem. Int. Ed. Engl. *19*, 140 (1980); b) *J. E. Johansen, Ch. Angst, Ch. Kratky, A. Eschenmoser, ibid. 92*, 141 (1980) and *19*, 141 (1980), respectively; c) *F.-P. Montforts, S. Ofner, V. Rasetti, A. Eschenmoser, W.-D. Woggon, K. Jones, A. R. Battersby, ibid. 91*, 752 (1979) and *18*, 675 (1979), respectively; d) *A. P. Johnson, P. Wehrli, R. Fletcher, A. Eschenmoser, ibid. 80*, 622 (1968) and 7, 623 (1968), respectively; *P. M. Müller*, Diss. ETH No. 5135 Zürich, 1973.

[2] Prepared by chlorination of 3,3',4,4'-tetramethylpyrromethene hydrochloride (*S. Ofner*, planned Dissertation, ETH Zürich) with chlorine in glacial acetic acid at RT, m.p. 180 °C (decomp.). Preliminary experiments showed that the reaction sequence *(6)→(8)* works also with the dibromo-pyrromethene derivative described in [1c].

[3] *Y. Yamada, D. Miljkovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müller, A. Eschenmoser*, Angew. Chem. *81*, 301 (1969); Angew. Chem. Int. Ed. Engl. *8*, 343 (1969); Dissertations, ETH Zürich: *R. Scheffold*, No. 3356, 1963; *E. Bertele*, No. 3357, 1963; *P. Wehrli*, No. 4043, 1967; *H. J. Wild*, No. 4848, 1972.

[4] *M. Roth, P. Dubs, E. Götschi, A. Eschenmoser*, Helv. Chim. Acta *54*, 710 (1971); *E. Götschi, W. Hunkeler, H. J. Wild, P. Schneider, W. Fuhrer, J.*

Gleason, A. Eschenmoser, Angew. Chem. *85*, 950 (1973); Angew. Chem. Int. Ed. Engl. *12*, 910 (1973).
[5] *E. Bertele, H. Boos, J. D. Dunitz, F. Elsinger, A. Eschenmoser, I. Felner, H. P. Gribi, H. Gschwend, E. F. Meyer, M. Pesaro, R. Scheffold*, Angew. Chem. *76*, 393 (1964); Angew. Chem. Int. Ed. Engl. *3*, 490 (1964); *A. Eschenmoser*, Pure Appl. Chem. *20*, 1 (1969); Q. Rev. Chem. Soc. *24*, 366 (1970).
[6] Preliminary experiments to prepare *(6) via* the iminoester/enamine condensation, and experiments on the condensation of the thiomethyl iminoester derived from *(1)* with lithium *tert*-butyl acetate (cf. [1c]) failed.
[7] On access of air *(10)* is immediately oxidized to *(8)*; cf. the UV/VIS spectrum of *(10)* in Table 1.
[8] The UV/VIS-spectrum of *(12)* corresponds to the spectra of the nickel(II) octaethyl-1,2,3,7,8,20-hexahydroporphyrinates described in [1b] (X-ray analyses!).
[9] Plus 2% *(11)*.—Partial disproportionation of *(10)* was also observed under various reaction conditions (*e.g.* with acids other than formic acid) [11].
[10] For the exclusion of oxygen in these experiments cf. note [5] in [1a].
[11] For experimental details, cf. *R. Lattmann*, planned Dissertation, ETH Zürich.
[12] 1,8-Diazabicyclo[5.4.0]undec-7-ene (*H. Oediger, F. Möller, K. Eiter*, Synthesis *1972*, 591).
[13] Yield of *(6)* after crystallization: 55%. The mother liquors were reconverted to *(5)* with KCN in DMF (60 °C); yield of *(6)* based on reacted starting material: 92%.

Tetraphenylcyclobutadienecycloalkenenickel(0) Complexes

By *Heinz Hoberg* and *Christian Fröhlich*[*]

Unstable tetraphenylcyclobutadiene can be fixed both to nickel(II)[1] as well as to nickel(0)[2]. Bis(tetraphenylcyclobutadiene)nickel(0), with its 18-electron configuration, formally corresponds to bis(1,5-cyclooctadiene)nickel(0) and bis(cyclooctatetraene)nickel(0)[3].

We have found that also mono(tetraphenylcyclobutadiene)nickel(0) compounds are accessible if the chelate effect of 1,5-cyclooctadiene (COD) or cyclooctatetraene (COT) is utilized for the stabilization. Thus, reaction of (tetraphenylcyclobutadiene)nickel bromide *(1)* with sodium[4] in ether in the presence of COD or COT affords the new complexes *(2)* and *(3)*, respectively.

$$\underset{(1)}{[(C_6H_5)_4C_4]NiBr_2} + 2\,Na + COD \rightarrow \underset{(2),\ 66\%}{[(C_6H_5)_4C_4]Ni(COD)} + 2\,NaBr$$

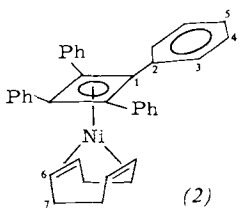
$$\underset{(1)}{[(C_6H_5)_4C_4]NiBr_2} + 2\,Na + COT \rightarrow \underset{(3),\ 77\%}{[(C_6H_5)_4C_4]Ni(COT)} + 2\,NaBr$$

(2) and *(3)* crystallize in the form of green prisms and are soluble in benzene, toluene, or tetrahydrofuran, giving intensely green solutions. In chlorinated hydrocarbons such as chloroform they gradually undergo decomposition. Both compounds are diamagnetic, astonishingly thermostable, and melt with decomposition at 220 and 260 °C, respectively.

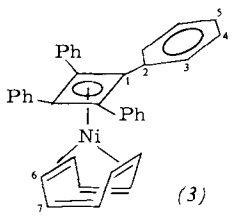
The mass spectra of *(2)* and *(3)* show, besides the respective molecular ions at $m/e = 552$ and 518, the characteristic fragmentation $m/e = 414$ ($[(C_6H_5)_4C_4]Ni$). The cryoscopically determined relative molecular masses of 515 for *(2)* and 532 for *(3)* in benzene afford proof of their monomeric structures. In the IR spectra (KBr) the aromatic absorptions are accompanied by a characteristic band in the C—C region (1620 cm^{-1}) only in the case of *(3)*. The ^1H-NMR spectrum (C_6D_6) of *(2)* shows, in addition to the signals of the aliphatic protons ($\delta = 2.3$, m, 8H), the signals of the vinyl protons which are shifted upfield by complexation ($\delta = 3.70$, broad, 4H). COT in *(3)*, like COD in *(2)*, functions as η^4-ligand ($\delta = 5.75$, s, 4H; $\delta = 3.69$, s, 4H).

The ^{13}C-NMR spectra[5] (Table 1) of *(2)* and *(3)* each contain only seven signals and thus suggest a η^4-coordination of the tetraphenylcyclobutadiene.

Table 1. ^{13}C-NMR spectra (25.2 MHz, Varian-XL-100A-15) of *(2)* and *(3)* in [D_8]tetrahydrofuran at 34 °C referred to TMS.



(2)



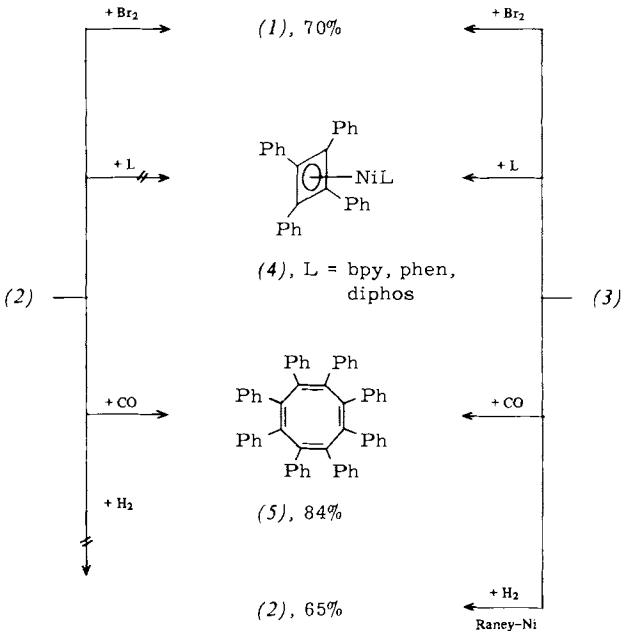
(3)

	C-1	C-2	C-3, 4		C-5	C-6	C-7
(2)	88.02	135.77	128.75	128.64	126.35	93.22	32.39
(3)	90.63	135.38	128.87	128.84	127.01	98.07	135.14
Mult.	s	s	d	d	d	d	*(2)*: t; *(3)*: d

The UV spectra of *(2)* and *(3)* (tetrahydrofuran) are identical in the region 240 to 500 nm. The band at 295 nm ($\lg \varepsilon = 4.6$) is assigned to the cyclobutadiene groups[6].

Reaction of *(2)* and *(3)* with bromine in dichloromethane at −20 °C does not lead to bromination of the cyclobutadiene ring[7], but to formation of *(1)*. COT in *(3)* reacts with 2,2′-bipyridine (bpy), 1,10-phenanthroline (phen), and ethylenebis(diphenylphosphano) (diphos) (toluene, 80 °C, 48 h) to give tetraphenylcyclobutadiene(ligand)-nickel complexes *(4)* in 86, 83, and 76% yields, respectively. *(2)* does not react with these N- and P-donors.

Also on reaction with carbon monoxide (toluene, 1 atm) it is clear that COD in *(2)* is more firmly complexed than COT in *(3)*. Thus, even at 20 °C, 1 mol of *(3)* takes up to 4 mol of CO with displacement of both ligands, while such an uptake



Scheme 1. Reactions of *(2)* and *(3)*. The compounds *(4)* were characterized by elemental analysis, and by IR and mass spectra.

[*] Prof. Dr. H. Hoberg, Dipl.-Chem. C. Fröhlich
Max-Planck-Institut für Kohlenforschung
Postfach 01 13 25, D-4330 Mülheim-Ruhr 1 (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0202-0145 $ 02.50/0*

requires 50 °C in the case of *(2)*. Tetraphenylcyclobutadiene affords octaphenylcyclooctatetraene *(5)*.

(2) and *(3)* are inert towards molecular hydrogen at 20 °C/1 atm in tetrahydrofuran. *(3)* reacts with hydrogen to give *(2)* only on addition of Raney nickel (see Scheme 1).

Experimental

A mixture of *(1)* (10.4 g, 18.1 mmol), cycloalkene (10 ml, *ca.* 90 mmol) and sodium (833 mg, 36.2 mmol; spherules, ⌀ *ca.* 1 mm) in 200 ml diethyl ether is vigorously stirred at −50 °C. The suspension gradually turns dark green[8]. After three days the precipitate is filtered off on a cooled frit (−50 °C), washed with cold diethyl ether (2 × 50 ml), dried in a high vacuum at 20 °C, and finally taken up in 500 ml toluene. After removal of insoluble NaBr by filtration the filtrate is evaporated down to *ca.* 50 ml; addition of about 100 ml diethyl ether leads to precipitation of both *(2)* (6.2 g, 66%) as well as *(3)* (7.2 g, 77%) in microcrystalline, analytically pure form. *(2)* and *(3)* can be recrystallized from toluene : diethyl ether (1:1).

Received: June 29, 1979 [Z 391a IE]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 131 (1980)

[1] *H. H. Freedman*, J. Am. Chem. Soc. *83*, 2194 (1961).
[2] a) *H. Hoberg, R. Krause-Göing, C. Krüger, J. C. Sekutowski*, Angew. Chem. *89*, 179 (1977); Angew. Chem. Int. Ed. Engl. *16*, 183 (1977); b) *H. Hoberg, R. Krause-Göing, R. Mynott, ibid. 90*, 138 (1978) and *17*, 123 (1978); c) *H. Hoberg, C. Fröhlich*, J. Organomet. Chem. *168*, C52 (1979).
[3] *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Vol. 1. Academic Press, New York 1974.
[4] *H. Hoberg, U. Griebsch*, Angew. Chem. *90*, 1014 (1978); Angew. Chem. Int. Ed. Engl. *17*, 949 (1978).
[5] We thank Dr. *R. Mynott* for recording the ^{13}C-NMR spectra.
[6] *H. P. Fritz*, Z. Naturforsch. *B16*, 415 (1961).
[7] *H. H. Freedman, G. A. Doorakian*, Tetrahedron *20*, 2818 (1964).
[8] At higher temperatures considerable amounts of bis(tetraphenylcyclobutadiene)nickel [2c] and *(5)* are formed.

Photochemically Induced 1,2-Bis(dialkylalumination) of Diphenylacetylene

By *Heinz Hoberg* and *Fernando Aznar*[*]

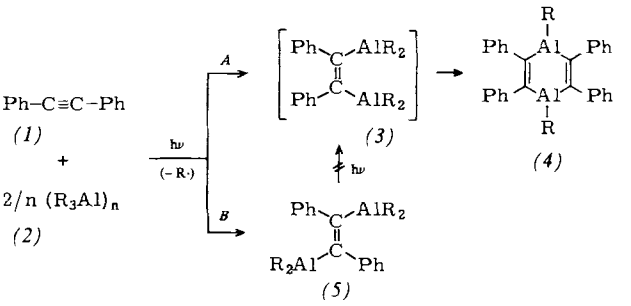
Trialkylaluminum/alkali metal[1] and dialkylaluminum halide/alkali metal[2] add to disubstituted alkynes, especially diphenylacetylene, in a dark reaction to give respectively *cis*- and *trans*-bis(alumino)alkenes, from which 1,4-dialuminacyclohexadienes *(4)* can be prepared[3,4].

We have now found that a 1,2-bis(dialkylalumination) of diphenylacetylene *(1)* with trialkylaluminum *(2)* is also possible photochemically in the absence of donors; it leads to 1,2-bis(aluminum compounds) *(4)* and *(5)*. The yield is highly dependent upon the nature of R and the temperature.

After 48 hours' irradiation at 25 °C triethylaluminum *(2a)* affords mainly the six-membered ring compound *(4a)*, which can be isolated as the crystalline bis-THF adduct (32%) (THF = tetrahydrofuran). At 60 °C, on the other hand, *(2a)* also reacts to give *(5)* (*ca.* 49%), which can be isolated as the bis-THF adduct in 30% yield.

The difference in the course of reaction (route A or B) can be attributed to the degree of association (*n*) of the trialkylaluminum compounds *(2)*[5]. Trimethylaluminum is only slightly reactive under the given conditions [yield of *(4)* and/or *(5)* < 1%].

[*] Prof. Dr. H. Hoberg, Dr. F. Aznar
Max-Planck-Institut für Kohlenforschung
Postfach 011325, D-4330 Mülheim-Ruhr 1 (Germany)



We assume that *(1)* reacts photochemically with dimeric trialkylaluminum compounds *(2)* with *cis*-1,2-addition *via (3)* to give *(4)*, while the monomeric trialkylaluminum compounds *(2)* afford mainly the *trans*-1,2-addition products *(5)* (Table 1). It should be mentioned that *(5)* cannot be isomerized photochemically to the *cis*-form *(3)* or its secondary products *(4)* in the absence of donors (Et_2O, THF)[4].

Table 1. Yield (GC) of *cis*- and *trans*-stilbene after irradiation of *(1)* and R_3Al *(2)* (molar ratio 1:2, 48 h) and hydrolysis [a]. *cis*-Stilbene is formed from *(4)*, *trans*-stilbene from *(5)*.

	R	*n*	Stilbene [Yield] *cis* [%]	*trans* [%]	*T* [°C]
(2a)	C_2H_5	2	4	2	0
(2a)	C_2H_5	2	52	14	25
(2a)	C_2H_5	2	4	49	60
(2b)	*i*-C_3H_7	≈1	8	40	25
(2c)	*i*-C_4H_9	≈1	3	7	0
(2c)	*i*-C_4H_9	≈1	12	43	25
(2d)	*t*-C_4H_9	≈1	11	42	25

[a] For determination of the yields a solution of *(1)* and *(2)* was irradiated (see Experimental), hydrolyzed with 0.1 N H_2SO_4, and extracted with diethyl ether. The ethereal phase was evaporated down and the residue chromatographically analyzed.

On irradiation in the presence of *(1)* the ethyl groups in *(2a)* are eliminated in the form of C_2H_4, C_2H_6, C_4H_{10}, and H_2.

Experimental

(4a)·2THF: A solution of *(1)* (12.0 g, 67.4 mmol) and *(2a)* (15.4 g, 19.2 ml, 134.8 mmol) in toluene (200 ml) is irradiated with a Philips HPK 125 lamp for 48 h at 25 °C in a quartz-glass immersion apparatus. All but *ca.* 80 ml of the toluene is then removed by evaporation and the remaining solution treated with 15 ml THF and cooled to 0 °C. After six days the crystals are filtered; yield 6.6 g (32%). Melting point and IR spectrum agree with those given in Ref.[3].

(5b)·2THF: For the preparation of *(4a)* a solution of *(1)* (8.93 g, 50.16 mmol) and *(2b)* (19.84 g, 24.8 ml, 100.4 mmol) in 200 ml of toluene is irradiated for 48 h. The toluene is then evaporated down to *ca.* 50 ml; after addition of 15 ml THF and 100 ml hexane the solution is cooled to 0 °C. After six days the crystals are filtered; yield 8.0 g (26%). Melting point and IR spectrum are identical with those given in Ref. [2].

Received: September 27, 1979 [Z 391b IE]
German version: Angew. Chem. *92*, 132 (1980)

[1] *H. Lehmkuhl, J. Culjkovic, H. Nehl*, Justus Liebigs Ann. Chem. *1973*, 666.
[2] *H. Hoberg, V. Gotor*, J. Organomet. Chem. *127*, C32 (1977).
[3] *H. Hoberg, V. Gotor, A. Milchereit, C. Krüger, J. C. Sekutowski*, Angew. Chem. *89*, 563 (1977); Angew. Chem. Int. Ed. Engl. *16*, 539 (1977).
[4] *H. Hoberg, F. Aznar*, J. Organomet. Chem. *164*, C13 (1977).
[5] *H. Lehmkuhl, K. Ziegler* in Houben-Weyl-Müller: Methoden der organischen Chemie, 4th Edit., Vol. XIII/4, Thieme, Stuttgart 1970; *M. B. Smith*, J. Phys. Chem. *71*, 364 (1967).

Heterogeneously Catalyzed Gas-Phase Bromination of Trifluoromethane[1]

By *Hans Bock, Jan Mintzer, Jörg Wittmann,* and *Jürgen Russow*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Owing to its suitability as a highly effective fire-extinguishing medium in automatic extinguishing installations for the protection of valuable goods[2], considerable interest attaches to a facile preparation of trifluorobromomethane. One possible pathway is the gas phase bromination of trifluoromethane:

$$F_3CH + Br_2 \rightarrow F_3CBr + HBr \quad (1)$$

Useful yields of *ca.* 70% are obtained in the thermal reaction only above about 600 °C[3,4] (cf. Table 1); however, undesired side-products are formed at such high temperatures and corrosion problems also occur. Experiments with catalysts[5] have so far failed to give improved yields at lower temperatures.

Optimization of the heterogeneously catalyzed gas-phase bromination (1) was accomplished in three steps:

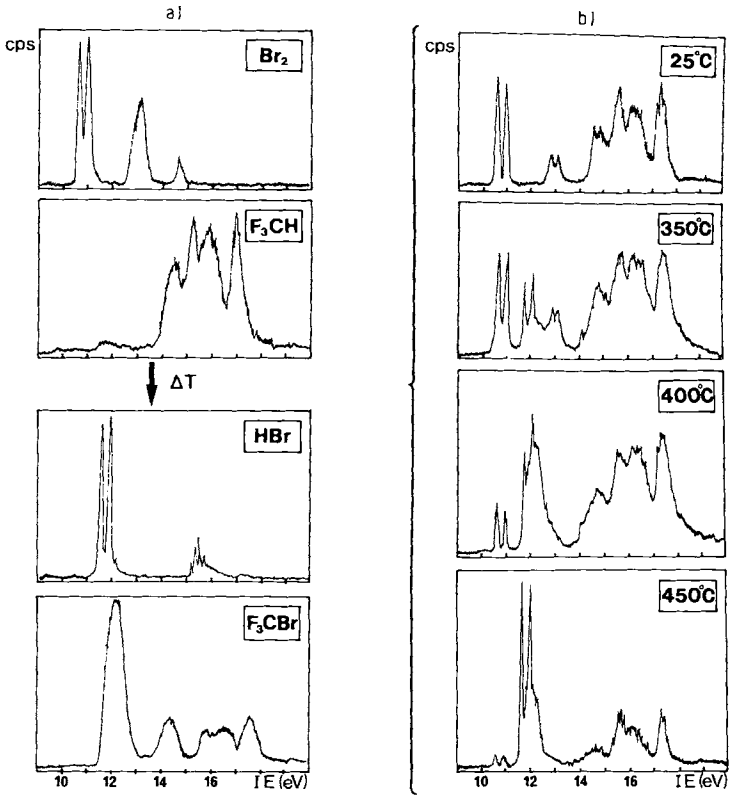


Fig. 1. a) PE spectra of reactants Br_2 and F_3CH and the products HBr and F_3CBr. The bands are seen not to overlap completely. The two double needles assigned to spin/orbit coupled states each of $Br_2^{\oplus}$ and $HBr^{\bullet\oplus}$ [6] are particularly suitable for gas analysis. b) Bromination of F_3CH over a $CuCl_2$/active charcoal catalyst as function of temperature: The 1:1 mixture (25 °C) reacts above 350 °C. The Br_2 double peak at 10.6/10.9 eV disappears and that of HBr appears at 11.7/12.0 eV. At the same time, the first F_3CH band at 14.8 eV is replaced by the second one of F_3CBr at 14.3 eV.

[*] Prof. Dr. H. Bock, Dipl.-Chem. J. Mintzer, Dipl.-Chem. J. Wittmann
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Dr. J. Russow
Hoechst Aktiengesellschaft
D-6230 Frankfurt am Main 80 (Germany)

1) On the basis of the partly published[6] and not completely overlapping photoelectron spectra of the reactants F_3CH and Br_2 and those of the products F_3CBr and HBr (Fig. 1a), a gas-analytical technique could be worked out for mixtures of any composition[7], which permits continuous monitoring of all components of the four-component system.

2) The catalyst screening—fast and with small sample quantities [7,8]—was by PE spectroscopy (Fig. 1b): determining at what temperature the same result is obtained as in the thermal reaction (*e.g.* in a tube packed with quartz rings, see Table 1). The gas-analytical approach chosen also proved advantageous, in that fluorination of oxide support material such as SiO_2 and γ-Al_2O_3 occurring mainly at high temperature can be recognized from the appearance of the characteristic ionization bands of H_2O (12.6 eV), CO_2 (13.8 eV), and/or CO (14.0 eV)[6].

3) Conversion and yield under reaction conditions optimized by PE spectroscopy are determined at atmospheric pressure on a preparative scale by conventional analysis: after passage through the heated catalyst compartment the excess of Br_2 is condensed out of the gas mixture; the bromine balance (% conversion) is established by addition of the bromine to cyclohexene. HBr is subsequently absorbed in 1 N NaOH; back titration gives the yield (%). The F_3CH/F_3CBr ratio in the residual gas is determined by gas chromatography.

Table 1. Yield of F_3CH bromination according to Eq. (1) as function of catalyst, furnace temperature T, and contact time $t_{contact}$.

Catalyst	T [°C]	$t_{contact}$ [s] [a]	Yield [%]
Quartz rings	450	19	51
	500	10	66
	600	14	68
	600	6	72
Activated charcoal	450	12	52
$CuCl_2$/activated charcoal	450	4	56
	450	12	59
$FeCl_3$/activated charcoal	450	15	66
KBr/activated charcoal	450	15	51
$FeCl_3$/KBr/activated charcoal [b]	450	12	71

[a] Conventionally defined as 1/[l gas/time·l catalyst]. [b] See procedure.

Table 1 shows that the thermal gas-phase bromination in a tube packed with quartz rings at 600 °C affords yields up to 72% depending upon the contact time; prolonged residence times promote decomposition reactions. Activated charcoal is ineffective, but is suitable as an inert carrier under the reaction conditions. Metal salts such as $CuCl_2$ and $FeCl_3$ catalyze the reaction, while KBr acts as a promoter.

Procedure

$FeCl_3$/KBr/C catalyst: HCl is passed over activated charcoal (30 g; Alfa 88765/28 mesh) at 150 °C for 1 h. After cooling in a stream of HCl, the substrate is impregnated with anhydrous $FeCl_3$ (5.6 g; corresponding to about 6% Fe on the carrier) and KBr (0.6 g) in CH_3OH (0.6 g). After stripping off the solvent *in vacuo* in a rotatory evaporator, the material is fluorinated in a stream of F_3CH (1/2 h at 30 °C, 1 h at 280 °C, 2 h at 300 °C, 3 h at 350 °C, and finally 5 h at 450 °C). It is important that the temperature be raised very slowly between 280 and 320 °C owing to transformation of $FeCl_3$ (m.p. 304 °C) into FeF_3 (m.p. 1030 °C).

Received: December 3, 1979 [Z 393 IE]
German version: Angew. Chem. *92*, 136 (1980)

[1] Analysis and Optimization of Gas-Phase Reactions, Part 16.—Part 15: *B. Solouki, P. Rosmus, H. Bock, G. Maier*, Angew. Chem. *92*, 56 (1980); Angew. Chem. Int. Ed. Engl. *19*, 51 (1980).

[2] Cf., *e.g., K. Weissermel, H.-J. Arpe:* Industrielle Organische Chemie. Verlag Chemie, Weinheim 1976, p. 51.

[3] *T. J. Brice*, J. Am. Chem. Soc. *68*, 968 (1946).

[4] *I. Yuichi, K. Kazuharu*, Jap. Pat. 7762208 (1977); Onoda Chem. Co.; Chem. Abstr. *87*, 133857 (1977).

[5] *K. Norihisa, I. Fumio, M. Kimiaki*, Jap. Pat. 7834705 (1978); Central Glass Co.; Chem. Abstr. *89*, 540 (1978): max. conversion achieved on $CrCl_3/AlF_3/Al_2O_3$ was 57% at 450 °C (cf. Table 1).

[6] Cf. collections of spectra, such at that of *D. W. Turner, C. Baker, A. D. Baker, C. R. Brundle:* Molecular Photoelectron Spectroscopy. Wiley-Interscience, London 1970.

[7] Cf. *H. Bock, B. Solouki, J. Wittmann*, Angew. Chem. *90*, 985 (1978); Angew. Chem. Int. Ed. Engl. *17*, 932 (1978); *H. Bock, B. Solouki, G. Bert, T. Hirabayashi, S. Mohmand, P. Rosmus*, Nachr. Chem. Tech. Lab. *26*, 634 (1978).

[8] Cf. also *H. Bock, B. Solouki, J. Wittmann, H.-J. Arpe*, Angew. Chem. *90*, 986 (1978); Angew. Chem. Int. Ed. Engl. *17*, 933 (1978).

BOOK REVIEWS

Ullmanns Encyklopädie der technischen Chemie [Ullmann's Encyclopedia of Industrial Chemistry]. Editorial board *E. Bartholomé, E. Biekert, H. Hellman, H. Ley* (deceased), *W. M. Weigert* (deceased), and *E. Weise*. Volume 17: Milchsäure to Petrolkoks. Verlag Chemie, Weinheim 1979. 4th edition, xv, 733 pages, bound, DM 425.00.

The individual volumes of Ullmann's fourth edition[*] are appearing with admirable regularity. A scan through this particular volume confirms that Ullmann is a genuine encyclopedia, going beyond the specific realm of industrial chemistry to deal with the necessary foundations and to include related fields. Individual overlapping entries treat special areas, such as the "oxidation" entry in the present volume, which describes in summary the oxidation processes for the preparation of organic intermediates; the many references to other entries for further information on certain processes are particularly valuable. To name some of the volume's entries taken from the sphere of inorganic chemistry, we have molecular sieves (10 pages), molybdenum (28 pages), sodium (87 pages), nickel (64 pages), and niobium (12 pages), including their compounds and alloys (especially important compounds such as sodium chloride and sodium hydroxide have their own entries), nitrides (7 pages), oxide ceramics (15 pages), and peroxo compounds (38 pages). From organic chemistry there are lactic acid (7 pages), naphthalene and derivatives (50 pages), aliphatic (10 pages) and aromatic (6 pages) nitriles, nitroso compounds (7 pages), aliphatic (10 pages) and aromatic (34 pages) nitro compounds, optically active compounds (7 pages), oxalic acid (8 pages), and peroxides and peroxy acids (30 pages). From the sphere of dye chemistry we can quote naphthalimide dyes (6 pages), naphthoquinone and benzoquinone dyes (5 pages), nitro and nitroso dyes (9 pages), and optical brighteners (15 pages), and from the sphere of pharmacology anesthetics (7 pages), nucleic acids and their derivatives (6 pages), and parasitoses (8 pages). Interested in fossil fuels? There are 14 pages on oil sands, 14 on oil shale, 5 on petroleum coke, and 20 on motor fuels; this last entry is restricted to gasoline, as diesel and turbine fuels are discussed under fuel oils. In addition, the following application-oriented entries should be mentioned: perfumes (5 pages), furs (9 pages), nitrocellulose (12 pages), and in particular paper, subdivided into fibrous raw materials (46 pages) and manufacture (59 pages).

The present volume is the equal of its predecessors in quality of presentation and material. This is undoubtedly due in essence to the editors' efforts in finding competent authors for the wide range of topics and then in coordinating their contributions.

Ulfert Onken [NB 497 IE]

The Chemical Applications of Transmission Electron Microscopy. *J. R. Fryer.* Academic Press, London 1979. x, 286 pages, 126 figures, 4 tables, bound, $ 38.00.

The present monograph treats the principles of image formation and image contrast in an electron microscope, microscope attachments, specimen preparation, high-resolution microscopy, and phase contrast, as well as the study of surface phenomena, crystal structures, and precipitates from solutions. The fascinating possibility of an *in-situ* observation of a chemical reaction in an electron microscope is considered in the last of the eight chapters. The book gives a good balance between theory and empiricism, the current state of the art in high-resolution microscopy being emphasized in preference to the physical principles of electron optics. The examples have been taken mainly from the author's own work. It is rather unfortunate that the technical details are explained predominantly for the example of the Siemens apparatus used in Glasgow, especially as Siemens no longer produce electron microscopes.

On the subject of high resolution, supplementary information would be desirable in a new edition, such as data on structural features that favor the use of this method and a more extensive discussion of the studies on oxides, in which the most recently published, higher-resolution pictures are taken into consideration. The table of the graphite compounds requires revision: it contains many printing errors and does not correspond to the current state of the art.

It was the author's intention that the bibliography should provide information on the work of other authors on subjects treated in less detail here. To achieve this aim revision is necessary to include further authors, such as *S. Andersson* and *L. Kihlborg*.

Finally, it should be emphasized that the book is a handy and practically-oriented summary with emphasis on providing a really useful introduction to the field, up to now not easily available to those who wanted to familiarize themselves with the methods of transmission electron miscroscopy.

Reginald Gruehn [NB 494 IE]

[*] Cf. Angew. Chem. Int. Ed. Engl. *18*, 491 (1979).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0202-0148 $ 02.50/0

Treatise on Analytical Chemistry. Part I: Theory and Practice. Edited by *I. M. Kolthoff et al.* John Wiley & Sons, New York 1979. 2nd edit., xxviii, 881 pages, bound, $ 78.50.

If the first edition of the present monograph was a boon to the teacher, practical chemist, and student alike, then the first volume of the second edition is a still more valuable addition to basic analytical literature.

The publishers invited expert authors to write on general and fundamental problems. The 14 chapters, arranged in four sections, contain excellent discussions of the rudiments of analytical chemistry in general (2 chapters), methodology (4 chapters), the relationship of general chemistry and analytical chemistry (5 chapters), and above all solution equilibria (3 chapters).

Kolthoff's scientific background and his love of the already classical direction of analytical chemistry come across clearly in the first chapter. One could wish for a more comprehensive account of the physical aspects of modern methods involving the interactions of elementary particles (use of electron and ion beams). This is not to say that anything else should be omitted, but rather that some expansion of this kind, perhaps with philosophical reflections, would emphasize the interdisciplinary nature of analytical chemistry still more strongly.

In comparison with the excellent methodological section—and here the chapters on "Sampling", "Precision", and "Standards" deserve particular praise—the contribution on "Education" loses a little. The editors have succeeded very well, however, in incorporating general and physicochemical aspects, such as the structural considerations relating to the process of dissolution.

In summary, it must be said that the work is of a high standard as regards the description of general data and methods of working; it can only be hoped that the same standard will be maintained in the subsequent volumes. The acquisition of this work is a must for every institution concerned with analytical chemistry, since it is practically compulsory reading for any budding analyst.

Hanns Malissa [NB 492 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Progress in Biomass Conversion, Vol. 1. Edited by *K. V. Sarkanen* and *D. A. Tillman.* Academic Press, New York 1979. xii, 259 pp., bound, $ 16.50.—ISBN 0-12-535901-2

Physical and Mechanistic Organic Chemistry. By *R. A. Y. Jones.* Cambridge University Press, Cambridge 1979. x, 357 pp., sewed, £ 8.50.—ISBN 0-521-29596-3

Guide to Gas Chromatography Literature, Vol. 4. By *A. V. Signeur.* Plenum Press, New York 1979. vii, 1321 pp., bound, $ 145.00.—ISBN 0-306-68204-4

Life Sciences Research Report 12. Light-Induced Charge Separation in Biology and Chemistry. (Dahlem Conferences). Edited by *H. Gerischer* and *J. J. Katz.* Verlag Chemie, Weinheim 1979. 562 pp., sewed, DM 75.00.—ISBN 3-527-12001-7

Life Sciences Research Report 13. Strategies of Microbial Life in Extreme Environments. (Dahlem Conferences). Edited by *M. Shilo.* Verlag Chemie, Weinheim 1979. 513 pp., sewed, DM 72.00.—ISBN 3-527-12002-5

Life Sciences Research Report 14. The Role of Intercellular Signals. Navigation, Encounter, Outcome. (Dahlem Conferences). Edited by *J. G. Nicholls.* Verlag Chemie, Weinheim 1979. 307 pp., sewed, DM 44.00.—ISBN 3-527-12016-5

Characterisation of Porous Solids. Edited by *S. J. Gregg, K. S. W. Sing,* and *H. F. Stoeckli.* Society of Chemical Industry, London 1979. xiii, 392 pp., bound, £ 21.00.—ISBN 090100-157-0

Polymer-Polymer Miscibility. By *O. Olabisi, L. M. Robeson,* and *M. T. Shaw.* Academic Press, New York 1979. xii, 370 pp., bound, $ 42.50.—ISBN 0-12-525050-9

Chemistry Reviews, Vol. 1. Edited by *M. E. Vol'pin.* Soviet Scientific Reviews/Harwood Academic Publ., Amsterdam 1979. ix, 277 pp., bound, $ 46.00.—ISBN 33-7186-0008-0

Spectroscopic Properties of Inorganic and Organometallic Compounds, Vol. 11. Senior Reporter: *E. Ebsworth.* The Chemical Society, London 1979. xii, 455 pp., bound, DM 160.00.—ISBN 0-85186-103-2.—A volume of the series "Specialist Periodical Reports"

Terpenoids and Steroids, Vol. 9. Senior Reporter: *J. Hanson.* The Chemical Society, London 1979. xii, 352 pp., bound, DM 140.00.—ISBN 0-85186-650-6.—A volume of the series "Specialist Periodical Reports"

Electron Spin Resonance, Vol. 5. Senior Reporter: *P. B. Ayscough.* The Chemical Society, London 1979. xiii, 378 pp., bound, DM 150.00.—ISBN 0-85-186-791-X.—A volume of the series "Specialist Periodical Reports"

Organometallic Compounds, Vol. 1. The Main Group Elements, Part 2, Groups IV and V. By *B. J. Aylett.* Chapman and Hall, New York 1979. 4th edit. xi, 521 pp., bound, £ 32.50.—ISBN 0-412-13020-3

Gesundheitsschädliche Arbeitsstoffe, Band III. Edited by *D. Henschler.* Verlag Chemie, Weinheim 1979. xxii, 140 pp., looseleaf file, DM 68.00.—ISBN 3-527-25847-7

German-Jewish Pioneers in Science 1900—1933. By *D. Nachmansohn.* Springer-Verlag, Berlin 1979. xx, 388 pp., bound, DM 60.00.—ISBN 3-540-90402-6

Chemistry and Agriculture—Bristol 1979. The Chemical Society, London 1979. xiv, 287 pp., sewed, DM 35.00.—ISBN 0-85186-680-8

Comprehensive Biochemistry, Vol. 33B. A History of Biochemistry. Edited by *M. Florkin* and *E. H. Stotz.* Elsevier Scientific Publishing Co., Amsterdam 1979. xix, 320 pp., bound, $ 52.75.—ISBN 0-444-80068-9

Theorie und Methoden der Enzymkinetik. By *H. Bisswanger.* Verlag Chemie, Weinheim 1979. xii, 239 pp., sewed, DM 48.00.—ISBN 3-527-25845-0

Nuclear Magnetic Resonance, Vol. 8. Senior Reporter: *R. Abraham.* The Chemical Society, London 1979. xxxiv, 351 pp., bound, DM 140.00.—ISBN 0-85186-322-1.—A volume of the series "Specialist Periodical Reports"

Topics in Stereochemistry, Vol. 11. Edited by *N. L. Allinger* and *E. L. Eliel.* John Wiley & Sons, Chichester 1979. 344 pp., bound, £ 26.00.—ISBN 0-471-05445-3

Carbanions in Organic Synthesis. By *J. C. Stowell.* John Wiley & Sons, Chichester 1979. xi, 247 pp., bound, £ 13.75.—ISBN 0-471-02953-X

Metal and Metalloid Amides. By *M. F. Lappert, P. P. Power, A. R. Sanger,* and *R. C. Srivastava.* John Wiley & Sons, Chichester 1980. 847 pp., bound, £ 50.00.—ISBN 0-85312-098-6

Advances in Inorganic Chemistry and Radiochemistry, Vol. 22. Edited by *H. J. Emeléus* and *A. G. Sharpe.* Academic Press, New York 1979. ix, 457 pp., bound, $ 48.00.—ISBN 0-12-023622-2

Populäre Schriften. By *L. Boltzmann.* Selected by *E. Broda.* Vieweg & Sohn, Braunschweig 1979. iv, 290 pp., sewed, DM 29.80.—ISBN 3-528-08442-1

How to Succeed in Organic Chemistry. By *J. E. Gordon.* John Wiley & Sons, Chichester 1979. xiv, 594 pp., sewed, $ 4.95.—ISBN 0-471-03010-4

Physikalische Prinzipien und ihre Anwendung in der Chemie. By *G. M. Barrow* and *G. W. Herzog.* Vieweg & Sohn, Braunschweig 1979. xii, 377 pp., sewed, DM 39.80.—ISBN 3-528-03579-X

Wörterbuch der Chemie und der chemischen Verfahrenstechnik. Vol. 2: English/German. Verlag Chemie, Weinheim 1979. 2nd revised and enlarged edition. ix, 781 pp., bound, DM 220.00.—ISBN 3-527-25781-0

Gel Chromatography. By *T. Kremmer* and *L. Boross.* John Wiley & Sons, Chichester 1979. 298 pp., bound, £ 16.50.—ISBN 0-471-99548-7

Carcinogens and Related Substances. By *M. C. Bowman.* Marcel Dekker, Basel 1979. vii, 316 pp., bound, SFr. 78.00.—ISBN 0-8247-6885-X

Reaktionszwischenstufen der Organischen Chemie. By *N. S. Isaacs.* Verlag Chemie, Weinheim 1980. xii, 417 pp., sewed, DM 68.00.—ISBN 3-527-25728-4

Urea-Formaldehyde Resins. By *B. Meyer.* Addison-Wesley Publishing Co., London 1979. xi, 423 pp., bound, $ 29.50.—ISBN 0-201-04558-3

Organic Compounds of Sulphur, Selenium, and Tellurium, Vol. 5. Senior Reporter: *D. R. Hogg.* The Chemical Society, London 1979. xxiv, 523 pp., bound, DM 195.00.—ISBN 0-85186-620-4.—A volume of the series "Specialist Periodical Reports"

Explosivstoffe. By *R. Meyer.* Verlag Chemie, Weinheim 1979. 5th revised and enlarged edition. ix, 407 pp., sewed, DM 88.00.—ISBN 3-527-25846-9

Surface Contamination. Genesis, Detection, and Control. Edited by *K. L. Mittal.* Plenum Press, New York 1979. Vol. 1: xvi, 523 pp., bound, $ 39.50.—ISBN 0-306-40176-2; Vol. 2: xvi, pp. 527—1056, bound, $ 39.50.—ISBN 0-306-40177-0

Contemporary Topics in Polymer Science, Vol. 3. Edited by *M. Shen.* Plenum Press, New York 1979. xii, 340 pp., bound, $ 37.50.—ISBN 0-306-40283-1

Fundamentals of Crystal Growth I. By *F. Rosenberger.* Springer-Verlag, Berlin 1979. x, 530 pp., bound, DM 79.00.—ISBN 3-540-09023-1

Max-Planck-Gesellschaft—Jahrbuch 1979. Verlag Vandenhoeck & Ruprecht, Göttingen 1979. 770 pp., bound, DM 68.00.—ISBN 3-525-85382-3

Handbook of Liquid Crystals. By *H. Kelker* and *R. Hatz.* Verlag Chemie, Weinheim 1980. xviii, 917 pp., bound, DM 420.00.—ISBN 3-527-25481-1

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar,* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 3
March 1980
Pages 151–230

Electrophilic Reagents—Recent Developments and Their Preparative Application

By Franz Effenberger[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The most widely known electrophilic agents are protic acids and compounds with an electron-sextet partial structure. Recent research has aimed at the development of new electrophilic reagents, with greater reactivity on the one hand and higher selectivity on the other, which would largely obviate the addition of Lewis acids (Friedel-Crafts catalysts), and also allow control of the isomer ratio in reactions with ambivalent substrates. Compounds with "super-leaving groups", such as trifluoromethanesulfonate and fluorosulfate, have been demonstrated as most advantageous in this respect since they are sufficiently polarized or dissociated for reactions to take place even in the absence of Friedel-Crafts catalysts. Heterocycles such as pyridones or imidazole are likewise suitable leaving groups; they are employed for their high selectivity, and also because they allow working under non-aqueous conditions.

1. Introduction

The terms "electrophile" and "electrophilic reagent" were introduced into organic chemistry by *C. K. Ingold*[1a]; his definitions, given in a comprehensive review[1b] and in his standard work "Structure and Mechanism in Organic Chemistry"[1c], are still valid today:

> "Reagents which act by acquiring electrons, or share in electrons which previously belonged to a foreign molecule will be called electrophilic reagents, or sometimes electrophiles."

Ingold distinguishes here between electrophiles which actually take over the electrons from another molecule (oxidants in the true sense), and those which form covalent bonds and thence place only a partial demand on the substrate electrons. This definition smoothly accommodates both protic acids and compounds with an electron-sextet structure which coordinate with lone electron pairs of other molecules in an electrophilic manner.

[*] Prof. Dr. F. Effenberger
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

The basic principle underlying the interaction between acid/base, acceptor/donor, and electrophile/nucleophile has been a controversial issue for a long time, and has led to frequent attempts at an optimum systematization or classification[2]. *Ingold* had already recognized clearly, though, that a formal (electric) charge is not prerequisite for the electrophilicity of a certain species; rather, the actual electrophilic moiety may be formed *in situ* in the reactant mixture.

In electrophilic bond formation, the bonding electrons must by definition stem from the substrate. Thus only compounds with lone pairs or π-electrons are as a rule susceptible to electrophilic attack; electrophilic reactions of σ bonds remain exceptional for energetic reasons[3]. Alcohols and amines, as compounds with lone electron pairs, consequently number among the most important substrates for electrophiles, *e.g.* in alkylation or acylation. Usually, these reactions are considered under the aspect of the nucleophile; because of the considerable influence of the electrophilic partner, however, recent developments in this field will be discussed here too.

The most frequently employed reactions of unsaturated compounds are the electrophilic substitution of arenes and hetarenes, the electrophilic addition to alkenes and alkynes, respectively, and their substitution; in this context, enols and

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-151 $ 02.50/0

enol derivatives (enol ethers, acylates, and silyl enol ethers) as well as enamines must be considered as specially substituted olefins.

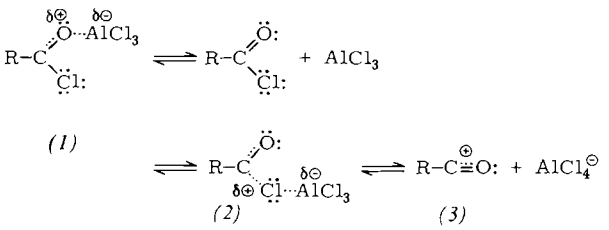
The quest for new electrophiles has been directed primarily towards greater reactivity and higher selectivity; such reagents should render the addition of equimolar amounts of Friedel-Crafts catalysts superfluous, and allow at least some control of the isomer distribution in reactions with ambivalent substrates (*e.g.* substituted aromatics or enols).

A decisive factor for both the generation and the reaction potential of an electrophile is whether the reagent is dissociated into anion and cation (as the actual electrophilic species), or whether a more or less polarized bond is cleaved in the desired direction only under the influence of the co-reactant:

$$E-A \leftrightarrow E^{\delta\oplus} \blacktriangleleft A^{\delta\ominus} \rightleftharpoons E^{\oplus}\,A^{\ominus} \rightleftharpoons E^{\oplus} + A^{\ominus}$$

In the absence of a suitable substrate, bond polarization is determined primarily by the electronegativity difference between E and A; the extent of bond cleavage mainly depends on the stability of the ions $E^{\oplus}$ and $A^{\ominus}$ in a given solvent, as long as the system provides the necessary energy for dissociation.

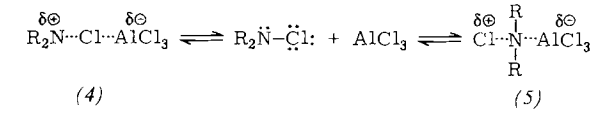
The described bond polarization or cleavage of a reagent E–A is frequently catalyzed by electron acceptors (Brønsted or Lewis acids) which in this context are generally designated summarily as Friedel-Crafts catalysts. The mode of interaction of these electron acceptors is not the same, though, for the various potential electrophiles—as, for example, in Friedel-Crafts alkylation and acylation; a general classification with respect to their catalytic effectiveness is therefore not feasible. A compound with lone pairs at different atoms, for example, can be attacked by the catalyst at each of the nucleophilic sites; this in turn may lead to the formation of different electrophiles, rendering predictions as to the actual reagent rather difficult. The presence of both oxonium complexes *(1)* and acylium ions *(3)*, for instance, has been established for Friedel-Crafts acylation with acyl chlorides and $AlCl_3$[4a,b]. Additionally, the acyl halide suffers halogen exchange—proven by isotopic labeling—which also can be rationalized only *via* the intermediate *(2)* and an equilibrium with the acylium ion *(3)*[4c].



(1) *(2)* *(3)*

From kinetic experiments, it has been deduced that a further intermediate is involved in the formation of *(3)* in which the carbonyl oxygen is likewise complexed by $AlCl_3$[4d]. All three potential electrophiles [*(1), (2), (3)*] now can act as the effective acylating agent in Friedel-Crafts acylation.

Another striking example is the amination with chloroamines in the presence of Friedel-Crafts catalysts. Attack of the Lewis acid at a lone pair of the chlorine atom produces an aminating agent *(4)*, whereas attack at the nitrogen lone pair results in the formation of a chlorinating agent *(5)*[5].



(4) *(5)*

This problematical situation in electrophilic reactions with Friedel-Crafts catalysts has been dealt with comprehensively in several reviews[6]. In the development of new, both more reactive and selective electrophiles, attempts have been made to eliminate the difficulties inherent in the application of Lewis acids, and, by introducing better leaving groups, to achieve sufficient polarization or dissociation of the reagents E—A *per se*. The present review will focus attention primarily on these aspects.

2. Importance of the Leaving Group for Electrophile Formation

A decisive factor for the reactivity of an electrophile is the degree of its polarization or dissociation. Numerical values for the leaving tendency of different groups have been derived mainly from the kinetics of nucleophilic substitution at a saturated carbon atom. For estimating relative reactivities of electrophiles with different leaving groups, solvolysis probably represents the best model; here, the dissociation step is rate-determining and, consequently, the influence of the leaving group on the reaction rate far greater than in S_N2 substitution[7]. For some of the more common leaving groups, relative rates in S_N1 reactions are given below (relative to bromide):

Leaving group $Z^{\ominus}$:	$CF_3SO_3^{\ominus}$	p-CH_3—C_6H_4—$SO_3^{\ominus}$	$Br^{\ominus}$
k_Z/k_{Br}:	5×10^8	5×10^3	1
Leaving group $Z^{\ominus}$:	$Cl^{\ominus}$	p-O_2N—C_6H_4—$COO^{\ominus}$	
k_Z/k_{Br}:	2.5×10^{-2}	2×10^{-6}	

Yet even in S_N1 reactions, the influence of the leaving group on the reaction rate depends to some extent on the stability of the carbenium ion formed upon dissociation, diminishing with increasing cation stability[7]. If dissociation of E–A, as stated above, is in fact determined principally by the stability of the ions $E^{\oplus}$ and $A^{\ominus}$, then, for any given electrophile $E^{\oplus}$, the stability of $A^{\ominus}$ alone should determine its leaving tendency; in this case, the pK_a of the conjugate acid could provide a quantitative measure. Good correlation indeed exists between leaving tendency and conjugate acid strength in many cases, even though pK_a values are defined for H–A bond dissociation while in S_N1-type solvolyses >C–A bonds are cleaved heterolytically. Within the halide series, for instance, the leaving tendencies parallel the pK_a values of the hydrohalic acids (I > Br > Cl > F).

For the solvolysis of sulfonates, with C–O bond cleavage, a good correlation has been established between the leaving tendency of the sulfonate anion, $XSO_3^{\ominus}$, and the acid strength of XSO_3H (X = CF_3, F, C_6F_5, p-CH_3—C_6H_4)[8].

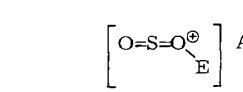
According to a recent investigation, acid strength and leaving tendency are loosely correlated even for very strong acids[9]. The rates of solvolysis of methyl trifluoromethanesulfonate (= methyl triflate), fluorosulfate, and perchlorate, for instance, are graduated comparably in the three solvent media water, methanol, and acetonitrile ($CF_3SO_3CH_3$ >

$FSO_3CH_3 > ClO_4CH_3$); the differences, though, are fairly small. Conductometric determinations in aprotic media and in CH_3COOH, on the other hand, give similar acidities for perchloric and trifluoromethanesulfonic acid, and a somewhat lower value for fluorosulfuric acid[10].

The exceptionally high leaving tendency of the trifluoromethanesulfonate ("triflate") ion has been attributed to specific electronic interaction of the CF_3 group in the dissociation step[11]. However, the paramount importance of triflate as leaving group is due to the extraordinary thermal stability and resistance towards oxidative and reductive degradation of both triflate ion and the free acid. In a recent summary of preparative applications of trifluoromethanesulfonic acid and its derivatives, *Howells* and *McCown* have particularly stressed this point[12].

Since the quantitative data on the leaving tendency of various moieties Z have all been derived from the solvolysis of C—Z bonds, they are not directly applicable to "hetero-electrophiles" (O, N, halogen electrophiles). For this, the other types of bonds involved in heterolysis, the changed bond polarization due to the altered electronegativity differences, and the disparate cation stabilization must all be taken into account. Nevertheless, the correlations between reactivity and stability of the leaving group, established for carbon electrophiles, have been applied successfully also in the development of new hetero-electrophiles.

A fundamental problem which so far has thwarted satisfactory quantification is the solvent effect in reactions with electrophiles. In the case of nucleophiles, reactivity is affected by solvent and gegenion in a well defined manner[13]. In contrast to these generally stable particles, most cationic electrophiles are stable and detectable only in superacid systems[13,14]; their high reactivity additionally limits the choice of organic reaction media to haloalkanes, nitriles, sulfones, and the like. Even so, most electrophiles do not undergo regular solvation; rather, they form definite 1:1 adducts with the solvent which constitute the actual electrophilic species. Thus, upon reaction in acetonitrile, nitrilium salts are produced[9,15], and in haloalkanes halonium derivatives[16]; even in SO_2, addition compounds of the following type are observed[14a,16].



This, of course, severely affects the reactivity of the electrophiles. Nitronium salts, for instance, in inert solvents such as dichloroethane or sulfolane are weaker nitrating agents—despite their established ionic structure $[NO_2^{\oplus}]Z^{\ominus}$—than the normal mixtures of HNO_3 and H_2SO_4[17] since in the less nucleophilic acid mixture electrophile/solvent interaction is much less pronounced. Some information about the influence of solvation on carbenium ions has been obtained from a comparison of the relative stabilities of cations in the gas phase and in solution[18].

3. Halogen Electrophiles[19]

Apart from perchloryl fluoride, which is utilized for introducing the ClO_3 group into aromatics[20], the only halogen electrophiles of practical interest are the monovalent cations $I^{\oplus}$, $Br^{\oplus}$, $Cl^{\oplus}$, and $F^{\oplus}$. So far, however, they have not been observed directly either in solution or in the solid state[21a]; attempts at their generation, usually in superacid systems, always afforded only $X_2^{\oplus}$ and $X_3^{\oplus}$ species[21b]. The stability of these poly-ions increases, as expected, in the order $F < Cl < Br < I$, and with the number of halogen atoms incorporated, *i.e.* from $X_2^{\oplus}$ to $X_3^{\oplus}$[22]. Several of these polyhalo cations have been isolated in the solid state[23], yet nothing has been reported about their use as electrophilic halogenating agents.

Preferentially, therefore, reagents of the type $Z^{\delta\ominus} \blacktriangleright X^{\delta\oplus}$ are employed in electrophilic halogenation where the crucial bond is polarized in the requisite direction by linking the halogen to a more electronegative element (O, N, or another halogen), and Z at the same time is a good leaving group. These conditions are met, *inter alia*, by interhalogen compounds, halogen nitrates, fluorosulfates, and trifluoromethanesulfonates, by the hypohalites and some organic *N*-halo derivatives, as well as by carbon-halogen compounds with a $C \blacktriangleright X$ bond polarized sufficiently by electron withdrawing substituents.

With interhalogen compounds themselves only iodination and bromination of activated arenes such as phenols and aromatic amines is possible[24]. Mixtures of $SbCl_5$ and Br_2 or I_2 in which interhalogens are also assumed to be present as reactive species allow the substitution of less reactive aromatics too, for instance *meta*-bromination of nitrobenzene in 65% yield[25].

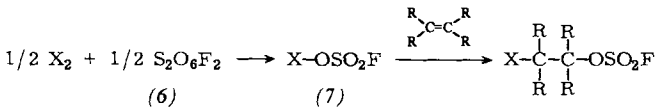
Halogen nitrates are prepared either from the anhydrides of the constituent acids[26] or, as pyridine complexes, with silver nitrate in pyridine directly from the halogens[27a]. The positivation of the halogen atoms in these reagents has been ascertained from spectroscopic results[28] as well as from their reaction behavior[26]: for example, their addition to double bonds proceeds both regioselectively and—*via* halonium intermediates—stereospecifically to give the *trans* adduct[27b].

$$Cl_2O + N_2O_5 \xrightarrow{0\,^{\circ}C} 2\,Cl{-}ONO_2$$

$$X_2 + AgNO_3 \xrightarrow[\text{Pyridine}]{CHCl_3} [X \cdot 2\,\text{Pyridine}]^{\oplus}NO_3^{\ominus} + AgX$$

$X = Br, I$

Halogen fluorosulfates *(7)* are usually prepared from the halogens with peroxodisulfonyl difluoride *(6)*[29,30]; their facile addition to olefins has been investigated extensively and is supposed to proceed *via* an electrophilic mechanism.



(6) *(7)*

X = F, Cl, Br; R = H, F, Cl

Recent investigations have confirmed the exceptional halogenating potential of halogen triflates *(8)*. Iodine triflate *(8a)*, for instance, though known for some time[31], has only recently been employed in iodination reactions.

$$6\,CF_3SO_3H + I_2 + 3\,S_2O_6F_2 \xrightarrow[-6\,HSO_3F]{} 2\,I(OSO_2CF_3)_3$$

(6)

$$\xrightarrow[140\,^\circ C]{+2\,I_2} 6\,I{-}OSO_2CF_3$$

(8a)

Chlorine triflate *(8b)* was synthesized almost simultaneously by two independent pathways[32,33].

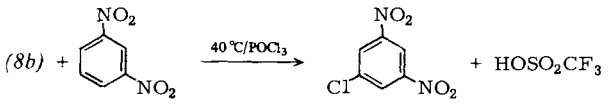
$$CF_3SO_3H + ClF \xrightarrow[-HF]{-111\text{ to }-78\,^\circ C} Cl{-}OSO_2CF_3$$

(8b)

$$\xrightleftharpoons{-80\text{ to }-40\,^\circ C} 1/2\,Cl_2O + 1/2\,(CF_3SO_2)_2O$$

Not unexpectedly, *(8b)* is an extremely powerful electrophile and chlorinates even *m*-dinitrobenzene in good yield[33]. Since the trifluoromethanesulfonic acid liberated in the course of the reaction is converted back into trifluoromethanesulfonic anhydride by the solvent $POCl_3$, only 20 mol-% need be employed[33].

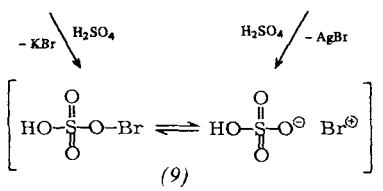
$$Cl_2O + (CF_3SO_2)_2O \rightleftharpoons 2\ (8b)$$



$$2\,CF_3SO_2OH + POCl_3 \longrightarrow (CF_3SO_2)_2O + Cl_2P(=O)OH + HCl$$

Bromine[34] and iodine triflate *(8a)*[35], prepared *in situ* from silver triflate and bromine or iodine, respectively, have also been successfully employed for the halogenation of deactivated arenes[34]. The findings with other halogen sulfonates[34] have led to the conclusion that for brominations in sulfuric acid, bromine hydrogen sulfate *(9)* is the reactive species, both in the presence of silver sulfate[36a] and with potassium peroxodisulfate[34].

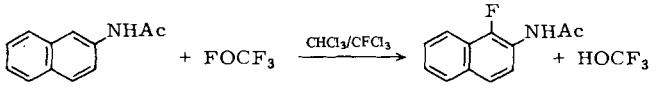
$$1/2\,K_2S_2O_8 + Br_2 \qquad 1/2\,Ag_2SO_4 + Br_2$$



(9)

Cesium fluoroxysulfate, obtained from cesium sulfate and fluorine, is both a powerful oxidant and fluorinating agent[36b].

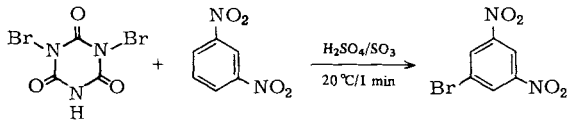
Among the hypohalites, which have long been used as main source of electrophilic halogen, fluoroxytrifluoromethane *(10)* has gained increasing importance[37a], particularly for the introduction of fluorine into the steroid skeleton. Reaction with both π- and σ-bonds[37b] most probably proceeds *via* an electrophilic mechanism.



(10) > 50%

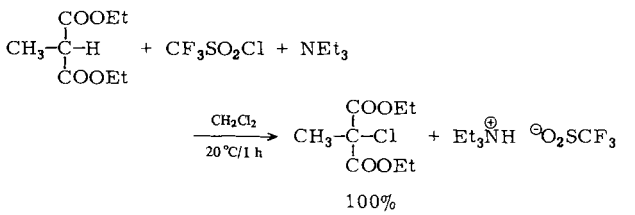
The XeF_6-graphite occlusion compound $C_{19}\cdot XeF_6$ which is more stable and thence easier to handle than the usually employed XeF_2[19b], has been applied specially for the fluorination of polycyclic arenes[38].

The halogen in the widely used *N*-halo derivatives can react either as radical or as electrophile[19b], depending on the further substituents at the nitrogen. With the extremely reactive *N,N*-dibromocyanuric acid *(11)*, for example, even strongly deactivated arenes are brominated in 15% oleum in good yield[39a], protonated *(11)* most likely being the reactive species[39b].



(11) 86%

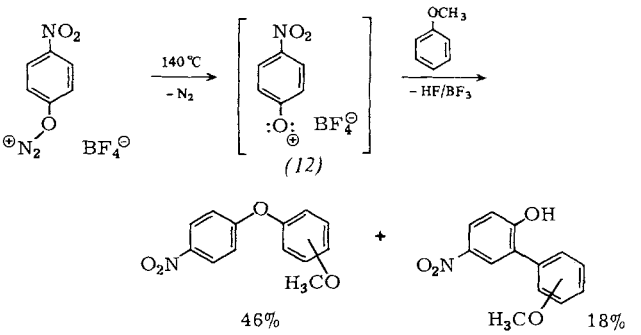
A very mild reagent for the chlorination of CH-acidic substrates is trifluoromethanesulfonyl chloride; it gives much better yields than *N*-chlorosuccinimide[40].



100%

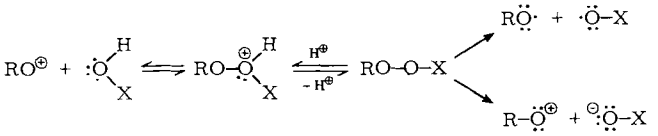
4. Oxygen Electrophiles

The oxygen electrophiles mainly used are compounds $RO^{\delta\oplus} \blacktriangleleft Z^{\delta\ominus}$ (R = H, organic group), with a sufficiently polarized O—Z bond and a good leaving group; because of the high electronegativity of oxygen itself, this must be either fluorine, another oxygen moiety, or a positively charged function ($-N_2^{\oplus}$, $-S^{\oplus}R_2$). The aryloxylium ion *(12)* so far is the only cationic oxygen electrophile $R-\ddot{O}^{\oplus}$ for which there is definite proof[41].

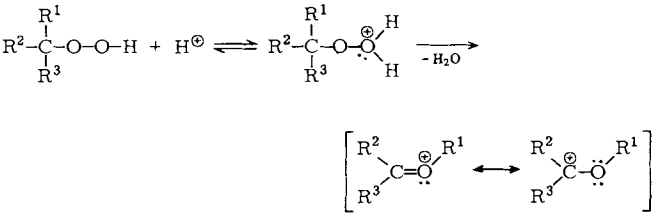


(12)

In practice, oxygen electrophiles are obtained mainly from hydrogen peroxide and its derivatives (peroxides, hydroperoxides, peroxo acids, peroxycarboxylic acids)[42]. Preferentially, peroxy functions are cleaved homolytically; a polar cleavage of the fairly weak O—O bond can be achieved, though, in polar solvents, also by substituents which are able to stabilize charges, and under the influence of proton or Lewis acids which polarize the O—O bond and, at the same time, generate better leaving groups[43].

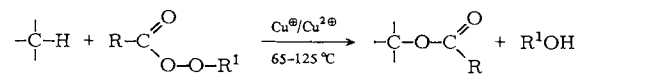


In generating oxygen electrophiles from peroxy precursors, heterolysis of the O–R bond may occur besides O–O bond cleavage[44]. Much more frequent and detrimental, however, is the rearrangement of the primarily formed cations into the well-stabilized carbenium ions[44].



Since in aryloxylium ions, *e.g. (12)*, analogous rearrangements are not possible, their existence could be demonstrated unequivocally by follow-up reactions[41].

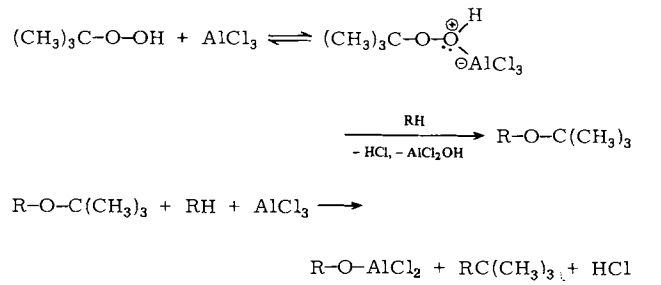
Acoxylation with peroxides is carried out with addition of transition metal ions; the reaction is employed regularly, and proceeds *via* radical intermediates[45].



R^1 = *t*Bu, ArylCO,...

An electrophilic mechanism, on the other hand, is assumed—on the basis of reactivity gradation and isomer distribution—for the reactions of the more electrophilic diaryl- and bis(arylsulfonyl) peroxides with nucleophilic arenes[46].

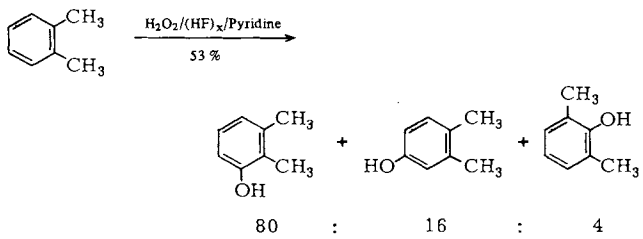
In the electrophilic hydroxylation of aromatics, the main problems are secondary (poly)hydroxylation—due to the enhanced reactivity of the hydroxyarenes formed—and oxidative processes which lead to a wide spectrum of products[47]. Polyhydroxylation can be avoided by using *tert*-butylperoxy isopropyl carbonate[48] or *tert*-butyl hydroperoxide[49] in the presence of Friedel-Crafts catalysts; in this case, the primary product, aryl *tert*-butyl ether, is transformed into the aryloxyaluminum dichloride *(13)* and thus deactivated.



R = Aryl *(13)*

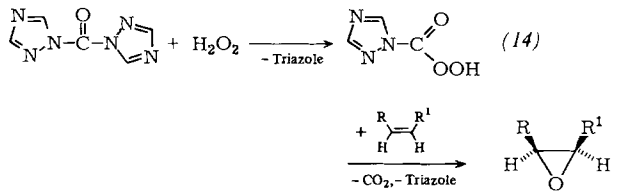
Electrophilic hydroxylation with peroxycarboxylic acids has gained increasing importance[42], especially since the ready accessibility of various peracids allows variation of the electrophilic potential within wide limits[50]. The yields in arene hydroxylation can be improved by addition of BF_3[51]; addition of $AlCl_3$ or $SbCl_5$, on the other hand, only favors the formation of oxidation products[47]. So far, inorganic peracids have found little use for arene hydroxylation—probably because of their instability in non-aqueous media. One example is the hydroxylation of alkyl- and hydroxybenzenes with peroxomonophosphoric acid; the high percentage of *ortho*-substitution products has led to the assumption of a cyclic transition state for this reaction[52].

Attempts within the past few years to utilize hydrogen peroxide itself as source of electrophilic oxygen were highly successful, and have made arene hydroxylation now possible on an industrial scale. Good yields of mono-hydroxylation products are thus obtained with highly concentrated hydrogen peroxide in the presence of $AlCl_3$[53] or strong acids[54] since in this case secondary reactions of the newly formed phenols are largely suppressed by protonation or complexation. The mixtures H_2O_2/HF[55a,b] and $H_2O_2/(HF)_x$/pyridine[55c] have proven exceptionally advantageous in this respect.

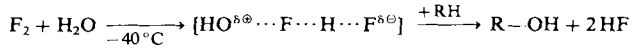


Surprisingly, poly-hydroxylation is also largely suppressed by the addition of CO_2[55a]. With H_2O_2/urea adducts and $AlCl_3$, arenes can likewise be hydroxylated in good yields[56].

Reaction of concentrated hydrogen peroxide with isocyanates[57a] or carbonyldiazolides[57b] affords peroxycarbamidic acids *(14)* which can serve as source of electrophilic oxygen in absolutely neutral medium, *e.g.* for the epoxidation of acid-labile olefins.



Hypofluoric acid HOF is one of the few oxygen electrophiles not derived from hydrogen peroxide. Other than HOCl, it yields only phenols in the reaction with arenes and no halogen derivatives. It has been supposed[58] that the electrophilicity of HOF is significantly enhanced by formation of the adduct *(15)* since with H_2O_2/HF no hydroxylation occurs under these conditions.



(15)

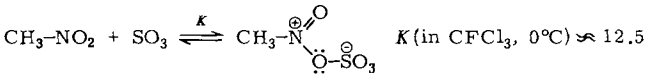
R = aryl

5. Sulfur Electrophiles

Among the reactions with electrophilic sulfur derivatives, sulfonation, sulfonylation, and likewise sulfenylation are of great importance; reactions with sulfurous acid derived electrophiles, on the other hand, have attracted much less attention[59].

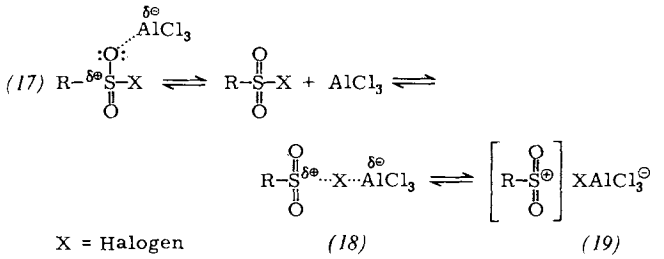
5.1. Sulfonation and Sulfonylation

Sulfonation is carried out prevalently with sulfuric acid of varying concentration—aqueous, concentrated, or SO_3-containing; SO_3-content and acid strength strongly affect both the formation of the electrophile and its reaction behavior[60]. With higher SO_3 concentration, for instance, more pyrosulfuric acids are formed ($H_2S_2O_7$, $H_2S_4O_{13}$) whose enhanced sulfonating potential is rationalized in terms of the higher leaving tendency of the respective larger anions[60b]. Adducts of SO_3 and cyclic ethers, pyridine, or tertiary amines are employed as selective sulfonating agents[61]. An addition complex *(16)* is present, too, in equilibrium in the sulfonation with SO_3 in nitromethane or nitrobenzene; though less reactive, *(16)* is significantly more selective than free SO_3 in haloalkane media[62].



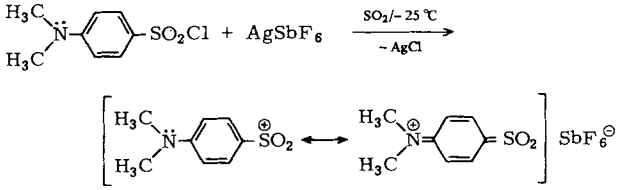
(16)

Sulfonylations are usually carried out with sulfonyl halides in the presence of Friedel-Crafts catalysts; as active electrophile in this case, either the oxygen- or the halogen-complexed intermediates, *(17)* or *(18)*, respectively, or the sulfonylium salts *(19)* are to be considered.

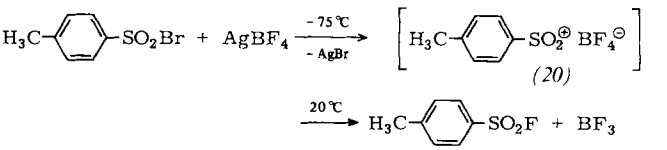


X = Halogen *(18)* *(19)*

Oxygen-addition products *(17)* result from the action of antimony pentahalides upon alkyl- and arylsulfonyl halides which bear no strong donor substituents[63a,b]; if the positive charge is sufficiently stabilized, *e.g.* by dialkylamino or alkoxy groups, sulfonylium salts *(19)* are formed[63b,c].

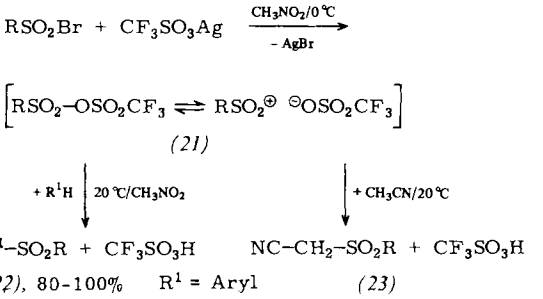


Klages et al.[64] who first investigated the reaction of toluenesulfonyl halides with silver perchlorate and tetrafluoroborate had already recognized the ionic nature of the powerful sulfonylating agents formed at low temperature with silver halide precipitation. Isolation of these sulfonylium salts

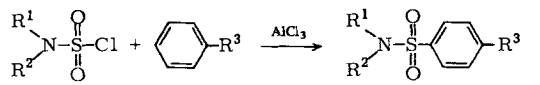


is not possible, though, since they decompose at slightly higher temperatures. The electrophilic potential of the *p*-toluenesulfonylium ion in *(20)*, for instance, is sufficient to strip off one fluoride from the gegenion $BF_4^{\ominus}$[64b].

In preparing new sulfonylating agents from aliphatic and aromatic sulfonyl bromides and silver triflate, the considerable stability of the triflate ion could be utilized to great advantage: The mixed anhydrides *(21)* can thus be obtained in neat form; their exceptional electrophilic potential allows, for instance, arylsulfone *(22)* formation in very good yields already at room temperature without addition of any Friedel-Crafts catalyst[65]. If preparation of the anhydrides *(21)* is attempted in acetonitrile as solvent, the cyanomethyl sulfones *(23)* are formed.



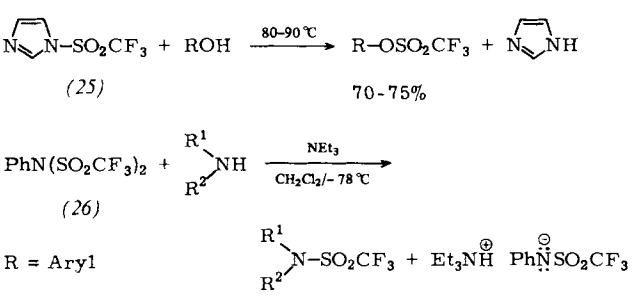
The way in which the relative reactivities in aryl sulfonylation depend on the rest R in the sulfonyl moiety indicate the dissociated form of *(21)* as the reactive species. The aliphatic anhydrides *(21)*, R = alkyl, are thermally labile; their rate of decomposition increases with increasing stability of the alkyl cations generated upon SO_2 expulsion ($CH_3^{\oplus} < C_2H_5^{\oplus} < (CH_3)_2CH^{\oplus}$)[65a].



(24) 50-100%

R^1, R^2 = C_2H_5, $-(CH_2)_5-$; R^3 = H, CH_3, Cl

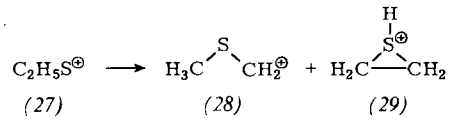
With the dialkylsulfamoyl chlorides *(24)*, *N,N*-dialkylsulfamoyl groups may be introduced into the *p*-position of mono-substituted arenes[66]. For the sulfonylation of OH- and NH-functions, both *N*-trifluoromethylsulfonylimidazolide *(25)*[67] and phenyl-*N,N*-bis(trifluoromethylsulfonyl)amide *(26)*[68] are very mild and highly selective reagents.



R = Aryl

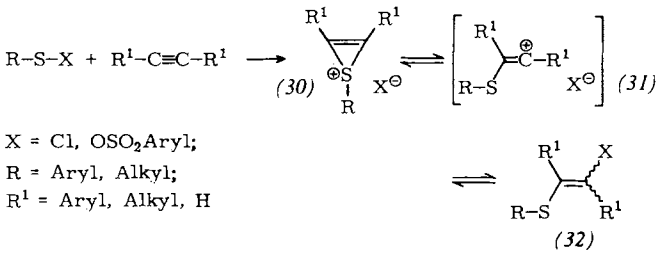
5.2. Sulfenylation

A comprehensive review of sulfenylium ions and other sulfenylating agents has appeared in 1976[69]; therefore, only work of the last few years will be commented upon here. Despite many efforts, free sulfenylium ions could so far not be detected in solution; once formed, they immediately stabilize by interaction or co-ordination with the solvent. In the gas phase, sulfenylium ions very rapidly rearrange into more stable species (*e.g.* the ethanesulfenylium ion *(27)* into *(28)* and *(29)*[70]). In general, electrophilic sulfenylating agents are generated from sulfenyl halides with Friedel-Crafts catalysts or *via* substitution of the halogen by a better leaving group[69].



(27) *(28)* *(29)*

The electrophilic addition of sulfenic acid derivatives to olefins[71] and acetylenes[72] has been investigated most extensively. Thiirenium salts *(30)* could be isolated from the reactions with acetylenes, partly in crystalline form. In solution, an equilibrium exists between these salts and the vinyl cations *(31)* and vinyl sulfides *(32)*; this equilibrium is the more shifted towards the side of the vinyl sulfides *(32)* the more nucleophilic the anion $X^{\ominus}$[72].

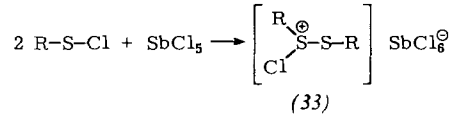


(30) *(31)*

X = Cl, OSO_2Aryl;
R = Aryl, Alkyl;
R^1 = Aryl, Alkyl, H

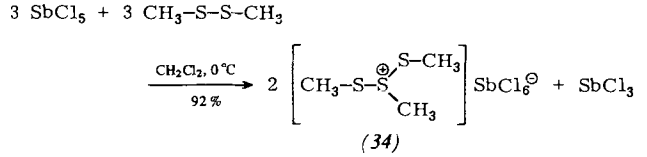
(32)

No free sulfenylium ions could be detected either in these reactions; rather, the attack of Lewis acids upon sulfenyl chlorides leads to the addition compounds *(33)* which then react as actual electrophilic species with the alkyne[72].



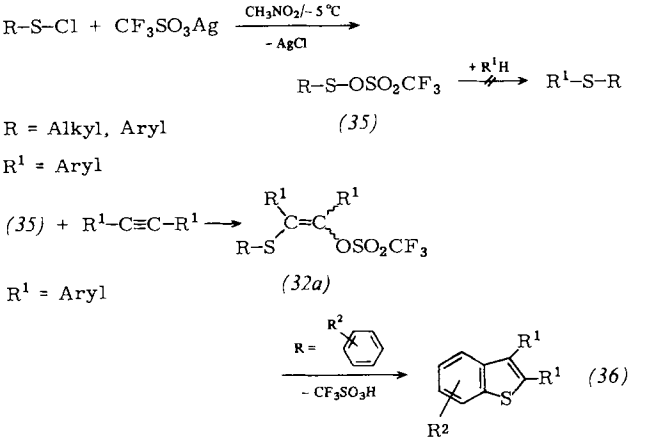
(33)

The sulfonium salts *(34)*, easily accessible from disulfides and antimony pentachloride, are excellent sulfenylating reagents[73].



(34)

The electrophilicity of the sulfenylating agents *(35)*, obtained from sulfenyl chlorides and silver triflate[74], does not suffice for arene sulfenylation; they add smoothly, though, to acetylenes. Due to the presence of the good triflate leaving group, the vinyl sulfides *(32a)* thus formed are subject to facile dissociation into vinyl cations; in the case of R = aryl, benzothiophenes *(36)* are formed in good yield by rearrangement of these vinyl cations[74].



(35)

R = Alkyl, Aryl
R^1 = Aryl

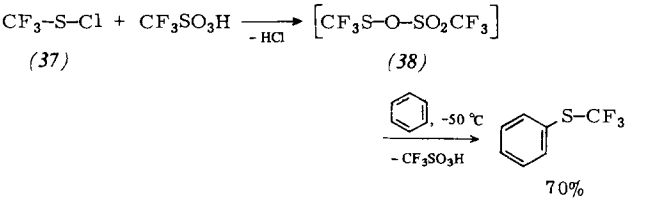
(32a)

R^1 = Aryl

(36)

An analogous benzothiophene formation upon heating arylsulfenic trinitrobenzenesulfonic anhydride with acetylenes had already been observed in earlier work[75].

The CF_3S function can be introduced directly into arenes and hetarenes with trifluoromethanesulfenyl chloride *(37)* in the presence of trifluoromethanesulfonic acid, for which the sulfenic sulfonic anhydride *(38)* formed intermediately is assumed as effective electrophile[76].

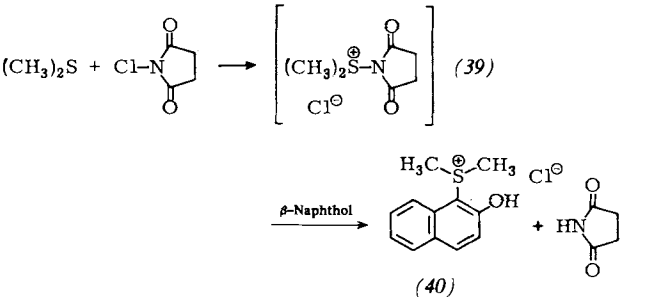


(37) *(38)*

70%

Iron[77] and silica gel[78] have proven exceptionally good catalysts for electrophilic aromatic substitution with sulfenyl halides.

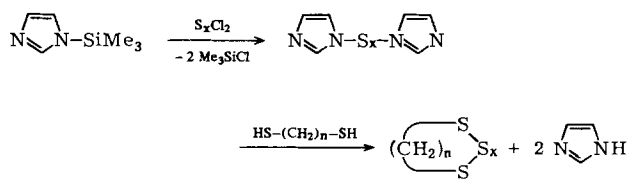
Salts of the type *(39)*[79], prepared from sulfides with chlorine[80] or from sulfoxides with mineral acids, allow electrophilic introduction of the R_2S moiety into arenes with formation of sulfonium salts such as *(40)*[69,81].



(39)

(40)

Electrophilic sulfurization has recently been carried out by utilizing the imidazolide procedure[82].



A mixture of $Pb(SCN)_2$ and $SbCl_5$ in CCl_4 permits introduction of the thiocyanato function into alkyl- and halobenzenes, probably *via* $(SCN^{\oplus}SbCl_6^{\ominus})$ as reactive species[83].

6. Nitrogen Electrophiles

Organic derivatives are known of practically all oxidation states of the N atom. Among the reactions with nitrogen electrophiles, though, only nitration, amination, nitrosation, and diazonium coupling reactions are of practical significance. Our discussion will be focused primarily on nitration and amination since, as far as diazonium salts as electrophiles are concerned, no fundamentally new aspects have appeared in recent years, and since, on the other hand, conditions for nitrosation are fairly similar to those for nitration.

6.1. Nitration and Nitrosation

Aromatic nitration is of great technical and scientific consequence and has therefore been investigated very thoroughly; the relevant earlier literature is adequately covered in some recent summaries[84–87].

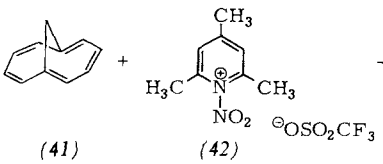
Replacement of the sulfuric acid in the usual nitration mixtures, made up of nitric acid and sulfuric acid of varying concentration, has a marked effect on the product spectrum in aromatic nitration. Thus trifluoromethanesulfonic acid[88a] and HF[88b] have both proven most advantageous for directing anthraquinone nitration into the 1-position. With combinations of nitric acid and either an arylsulfonic or phosphoric acid[89], a significantly higher *o/p*-ratio results on toluene nitration.

Since the use of HNO_3/H_2SO_4 mixtures is ecologically rather problematical, considerable efforts are being made to either curtail their use or, better, to completely replace them by other nitrating agents. Use of dichloromethane as solvent for nitrations with HNO_3/H_2SO_4 mixtures not only gives higher yields, *e.g.* in the reaction with equimolar amounts of nitric acid, since much less oxidation and sulfonation products are formed, but also permits recovery of sulfuric acid from the reaction mixture[90].

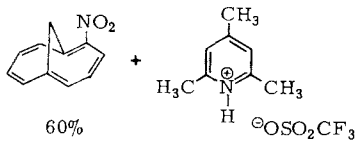
Nitryl salts were introduced by *Olah* and *Kuhn*[87,91] into preparative organic chemistry as effective nitrating reagents; they also allow nitration under non-aqueous conditions which is especially advantageous in the case of solvolysis- or oxidation-prone substrates.

Salts of the nitryl ion $NO_2^{\oplus}$ with complex perfluoro anions (*e.g.* $BF_4^{\ominus}$, $PF_6^{\ominus}$, $SbF_6^{\ominus}$, $SeF_5^{\ominus}$, $IF_6^{\ominus}$) have been known for some time; their spectral properties have recently been critically evaluated[92]. In addition, nitryl triflate[17,93] as well as the respective hydrate[94] and also nitryl hydrogen sulfate[90] have been synthesized in recent years. The reactivity of these various nitryl salts in organic solvents critically depends on both solubility and the extent of ion/solvent interaction[17].

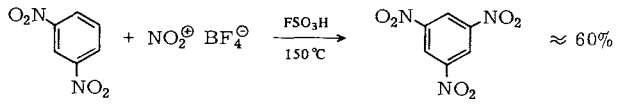
Just as in the case of the well-known reactions with *N*-nitropyridinium salts[95,96], highly interesting results may still be expected[87] from the adducts of nitryl salts with donor molecules (alcohols, ethers, sulfides), namely with respect to special selectivity in nitration. With the 1:1-addition compound *(42)* of nitryl triflate and collidine[97], which is readily soluble in dichloromethane, acid-labile substrates such as 1,6-methano[10]annulene *(41)* can be selectively nitrated in good yield[98].



(41) *(42)*

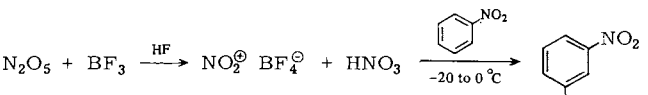


Nitryl tetrafluoroborate in fluorosulfuric acid represents an exceptionally reactive nitrating species which converts *m*-dinitrobenzene into trinitrobenzene in relatively high yield[99].



Nitration with nitryl halides in the presence of Friedel-Crafts catalysts[87], though possible in principle, so far has gained no practical significance. On the one hand, the nitrogen-halogen bond is not polarized unequivocally because of the comparable electronegativities of N and the halogens, and on the other, attack of the catalyst at an oxygen atom of the nitro group can render the nitryl halide a potential halogenating species.

Among the oxides of nitrogen, both dinitrogen tetroxide and dinitrogen pentoxide can be employed for nitration reactions; nitrations with N_2O_5 are well known and have been investigated extensively[87]. Nitryl salts are generated from N_2O_5 by the action of protic or Lewis acids, which then react as described above; if HF is used as solvent, or the pyridinium/polyhydrogen fluoride mixture[4] which is experimentally easier to handle, an effective electrophile of especially high nitrating potential is obtained.



> 90%

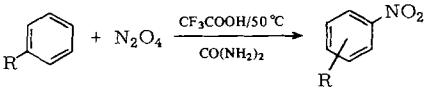
Sensitive substrates are nitrated preferentially in organic solvents[100], *e.g.* CCl_4, where N_2O_5 apparently reacts in the undissociated form.

Dinitrogen tetroxide, which as a rule dissociates into two NO_2 radicals, can also be cleaved heterolytically under the influence of Lewis acids. Since a potential nitrating and nitrosating agent are generated simultaneously, this has no great practical importance[87,101].

$$N_2O_4 + 3\,H_2SO_4 \rightleftharpoons NO_2^{\oplus} + NO^{\oplus} + H_3O^{\oplus} + 3\,HSO_4^{\ominus}$$
$$3\,N_2O_4 + 8\,BF_3 \rightarrow 3\,NO_2^{\oplus}\,BF_4^{\ominus} + 3\,NO^{\oplus}BF_4^{\ominus} + B_2O_3$$

Use of N_2O_4 as nitrating species is limited to some special cases, for instance the nitration of arylthallium compounds; toluene thus can be nitrated prevalently in *para*-position in

an overall yield of 98% (*o/m/p*-ratio 11:2:87)[102]. High yields are likewise achieved for N_2O_4 nitration in the presence of palladium salt catalysts[103], in trifluoroacetic acid with addition of at least a molar amount of urea—in this case without any Pd salts—[103], and in the case of reactive arenes even without added urea[104]. In all these N_2O_4 reactions, effective trapping of the nitrous acid seems to be the decisive factor.



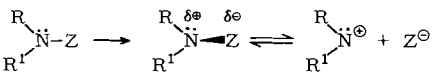
R	Yield [%]	Ratio of isomers *o* : *m* : *p*
H	99	
CH_3	76	55 : 2 : 43
Cl	100	36 : — : 64

In the presence of Lewis acids, *e.g.* Nafion-H (a perfluorosulfonic resin) or BF_3, alkyl nitrates and 1-cyano-1-methylethyl nitrate ("acetone cyanohydrin nitrate") are mild, non-oxidating nitrating reagents[105]. Titanium(IV) nitrate, employed for arene nitration in CCl_4, might, because of its low substrate selectivity, gain some preparative interest for the nitration of deactivated arenes and hetarenes[106].

The practical importance of nitrosation is much less than that of nitration. Since the weak electrophilicity of the nitrosating reagents is coupled with a relatively high oxidation potential, only strongly activated arenes such as phenols or aminobenzenes can be nitrosated successfully. The preparative aspects of nitrosation with the more common reagents have been summarized recently[84]. Nitrosyl salts[91b]—readily prepared and easy to handle—likewise are only weakly electrophilic, yet strongly oxidizing[107]; they are widely employed for the nitrosation of amines, alcohols, and anionic species[91b,107]. However, their electrophilic potential is not sufficient for rection with scarcely activated aromatic substrates.

6.2. Amination[108]

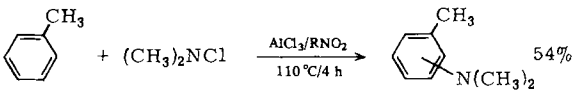
By introducing a good leaving group Z, ammonia and amines can be converted into electrophilic aminating agents. For all H_2N–Z derivatives reported so far, only N–Z bond polarization may be assumed; there are no indications for the existence of free $NH_2^{\oplus}$[109]. Investigations by *Gassman et al.* on the occurrence and chemical behavior of nitrenium ions $RR^1N^{\oplus}$ (R, R^1 = alkyl, aryl) have shown that these ions are much less stable than the structurally analogous carbenium ions[109]. The effect of the leaving group on heterolysis of the N–Z bond displays the same graduation as in carbenium ion formation[110]. Because of their high electronegativity, halogen and oxygen functions are mainly incorporated as leaving groups Z.



R, R^1 = H, Alkyl, Aryl

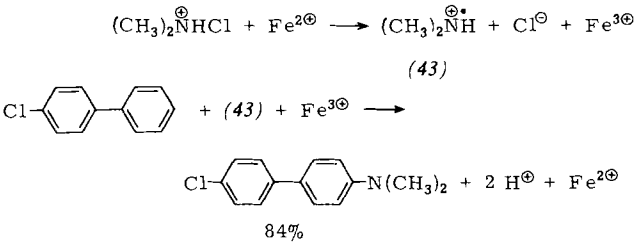
The long-known electrophilic introduction of amino groups with haloamines has been reviewed in considerable detail[108,111]. Satisfactory yields of amination products are generally obtained only with relatively strong nucleophiles (*e.g.* amines, alcohols), indicating a S_N2 character of these reactions[112]. With weakly nucleophilic substrates such as arenes, one observes competing electrophilic amination, amination *via* radical intermediates, and halogenation[111]. The isomer distribution for the amination of toluene with chlorodimethylamine, under the conditions given in the scheme below, points towards an electrophilic mechanism (R = CH_3, n-C_3H_7, $C(CH_3)_3$, C_6H_5).

Reaction of anisole with chlorodimethylamine under comparable conditions, on the other hand, exclusively affords chlorinated products (67% yield)[113].

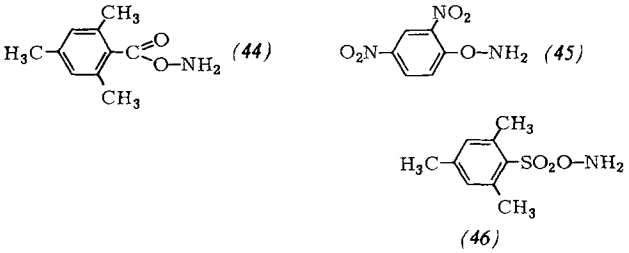


o:*m*:*p* = 7:15:32

The amination of arenes with chloroamines in highly acidic medium and in the presence of redox catalysts ($Fe^{2\oplus}$, $Ti^{3\oplus}$) is of great preparative value because of the good yields and high selectivities obtained[114]. Amino radical cations *(43)*, which have some electrophilic character, are the reactive species in this case[114]; the only isomers formed are the 4,4′-disubstituted biphenyls.



Far more important for electrophilic aminations than the haloamines are hydroxylamine derivatives. For this, however, the hydroxylamine OH function must first be converted into a good leaving group (as in the case of the alcohols in the carbon compound domain). Hydroxylamine-*O*-sulfonic acid[115] was the first and, for quite some time, the only such derivative whose manifold reactions with nucleophiles were investigated extensively[108]. Because of their higher reactivity, due to the presence of a better leaving group, the reagents *(44)*, *(45)*, and *(46)*[116,117] are now mainly used in practice.



The instability of some of these aminating agents is a great drawback. For instance, *(46)* is highly explosive[118]; all attempts to prepare the triflate derivative *(47)* *via* the hydroxyl-

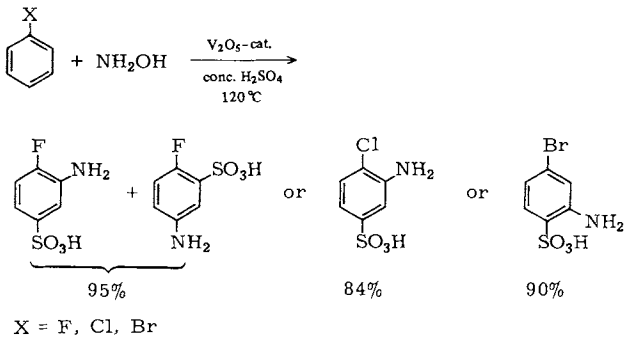
amine thallium salt have likewise failed[119]. This instability of the hydroxylamine derivatives could be due to an α-elimination to give nitrene and follow-up reactions.

$$H_2N{-}O{-}Tl + Cl{-}SO_2CF_3 \xrightarrow[-TlCl]{-40\,^\circ C} [H_2N{-}OSO_2CF_3] \xrightarrow{?} [\ddot{N}H] \rightarrow \cdots$$

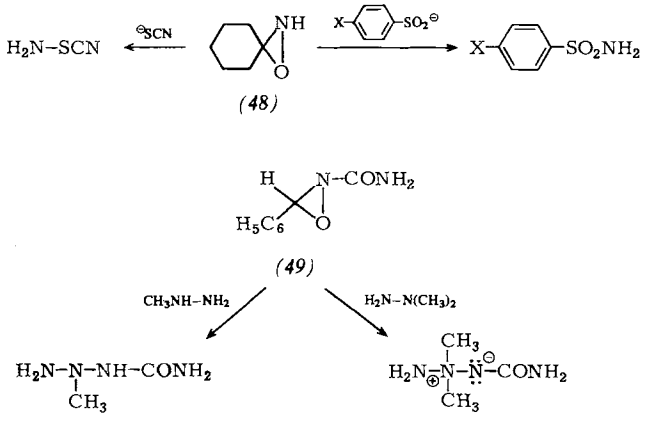
(47)

If α-elimination is prevented by suitable *N*-substituents, stable compounds result, *e.g.* the bis(trimethylsilyl) derivatives[120] of *(44)* and *(46)* and a *N,N*-diacyl derivative of *(47)*[121]. Nothing is known, though, about the usefulness of these compounds as aminating agents[121]. Besides nitrogen- and sulfur-containing substrates, carbanions have also been aminated with *N,N*-dialkyl derivatives of *(46)*[117].

Amination of haloarenes with acidic solutions of hydroxylamine according to the Turski method gives good yields[123]; however, the product distribution is strongly dependent on the halogen substituent. No radical intermediates could be detected in this process[122].



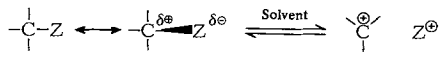
The oxaziridines *(48)* and *N*-carbamoyloxaziridines *(49)*, prepared *via* electrophilic amination processes, are themselves aminating agents which can be used for transferring amino or ureido functions respectively[108].



7. Alkylating Agents[6b, 124]

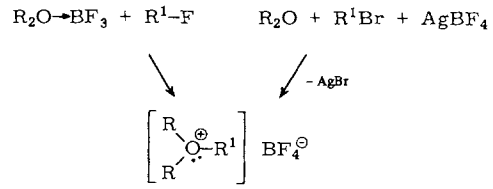
The electrophilic introduction of alkyl groups into organic compounds, under formation of a new C—C, C—O, C—N, or C—S bond, is preparatively of the utmost importance, but has also played a decisive role in the development of mechanistic concepts: carbocations were first postulated as intermediates in organic reactions for this type of reactions—with all the ensuing consequences.

The various alkylating reagents differ primarily in the degree of positivation of the reactive carbon center. In principle, this covers the whole range from mere bond polarization to the formation of free carbenium ions, influenced, as many investigations have shown, by the stability of the cation formed, by the leaving tendency of Z, and by the solvent medium[125].

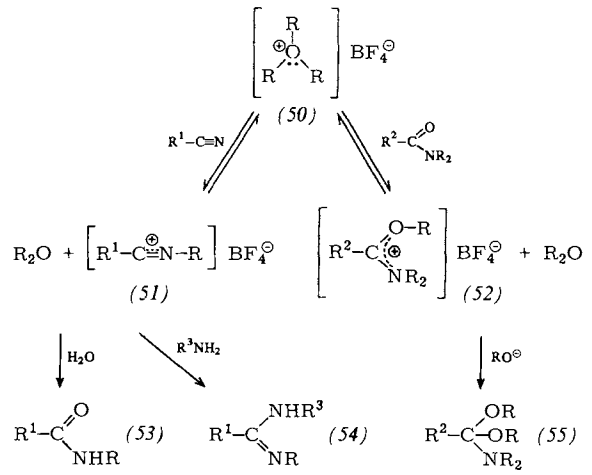


The electrophilicity of a given alkylating agent goes up, of course, with increasing positivation of the carbon center. Thus, alkyl halides react with strong nucleophiles—such as anions, amines, and alcohols—even in non-dissociated form; the reaction with weakly nucleophilic substrates (arenes, olefins, σ-bonds), on the other hand, requires the addition of Friedel-Crafts catalysts. In the following, our attention will be directed primarily to those alkylating reagents with good leaving groups which were developed within the last few years in the course of the investigation of onium structures[91b] and have found a broad preparative application.

Among the onium compounds, the trialkyloxonium salts discovered by *Meerwein et al.*[126] have long been known as excellent alkylating agents. They are prepared from alkyl halides with BF_3, SbF_5, or $SbCl_5$ in ethereal solution[127].

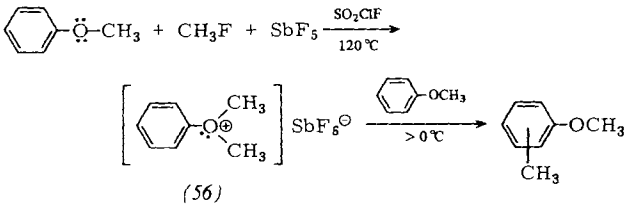


Although their electrophilic potential is not sufficient for alkylation of normal arenes, reactions are possible already with substrates which have such slight nucleophilic character as azulenes, nitriles, and carboxamides[126a].



The salts *(51)* and *(52)*, formed from nitriles and amides, respectively, and in equilibrium with the oxonium precursors *(50)*, are themselves alkylating agents. However, their addition to nucleophiles (water, amines, alcohols) affords *N*-alkyl amides *(53)*, amidines *(54)* and amide acetals *(55)*.

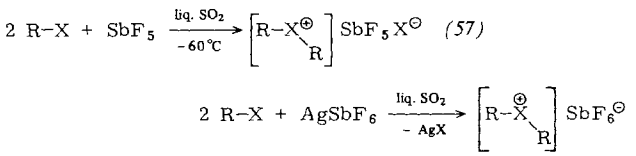
Dialkylaryloxonium salts *(56)*, accessible by alkylation of aryl alkyl ethers, have a higher alkylating potential than the trialkyl analogues and can be employed for arene alkylation[128].



(56)

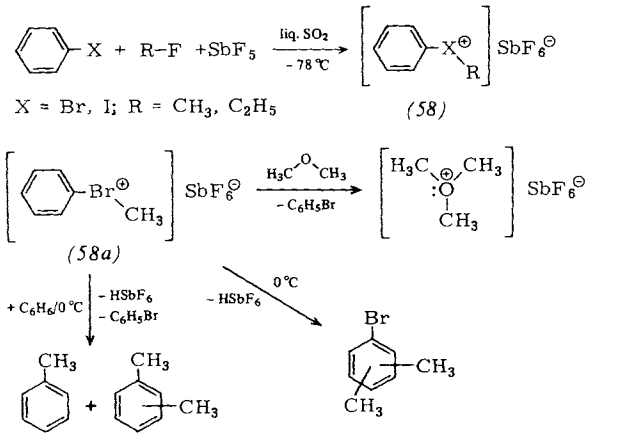
Triaryloxonium salts may be obtained in $<2\%$ yield from diaryl ethers and benzenediazonium salts; since they are practically inert towards nucleophiles, they are of no consequence as arylating agents[129].

The alkylhalonium compounds *(57)*, recently prepared by *Olah* and *DeMember*, can be used as highly reactive alkylating agents in the same manner as the oxonium salts[130, 131].



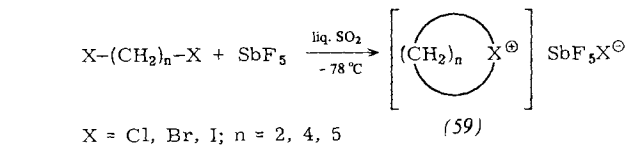
X = Cl, Br, I; R = CH_3, C_2H_5, $(CH_3)_2CH$

Alkylarylhalonium salts *(58)* are accessible analogously from halobenzenes[132] and are likewise used as powerful alkylating agents[130, 132].



(58a)

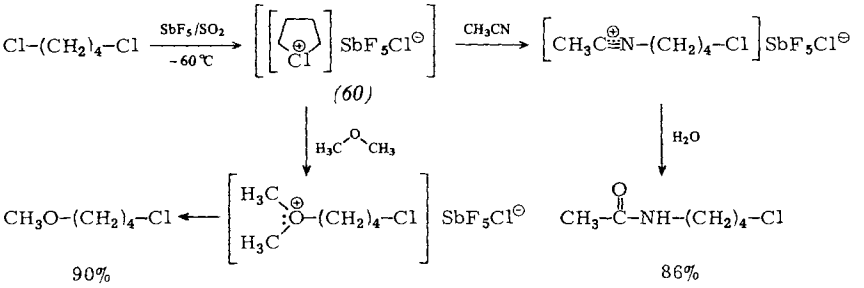
The cyclic halonium ions *(59)*, postulated as intermediates in the electrophilic addition of halogens to olefins for a long time, could now be isolated under like conditions as the open-chain analogues as well as directly from the halogenation of olefins[130, 133].



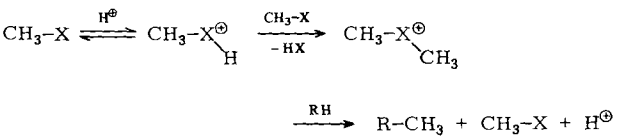
X = Cl, Br, I; n = 2, 4, 5 *(59)*

These cyclic halonium derivatives, *e.g. (60)*, have also proven to be effective alkylating agents[133].

From our present knowledge about halonium salts, many Friedel-Crafts alkylations with primary and partly also with secondary alkyl halides now are assumed to proceed *via* dialkylhalonium ions; they have definitely been established as intermediates in proton-catalyzed alkylations[134].

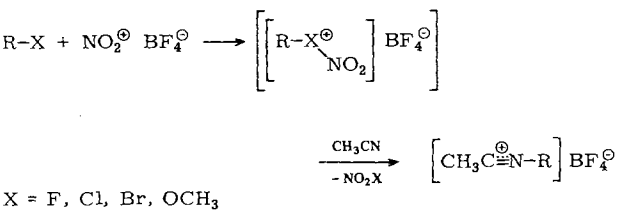


(60)



X = Cl, Br, I; R = Aryl

Onium complexes are formed from alkyl halides and ethers also with other strong electrophiles, such as nitryl[135a] or nitrosyl[135b] salts; they react as powerful alkylating agents.



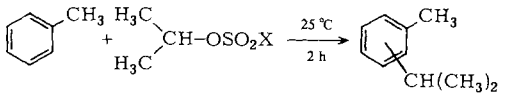
X = F, Cl, Br, OCH_3

Apart from these efforts to improve the reactivity, chemists have also endeavored to suppress secondary alkylation and isomerization in the Friedel-Crafts alkylation of arenes as far as possible; attempts with heterogeneous catalysts ($AlCl_3$ on graphite[136] or Nafion-H[137]) have met with at least partial success. Solvents such as nitroalkanes where the effectiveness of the catalyst is attenuated by complexation likewise improve the selectivity and curb isomerization[138].

Arene alkylation with secondary or tertiary carbenium ions in the gas phase gives a product spectrum comparable with that obtained for reactions of strong alkylating agents in a weakly solvating medium[139].

Among the new alkylating reagents, alkyl triflates[12] command special interest, due not only to the good leaving properties of the triflate ion but, as outlined above, also because of the high stability of both the trifluoromethanesulfonic acid and its alkyl esters. The instability of alkyl perchlorates[141], in contrast, renders them unsuitable as practical alkylating agents even though most can be prepared in high yield[140], and in spite of the good leaving group $ClO_4^{\ominus}$.

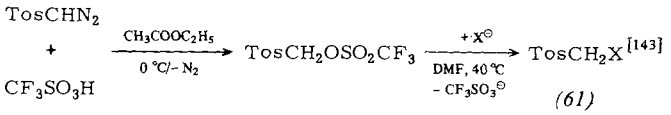
Isopropyl triflates and fluorosulfates allow the non-catalyzed alkylation of arenes such as benzene and toluene in good yield; the esters of primary alcohols, on the other hand, still require Friedel-Crafts catalysts[142].



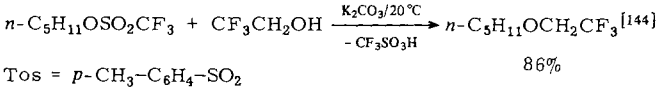
≈ 50%

X	*o*	: *m*	: *p*
F	44.3	17.7	38.0
CF_3	46.5	19.1	34.4

In the alkylation of anions[143] and of highly acidic alcohols[144], good yields could likewise be obtained only with alkyl triflates; for example, 96, 82, 79, and 76% of *(61)* were obtained with X = Cl, I, N_3, and SCN, respectively. In contrast, elimination and rearrangements are observed to a large extent under the rather more severe reaction conditions required for the usual alkylating agents such as tosylates.



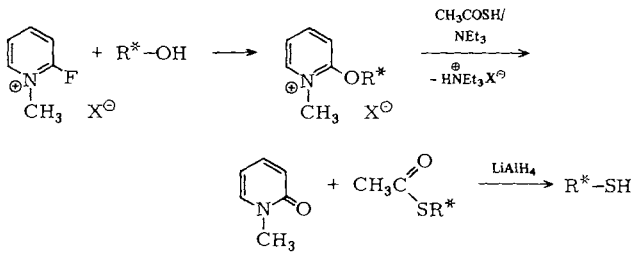
(61)



Tos = *p*-CH_3–C_6H_4–SO_2

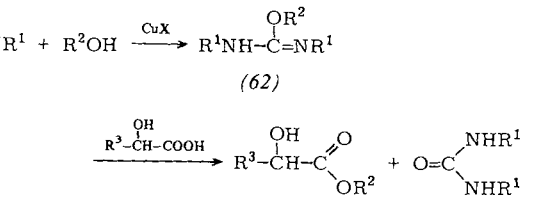
Generation and unequivocal proof of the existence of the extremely unstable vinyl cations was also achieved only by solvolysis of the respective triflates[145]. Deactivated arenes (*e.g.* halobenzenes) have already been alkenylated with vinyl cations without added Friedel-Crafts catalyst although their preparative application is still in its preliminary stages[146].

Heterocyclic moieties sometimes have proven to be advantageous leaving groups in alkylation processes. Thiols, for instance, can be prepared smoothly by reaction of thiolacetic acid with 2-alkoxy-*N*-methylpyridinium salts *(61)* and subsequent hydrogenolysis; optically active alcohols show Walden inversion in this reaction[147].

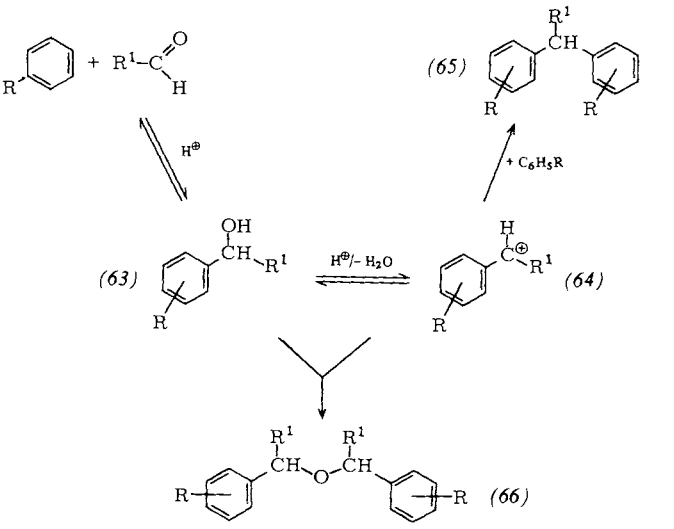


Pyridine itself has also been employed as leaving group in alkylation reactions[148], as have ureas. With *O*-alkylisoureas *(62)*, for instance, obtained by addition of alcohols R^2OH to carbodiimides, the alkylation of carboxylic and phosphoric acids, of thiols, amines and alcohols can be carried out under very mild conditions[149]. These reactions proceed with good yields and high selectivity, and thence are especially applicable in natural product synthesis.

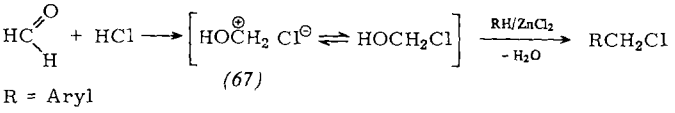
The term hydroxyalkylation denotes reactions of aldehydes and ketones with nucleophilic arenes[124]. These reactions frequently are complicated by secondary processes since, under the conditions employed, the hydroxyalkyl products *(63)* are readily converted into the carbocations *(64)*; once formed, these immediately react either with the nucleophilic substrate still present to give *(65)*, or with the primary products *(63)* to give *(66)*. Both of these secondary products for their part can again be alkylated by unreacted carbonyl compound.



(62)

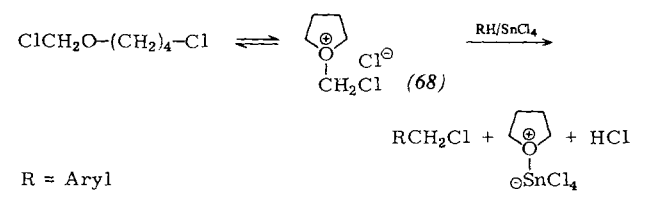


These reactions are of great technical significance in the synthesis of resins (*e.g.* phenol/formaldehyde, urea/formaldehyde). Undesirable secondary reactions can be circumvented by the use of hydrohalic acids which trap the carbenium ions, as soon as they are set free, in the form of haloalkyl derivatives (haloalkylation)[24]. Direct chloromethylation with formaldehyde/HCl[150], in which the carcinogenic hydroxymethyl cation *(67)* is considered as the attacking species, is preparatively very important.



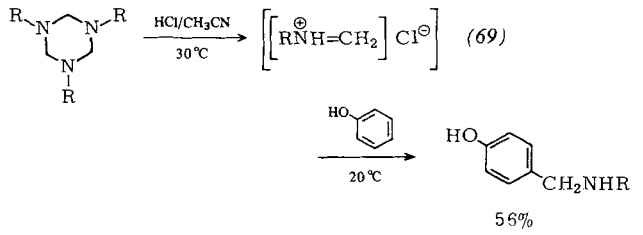
R = Aryl

Instead of formaldehyde/HCl, α-halo ethers may be applied; they likewise have been shown to be carcinogenic. Efforts to replace chloromethylation, especially in technical processes, by less precarious procedures so far have met only with limited success. In one variant, less volatile reagents such as *(68)* are employed[151]; in another, the iminium deri-



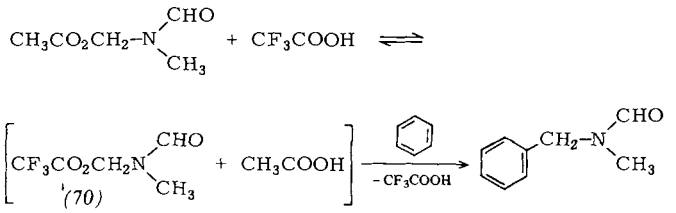
R = Aryl

vatives *(69)* of the parent carbonyl compounds are utilized as electrophiles[152]. This reaction results in aminoalkylation, and has successfully been applied to carbanions (Mannich reaction), heteroatom-H bonds, electron-rich π-systems (enol ethers, enamines, ynamines), and reactive arenes and hetarenes (*e. g.* phenols or furans[153]).



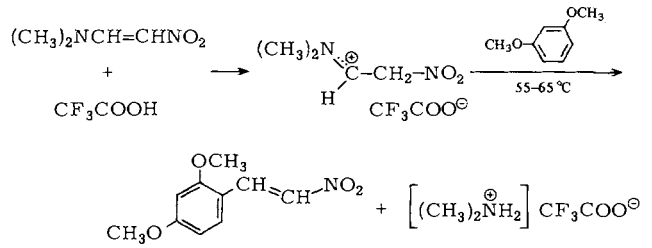
(69)

Aminoalkylation of less reactive arenes requires amino reagents such as *(70)* where the electrophilic potential is enhanced by both electron-withdrawing N-substituents and by a good leaving group as gegenion ($ClO_4^\ominus$, $BF_4^\ominus$, $CF_3COO^\ominus$)[154,155].

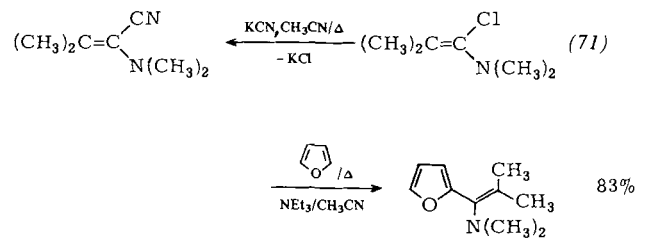


(70)

The nitro-olefination of indenes and electron-rich arenes such as resorcinol dimethyl ether actually is an aminoalkylation too; dimethylamine is immediately eliminated in the process, though, and the more favorable conjugated system developed[156].

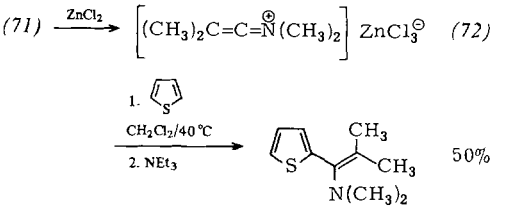


Reaction of nucleophiles with α-halo enamines *(71)* likewise represents a variant of aminoalkylation[157].



(71)

With less nucleophilic aromatic substrates, ketene-iminium chlorides, formed in a predissociation step, are assumed as reactive species. The primary formation of such a salt *(72)* has been established for the reactions with thiophene and anisole whose lower reactivity requires addition of a Lewis acid[157].



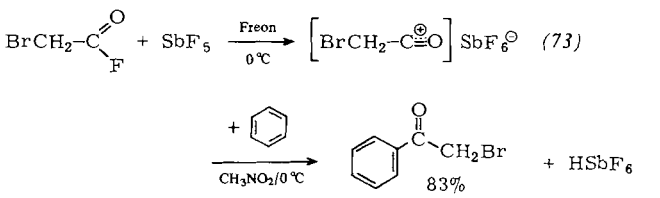
(72)

8. Acylating Agents

In electrophilic acylation, carboxylic acid derivatives are made to react with hetero- or carbon-nucleophiles, usually with substitution of a hydrogen atom[158]; in this review, the accent is placed on new, highly reactive acylating reagents for aromatic substrates.

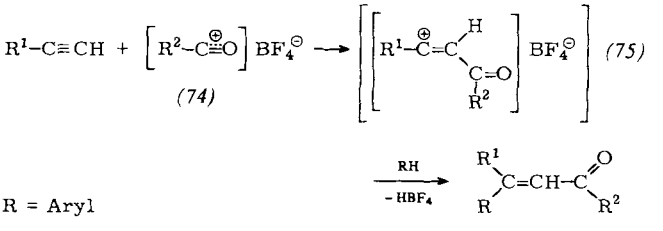
For arene acylation, the electrophilicity of regular acyl derivatives—esters, halides, anhydrides—has to be enhanced, as a rule by addition of a Friedel-Crafts catalyst (proton or Lewis acid)[6a,159]. The actual attacking electrophile in these catalyzed processes is not known with certainty; as outlined in the introduction, equilibria have been established for these systems in which both oxonium species *(1)* and acylium ions *(3)* are present[4b,160].

Since Friedel-Crafts acylation normally requires at least equimolar amounts of Lewis acid for acceptable yields, interest has recently been concentrated on truly catalytic processes. Thus, several groups almost simultaneously reported the catalytic effectiveness of traces of Fe salts (≤1 mol-%)[161]. On the basis of our present knowledge of the structure of acylating reagents, it was an obvious step to also try isolated salts of acylium ions *(3)*. An acylium salt was characterized for the first time by *Seel*[162]; the general modes of preparation and especially the preparative applicability of acylium salts have been investigated extensively by *Olah et al.*[159,160,163]. As a rule, these hygroscopic salts, *e.g. (73)*, are treated with a large excess of aromatic substrate in nitromethane solution.



(73)

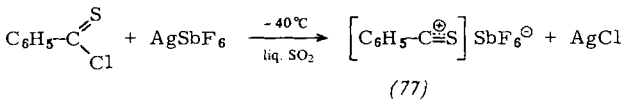
So far, this method of arene acylation has been utilized only sparingly—despite the very good yields of phenone products obtained in most cases. With olefinic[164] and acetylenic substrates[165], however, acylium salts undoubtedly have their advantages compared with the usual acylation reagents. Acylation at low temperature of alkynes with acylium tetrafluoroborates *(74)*, for instance, in the presence of arenes yields the α,β-unsaturated ketones *(76)*[165], *via* reaction of



(74) *(75)* *(76)*

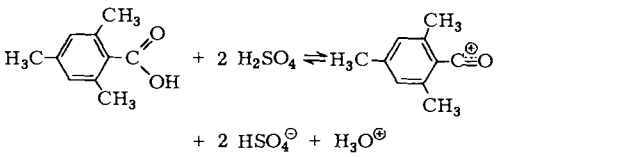
the primarily formed vinyl cations *(75)* with the aromatic substrate.

Thioacylium salts *(77)* are easily prepared[166a]; apparently, they are more stable than the O-analogues[166b].

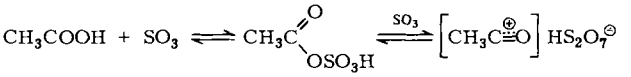


(77)

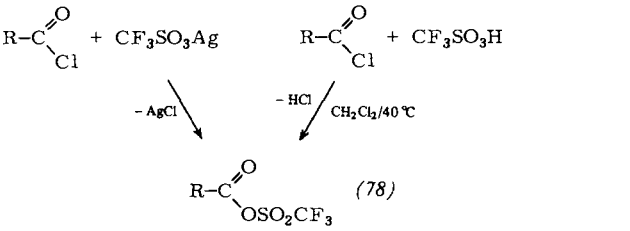
From the observed freezing point depression, it was deduced fairly early that acylium ions are generated by the action of strong mineral acids on carboxylic acids, esters, or anhydrides[167]. This acylium ion formation is particularly pronounced with 2,6-disubstituted benzoic acids.



If carboxylic anhydrides or SO_3-containing sulfuric acid are employed, primary formation of mixed anhydrides is assumed which then dissociate into acylium ions under the influence of a second molecule of SO_3[160,168].

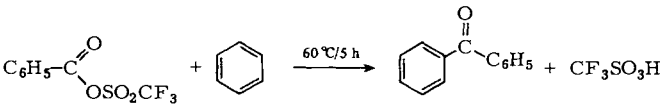


Even diacylium salts of substituted terephthalic acids could thus be obtained and made to react with several nucleophiles[169]. Spectroscopic investigations have shown the presence of mixed anhydrides between carboxylic and very strong inorganic acids in equilibrium with acylium ions and protonated species[160,170]. The reaction of acyl chlorides with silver triflate, and also that of acyl chlorides with trifluoromethanesulfonic acid in inert solvents, gives good yields of carboxylic trifluoromethanesulfonic anhydrides *(78)* in pure form[171].



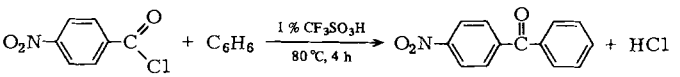
The anhydrides *(78)* can likewise be prepared by reaction of *S*-methyl thiolcarboxylic esters with methyl triflate (with dimethyl sulfide elimination)[172a] or by dehydration of a 1:1-mixture of trifluoroacetic and trifluoromethanesulfonic acid with P_2O_5[172b].

From the high leaving tendency of the triflate ion, the anhydrides *(78)* could be expected to be good acylating agents. This was fully confirmed: their acylation potential is greater than that of all known reagents. With other carboxylic sulfonic anhydrides, for instance, xylenes show no reaction after 24 h at 100 °C[173]; in contrast, the even less reactive benzene is smoothly acylated upon warming with *(78a)* without addition of any Friedel-Crafts catalyst[171]. The trifluoromethanesulfonic acid liberated in the course of the reaction can be recovered quantitatively as barium salt.



(78a) 90%

Since the anhydrides *(78)*, on the other hand, are accessible also directly from the acyl chlorides and trifluoromethanesulfonic acid, a way was open for the development of a catalytic arene acylation. The general procedure, worked out along these lines, is specially suited for substrates that otherwise give undesirable side-reactions with the usual Friedel-Crafts catalysts (*e.g.* nitro compounds)[174].

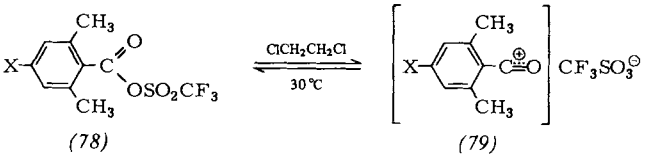


82%

The exceptional position of trifluoromethanesulfonic acid in this respect is exemplified strikingly if one compares the yields for the acylation of *p*-xylene with benzoyl chloride under addition of one 1% each of various strong acids[174]. Heterogeneous acid catalysis for Friedel-Crafts acylation with Nafion-H has recently also been reported[175].

Acid:	CF_3SO_3H	FSO_3H	*p*-H_3C C_6H_4	SO_3H
Ketone yield [%]:	82	20	31	
Acid:	conc. H_2SO_4	$HClO_4$	CF_3COOH	$HPOF_2$
Ketone yield [%]:	28	14	21	4

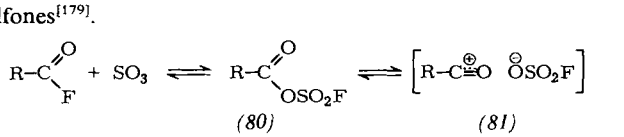
The extent to which the anhydrides *(78)* are dissociated in inert solvents, *e.g.* dichloroethane, depends in the expected manner on steric and electronic factors in the acyl moiety; the equilibrium concentration of the acylium ions *(79)* correlates fairly well with *Brown*'s σ^+-constants for the substituents X[176], and thus with former results on the relative stability of benzoyl cations[177].



(78) *(79)*

X	X= OCH_3	CH_3	H	Cl	NO_2
Eq. conc. of *(79)* [%]	= 87	66	45	33	10

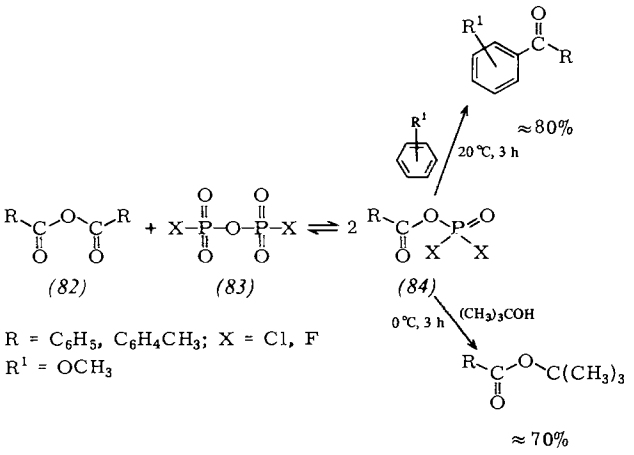
Mixed anhydrides could also be prepared from carboxylic acids and other strong inorganic acids; however, they exhibited no special potential for the acylation of arenes. The carboxylic fluorosulfuric anhydrides *(80)*, for instance, were synthesized by insertion of SO_3 into the C–F bond of acyl fluorides[178,179]. In solution, the anhydrides *(80)* are dissociated into acylium ions *(81)* and fluorosulfate anions[179]; upon reaction with arenes, though, only moderate yields of ketones are obtained, the main side-products being diaryl sulfones[179].



(80) *(81)*

R	= C_6H_5	*p*-CH_3 C_6H_4	*p*-Cl C_6H_4
Yield of *(80)* [%]	= 70	50	50

The anions of dihalophosphoric acids are likewise good leaving groups[180] but, with few exceptions[181], have not yet been applied in organic preparative practice. Recently, carboxylic dihalophosphoric anhydrides *(84)* were prepared in good yield from the anhydrides of the constituent acids, *(82)* and *(83)*. Upon investigation of their reaction behavior[182], they were found to display an exceptional acylation potential which, for example, allows arene acylation under mild conditions without addition of Friedel-Crafts catalysts, and also the esterification of tertiary alcohols in good yield.



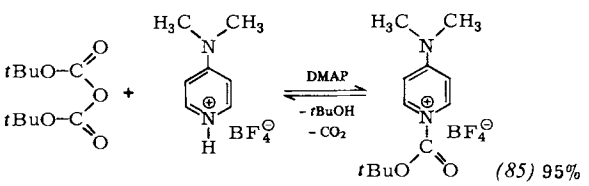
(82) *(83)* *(84)*

R = C_6H_5, $C_6H_4CH_3$; X = Cl, F
R^1 = OCH_3

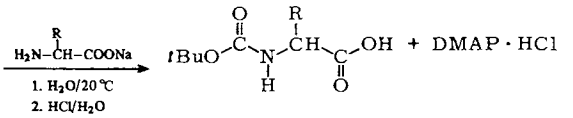
The anhydrides *(84a)*, X = Cl, are also formed as intermediates in the reaction of carboxylic acids with $POCl_3$[182], as already postulated by *Th. Wieland*[183]. Carboxylic perchloric anhydrides, which can be prepared in good yield from acyl chlorides and silver perchlorate, are explosive and therefore unsuitable as practical acylating reagents[184].

Acylium ions are certainly the reactive species in many normal Friedel-Crafts acylations and also frequently in reactions of the mixed anhydrides of carboxylic and strong inorganic acids described above; it has been doubted[160], though, whether they are sufficiently electrophilic to react with σ-bonds. Protonated acylium ions have therefore been postulated as the effective electrophile in superacid systems[160]; recent calculations have provided additional strong evidence for their existence[185].

The interest of preparative chemists is naturally focused on acylating agents which react both very selectively *and* under mild conditions. Out of the multitude of investigations on reagents for the acylation of OH, NH, and SH functions, we shall discuss primarily those in which heterocyclic moieties are employed as leaving groups. The acylazolides developed by *Staab*'s group[186] are among the most versatile reagents of this type.

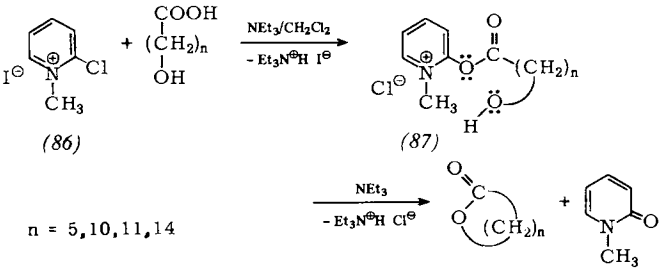


(85) 95%



In recent years, the importance also of pyridines and pyridones as leaving groups has grown steadily. Acylation with anhydrides or acyl chlorides in the presence of pyridine has been known for a long time; however, the acceleration of acylation on use of 4-dimethylaminopyridine (DMAP) instead of pyridine was not recognized until comparatively late[187]. The best yields in this procedure are obtained with carboxylic anhydrides and catalytic amounts of DMAP in aprotic and slightly polar solvents; thus, a 96% yield of *N-tert*-butoxycarbonyl amino acid is obtained in the reaction shown below. Pyridinium salts *(85)*, in equilibrium with the reactants, are considered as the reactive electrophiles. Sometimes it is better to employ isolated pyridinium salts, preferentially with anions of low nucleophilicity, in aqueous medium as acylating agents[188]. L-Proline, for instance, can thus be transformed into *N*-butoxycarbonyl L-proline in 96% yield.

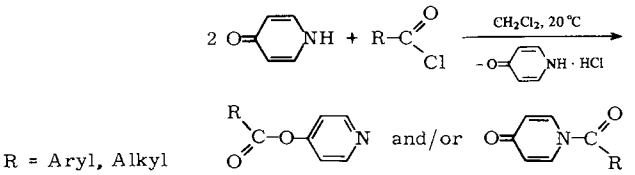
The reagents, prepared by *Mukaiyama et al.* from the *N*-alkyl-2-halopyridinium salts *(86)* and carboxylic acids, *e.g. (87)*, allow reaction under very mild conditions[189]; apart from acylated alcohols, thiols, and amines, difficultly accessible lactones could likewise be obtained in good yield by this method[189].



(86) *(87)*

n = 5,10,11,14

Upon acylation of 4-pyridones, acyloxypyridines *(88)* and/or *N*-acylpyridones *(89)* are formed in good yields, respectively, *via N*- or *O*-reaction[190].



R = Aryl, Alkyl

(88) *(89)*

Acylation with these nonionic acylpyridones, *(88)* and *(89)*[190], as well as with the 2-acyloxypyridines[191], can be carried out in inert solvents under neutral or weakly acidic conditions. In solution, *(88)* and *(89)* are in equilibrium at room temperature; its position strongly depends on the nature of the acyl moiety[190, 192], and in the case of the 2-pyridone is shifted more to the *O*-acyl side[191, 193].

Pentafluorophenyl acetate has recently been reported as a highly selective agent for the acetylation of amino alcohols[194].

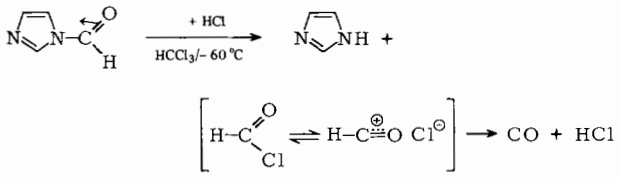
9. Formylating and Carboxylating Reagents

Formylation and carboxylation differ from the principally comparable acylation reactions mainly in generation, stability, and reactivity of the requisite electrophiles. For instance, the formyl derivatives required for a Friedel-Crafts formylation are unstable even at room temperature. Interaction be-

tween Friedel-Crafts catalysts and carbonic acid derivatives, the appropriate electrophiles for carboxylation, appears even more complex than for the carboxylic acid derivatives. Furthermore, the electrophilic potential of carboxylating agents is lowered substantially, relative to that of acylating reagents, by the mesomeric influence of yet another heteroatom (O, N).

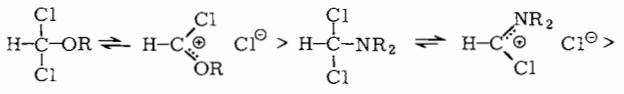
9.1. Formylation[195]

The facile decarbonylation of an intermediate formyl cation *(90)* makes formylations with formyl derivatives problematical; this decomposition reaction is probably also responsible for the instability of formyl chloride and formic anhydride[196].

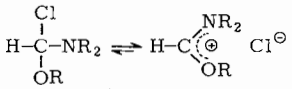


(90)

With formyl reagents where the oxygen atom is suitably substituted or replaced by a nitrogen function, CO elimination can be avoided[197,198]. *(91)*, *(92)*, and *(93)*, for instance, meet these requirements; their definite graduation of reactivity can be derived straightforwardly from the general substituent effects.

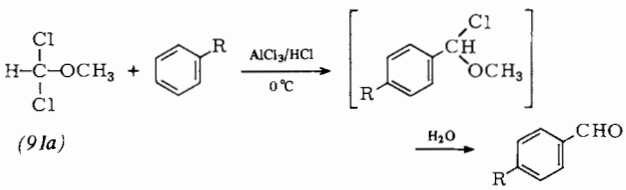


(91) *(92)*



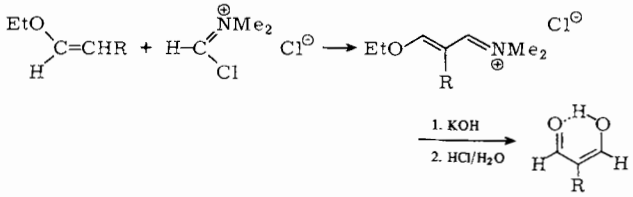
(93)

The stability of the cations generated upon dissociation increases markedly from *(91)* to *(93)*; of course their formylation potential declines concomitantly[197,199]. The non-dissociated α,α-dichlorodimethyl ether *(91a)*, for example, allows formylation even of non- or slightly-activated arenes in the presence of a Friedel-Crafts catalyst; thus, benzene is formylated in 37% yield, and toluene even in 80% yield[200].



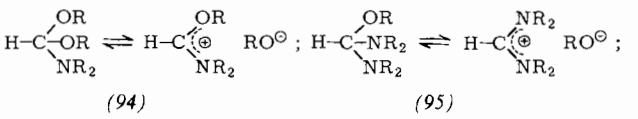
(91a)

The α,α-dichlorotrialkylamines *(92)* (chloromethyliminium chlorides), which are fully dissociated, can be used as formylating agents without Friedel-Crafts catalysis, though only for the more reactive arenes[195,201]. They are also employed in the Vilsmeyer-Haack-Arnold formylation of activated olefins (enol ethers and acetates, enamines); this reaction is of great consequence since it makes polycarboxy compounds accessible, *e.g.* malondialdehyde[202], which constitute important synthetic building blocks.

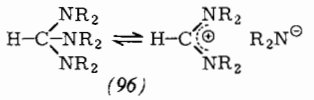


The graduated reactivity of the various formylating agents, accessible from dimethylformamide and, *inter alia,* phosgene, phosphorus oxide chloride, dimethyl sulfate, and mineral acids, has been the subject of a comprehensive investigation[203]. The (expected) reactivity difference between compounds of type *(92)* and *(93)* was shown to depend not only on the stability of the carbenium ion, but also on the nature of the anion[203]. In the formylation of *N,N*-dimethylaniline, the unequal reactivity of some carboxamide complexes of type *(92)* had already been recognized before[204].

Orthoformic acid derivatives have found general interest as formylating agents only since the monoamide diesters *(94)*, diamide esters *(95)*, and triamides *(96)* have become available[205]; their autodissociation (as indicated above) could be demonstrated by conductivity measurements[206].



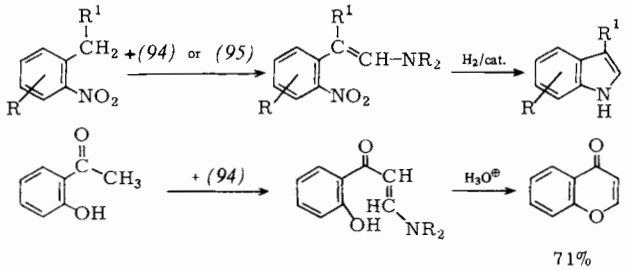
(94) *(95)*



(96)

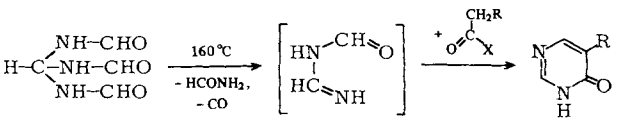
Reactivity decreases markedly in the order *(96)* > *(95)* > *(94)*. This can be rationalized (i) in terms of the degree of dissociation (which in turn is determined by the stability of the ions generated) and (ii) in terms of the different base strength of compounds *(94)*—*(96)*. Higher base strength of the orthoamide derivatives or of the anions $RO^{\ominus}$ and $R_2N^{\ominus}$, respectively, promotes the formation of anions from the CH-acidic substrate which is to be formylated, and hence favors electrophilic attack.

Owing to their low electrophilicity, the orthoamide derivatives listed above are generally unsuitable for the formylation of arenes; they are especially effective formylating agents, though, for CH-acidic substrates[205,207]. Of the respective manifold applications, only a general indene synthesis[208] and a simple preparation of chromone[209] need be mentioned specifically. Sensitive substrates may be formylated in a straightforward manner with *tert*-butoxy-bis(dimethylamino)methane [*"Bredereck's* reagent", see *(95)*][210].



71%

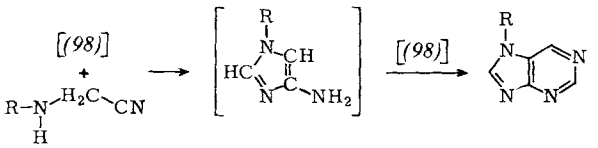
N,N',N''-Methylidinetriformamide *(97)*[211], *s*-triazine, and formamidine acetals [see *(95)*] all represent important formylating agents in the field of heterocyclic synthesis since they at the same time incorporate the amidine component for a subsequent ring closure. For instance, *N*-formyl formamidine *(98)*[212] which is liberated from *(97)* upon heating reacts with carbonyl substrates[213a] or nitriles[213b] smoothly and in good yields to give 5-substituted pyrimidines *(99)*.



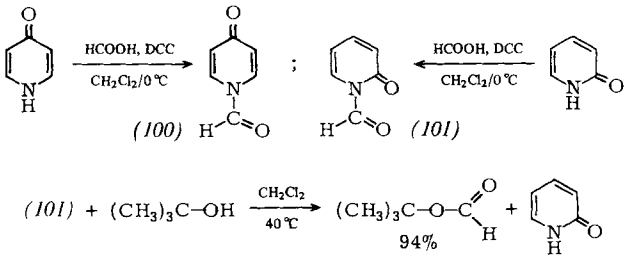
(97) *(98)* *(99)*

R = $COOR^1$, CN, $CONH_2$; X = OR^1, NH_2

This synthetic principle permits facile and efficient purine syntheses[214a], starting from aminoacetonitrile and proceeding *via* a 4-aminoimidazole with subsequent annelation of the pyrimidine ring[214b] (R = CH_3, C_2H_5, C_6H_5; yield 43, 46, 70%, respectively).



The *N*-formyl pyridones *(100)* and *(101)*, easily accessible from formic acid and dicyclohexylcarbodiimide (DCC), are excellent formylating agents for amines, alcohols, and thiols[215].

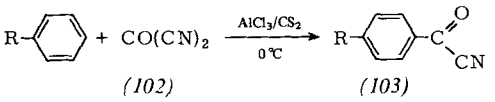


(100) *(101)*

(101) also allows a highly selective formylation of a mixture of primary, secondary, and tertiary alcohols, the tertiary substrates reacting least well, the primary ones best[215]. Even tertiary alcohols which are sterically severely hindered, such as 17α-hydroxyprogesterone, can be transformed into formates with *(101)* in dichloromethane at 40 °C[215]. Above 40 °C, *(101)* also shows a considerable extent of decarbonylation.

9.2. Carboxylation[6b, 159]

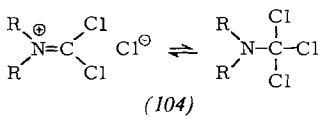
The general aspects of Friedel-Crafts acylation of course apply also to carboxylation; as in the case of the formylation reaction, though, there are no carbonic acid derivatives which might be used as generally applicable reagents[216]. For acylations, halides are nearly always employed in practice; the corresponding haloformates, however, decarboxylate under the action of Friedel-Crafts catalysts[217], and then act as alkylating agents. With the dihalide phosgene, aroyl chlorides are formed from arenes in the presence of Friedel-Crafts catalysts; as a rule, though, these are further converted into aromatic ketones under the reaction conditions. With carbonyl dicyanide *(102)* in place of phosgene, this secondary reaction is avoided[218], and aroyl cyanides *(103)* are obtained in good yield; the drawback of the procedure is that *(102)* is not as easily accessible as $COCl_2$[218].



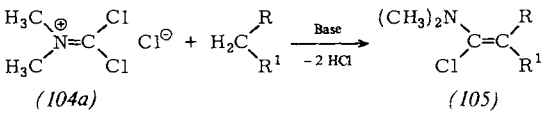
(102) *(103)*

R	= H	CH_3	Cl
Yield [%]	= 71	79	16

The more reactive dichloromethyleneiminium chlorides *(104)* (phosgeneiminium salts) constitute far better carboxylating agents[219]; they are specially suited for the carboxylation of CH-acidic substrates which are thus converted into α-chloroenamines *(105)*[219,220].



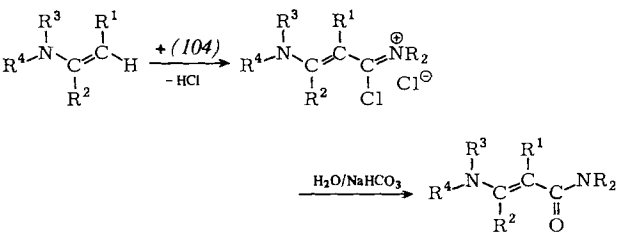
(104)



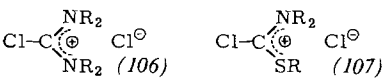
(104a) *(105)*

R	= CN	CN	COOEt
R^1	= CN	COOEt	$Ph_3P^{\oplus}$
Yield [%]	= 77	85	62

Enamines[221] and enol ethers[219] can likewise be carboxylated in good yield with these phosgeneiminium salts. However, their electrophilic potential in general is not sufficient for carboxamidation of arenes, except in the case of highly activated substrates such as *N,N*-dimethylaniline or resorcinol dimethyl ether[219].

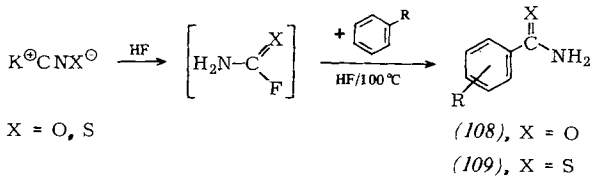


On replacement of one Cl atom in the phosgeneiminium salts *(104)* by another hetero substituent, they still remain potential carboxylating agents; since the higher +*M* effect of these substituents diminishes their reactivity, however, chloro formamidinium salts *(106)*[222a] and also the sulfur compounds *(107)*[222b] are of little significance as carboxylating agents.



(106) *(107)*

The carboxamidation of arenes (Gattermann amide synthesis) presents some preparative problems since the unstable carbamidic chloride is difficult to handle. This disadvantage can be avoided by using KOCN in HF[223]; under these conditions, the carbamoyl fluoride formed *in situ* immediately reacts with the aromatic substrate to give the benzamides *(108)*. Potassium rhodanide may analogously be employed for the synthesis of *thio*amides *(109)*[223].

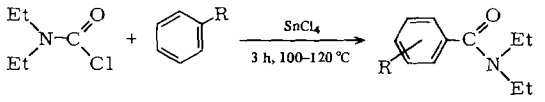


X = O, S

(108), X = O
(109), X = S

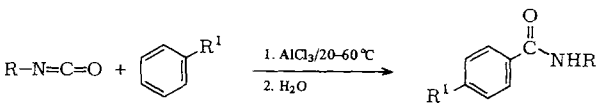
R	= H	CH_3	Cl
Yield of *(108)* [%]	= 63	70	9

Carboxamidation of alkyl arenes with *N,N*-diethylcarbamoyl chloride is less complicated and gives better yields[224].



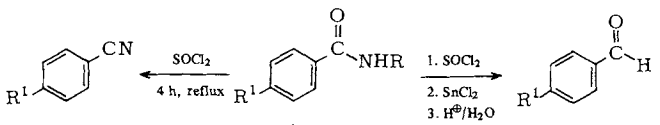
R = Alkyl 69-93% (≥80% *p*-Isomer)

Arene carboxylation with isocyanates and isothiocyanates has proven exceptionally advantageous. *Leuckart* had already obtained *N*-substituted amides *(110)* from the reaction of aromatic isocyanates with activated arenes in the presence of $AlCl_3$[225]. This facile synthesis for aromatic carboxamides was later extended also to less activated aromatic substrates and aliphatic isocyanates[226a].



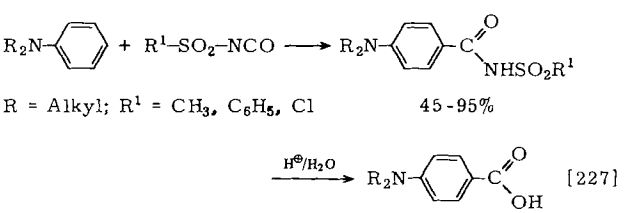
R^1 = Alkyl, Halogen, Alkoxy *(110)* 65-100%

Use of aliphatic isocyanates is preparatively advantageous since the *N*-alkyl amides *(110a)*, R = alkyl, offer the possibility of further chemical conversion; upon warming with thionyl chloride, for instance, they are transformed into the nitriles *(111)*, and, *via* the imidoyl chlorides, with Sn(II) chloride into the aldehydes *(112)*[226b].



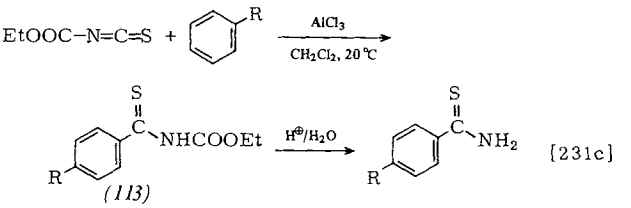
(111), 90-100% *(110a)* *(112)*
R^1 = F, 83%

With the more reactive sulfonyl isocyanates, *Seefelder*[227] and *Graf*[228] succeeded in carboxamidating electron-rich arenes (dialkylanilines, resorcinol dimethyl ether) and hetarenes (pyrrole, thiophene, indene, carbazole) in good yields even without addition of Friedel-Crafts catalysts[229,230].



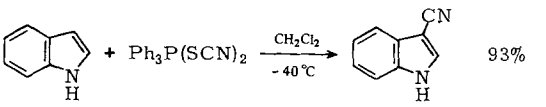
R = Alkyl; R^1 = CH_3, C_6H_5, Cl 45-95% [227]

Isothiocyanates can similarly be reacted with arenes, though in the presence of $AlCl_3$, to *N*-substituted thioamides *(113)*[231].



R	= H	CH_3	*t*-Bu	CH_3O	Cl
Yield of *(113)* [%]	= 52	63	41	90	29

By the use of cyanogen halides or alkyl cyanates, a direct electrophilic introduction of the CN function is possible with highly nucleophilic groups (OH, SH, NH); only poor yields are obtained with aromatic substrates[232]. Good yields of cyanation products are achieved with triphenylphosphane/dirhodane in the case of reactive hetarenes (indene, pyrrole)[233].



10. Concluding Remarks

I have tried in this contribution to delineate the general trends in the development of new electrophilic species and, at the same time, to show up the preparative advantages and the applicability of these novel reagents.

The "super-leaving groups", known from carbenium ion chemistry (*e.g.* triflate and fluorosulfate), are doubtless of crucial importance in this context. Since their paramount importance in solvolysis reactions had already been recognized in the sixties, it is indeed surprising that their specific properties were not utilized until so much later for the development of new, highly effective electrophiles.

A second trend noted in recent years is towards more and more selective electrophiles. To this end, heterocyclic moieties in particular have been employed as leaving groups; in many instances, this also allows working under neutral and/or aprotic conditions. At the same time, it has been recognized more and more clearly that the interaction of charged electrophiles with solvents containing lone pairs (*e.g.* nitriles, tertiary amines, ethers, thioethers, nitro and halo compounds) constitutes a decisive factor; reactivity and selectivity of the electrophile can thus be varied in a controlled fashion.

Electrophilic metalation, phosphorylation, and silylation have deliberately been excluded from this account, since the alternative mechanistic routes which would have to be discussed for these reactions lie outside the scope of this review.

My sincere thanks go to my dedicated co-workers, both former and present, who have collaborated in the work cited here. Generous support of our investigations by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: December 3, 1979 [A 305 IE]
German version: Angew. Chem. *92*, 147 (1980)
Translated by Priv.-Doz. Dr. *Peter Fischer*, Stuttgart

[1] a) *C. K. Ingold*, J. Chem. Soc. *1933*, 1120; b) Chem. Rev. *15*, 225 (1934); c) Structure and Mechanism in Organic Chemistry. Cornell University Press, Ithaca 1953, p. 201.

[2] a) *V. Gutman:* The Donor-Acceptor Approach to Molecular Interactions. Plenum Press, New York 1978; b) *W. B. Jensen*, Chem. Rev. *78*, 1 (1978).

[3] a) *G. A. Olah*, Angew. Chem. *85*, 183 (1973); Angew. Chem. Int. Ed. Engl. *12*, 173 (1973); b) *G. A. Olah, N. Yoneda, D. G. Parker*, J. Am. Chem. Soc. *99*, 483 (1977); c) *R. D. Bach, J. W. Holubka, R. C. Badger, S. J. Rajan, ibid. 101*, 4416 (1979).

[4] a) *G. A. Olah:* Friedel Crafts Chemistry. Wiley, New York 1973, p. 488; b) *B. Chevrier, R. Weiss*, Angew. Chem. *86*, 12 (1974); Angew. Chem. Int. Ed. Engl. *13*, 1 (1974); c) *G. Oulevey, B. P. Susz*, Helv. Chim. Acta *47*, 1828 (1964); d) *R. Corriu, M. Dore, R. Thamassin*, Tetrahedron *27*, 5601, 5819 (1971).

[5] *H. Bock, K. L. Kompa*, Chem. Ber. *99*, 1361 (1966).

[6] a) *G. A. Olah:* Friedel Crafts and Related Reactions. Vol. I—IV. Interscience, New York 1963; b) Friedel Crafts Chemistry. Wiley, New York 1973.

[7] a) *Th. H. Lowry, K. Schueller Richardson:* Mechanism and Theory in Organic Chemistry. Harper & Row, New York 1976, pp. 222ff.; b) *Ch. J. M. Stirling*, Acc. Chem. Res. *12*, 198 (1979).

[8] *R. K. Crossland, W. E. Wells, V. H. Shiner, Jr.*, J. Am. Chem. Soc. *93*, 4217 (1971).

[9] *D. N. Kevill, G. M. L. Lin*, Tetrahedron Lett. *1978*, 949.

[10] *T. Sujinaga, I. Sakamoto*, J. Electroanal. Chem. Interfacial Electrochem. *85*, 185 (1977).

[11] *P. J. Stang, A. G. Anderson*, J. Org. Chem. *41*, 781 (1976).

[12] *R. D. Howells, J. D. McCown*, Chem. Rev. *77*, 69 (1977).

[13] *C. Reichardt:* Solvent Effects in Organic Chemistry. Verlag Chemie, Weinheim 1979, pp. 144ff.

[14] a) *G. A. Olah, D. J. Donovan*, J. Am. Chem. Soc. *100*, 5163 (1978); b) *J. Sommer, S. Schwartz, P. Rimmelin, P. Canivet, ibid. 100*, 2576 (1978); c) *S. Kobayashi*, Yuki Gosei Kagaku Kyokai Shi *33*, 861 (1975); Chem. Abstr. *84*, 120621j (1976).

[15] *R. D. Bach, J. W. Holubka, T. A. Taffee*, J. Org. Chem. *44*, 1739 (1979).

[16] *G. A. Olah, M. R. Bruce*, J. Am. Chem. Soc. *101*, 4765 (1979).

[17] *F. Effenberger, J. Geke*, Synthesis *1975*, 40.

[18] *R. D. Wieting, R. H. Staley, J. L. Beauchamp*, J. Am. Chem. Soc. *96*, 7552 (1974).

[19] a) *K. Dehnicke*, Chimia *27*, 309 (1973); b) *P. B. D. De la Mare:* Electrophilic Halogenation. Cambridge University Press, Cambridge 1976; comprehensive summary of electrophilic halogenation; c) *M. Hudlicky*, Org. Prep. Proced. Int. *1978*, 10, 181.

[20] a) *C. E. Inman, R. E. Oesterling, E. A. Tyczkowski*, J. Am. Chem. Soc. *80*, 5286 (1958); b) *K. O. Christie, C. J. Schack*, Adv. Inorg. Chem. Radiochem. *18*, 319 (1976); c) *B. Lunelli*, Ind. Eng. Chem. Prod. Res. Develop. *1976*, 15, 278.

[21] a) *R. J. Gillespie, J. Passmore*, Adv. Inorg. Chem. Radiochem. *17*, 49 (1975); b) *R. J. Gillespie, M. J. Morton*, Q. Rev. Chem. Soc. *25*, 553 (1971).

[22] *R. J. Gillespie, M. J. Morton*, Inorg. Chem. *11*, 586, 591 (1972).

[23] a) *O. Glemser, A. Šmalc*, Angew. Chem. *81*, 531 (1969); Angew. Chem. Int. Ed. Engl. *8*, 517 (1969); b) *W. W. Wilson, B. Landa, F. Aubke*, Inorg. Nucl. Chem. Lett. *11*, 529 (1975).

[24] *G. J. Fox, G. Hallas, J. D. Hepworth, K. N. Paskins*, Synthesis *55*, 20 (1976), and references cited therein.

[25] *S. Uemura, A. Onoe, M. Okano*, Bull. Chem. Soc. Jpn. *47*, 147 (1974).

[26] *M. Schmeisser, K. Brändle*, Angew. Chem. *73*, 388 (1961).

[27] a) *J. W. Lown, A. V. Joshua*, J. Chem. Soc. Perkin Trans. I *1973*, 2680; Can. J. Chem. *55*, 122 (1977); b) *55*, 508 (1977).

[28] *K. O. Christe, C. J. Schack, R. D. Wilson*, Inorg. Chem. *13*, 2811 (1974).

[29] *W. P. Gilbreath, G. H. Cady*, Inorg. Chem. *2*, 496 (1963).

[30] *F. Aubke, R. J. Gillespie*, Inorg. Chem. *7*, 599 (1968).

[31] *J. R. Dalziel, F. Aubke*, Inorg. Chem. *12*, 2707 (1973).

[32] a) *D. D. DesMarteau*, J. Am. Chem. Soc. *100*, 340 (1978); b) *Y. Katsuhara, D. D. DesMarteau, ibid. 101*, 1039 (1979).

[33] *F. Effenberger, U. Kußmaul, K. Huthmacher*, Chem. Ber. *112*, 1677 (1979).

[34] *K. Huthmacher, F. Effenberger*, Synthesis *1978*, 693.

[35] *Y. Kobayashi, I. Kumadaki, T. Yoshida*, J. Chem. Res. (S) *1977*, 215.

[36] a) *D. H. Derbyshire, W. A. Waters*, J. Chem. Soc. *1950*, 573; b) *E. H. Appelmann, L. J. Basile, R. C. Thompson*, J. Am. Chem. Soc. *101*, 3384 (1979).

[37] a) *D. H. R. Barton, A. K. Ganguly, R. H. Hesse, S. N. Loo, M. M. Pechet*, Chem. Commun. *1968*, 806; b) *D. H. R. Barton, R. H. Hesse, R. E. Markwell, M. M. Pechet, H. T. Toh*, J. Am. Chem. Soc. *98*, 3034 (1976).

[38] *I. Agranat, M. Rabinovitz, H. Selig, Ch. H. Lin*, Synthesis *1977*, 267.

[39] a) *W. Gottardi*, Monatsh. Chem. *99*, 815 (1968); b) *108*, 1067 (1977).

[40] *G. H. Hakimelahi, G. Just*, Tetrahedron Lett. *1979*, 3643.

[41] a) *R. A. Abramovitch, G. Alvernhe, M. N. Inbasekaran*, Tetrahedron Lett. *1977*, 1113; b) *Y. Endo, K. Shudo, T. Okamoto*, J. Am. Chem. Soc. *99*, 7721 (1977).

[42] *W. M. Weigert, W. Merk, H. Offermanns, G. Prescher, G. Schreyer, O. Weiberg*, Chem.-Ztg. *99*, 106 (1975).

[43] *A. Blaschette, D. Brandes*, Chem.-Ztg. *99*, 125 (1975).

[44] *G. A. Olah, D. G. Parker, N. Yoneda*, Angew. Chem. *90*, 962 (1978); Angew. Chem. Int. Ed. Engl. *17*, 909 (1978).

[45] *D. J. Ravlinson, G. Sosnovsky*, Synthesis *1972*, 1.

[46] a) *D. H. R. Barton, P. D. Magnus, M. J. Pearson*, J. Chem. Soc. *C 1971*, 2231, and references cited therein; b) *R. L. Dannley, J. E. Gagen, K. Zak*, J. Org. Chem. *38*, 1 (1973).

[47] *D. Jahn*, Diplomarbeit, Universität Stuttgart 1976.

[48] *P. Kovacic, M. E. Kurz*, J. Org. Chem. *31*, 2459 (1966).

[49] *S. Hashimoto, W. Koike*, Bull. Chem. Soc. Jpn. *43*, 293 (1970).

[50] a) *S. N. Lewis* in *R. L. Augustine:* Oxidation. Vol. 1. Marcel Dekker, New York 1969, pp. 213ff.; b) *A. A. Akhrem, P. A. Kiselev, D. I. Metelitsa*, Dokl. Akad. Nauk SSSR *1975*, 220, 593; Chem. Abstr. *82*, 111307t (1975).

[51] *H. Hart, C. A. Buehler*, J. Org. Chem. *29*, 2397 (1964).

[52] *Y. Ogata, I. Urasaki, K. Nagura, N. Satomi*, Tetrahedron *30*, 3021 (1974).

[53] *M. E. Kurz, G. J. Johnson*, J. Org. Chem. *36*, 3184 (1971).

[54] a) *J. Varagnat*, Ind. Eng. Chem. Prod. Res. Develop. *1976*, 15, 212; b) *G. A. Olah, R. Ohnishi*, J. Org. Chem. *43*, 865 (1978).

[55] a) *J. A. Vesely, L. Schmerling*, J. Org. Chem. *35*, 4028 (1970); b) *J. A. Vesely*, US-Pat. 3839467 (1974), Universal Oil Products Co.; Chem. Abstr. *82*, 3974z (1975); c) *G. A. Olah, T. Keumi, A. P. Funk*, Synthesis *1979*, 536.

[56] *J. Sugano, Y. Kuriyama, Y. Ishiuchi, K. Minamikawa*, Jap. Kokai *74 07*, 234 (1974); Chem. Abstr. *80*, 120535b (1974).

[57] a) *E. Höft, S. Ganschow*, J. Prakt. Chem. *314*, 145 (1972); b) *J. Rebek, Jr., S. F. Wolf, A. B. Mossmann*, J. Chem. Soc. Chem. Commun. *1974*, 711.

[58] *E. H. Appelman, R. Bonnett, B. Mateen*, Tetrahedron *33*, 2119 (1977).

[59] a) *H. H. Takimoto, G. C. Denault*, J. Org. Chem. *29*, 759 (1964); b) *S. Bast, K. H. Andersen, ibid. 33*, 846 (1968); c) *G. A. Olah, J. Nishimura, ibid. 39*, 1203 (1974).

[60] a) *H. Cerfontain:* Mechanistic Aspects in Aromatic Sulfonation and Desulfonation. Interscience, New York 1968; b) *H. Cerfontain, C. W. F. Kort*, Int. J. Sulfur Chem. *C 1971*, 6, 123.

[61] a) *L. F. Fieser, M. Fieser:* Reagents for Organic Synthesis. Vol. 1. Wiley, New York 1967, pp. 1125ff., and references cited therein; b) *K. Hofmann, G. Simchen*, Synthesis *1979*, 699.

[62] a) *N. H. Christensen*, Acta Chem. Scand. *18*, 954 (1964); b) *H. Cerfontain, A. Koeberg-Telder*, Rec. Trav. Chim. Pays-Bas *89*, 569 (1970).

[63] a) *G. A. Olah, H. C. Lin*, Synthesis *1974*, 342; b) *G. A. Olah, S. Kobayashi, J. Nishimura*, J. Am. Chem. Soc. *95*, 564 (1973); c) *E. Lindner, H. Weber*, Chem. Ber. *101*, 2832 (1968).

[64] a) *F. Klages, K. Hoheisel, E. Mühlbauer, F. E. Malecki*, Chem. Ber. *96*, 2057 (1963); b) *F. Klages, F. E. Malecki*, Justus Liebigs Ann. Chem. *691*, 15 (1966).

[65] a) *K. Huthmacher, G. König, F. Effenberger*, Chem. Ber. *108*, 2947 (1975); b) *F. Effenberger, K. Huthmacher, ibid. 109*, 2315 (1976).

[66] *S. K. Gupta*, Synthesis *1977*, 39.

[67] a) *H. A. Staab, K. Wendel*, Chem. Ber. *93*, 2902 (1960); b) *F. Effenberger, K. E. Mack*, Tetrahedron Lett. *1970*, 3947.

[68] *J. B. Hendrickson, R. Bergeron*, Tetrahedron Lett. *1973*, 4607.

[69] *J. P. Marino* in *A. Senning:* Topics in Sulfur Chemistry. Vol. 1. Thieme, Stuttgart 1976, p. 1.

[70] *B. van de Graaf, F. W. McLafferty*, J. Am. Chem. Soc. *99*, 6808 (1977).

[71] a) *G. H. Schmid, T. T. Tidwell*, J. Org. Chem. *43*, 460 (1978); b) *K. Toyoshima, T. Okuyama, T. Fueno, ibid. 43*, 2789 (1978); c) *W. A. Smit, N. S. Zefirov, I. V. Bodrikov, M. Z. Krimer*, Acc. Chem. Res. *1979*, 282.

[72] *G. Capozzi, V. Lucchini, G. Modena*, Rev. Chem. Intermediates *2*, 347 (1979).

[73] *R. Weiss, C. Schlierf*, Synthesis *1976*, 323.

[74] *W. Russ*, Dissertation, Universität Stuttgart 1980.

[75] *G. Capozzi, G. Melloni, G. Modena*, J. Chem. Soc. *C 1970*, 2621.

[76] *A. Haas, V. Hellwig*, J. Fluorine Chem. *6*, 521 (1975).

[77] *T. Fujisawa, T. Kobori, N. Ohtsuka, G. Tsuchihashi*, Tetrahedron Lett. *1968*, 5071.

[78] *M. Hojo, R. Masuda*, Synth. Commun. *1975*, 169.

[79] *E. Vilsmaier, W. Sprügel*, Tetrahedron Lett. *1972*, 625.

[80] *P. Claus, W. Rieder*, Tetrahedron Lett. *1972*, 3879.

[81] *A. Winkler*, DOS 2644591 (1978), Bayer; Chem. Abstr. *89*, 23960f (1978).

[82] *D. N. Harpp, K. Stehou, T. H. Chan*, J. Am. Chem. Soc. *100*, 1222 (1978).

[83] *S. Uemura, A. Onoe, H. Okazaki, M. Okono*, Bull. Chem. Soc. Jpn. *48*, 619 (1975).

[84] *H. G. Padeken* in *Houben-Weyl:* Methoden der Organischen Chemie, 4th Edit., Vol. 10/1. Thieme, Stuttgart 1971, p. 1.

[85] *S. R. Hartshorn, K. Schofield*, Progr. Org. Chem. *8*, 278 (1973).

[86] *L. M. Stock*, Progr. Phys. Org. Chem. *12*, 21 (1976).

[87] *L. F. Albright, C. Hanson:* Industrial and Laboratory Nitrations. ASC-Symp. Ser. *22* (1975), American Chemical Society, Washington 1976.

[88] a) *C. L. Coon, M. E. Hill*, US-Pat. 3714272 (1973); Chem. Abstr. *78*, 97303x (1973); b) *Ch. Comninellis, Ph. Javet, E. Plattner*, Tetrahedron Lett. *1975*, 1429.

[89] a) *T. Kameo, O. Manabe*, Chem. Lett. *1972*, 33; b) *T. Kameo, O. Manabe*, Nippon Kagaku Kaishi *1974*, 195, 2396.

[90] *G. C. Davis, N. C. Cook*, Chemtech. *1977*, 7 626; Chem. Abstr. *88*, 6463 s (1978).

[91] a) *S. J. Kuhn, G. A. Olah,* J. Am. Chem. Soc. *83*, 4564 (1961); b) *G. A. Olah,* Aldrichimica Acta *6*, 7 (1973).
[92] *J. E. Griffiths, W. A. Sunder,* J. Fluorine Chem. *6*, 533 (1975).
[93] a) *M. Schmeisser, P. Sartori, B. Lippsmeier,* Z. Naturforsch. *B 28*, 573 (1973); b) *L. M. Yagupol'skii, I. I. Maletina, V. V. Orda,* Zh. Org. Khim. *10*, 2226 (1974); c) *S. K. Yarbo, R. E. Noftle,* J. Fluorine Chem. *6*, 187 (1975).
[94] *C. L. Coon, W. G. Blucher, M. E. Hill,* J. Org. Chem. *38*, 4243 (1973).
[95] *C. A. Cupas, R. L. Pearsons,* J. Am. Chem. Soc. *90*, 4742 (1968).
[96] *G. A. Olah, S. C. Narang, R. L. Pearson, C. A. Cupas,* Synthesis *1978*, 452.
[97] *F. Effenberger, J. Geke,* unpublished.
[98] *F. Effenberger, H. Klenk,* Chem. Ber. *109*, 769 (1976).
[99] *G. A. Olah, H. C. Lin,* Synthesis *1974*, 444.
[100] a) *E. Spreckels,* Chem. Ber. *52*, 315 (1919); b) *K. E. Cooper, C. K. Ingold,* J. Chem. Soc. *1927*, 836.
[101] *A. Schaarschmidt,* Chem. Ber. *57*, 2065 (1924); Angew. Chem. *39*, 1457 (1926).
[102] *B. Davies, C. B. Thomas,* J. Chem. Soc. Perkin Trans. I *1975*, 65.
[103] *R. O. C. Norman, W. J. E. Parr, C. B. Thomas,* J. Chem. Soc. Perkin Trans. I *1974*, 369.
[104] *G. R. Underwood, R. S. Silverman, A. Vanderwalde,* J. Chem. Soc. Perkin Trans. II *1973*, 1177.
[105] a) *G. A. Olah, S. C. Narang,* Synthesis *1978*, 690; b) *G. A. Olah, R. Malhotra, S. C. Narang,* J. Org. Chem. *43*, 4628 (1978); c) *S. C. Narang, M. J. Thompson,* Aust. J. Chem. *31*, 1839 (1978).
[106] a) *D. W. Amos, D. A. Baines, G. W. Flewett,* Tetrahedron Lett. *1973*, 3191; b) *R. G. Coombes, L. W. Russell,* J. Chem. Soc. Perkin Trans. II *1974*, 830.
[107] *M. T. Mocella, M. S. Okamoto, E. K. Barefield,* Synth. React. Inorg. Met. Org. Chem. *4*, 69 (1974).
[108] a) *A. Schmitz,* Russ. Chem. Rev. *45*, 16 (1975); b) *J. Kimijina,* Senryo To Yakuhin *1977*, 22, 241; Chem. Abstr. *89*, 214998t (1978).
[109] *P. D. Gassman,* Acc. Chem. Res. *3*, 26 (1970).
[110] *P. D. Gassman, G. D. Hartman,* J. Am. Chem. Soc. *95*, 449 (1973).
[111] *P. Kovacic, M. K. Lowery, K. W. Field,* Chem. Rev. *70*, 639 (1970).
[112] *G. Yagil, M. Anbar,* J. Am. Chem. Soc. *84*, 1797 (1962).
[113] *H. Bock, K.-L. Kompa,* Chem. Ber. *99*, 1361 (1966).
[114] *F. Minisci,* Top. Curr. Chem. *62*, 1 (1976).
[115] *F. Sommer, O. F. Schulz, M. Nassau,* Z. Anorg. Chem. *147*, 142 (1925).
[116] *Y. Tamura, J. Minamikawa, M. Ikeda,* Synthesis *1977*, 1.
[117] a) *T. Sheradsky, G. Salemnick, Z. Nir,* Tetrahedron *28*, 3833 (1972); b) *T. Oguri, T. Shioiri, S.-I. Yamada,* Chem. Pharm. Bull. Jpn. *23*, 167 (1975); c) *D. I. Scopes, A. F. Kluge, J. A. Edwards,* J. Org. Chem. *42*, 376 (1977).
[118] *R. Y. Ning,* Chem. Eng. News *51*, p. 36 (1973).
[119] *P. Reiter,* Diplomarbeit, Universität Stuttgart 1971.
[120] *F. D. King, D. R. M. Walton,* Synthesis *1975*, 788.
[121] *T. M. Chapman, E. A. Freedman,* Synthesis *1971*, 591.
[122] *G. Boche, N. Mayer, M. Bernheim, K. Wagner,* Angew. Chem. *90*, 733 (1978); Angew. Chem. Int. Ed. Engl. *17*, 687 (1978).
[123] *W. Biernacki,* Rocz. Chem. *46*, 623 (1972); *47*, 963 (1973); Chem. Abstr. *77*, 101023e (1972) and *79*, 136662f (1973), respectively.
[124] *G. A. Olah:* Friedel Crafts and Related Reactions. Vol. II. Interscience, New York 1964.
[125] See ref. [7a], pp. 213ff., and references cited therein.
[126] a) *H. Perst:* Oxonium Ions in Organic Chemistry. Verlag Chemie, Weinheim 1971; b) *H. Perst* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions, Vol. V. Wiley, New York 1976, pp. 1961ff.; c) *V. G. Granik, B. M. Pyatin, R. G. Glushkov,* Russ. Chem. Rev. *40*, 747 (1971).
[127] a) *H. Meerwein* in *Houben-Weyl:* Methoden der Organischen Chemie. 4th Edit., Vol. VI/3. Thieme, Stuttgart 1965, p. 338; b) *R. A. Goodrich, P. M. Treichel,* J. Am. Chem. Soc. *88*, 3509 (1966).
[128] *G. A. Olah, E. G. Melby,* J. Am. Chem. Soc. *95*, 4971 (1973).
[129] *A. N. Nesmeyanov, L. G. Makarova, T. P. Tosstaya,* Tetrahedron *1*, 145 (1957).
[130] *G. A. Olah:* Halonium Ions. Wiley, New York 1975.
[131] *G. A. Olah, J. R. DeMember,* J. Am. Chem. Soc. *91*, 2113 (1969).
[132] *G. A. Olah, E. G. Melby,* J. Am. Chem. Soc. *94*, 6220 (1972).
[133] *P. E. Peterson, P. R. Clifford, F. J. Slama,* J. Am. Chem. Soc. *92*, 2840 (1970).
[134] *G. A. Olah, Y. Yamada, R. J. Spear,* J. Am. Chem. Soc. *97*, 680 (1975).
[135] a) *R. D. Bach, J. W. Holubka, T. A. Taffee,* J. Org. Chem. *44*, 1739 (1979); b) *G. A. Olah, B. G. B. Gupta, S. C. Narang,* Synthesis *1979*, 274.
[136] a) *J.-M. Lalancette, M.-J. Fournier-Breault, R. Thiffault,* Can. J. Chem. *52*, 589 (1974); b) *A. G. Freeman, S. E. Goh,* Pap.-London Int. Conf. Carbon Graphite, 4th *1974*, (Pub. 1976) 329; Chem. Abstr. *89*, 59433j (1978).
[137] a) *G. A. Olah, J. Kaspi, J. Bukala,* J. Org. Chem. *42*, 4187 (1977); b) *J. Kaspi, D. D. Montgomery, G. A. Olah, ibid. 43*, 3147 (1978).
[138] a) *G. Sosnovsky, M. W. Shende,* Synthesis *1972*, 423; b) Z. Naturforsch. *B 27*, 1339 (1972).
[139] *M. Attinà, F. Cacace, G. Ciranni, P. Giacomello,* J. Am. Chem. Soc. *99*, 2611, 5022 (1977).
[140] a) *D. M. Hoffmann,* J. Org. Chem. *36*, 1716 (1971); b) *D. N. Kevill, W. A. Reis, J. B. Kevill,* Tetrahedron Lett. *1972*, 957.
[141] *J. Radell, J. W. Conolly, A. J. Raymond,* J. Am. Chem. Soc. *83*, 3958 (1961).
[142] *G. A. Olah, J. Nishimura, J. Am. Chem. Soc. 96*, 2214 (1974).
[143] *K. Hovius, J. B. F. N. Engberts,* Tetrahedron Lett. *1972*, 2477.
[144] *C. D. Beard, K. Baum, V. Grakauskas,* J. Org. Chem. *38*, 3673 (1973).
[145] *M. Hanack,* Angew. Chem. *90*, 346 (1978); Angew. Chem. Int. Ed. Engl. *17*, 333 (1978).
[146] a) *P. J. Stang,* Acc. Chem. Res. *11*, 107 (1978); b) *P. J. Stang, A. G. Anderson,* J. Am. Chem. Soc. *100*, 1520 (1978).
[147] *K. Hajo, H. Yoshino, T. Mukaiyama,* Chem. Lett. *1977*, 133.
[148] *J. B. Bapat, R. J. Blade, A. J. Boulton, J. Epstajn, A. R. Katritzky, J. Lewis, P. Molina-Buendia, P.-L. Nie, C. A. Ramsden,* Tetrahedron Lett. *1976*, 2691.
[149] *L. J. Mathias,* Synthesis *1979*, 561.
[150] *L. I. Belen'kii, Yu. B. Vol'kenshtein, I. B. Karamanova,* Usp. Khim. *46*, 1698 (1977); Chem. Abstr. *87*, 200267a (1977).
[151] a) *G. A. Olah, D. A. Beal, J. A. Olah,* J. Org. Chem. *41*, 1627 (1976); b) *G. A. Olah, M. R. Bruce,* J. Am. Chem. Soc. *101*, 4765 (1979); c) *G. A. Olah, D. A. Beal, S. H. Yu, J. A. Olah,* Synthesis *1974*, 560.
[152] *H. Böhme, M. Haake* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry. Part 1. Interscience, New York 1976, pp. 107ff.
[153] a) *J. Gloede, J. Freiberg, W. Bürger, G. Ollmann, H. Gross,* Arch. Pharm. (Weinheim) *302*, 354 (1949); b) *D. D. Reynolds, B. C. Cossar,* J. Heterocycl. Chem. *8*, 605 (1971).
[154] a) *K. Nyberg,* Acta Chem. Scand. *B 28*, 825 (1974); b) *A. K. Sheinkman, E. N. Nelin, A. I. Kostin, V. P. Marshtupa,* Zh. Org. Khim. *14*, 1289 (1978).
[155] *H. E. Zaugg,* Synthesis *1970*, 49.
[156] *G. Büchi, C.-P. Mak,* J. Org. Chem. *42*, 1784 (1977).
[157] *L. Ghosez, J. Marchand-Boynaert,* see ref. [152], p. 421.
[158] a) *D. P. N. Satchell,* Q. Rev. Chem. Soc. *17*, 160 (1963); b) *D. P. N. Satchell,* Chem. Ind. (London) *1974*, 683; c) *C.-W. Schellhammer* in *Houben-Weyl:* Methoden der organischen Chemie. 4th Edit., Vol. VII/2a. Thieme, Stuttgart 1973, pp. 15ff.
[159] *G. A. Olah:* Friedel Crafts and Related Reactions. Vol. III, Parts 1 and 2. Interscience, New York 1964.
[160] *G. A. Olah, A. Germain, A. M. White* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Vol. V. Wiley, New York 1976, pp. 2049ff.
[161] a) *D. E. Pearson, C. A. Buehler,* Synthesis *1972*, 533; b) *F. Effenberger, G. Epple, K. Hutzmacher,* DOS 2202973 (1973), BASF; Chem. Abstr. *79*, 115315e (1973); c) *Kh. Yu. Yuldashev, N. G. Siderova, K. Agzomova, A. R. Abdurasuleva, Kh. Tadzhimukhamedov, I. Stempnevskaya, S. I. Tabachkova, A. Khaitbaeva,* USSR-Pat. 405850 (1973); Chem. Abstr. *80*, 82352e (1974); d) *K. Arata, K. Yabe, I. Toyoshima,* J. Catal. *1976*, 44, 385; Chem. Abstr. *86*, 88657d (1977); e) *J. O. Morley,* Synthesis *1977*, 54.
[162] *F. Seel,* Z. Anorg. Allg. Chem. *250*, 331 (1943).
[163] *G. A. Olah, H. C. Lin, A. Germain,* Synthesis *1974*, 895.
[164] *W. A. Smit, A. V. Semenovsky, V. F. Kucherov, T. N. Chernova, M. Z. Krimer, O. V. Lubinskaya,* Tetrahedron Lett. *1971*, 3101.
[165] *A. A. Scheglov, W. A. Smit, S. A. Khurshudyan, V. A. Chertkov, V. F. Kucherov,* Synthesis *1977*, 324.
[166] a) *E. Lindner,* Angew. Chem. *82*, 143 (1970); Angew. Chem. Int. Ed. Engl. *9*, 160 (1970); b) *R. Mayer, P. Schönfeld, J. Fabian,* Z. Chem. *15*, 484 (1975).
[167] *H. P. Treffers, L. P. Hammett,* J. Am. Chem. Soc. *59*, 1708 (1937).
[168] *A. Casadevall, A. Commeyras, P. Paillous, H. Collet,* Bull. Soc. Chim. Fr. *1970*, 719.
[169] *J. O. Knobloch, F. Ramirez,* J. Org. Chem. *40*, 1101 (1975).
[170] *A. Germain, A. Commeyras, A. Casadevall,* Bull. Soc. Chim. Fr. *1973*, 2527, 2537.
[171] *F. Effenberger, G. Epple,* Angew. Chem. *84*, 294 (1972); Angew. Chem. Int. Ed. Engl. *11*, 299 (1972).
[172] a) *H. Minato, T. Miura, M. Kobayashi,* Chem. Lett. *1977*, 609; b) *T. R. Forbus, Jr., J. C. Martin,* J. Org. Chem. *44*, 313 (1979).
[173] a) *M. H. Karger, Y. Mazur,* J. Org. Chem. *36*, 528, 532, 540 (1971); b) *E. Sarlo, T. Lanigan,* Org. Prep. Proced. *1*, 157 (1969).
[174] *F. Effenberger, G. Epple,* Angew. Chem. *84*, 295 (1972); Angew. Chem. Int. Ed. Engl. *11*, 300 (1972).
[175] *G. A. Olah, R. Malhotra, S. C. Narang, J. A. Olah,* Synthesis *1978*, 672.
[176] a) *G. Epple,* Dissertation, Universität Stuttgart 1972; b) *J. K. Eberhard,* Dissertation, Universität Stuttgart 1978.
[177] *J. W. Larsen, P. A. Bouis,* J. Am. Chem. Soc. *97*, 4418 (1975).
[178] *C. G. Krespan, D. C. England,* J. Org. Chem. *40*, 2937 (1975).
[179] *F. Effenberger, M. Keil,* unpublished.
[180] *E. Fluck, E. Beuerle,* Z. Anorg. Allg. Chem. *411*, 125 (1975).
[181] a) *Z. Arnold, H. Holý,* Collect. Czech. Chem. Commun. *27*, 2886 (1962); b) *G. Martin, M. Martin,* Bull. Soc. Chim. Fr. *1963*, 1637.
[182] *F. Effenberger, G. König, H. Klenk,* Angew. Chem. *90*, 740 (1973); Angew. Chem. Int. Ed. Engl. *17*, 695 (1978).
[183] *Th. Wieland, K. H. Shin, B. Heinke,* Chem. Ber. *91*, 483 (1968).
[184] *K. Baum, C. D. Beard,* J. Org. Chem. *40*, 81 (1975).
[185] *P. Cremaschi, M. Simonetta,* Theor. Chim. Acta *43*, 351 (1977).
[186] *H. A. Staab, W. Rohr* in *W. Foerst:* Neuere Methoden der präparativen organischen Chemie. Vol. V. Verlag Chemie, Weinheim 1967, pp. 53ff.

[187] a) G. Höfle, W. Steglich, H. Vorbrüggen, Angew. Chem. 90, 602 (1978); Angew. Chem. Int. Ed. Engl. 17, 569 (1978), exhaustive literature references; b) A. Hassner, V. Alexanian, Tetrahedron Lett. 1978, 4475.
[188] E. Guibé-Jampel, M. Wakselman, Synthesis 1977, 772.
[189] a) T. Mukaiyama, Angew. Chem. 91, 798 (1979); Angew. Chem. Int. Ed. Engl. 18, 707 (1979); b) T. M. Mukaiyama, M. Usui, K. Saigo, Chem. Lett. 1976, 49; c) T. M. Mukaiyama, K. Narasaka, K. Kikuchi, ibid. 1977, 441.
[190] a) A. O. Mück, Dissertation, Universität Stuttgart 1971; b) E. Bessey, Dissertation, Universität Stuttgart 1977.
[191] a) Y. Ueno, T. Takaya, E. Imoto, Bull. Chem. Soc. Jpn. 37, 864 (1964); b) A. S. Dutta, J. S. Morley, J. Chem. Soc. C 1971, 2896.
[192] I. Fleming, D. Philippides, J. Chem. Soc. C 1970, 2426.
[193] A. W. K. Cahn, W. D. Crow, I. Gosney, Tetrahedron 26, 2497 (1970).
[194] L. Kisfaludy, T. Hahacsi, M. Low, F. Drexler, J. Org. Chem. 44, 654 (1979).
[195] a) G. A. Olah, S. J. Kuhn, see [159], pp. 1153ff.; b) G. A. Olah in [6b], pp. 115ff.
[196] a) H. A. Staab, A. P. Datta, Angew. Chem. 75, 1203 (1963); Angew. Chem. Int. Ed. Engl. 3, 132 (1964); b) G. A. Olah, Y. D. Vankar, M. Arvanaghi, J. Sommer, ibid. 91, 649 (1979) and 18, 614 (1979).
[197] C. Jutz, see ref. [152], pp. 225ff.
[198] W. Kantlehner, see ref. [152], Part 2 (1979), pp. 5ff.
[199] S. Hünig, Angew. Chem. 76, 400 (1964); Angew. Chem. Int. Ed. Engl. 3, 548 (1964).
[200] A. Rieche, H. Gross, E. Höft, Chem. Ber. 93, 88 (1960).
[201] P. Linda, A. Lucarelli, G. Marino, G. Savelli, J. Chem. Soc. Perkin Trans. II 1974, 1610.
[202] Z. Arnold, F. Šorm, Collect. Czech. Chem. Commun. 23, 452 (1958).
[203] H. Bredereck, F. Effenberger, G. Simchen, Chem. Ber. 97, 1403 (1964).
[204] H. H. Bosshard, H. Zollinger, Helv. Chim. Acta 42, 1659 (1959).
[205] G. Simchen, see ref. [152], Part 2 (1979), pp. 393ff.
[206] G. Simchen, H. Hoffmann, H. Bredereck, Chem. Ber. 101, 51 (1968).
[207] a) H. Bredereck, F. Effenberger, H. J. Botsch, Chem. Ber. 97, 3397 (1964); b) H. Bredereck, F. Effenberger, Th. Brendle, H. Muffler, ibid. 101, 1885 (1968).
[208] a) H. Bredereck, Pharm. Ztg. 116, 780 (1971); b) A. D. Balchor, W. Leimgruber, DOS 2057840 (1971), Hoffmann-La Roche; Chem. Abstr. 75, 63605v (1971).
[209] B. Föhlisch, Chem. Ber. 104, 348 (1971).
[210] S. Danishefsky, E. Berman, L. A. Clizbe, M. Hirama, J. Am. Chem. Soc. 101, 4385 (1979).
[211] H. Bredereck, R. Gompper, H. Rempfer, K. Klemm, H. Keck, Chem. Ber. 92, 329 (1959).
[212] H. Bredereck, F. Effenberger, A. Hofmann, Chem. Ber. 96, 3260 (1963).
[213] a) H. Bredereck, R. Gompper, H. G. v. Schuh, G. Theilig, Angew. Chem. 71, 753 (1959); b) H. Bredereck, F. Effenberger, E. H. Schweizer, Chem. Ber. 95, 8003 (1962); c) F. Tsatsaronis, F. Effenberger, ibid. 94, 2876 (1961).
[214] a) H. Bredereck, F. Effenberger, G. Rainer, H.-P. Schosser, Justus Liebigs Abb. Chem. 659, 133 (1962); b) H. Bredereck, F. Effenberger, G. Rainer, ibid. 673, 82, 88 (1964).
[215] F. Effenberger, M. Keil, E. Bessey, Chem. Ber. 113 (1980).
[216] E. Kühle, Angew. Chem. 85, 633 (1973); Angew. Chem. Int. Ed. Engl. 12, 630 (1973).
[217] G. A. Olah, P. Schilling, J. M. Bollinger, J. Nishimura, J. Am. Chem. Soc. 96, 2221 (1974).
[218] O. Achmatowicz, O. Achmatowicz, Jr., Rocz. Chem. 35, 813 (1961); Chem. Abstr. 56, 7209i (1962).
[219] Z. Janousek, H. G. Viehe, see ref. [152], pp. 343ff.
[220] V. P. Kukhar, V. I. Pasternak, G. V. Pesotskaya, Zh. Org. Khim. 9, 39 (1973).
[221] a) H. G. Viehe, Th. van Vyve, Z. Janousek, Angew. Chem. 84, 991 (1972); Angew. Chem. Int. Ed. Engl. 11, 916 (1972); b) N. D. Bodnarchuk, V. V. Momot, L. A. Lazukina, G. V. Pesotskaya, V. P. Kukhar, Zh. Org. Khim. 10, 735 (1974).
[222] a) W. Kantlehner, see ref. [152], Part 2 (1979), pp. 143ff.; b) Part 2, pp. 173ff. (1979).
[223] A. E. Feiring, J. Org. Chem. 41, 148 (1976).
[224] Yu. A. Naumov, A. P. Isakova, A. N. Kost, V. F. Zakharov, V. P. Zvolinskii, N. F. Moiseikina, S. V. Nikeryasova, Zh. Org. Khim. 11, 370 (1975).
[225] R. Leuckart, Ber. Dtsch. Chem. Ges. 18, 873 (1885); J. Prakt. Chem. 41, 306 (1890).
[226] a) F. Effenberger, R. Gleiter, Chem. Ber. 97, 472 (1964); b) 97, 480 (1964).
[227] M. Seefelder, Chem. Ber. 96, 3243 (1963).
[228] a) R. Graf, Justus Liebigs Ann. Chem. 661, 111 (1963); b) Angew. Chem. 80, 179 (1968); Angew. Chem. Int. Ed. Engl. 7, 172 (1968).
[229] J. W. McFarland, Int. J. Sulfur Chem. B 1972, 7, 319.
[230] F. Effenberger, R. Gleiter, L. Heider, R. Niess, Chem. Ber. 101, 502 (1968).
[231] a) K. K. Ginwala, J. P. Trivedi, J. Indian Chem. Soc. 40, 897 (1963); Chem. Abstr. 60, 4056 (1967); b) P. A. S. Smith, R. O. Kan, J. Org. Chem. 29, 2261 (1964); c) E. P. Papadopoulos, ibid. 41, 962 (1976).
[232] D. Martin, S. Rackow, Chem. Ber. 98, 3662 (1965).
[233] Y. Tamaru, T. Kawasaki, M. Adachi, M. Tanio, Y. Kita, Tetrahedron Lett. 1977, 4417.

Coupling of Solvolysis and C—C Linkage: A Promising Synthetic Route to Functionalized Carboxylic Acids, Aldehydes, and Ketones

By Kaspar Bott[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Numerous additions of carbocations to chloroolefins or acetylenes can be coupled with a solvolysis step when performed in a suitable acid; the products are variously substituted carboxylic acids, aldehydes, and ketones. Factors determining the success of these syntheses are the stability of the intermediate carbocations and suppression of the competing addition of protons to the unsaturated reaction component. Under the conditions of the Tscherniac-Einhorn reaction, amidomethylation of chloroolefins and acetylenes, *i.e.* the introduction of acylaminomethyl groups, is shown not to involve a trigonal α-chloro carbocation or a linear vinyl cation, but instead to proceed *via* a cyclic oxazinium ion intermediate.

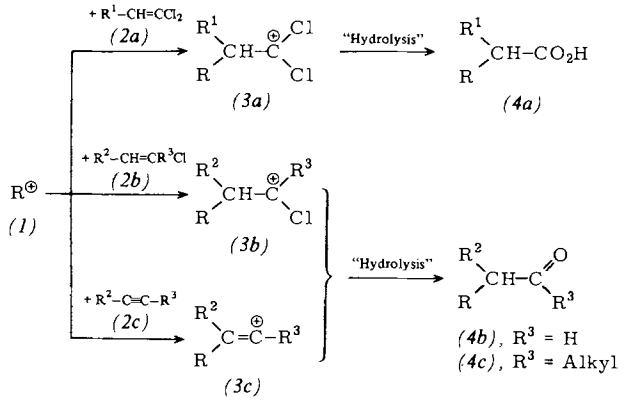
1. Introduction

Many syntheses in organic chemistry are possible only if C—C linkage is followed by an energetically favored step, such as salt formation. Typical examples of this strategy are the carbonylation of aromatic hydrocarbons according to *Gattermann-Koch*[1] and ester condensation according to *Claisen*[2].

In the following we shall survey those reactions in which the formation of an intermediate *(3a–c)* from the carbocation *(1)* and the unsaturated component *(2a–c)* is forcibly coupled with the energetically particularly favorable hydrolysis to

[*] Dr. K. Bott
Hauptlaboratorium der BASF Aktiengesellschaft
D-6700 Ludwigshafen (Germany)

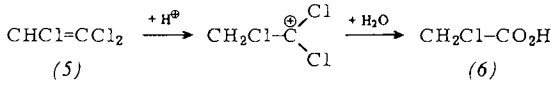
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-171 $ 02.50/0



give carboxylic acids *(4a)*, aldehydes *(4b)*, and ketones *(4c)*. Thus, subsequent elimination of *(1)* from the intermediate *(3)* is practically impossible.

As will be shown for a particular example (Section 2.3) the production of carbonyl compounds *(4a-c)* according to the given synthetic scheme has the decisive advantage that the adduct ions *(3a-c)* can be generated under much milder reaction conditions than is otherwise possible.

In the preferred reaction medium, *viz.* sulfuric acid, the synthetic step leading to *(3)* must compete with addition of a proton to the olefin *(2a,b)* or to the acetylene *(2c)*. For instance, chloroacetic acid *(6)* thus arises from trichloroethylene *(5)*:

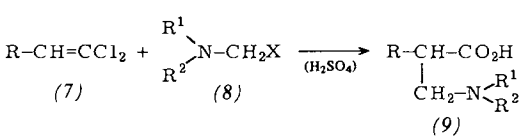


Carboxylic acids *(4a)*, aldehydes *(4b)*, and ketones *(4c)* can only be obtained in good yields if such competing saponifications can be forced into the background.

2. Synthesis of Carboxylic Acids

2.1. β-Acylamino Carboxylic Acids

The reaction named after *Tscherniac* and *Einhorn* permits the introduction of an acylaminomethyl group ("amidomethyl group") into an aromatic ring[3] or into an activated methylene group[4]. Since these syntheses normally take place in strong sulfuric acid, it was to be expected that suitable amidomethyl cations [from *(8)*] would react with the 1,1-dichloroolefins *(7)* to form *N*-acylated β-amino carboxylic acids.



According to available studies[5-7] (cf. Table 1) the weakly basic dichloroalkenes *(7)* require particularly electron-poor amidomethyl cations as reagents. In the choice of the amidomethylation agent *(8)* the phthalimido, maleimido, trichloroacetamido, and trifluoroacetamido group have proved of advantage as amide component, whereas not only the usual anionic substituents such as chlorine or hydroxyl, but also the carboxamide components R^1R^2N—, represent possible choices for X. A further possibility for generation of amidomethyl cations consists in dissolving the carboxamide R^1R^2NH and (oligomeric) formaldehyde in sulfuric acid prior to addition of the olefin *(7)*.

Table 1. β-Acylamino carboxylic acids *(9)* from 1,1-dichloroolefins *(7)* and amidomethylating reagents *(8)*.

Phthaloyl =  ; Maleoyl = 

	R	R₁ R²	X	Yield of *(9)* [%] [a]
(9a)	Cl	Phthaloyl	OH	94
(9b)	Cl	Cl_4-Phthaloyl	OH	92
(9c)	Cl	Maleoyl	OH	73
(9d)	Cl	H CCl_3CO	CCl_3 CO NH	88
		[b]		74
(9e)	Cl	H CF_3CO	OH	64
(9f)	Br	Phthaloyl	OH	91
(9g)	Br	Cl_4-Phthaloyl	OH	90
(9h)	Br	H CCl_3CO	[b]	60
(9i)	p-$NO_2C_6H_4CH_2$	Phthaloyl	OH	94
(9j)	p-$NO_2C_6H_4CH_2$	H CCl_3CO	OH	35
(9k)	Cl $(CH_2)_3$	Phthaloyl	OH	93
(9l)	p-$CH_3C_6H_4SO_2$ $(CH_2)_3$	Phthaloyl	OH	95
(9m)	p-$NO_2C_6H_4SO_2$ $(CH_2)_3$	Phthaloyl	OH	97
(9n)	p-$NO_2C_6H_4SO_2$ $(CH_2)_3$	Maleoyl	OH	98
(9o)	Phthalimido-$(CH_2)_3$	Phthaloyl	OH	95
(9p)	p-$NO_2C_6H_4$	Phthaloyl	OH	92

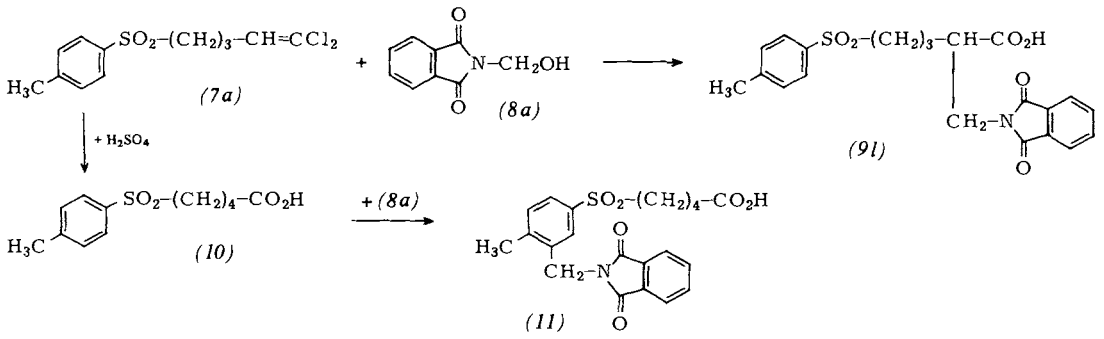
[a] The yields are based on the reactant used in substoichiometric amounts.
[b] Amidomethylation with trioxane + trichloroacetamide.

The 1,1-dichloroolefins *(7)* and chloroolefins *(46)* used in the synthesis of β-(acylamino) carbaldehydes exhibit a clear gradation of reactivity towards the electrophilic reagent *(8)*, which is manifested in the differing reaction temperatures. The temperature for reaction of vinyl chloride[8] is 0 to 5 °C, that for 1,1-dichloroethylene and its alkyl derivatives 5 to 15 °C, that for 1,2-dichloroethylene 30 to 35 °C, that for trichloroethylene and 1,1-dichloro-2-(*p*-nitrophenyl)ethylene is 40 to 50 °C, and finally that for 2-bromo-1,1-dichloroethylene is 50 to 60 °C.

Tscherniac-Einhorn syntheses with the 1,1-dichloroalkenes *(7)* are carried out in 95% sulfuric acid, and prove highly productive on use of *N*-(hydroxymethyl)phthalimide *(8a)* and its tetrachloro derivative. Comparison of the data listed in Table 1 shows that the yield always drops considerably upon incorporation of a trichloro- or a trifluoroacetamidomethyl group.

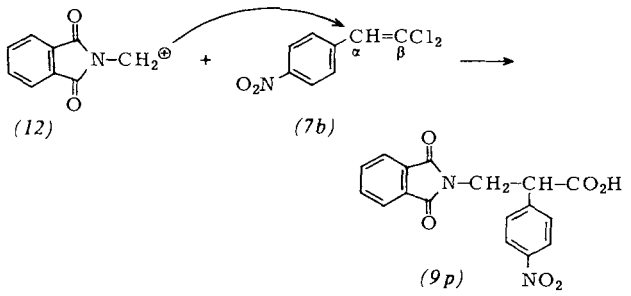
Preparation of *N*-acylated β-alanines in which R, as in *(9i)* and *(9j)*, is an arylalkyl group requires that the aryl group be protected against amidomethylation by a strongly electron-withdrawing substituent.

For the same reason, it is necessary to avoid an excess of *N*-(hydroxymethyl)phthalimide *(8a)* on preparation of 2-(phthalimidomethyl)-5-(*p*-toluenesulfonyl)valeric acid *(9l)*. If 1,1-dichloro-5-(toluenesulfonyl)-1-pentene *(7a)* is first allowed to react only with sulfuric acid at room temperature and the component *(8a)* is added on completion of "acidolysis", then the carboxylic acid *(11)* isomeric with *(9l)* results as

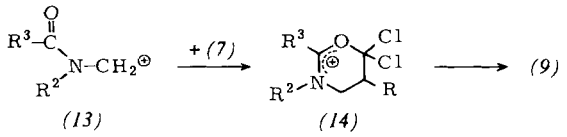


final product. The structure of *(9l)* follows unequivocally from the ^{1}H-NMR-spectrum.

The last example listed in Table 1, *viz.* 2-(*p*-nitrophenyl)-3-phthalimidopropionic acid *(9p)* is of interest because, in its formation, the "positive end" of the phthalimidomethyl cation *(12)* does not attack the β-position, as might have been expected, but only the α-C atom of the styrene skeleton of *(7b)*.



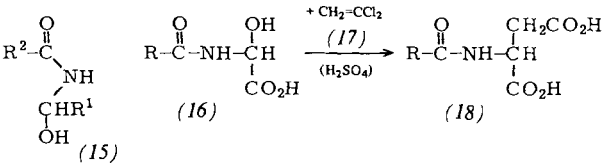
Evidence is available showing that the addition of the amidomethyl cation *(13)* to the dichloroolefins *(7)* does not proceed *via* an open-chain dichloro carbocation [such as *(3a)*] but can profit from concerted formation of a low-energy oxazinium intermediate *(14)*. Thus "true" carbocations react with trichloroethylene *(5)* (Section 2.3) in sulfuric acid only



at 80 to 110 °C whereas amidomethylation of the same olefin occurs under much milder conditions. As considered in more detail later (Section 3.1), the stereoisomeric cycloadducts can be isolated in high purity on treatment of the cation *(12)* with *cis/trans* isomeric olefins in chlorohydrocarbon solvents.

2.2. *N*-Acylaspartic Acids

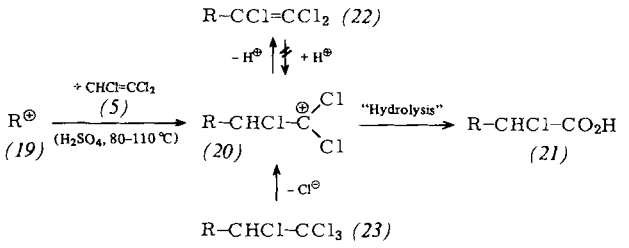
The use of amidomethylation agents *(15)* bearing an aliphatic group R^1 in the synthesis of β-amido carboxylic acids is subject to limitations because the substances *(15)* as aldehyde derivatives normally have a very short lifetime in sulfuric acid. In contrast, α-(acylamino)glycolic acids *(16)* (*N*-acyl-α-hydroxyglycines), accessible from glyoxylic acid (carboxylated formaldehyde), have a stability comparable with that of *N*-hydroxymethylcarboxamides *(8)*, X = OH, in concentrated mineral acids.



1,1-Dichloroethylene *(17)* is the only chloroolefin component tried so far in reactions of compounds *(16)* and butyl α-hydroxyhippurate[9,10]. The *N*-protected aspartic acids *(18)*, R = ethoxy or *n*-butoxy or phenyl, were obtained in yields of 47 to 87%, at reaction temperatures between 0 and 20 °C.

2.3. α-Chloro Carboxylic Acids

The addition of carbocations to 1,1-dichloroethylene *(17)* in sulfuric acid has already been surveyed in detail[11]. Application of this reaction proceeding under mild conditions (5 to 10 °C) to the less basic compound trichloroethylene *(5)* requires that the temperature be raised to 80 to 110 °C[12,13]. Under such drastic conditions the only substances that can react with *(5)* to give the α-chloro carboxylic acids *(21)* are those in which olefin formation from the intermediate carbocation *(19)* is strongly suppressed or completely ruled out.



In this context, it is of interest whether the products *(22)* and *(23)* resulting from the classical Prins reaction of an alkyl chloride RCl and *(5)* can be transformed into a substituted chloroacetic acid *(21)* *via* a common intermediate *(20)*. With the aid of readily accessible model substances it could be demonstrated[13] that 1,1,1,2-tetrachloro-3-(*p*-nitrophenyl)propane [*(23)*, R = *p*-nitrobenzyl] is hydrolyzed only slowly (25% conversion after 5 h) to α-chloro-*p*-nitrohydrocinnamic acid even at 115 °C, whereas 1,1,2-trichloro-3-(*p*-nitrophenyl)-1-propene [*(22)*, R = *p*-nitrobenzyl] and trichloro(2-norbornyl)ethylene [*(22)*, R = 2-norbornyl] are

largely oxidized by sulfuric acid. However, the trichloroolefins *(22)* were isolated in some cases as by-product of carboxylic acid synthesis from *(19)* and *(5)*.

2.3.1. Introduction of the Chloroacetic Acid Group into the Adamantane System[12,13]

Reaction of trichloroethylene *(5)* with the bromoadamantanes *(24a–c)*, which serve as precursors of 1-adamantyl cations *(26a–c)*, does not stop at α-chloro-1-adamantaneacetic acids *(25a–c)*. The greater part of *(25a–c)* reacts once again after hydride abstraction from the bridgehead position with *(5)* to give α,α′-dichloro-1,3-adamantanediacetic acids *(28a–c)* (see Table 2). The extent to which *(28a–c)* are formed expectedly depends upon the reaction temperature, the sulfuric acid concentration, and the degree of bridgehead substitution.

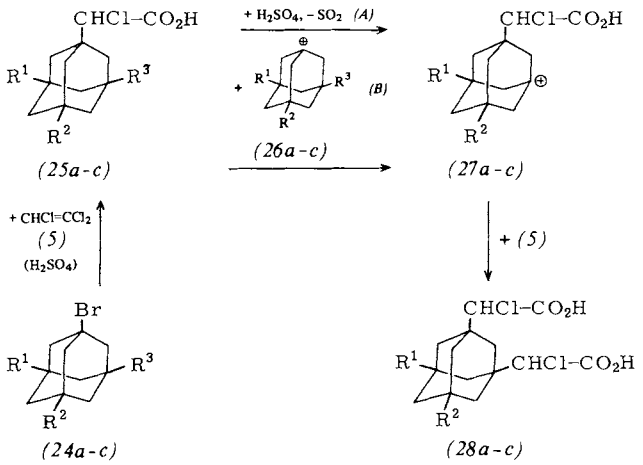


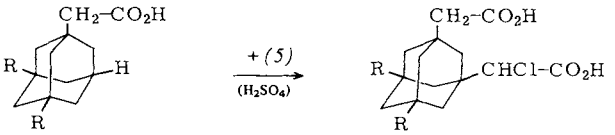
Table 2. Production of α-chloro-1-adamantaneacetic acids *(25)* and α,α′-dichloro-1,3-adamantanediacetic acids *(28)* from 1-bromoadamantanes *(24)* and trichloroethylene *(5)* in 90% sulfuric acid at 100 to 105 °C [a].

	R_1	R_2	R_3	Yields [%]	
(24a)	H	H	H	*(25a)* 15	*(28a)* 65
(24b)	CH_3	H	H	*(25b)* 26	*(28b)* 55
(24c)	CH_3	CH_3	H	*(25c)* 28	*(28c)* 37
(24d)	CH_3	CH_3	Br	—	*(28c)* 88
(24e)	CH_3	CH_3	CH_3	*(25e)* 94	—

[a] The yields of *(25a–c)* and *(28a–c)* are based on the amounts of *(24a–c)* used. The amount that is lost as (methylated) adamantane by addition of hydride to *(26a–c)* is disregarded.

The intermediate carbocations *(27a–c)* are generated from *(25a–c)* both by oxidation with sulfuric acid (path *A*) and by hydride transfer to *(26a–c)* (path *B*). Remarkably, the transformation of the 1-adamantyl cations *(26)* into 2-adamantanones observed by *Geluk* and *Schlatmann*[14,15] fails to take place in the presence of trichloroethylene.

In order to isolate the synthetic products *(25)* and *(28)*, their methyl esters are separated by fractional distillation. These esters arise as mixtures of the *meso* forms with the diastereomeric pairs of antipodes; the highly viscous oils do not show any particular tendency to crystallize. 1,3-Dibromo-5,7-dimethyladamantane *(24d)* and 1-bromo-3,5,7-trimethyladamantane *(24e)* may be regarded as ideal model substances for selective syntheses because they react with *(5)* to give high yields of α,α′-dichloro-5,7-dimethyl-1,3-adamantanediacetic acid *(28c)* and α-chloro-3,5,7-trimethyl-1-adamantaneacetic acid *(25e)*, respectively. If the 1-adamantaneacetic acids *(29a)* and *(29b)* are allowed to react with trichloroethylene *(5)* in 95% sulfuric acid, then only one chloroacetic acid group is introduced at the (unsubstituted) bridge-

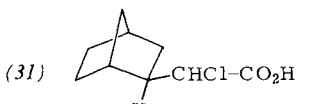


(29) *(a)*, R = H; *(b)*, R = CH_3 *(30)*

head position; the dicarboxylic acids *(30a)* and *(30b)* are formed highly selectively in yields of 85–86% based on the degree of conversion. The abstraction of hydrogen as hydride ion which precedes addition of trichloroethylene is relatively slow. Preparation of the 3-(carboxymethyl)-α-chloro-1-adamantaneacetic acids *(30a)* and *(30b)* requires temperatures between 105 and 115 °C. In order to perform the reaction under normal pressure, compound *(5)* must therefore be diluted with perchlorobutadiene since it boils at 87 °C. Formation of side products is minimized by keeping the conversion of *(29)* below 80%.

2.3.2. α-Chloro-2-*exo*-norbornaneacetic Acid

Another carbocation in the cycloaliphatic series which possesses considerable stability is the 2-norbornyl cation. Hence, α-chloro-2-*exo*-norbornaneacetic acid *(31)* can easily be synthesized from norbornene or norborneol and trichloroethylene (yield 66%).



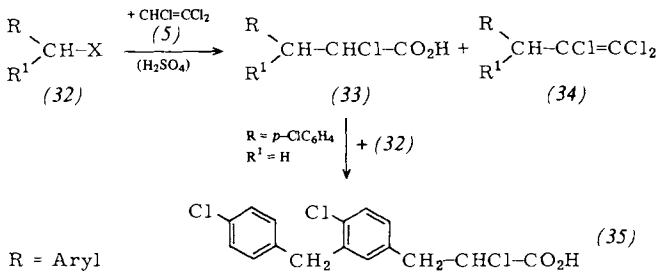
Proof of structure was obtained by dehalogenating the mixture of the two diastereomeric pairs of antipodes *(31)* with zinc. The anilide of the resulting *exo*-norbornaneacetic acid was identical with an authentic sample[16].

On introduction of a methyl group, the 2-norbornyl cation loses its ability to add to trichloroethylene. An alkyl substituent apparently facilitates formation of an olefinic double bond which undergoes secondary reactions such as oxidation, polymerization, or sulfonation.

2.3.3. α-Chlorohydrocinnamic Acids[13,17]

The preparation of α-chlorohydrocinnamic acids *(33)* from benzyl alcohols or their esters *(32)* and trichloroethylene *(5)* in sulfuric acid requires the presence of strongly electronegative substituents on the benzene ring. Otherwise, the initially formed carboxylic acids *(33)* undergo nuclear alkylation; this leads mainly to substances of higher molecular weight such as *(35)*.

It can be unequivocally demonstrated in the case of the reaction of *p*-chlorobenzyl alcohol *(32)*, R = *p*-chlorophenyl,



$R^1 = H$, X = OH, with *(5)* that the initial alkylation step leading to *(35)* is followed by further substitutions. This is the reason why no distillable products can be isolated even after esterification with methanol.

In the pentachlorobenzyl cation *(37)*, on the other hand, all the positions of the benzene ring could be blocked by substituents. For this reason, the pentachlorobenzyl half ester *(36)* of disulfuric acid, readily accessible by oxidation of pentachlorotoluene with sulfur trioxide, reacts without the complications mentioned with trichloroethylene *(5)* to give 3-(pentachlorophenyl)-2-chloropropionic acid *(38)*[18].

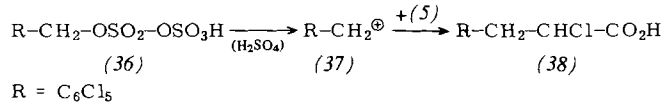


Table 3 surveys those substituents which can protect the benzene ring in compounds of type *(33)* from electrophilic attack and thus favor addition of phenylcarbenium ions to trichloroethylene *(5)*.

Table 3. Synthesis of α-chlorohydrocinnamic acids *(33)* from *(32)* and trichloroethylene *(5)*.

$RR^1CHX + CHCl{=}CCl_2 \rightarrow RR^1CH\ CHCl\ CO_2H$
(32) *(5)* *(33)*

	R	R_1	X	Yield of *(33)* [%]
(33a)	*p*-O_2N C_6H_4	H	CH_3CO_2	71 [a], 74 [b]
(33b)	*m*-O_2N C_6H_4	H	OH	82 [a]
(33c)	*p*-HO_2C C_6H_4	H	OH	38 [a, d]
(33d)	*m*-HO_2C C_6H_4	H	OH	39 [a, d]
(33e)	*p*-Cl-*m*-O_2N C_6H_3	H	CH_3CO_2	85
(33f)	*p*-CH_3SO_2 C_6H_4	H	OH	58 [a], 62 [b]
(33g)	*p*-$C_6H_5SO_2$ C_6H_4	H	OH	31 [c, e]
(33h)	*p*-C_6H_5CO C_6H_4	H	OH	71 [a]
(33i)	*p*-O_2N C_6H_4	*p*-O_2N C_6H_4	OH	77, 86 [b]
(33j)	*m*-O_2N C_6H_4	*m*-O_2N C_6H_4	Cl	71 [b]

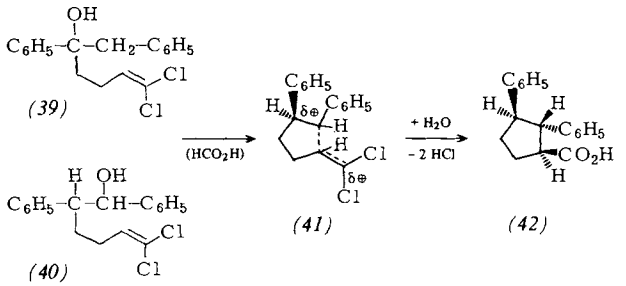
[a] Obtained as methyl ester. [b] Determined after conversion into the cinnamic acid derivative. [c] Isolated as methyl *p*-benzenesulfonylcinnamate. [d] A considerable amount of the product is destroyed by decarboxylation. [e] 51% of higher molecular carboxylic acids are also formed.

Apart from hydrocinnamic acids *(33)*, this synthesis also yields trichloroethylene derivatives *(34)*, isolable in yields between 2 and 6%.

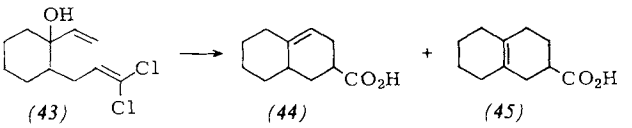
With regard to the production of α-chloro-β-arylhydrocinnamic acids such as *(33i)* and *(33j)*, the synthesis of carboxylic acids with trichloroethylene complements the Meerwein reaction[19], which can only be employed when $R^1 = H$. The preparative utility of these syntheses is underscored by the possibility of obtaining cinnamic acids in high yields by treating α-chloro-hydrocinnamic acids *(33)* with sodium hydroxide.

2.4. Cycloalkanecarboxylic Acids

Production of cycloalkanecarboxylic acids by intramolecular addition of a carbocation to a dichlorovinyl terminal group occupies a special place[20]. If five- or six-membered rings are to be constructed, C—C linkage is successful in formic acid as reaction medium. Refluxing a solution of the isomeric deoxybenzoins *(39)* or *(40)* in formic acid gives *trans,trans*-2,3-diphenyl-1-cyclopentanecarboxylic acid *(42)* (yield *ca.* 50%), regardless of which starting material is used.



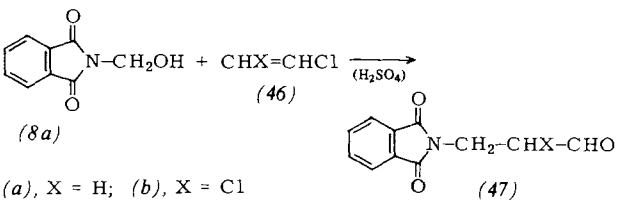
The result indicates that the carbocations formed initially from the alcohols *(39)* and *(40)* are in mutual equilibrium and that in the case of the energetically less favorable secondary carbocation [from *(40)*] the transition state *(41)* of the cyclization step has a lower energy content. In the same way, the allyl alcohol *(43)* can be transformed into a mixture of the double-bond isomeric octalincarboxylic acids *(44)* and *(45)* (overall yield 40%) while the likewise feasible ring closure to give cyclobutane fails to occur.



3. Synthesis of Aldehydes and Ketones

3.1. β-Acylamino Carbaldehydes and β-Acylamino Ketones

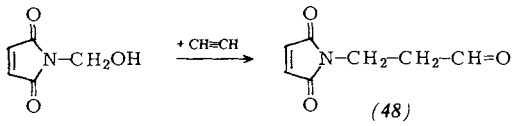
The reaction of vinyl chloride *(46a)* and *cis*- or *trans*-1,2-dichloroethylene *(46b)* with *N*-(hydroxymethyl)phthalimide *(8a)* in 90 to 96% H_2SO_4 provides a facile entry to 3-phthalimidopropionaldehydes *(47a)* and *(47b)* (yield 83 and 53%, respectively)[7,21].



Use of acetylene in place of *(46a)* proves just as successful. Reaction goes to completion within a few minutes at 5 to 10 °C under normal pressure, as can be seen from the cessation of acetylene take-up.

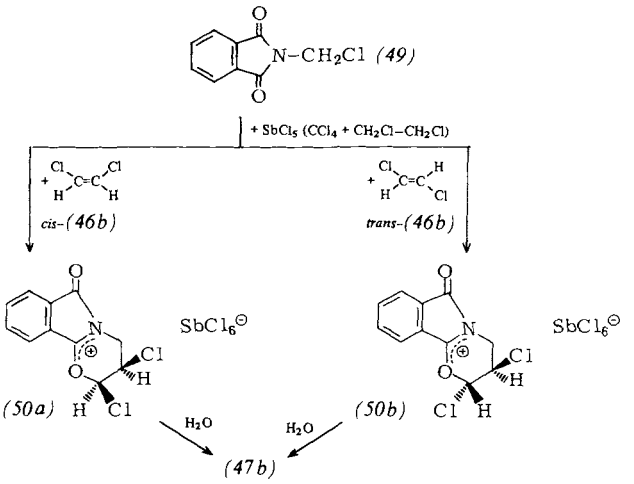
3-Maleimidopropionaldehyde *(48)* synthesized in the same way from *N*-(hydroxymethyl)maleimide and acetylene cannot be isolated in the pure state owing to its pronounced tendency to polymerize; however, titration of the crude product

against hydroxylammonium chloride solution shows the yield of aldehyde to be 80%.



(48)

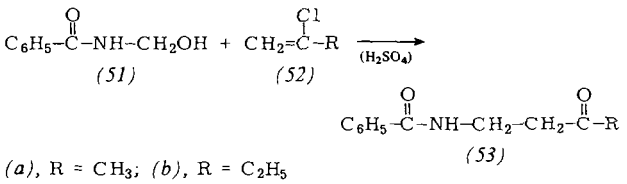
It is unlikely that the action of *N*-(hydroxymethyl)carboxamides on acetylene in sulfuric acid affords "free" vinyl cations which would be easily recognizable from their rearrangement products (cf. Section 3.2). Instead, as in the case of chloroolefins *(7)* and *(46)*, synchronous formation of a cyclic intermediate can be assumed. Such a reaction course can easily be detected by treating an equimolar mixture of antimony pentachloride and *N*-(chloromethyl)phthalimide *(49)* with the pure isomers of 1,2-dichloroethylene *(46b)* in chlorohydrocarbons. The expected cycloadducts *(50a)* and *(50b)* can be isolated as crystalline hexachloroantimonates[7].



The NMR spectra of the two dihydrooxazinium hexachloroantimonates reveal that *(50a)* and *(50b)* each contain at most 10% of the other isomer. Water rapidly transforms the isolated salts into the 2-chloro-3-phthalimidopropionaldehyde *(47b)*.

The proposed synchronous mechanism for the generation of the intermediate from a chloroolefin or acetylene and an amidomethyl cation suggests a low-energy transition state according to the Woodward-Hoffmann rule[22]. Further support for one-step construction of the dihydrooxazine comes from stereochemical results obtained by *R. R. Schmidt*[23] on amidomethylation of olefins more strongly basic than *(7)* and *(46)*.

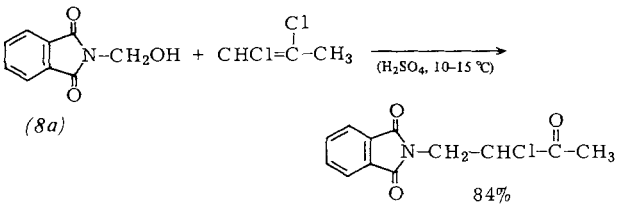
Replacement of the α-hydrogen by an alkyl group in the vinyl chloride *(46a)* affords the considerably more acid-sensitive 2-chloro-1-alkenes *(52)*. Consequently, it is not surprising that 2-chloro-1-propene *(52a)* is merely saponified to acetone by a solution of *N*-(hydroxymethyl)phthalimide *(8a)* in 80 to 90% sulfuric acid. At the same time, *(8a)* affords *N*-(chloromethyl)phthalimide *(49)*. Only on use of the more readily ionizing amidomethylation agent *N*-(hydroxymethyl)benzamide *(51)* is it possible to prepare the desired *N*-(3-oxobutyl)benzamide *(53a)* (yield 51%) and *N*-(3-oxopentyl)benzamide *(53b)* from *(52a)* and *(52b)*, respectively.



(51) (52) (53)

(a), R = CH_3; (b), R = C_2H_5

The introduction of a second chlorine atom into the vinyl group of *(52a)* markedly decreases the reactivity of the corresponding olefin towards strong acids. Thus 1,2-dichloro-1-propene is still capable of reacting with *N*-(hydroxymethyl)phthalimide *(8a)* to form *N*-(2-chloro-3-oxobutyl)phthalimide (84% yield), even though 95% sulfuric acid is used as the reaction medium.

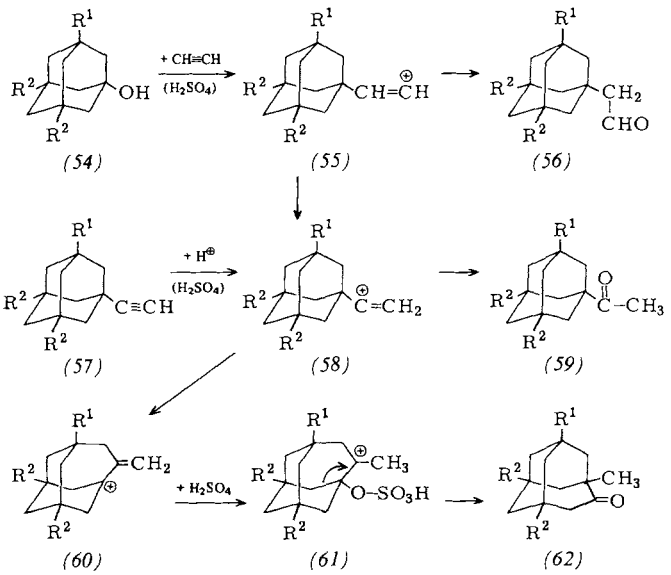


(8a)

3.2. Aldehydes and Ketones Belonging to the Adamantane Series

In 90 to 95% sulfuric acid, 1-adamantanol *(54a)* and its bridgehead methyl derivatives *(54b,c)* already react at 4 to 7 °C within just a few minutes with an equimolar amount of acetylene[24,25]. Subsequent hydrolysis affords 1-adamantaneacetaldehydes *(56a–c)*, 1-adamantyl methyl ketones *(59a–c)*, and homoadmantan-2-ones in overall yields between 88 and 95%. The following product composition is found for 1-adamantanol *(54a)*: 72% *(56a)*, 3% *(59a)*, and 25% *(62a)*.

Hydride exchange between the 1-adamantyl cations and the adamantaneacetaldehydes *(56a)* or *(56b)* with free bridgehead sites, giving mainly 1,3-adamantanediacetaldehydes and (methylated) adamantanes, can be avoided by



(54) (55) (56) (57) (58) (59) (60) (61) (62)

(a), $R^1 = R^2 = H$; (b), $R^1 = H$, $R^2 = CH_3$; (c), $R^1 = R^2 = CH_3$

Table 4. Relative yields of 1-adamantyl methyl ketones *(59)* and homoadamantan-2-ones *(62)*.

Reactants	$R^1 = R^2$	Relative yields	
		(59) [%]	*(62)* [%]
(54a) + C_2H_2	H	*(59a)* 11	*(62a)* 89
(54c) + C_2H_2	CH_3	*(59c)* 29	*(62c)* 71
(57a)	H	*(59a)* 31	*(62a)* 69
(57c)	CH_3	*(59c)* 48	*(62c)* 52

dropwise addition of solutions of the adamantanols *(54a)* and *(54b)* to sulfuric acid in an acetylene atmosphere.

Separation of the products *(56)*, *(59)*, and *(62)*, on a preparative scale can be accomplished by chemical means, *i. e.* by exploiting their significant gradation of reactivity [*(56)* > *(59)* > *(62)*] towards carbonyl reagents for selective precipitation of the semicarbazones[26].

As shown by the scheme, the adamantols *(54)* and acetylene initially form 2-(1-adamantyl)vinyl cations *(55)* which are then largely converted into the adamantaneacetaldehydes *(56)*. This stabilization step presumably proceeds *via* an enol sulfuric acid half ester[27,28]. A small proportion of *(55)* rearranges to the lower-energy 1-(1-adamantyl)vinyl cations *(58)* which can be generated directly by protonation of the adamantylacetylenes *(57)*. Cations *(58)* react to a lesser extent to give the adamantyl methyl ketones *(59)*; the principal reaction is transition to the "trigonal" carbocation *(60)* (see Table 4). This process is associated with a considerable gain in energy although no overlap of the spatially fixed π-bonding orbitals with the vacant orbital of the carbenium carbon atom is possible in *(60)*. The intermediacy of *(61)* can be assumed in the formation of the homoadamantan-2-one *(62)* from *(60)*.

Acidolysis of 1-adamantylacetylenes *(57a)* and *(57c)* in 90% sulfuric acid expectedly gives only the adamantyl methyl ketones *(59)* and the homoadamantanones *(62)*[26]. Table 4 shows that the molar ratio of the ketones *(59)* and *(62)* depends both upon the way in which they are generated and upon the number of bridgehead methyl groups.

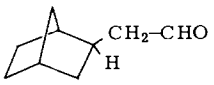
As shown by a study of the "detailed mechanism" of the reaction between 1-adamantol *(54a)* and acetylene[27,28], the proportion of 1-adamantaneacetaldehyde *(56a)* falls drastically in favor of homoadamantanone *(62a)* if the sulfuric acid concentration is lowered from 98 to 85% (Table 5). Use of boron trifluoride/ether complex as reaction medium even raises the absolute yield of *(62a)* to 60%.

Table 5. Relative yields of the reaction of 1-adamantol *(54a)* with acetylene at various concentrations of sulfuric acid.

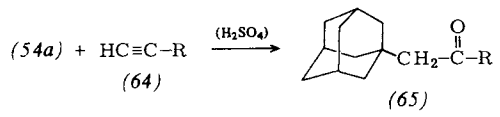
H_2SO_4 conc. [wt.-%]	Relative yields	
	(56a) [%]	*(62a)* [%]
98	89.1	10.9
92.5	71.2	28.8
90	66.0	34.0
87.6	60.0	40.0
85.5	57.0	43.0

Independently of the synthesis of the aldehyde *(56a)* and the ketone *(62a)* described above, the initially formed species *(56a)* is slowly transformed into 1-adamantyl methyl ketone *(59a)* in sulfuric acid without traversing a vinyl cation stage. Thus *Sasaki et al.*[29] demonstrated 1-adamantyl methyl ketone *(59a)* as the only product of the reaction between acetylene and 1-bromoadamantane *(24a)* which requires considerably longer reaction times than *(54a)*. The ketone can be obtained in 80% yield by this method[28].

Reactions of 1,3-adamantanediols with acetylene in sulfuric acid are complicated and have not been studied in detail. The synthesis of 2-*exo*-norbornaneacetaldehyde *(63)* (yield 19%) from norbornene and acetylene warrants mention as an example of reaction of a secondary carbocation in the cycloaliphatic series[25].

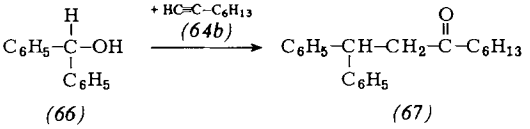
(63) 

On application of the addition reactions of carbocations to substituted acetylenes it was found that the expected ketones *(65a)* and *(65b)* are obtained in 40 to 43% yield from 1-pentyne *(64a)* or 1-octyne *(64b)* and 1-adamantol *(54a)*, while analogous preparation of 1,1-diphenyl-3-nonanone *(67)* from *(64b)* and benzohydrol *(66)* is far less productive (yield 23%).



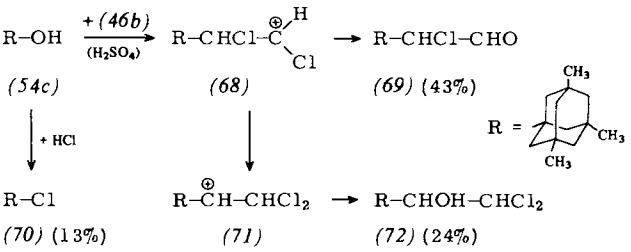
(a), R = n-C_3H_7; *(b)*, R = n-C_6H_{13}

The highly reactive phenylacetylene is mainly saponified to acetophenone under the conditions of this synthesis.



The scope of the above ketone syntheses from alkyl- and arylacetylenes is limited above all by the fact that protonation of the alkyne often plays a predominant role. In contrast, rearrangements of the secondary vinyl cations functioning as intermediates recede into the background.

An example of the production of an α-chlorocarbaldehyde is seen in the well-studied reaction of 3,5,7-trimethyl-1-adamantol *(54c)* with 1,2-dichloroethylene *(46b)*[21]. The initially formed α-chloro carbocation *(68)* can be stabilized in two ways. It can either hydrolyze directly to α-chloro-1-adamantaneacetaldehyde *(69)* or form 1-(1-adamantyl)-2,2-dichloroethanol *(72)* *via* the rearranged cation *(71)*. In addition, a small part of the reactant *(54c)* is transformed by liberated hydrogen chloride into the inert 1-chloroadamantane *(70)*. The yields given in the formula scheme are calculated from gas chromatographic analysis of the distilled reaction products.



Intramolecular additions of carbocations to a C—C triple bond or to a chlorovinyl group provide a pathway to cycloalkanones and cycloalkyl ketones. Such syntheses proceeding *via* ring closure which have already been reviewed[30,31] do not generally require a strongly acidic medium but can instead be performed in formic acid or trifluoroethanol.

4. Conclusion

The methods considered in this review for the synthesis of carboxylic acids, aldehydes, and ketones are not only of preparative importance but also permit a further insight into the chemical behavior of carbocations. Thus the first generation of a "primary" vinyl cation [*(55a)*] devoid of stabilizing substituents was accomplished by addition of the 1-adamantyl cation to acetylene and the reaction of this cation monitored. On the other hand, it has been found that the reactions of amidomethyl cations with chloroolefins in sulfuric acid do not involve a carbocation but an oxazonium ion as intermediate. These results could prove valuable for the planning of new syntheses. The availability of the starting materials should also encourage the exploitation of these reactions.

Received: December 17, 1979 [A 307 IE]
German version: Angew. Chem. *92*, 169 (1980)

[1] Review: *N. N. Crounse*, Org. React. *5*, 290 (1949).
[2] *Houben-Weyl:* Methoden der organischen Chemie. 4th Edit., Vol. VIII. Thieme, Stuttgart 1952, p. 642.
[3] Reviews: a) *H. E. Zaugg, W. B. Martin*, Org. React. *14*, 52 (1965); b) *H. E. Zaugg*, Synthesis *1970*, 49.
[4] *H. Hellmann, G. Aichinger, H. P. Wiedemann*, Justus Liebigs Ann. Chem. *626*, 35 (1959).
[5] *K. Bott*, Chem. Commun. *1969*, 1304
[6] *K. Bott*, Tetrahedron Lett. *1970*, 4185.
[7] *K. Bott*, Chem. Ber. *106*, 2513 (1973).
[8] Used as a gas under normal pressure.
[9] *D. Ben-Ishai*, DOS 2626127 (1976), Technion Research and Development Foundation, Haifa.
[10] *D. Ben-Ishai, R. Moshenberg, J. Altman*, Tetrahedron *33*, 1533 (1977).
[11] *K. Bott, H. Hellmann*, Angew. Chem. *78*, 932 (1966); Angew. Chem. Int. Ed. Engl. *5*, 870 (1966).
[12] *K. Bott*, Angew. Chem. *79*, 943 (1967); Angew. Chem. Int. Ed. Engl. *6*, 946 (1967).
[13] *K. Bott*, Chem. Ber. *103*, 3850 (1970).
[14] *H. W. Geluk, J. L. M. A. Schlatmann*, Tetrahedron *24*, 5361 (1968).
[15] *H. W. Geluk, J. L. M. A. Schlatmann*, Rec. Trav. Chim. Pays-Bas *88*, 13 (1969).
[16] *K. Bott*, Chem. Ber. *100*, 978 (1967).
[17] *K. Bott*, Tetrahedron Lett. *1968*, 4979.
[18] *V. Mark, L. Zengierski, V. A. Pattison, L. E. Walker*, J. Am. Chm. Soc. *93*, 3538 (1971).
[19] *C. S. Rondestvedt*, Org. React. *11*, 189 (1960).
[20] *P. T. Lansbury, R. C. Stewart*, Tetrahedron Lett. *1973*, 1569.
[21] *K. Bott*, Tetrahedron Lett. *1970*, 4301.
[22] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[23] *R. R. Schmidt*, Synthesis *1972*, 333.
[24] *K. Bott*, Tetrahedron Lett. *1969*, 1747.
[25] *K. Bott*, Justus Liebigs Ann. Chem. *766*, 51 (1972).
[26] *K. Bott*, Chem. Commun. *1969*, 1349.
[27] *D. R. Kell, F. J. McQuillin*, Chem. Commun. *1970*, 599.
[28] *D. R. Kell, F. J. McQuillin*, J. Chem. Soc. Perkin Trans. I 2100 (1972).
[29] *T. Sasaki, S. Eguchi, T. Toru*, Chem. Commun. *1968*, 780.
[30] *P. T. Lansbury*, Acc. Chem. Res. *5*, 311 (1972).
[31] *M. Hanack*, Angew. Chem. *90*, 346 (1978); Angew. Chem. Int. Ed. Engl. *17*, 333 (1978).

Synthesis of Intermediates by Rhodium-Catalyzed Hydroformylation

By Hardo Siegel and Walter Himmele[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The reaction of olefins with carbon monoxide and hydrogen to give aldehydes is referred to as hydroformylation (oxo reaction). As catalyst for this reaction rhodium is about three to four orders of magnitude more active than the more commonly employed cobalt. With special rhodium compounds, *e.g.* di-μ-chlorobis(η-1,5-cyclooctadiene)dirhodium $[RhCl(C_8H_{12})]_2$, in the presence of chiral phosphanes, even asymmetric hydroformylations can be achieved; however, the enantiomeric purity of the products (20–30%) is not high enough for industrial-scale syntheses.

1. Introduction

The hydroformylation or oxo reaction first carried out by *Roelen* in 1938 has developed into an industrially important process for the production of aldehydes and alcohols from olefins, carbon monoxide and hydrogen[1]. The world production of hydroformylation- and secondary-products, the main ones being *n*-butanol and 2-ethylhexanol, is at present *ca.* 4.5 million t/a.

Advances made in the area of homogeneous catalysis in the last ten years, mainly through the introduction of tailor-made metal complexes, have opened up new possibilities for the synthesis of higher-purity intermediates by high-pressure and catalytic methods. One example, which is also of interest in the industrial sector, is rhodium-catalyzed hydroformylation. Since rhodium is 10^3 to 10^4 times more active than cobalt, the reaction parameters pressure and temperature can

[*] Dr. H. Siegel, Dr. W. Himmele
Hauptlaboratorium der BASF Aktiengesellschaft
D-6700 Ludwigshafen

be widely varied, thus allowing better control of the selectivity. Olefins are transformed, usually in high yields, into aldehydes, which in turn can be converted by well-known industrially employed methods into alcohols, amines, or acids and find use in C—C coupling reactions such as condensations, Mannich, Wittig, and Grignard reactions, or ethynylations.

2. Selectivity of Hydroformylation with Rhodium Catalysts—Arylalkenes

In the catalytic hydroformylation of olefins with rhodium complexes the formyl group can, in principle, be inserted at each C-atom of the double bond.

$$RCH{=}CHR' \xrightarrow[\text{Rh cat.}]{CO/H_2} RCH(CHO)-CH_2R' + RCH_2-CH(CHO)R'$$

Important for the selectivity are the steric and electronic properties of the substituents R and R', the choice of reaction conditions such as temperature and pressure, special complex ligands, and the ratio of carbon monoxide to hydrogen. In addition side reactions such as isomerization and hydrogenation, which occur in every hydroformylation, can also influence the selectivity.

On hydroformylation with rhodium catalysts (100–700 bar, 70–150 °C) with or without complex ligands on the rhodium (molar ratio $<5:1$), the formyl group is generally incorporated at the electron-poorest C-atom if the electronic properties of the substituents at the double bond are decisive. If, however, the steric factors dominate, then the formyl group enters at that C-atom of the double bond least shielded by substituents.

(1) (2)

Table 1. Incorporation of the formyl group in the positions a, b, c of the olefins (1) and (2) (in %).

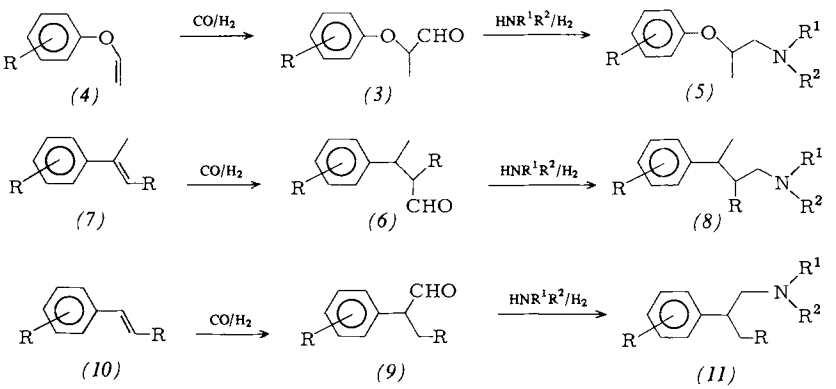
	(1)			(2)		
T[°C]	a	b	c	a	b	c
70	0	48	52	95	5	0
80	3	45	52	90	10	0
100	11	37	52	50	45	5
130	41	24	35	40	50	10

600 bar $CO/H_2 = 1:1$, 20 ppm Rh as $[RhCl(1,5\text{-cyclooctadiene})]_2$.

Temperature has a marked influence on the selectivity. This is immediately evident, *e.g.*, in the hydroformylation of eugenol *(1)* and isoeugenol *(2)*[2] (Table 1).

3. Intermediates for the Synthesis of Pharmacologically Active Compounds

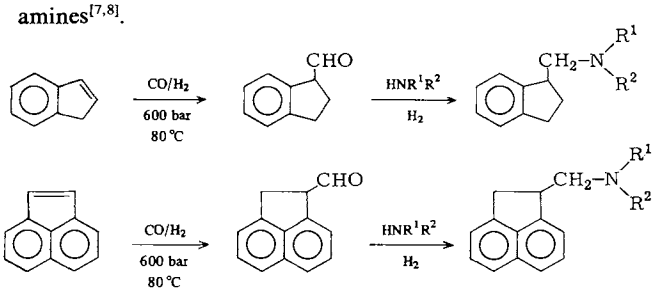
A few classes of substances which are of interest for the synthesis of pharmacologically active amines are readily accessible by hydroformylation with rhodium catalysts[3,4]. Thus, the 2-aryloxypropanals *(3)* obtained from aryl vinyl ethers *(4)* are used for the synthesis of (aryloxypropyl)amines *(5)*; 3-arylbutanals *(6)*, prepared from 2-arylalkenes *(7)*, are intermediates for the synthesis of 3-arylbutylamines *(8)*, and



2-arylpropanals *(9)*, obtained from 1-arylalkenes *(10)*, are precursors for the synthesis of β-phenylpropylamines *(11)*.

In order to achieve a high selectivity in the hydroformylation, the reaction is carried out in all cases at 600–700 bar CO/H_2 and $<100\,°C$ with rhodium concentrations in the ppm range.

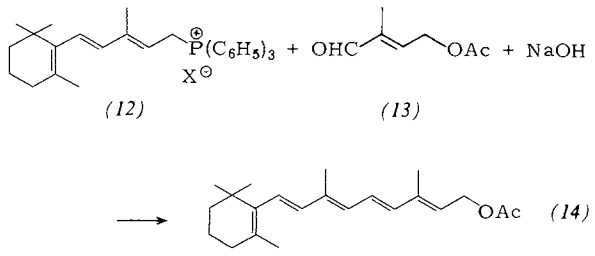
Modified β-phenylethylamines with interesting hypotensive properties are obtained by hydroformylation of indene[5] or acenaphthalene[6] in the presence of rhodium catalysts and subsequent reaction of the resulting aldehydes with amines[7,8].



4. Intermediates for Vitamin and Terpene Chemistry

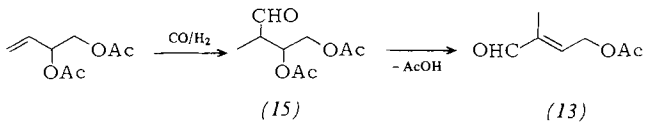
4.1. Unsaturated Aldehydes from 2-Alkenyl Acetates

In the process used at BASF for the industrial synthesis of vitamin A the ylide of a C_{15}-phosphonium salt is allowed to react with a C_5-aldehyde[9]. A phosphonium salt[11] *(12)*, prepared by reaction of vinyl β-ionol[10] and triphenylphosphane in the presence of an acid, serves as C_{15}-moiety and *trans*-3-formyl-2-butenyl acetate *(13)* as C_5-moiety. The synthesis, in presence of a base, leads directly to the vitamin A acetate *(14)*.



(12) (13) (14)

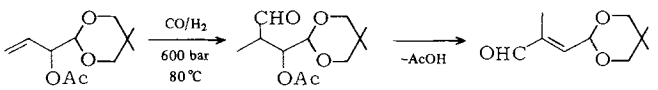
The unsaturated aldehyde *(13)* can be prepared *via* hydroformylation of 1-vinylethylene diacetate in the presence of a rhodium catalyst.



(15) (13)

High pressure and low temperature favor formation of the branched aldehyde *(15)*. At 80 °C and 600 bar CO/H_2 selectivities of up to *ca.* 80% can be achieved. The acetoxy group in the β-position to the formyl group is readily removed as acetic acid to give pure *trans-(13)*[12,13]. This synthesis of α,β-unsaturated aldehydes by hydroformylation of 2-alkenyl acetates and subsequent elimination of acetic acid can also be used for the production of further intermediates which are of interest in terpene chemistry.

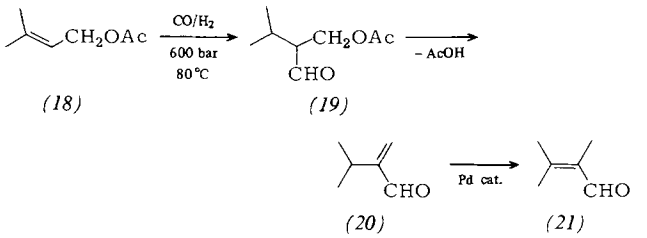
trans-2-Methyl-3-(5,5-dimethyl-1,3-dioxan-2-yl)acrylaldehyde *(17)*, an important intermediate for the synthesis of carotinoids[14], can be obtained in the same way from the acetal *(16)*.



(16) (17)

Reaction of *(17)* with the ylide of the C_{15}-phosphonium salt *(12)* and subsequent hydrolysis affords easy access to retinal (vitamin A aldehyde).

Hydroformylation of the 3-methyl-2-butenyl acetate *(18)* leads in high yields to 2-formyl-3-methylbutyl acetate *(19)*, elimination of acetic acid from *(19)* to α-isopropylacrylaldehyde *(20)*. This is isomerized in the presence of palladium catalysts to trimethylacrylaldehyde *(21)*, an important intermediate for the synthesis of irones[15].

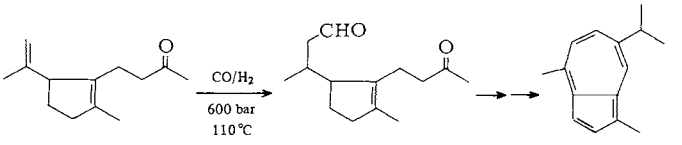


(18) (19) (20) (21)

4.2. Unsaturated Aldehydes by Hydroformylation of Non-Conjugated Diolefins

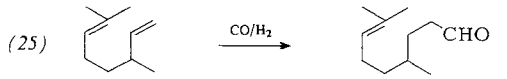
A further possibility for the synthesis of unsaturated aldehydes consists in the selective hydroformylation of non-conjugated diolefins. Here, steric factors play a decisive role regarding the degree of hydroformylation of the double bonds.

The ketone *(22)*[16] accessible from linalool is selectively hydroformylated at the isopropenyl group. An intramolecular ring closure of the resulting ketoaldehyde *(23)* followed by further reaction steps affords guaiazulene *(24)*[17].



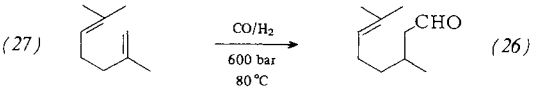
(22) (23) (24)

In citronellene *(25)* the formyl group is almost exclusively incorporated terminally (at 600 bar, 70 °C, with rhodium catalysts) owing to steric hindrance by the two methyl groups[18].



(25)

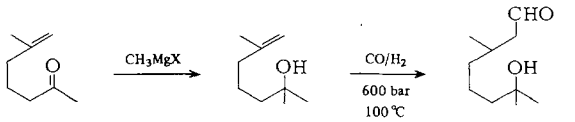
Synthesis of the industrially important citronellal *(26)* from 2,6-dimethyl-1,5-heptadiene *(27)*[19] proceeds in a similar fashion.



(27) (26)

4.3. Synthesis of Hydroxycitronellal

An industrial process for production of the important odorant hydroxycitronellal *(28)* consists in hydroformylation of the 2,6-dimethyl-6-hepten-2-ol *(30)*[20] obtainable from 6-methyl-6-hepten-2-one *(29)* *via* a Grignard reaction.



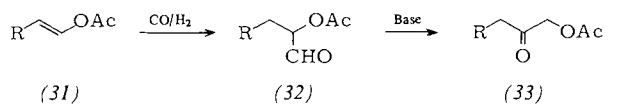
(29) (30) (28)

5. Intermediates for the Synthesis of Heterocycles

5.1. Furancarboxylic Acid Derivatives from 1-Alkenyl Acetates

In the hydroformylation of 1-alkenyl acetates *(31)*, which are readily accessible by formation of the enol acetate from the corresponding aldehydes, the formyl group is incorporated with a selectivity of >90% at the α-position to the acetoxy group [*(32)*] at 600 bar and *ca.* 110 °C.

In the presence of weak bases, *(32)* readily undergoes a type of Lobry-de-Bruyn-van-Ekenstein rearrangement to give the ketoacetate *(33)*[21].

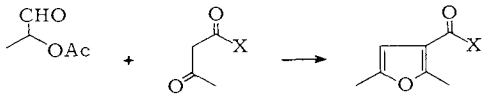


(31) (32) (33)

Hydroformylation of vinyl acetate affords 2-formylethyl acetate *(34)* in high yields. This ester, and also other 2-formylalkyl acetates, are important intermediates for a novel one-step synthesis of furancarboxylic acid derivatives.

Reaction of *(34)* with acetoacetamides *(35)* or acetoacetates *(37)* leads in high yields to the 2,5-dimethyl-3-furancarboxamides *(36)* or the corresponding esters *(38)*, respectively[22,23].

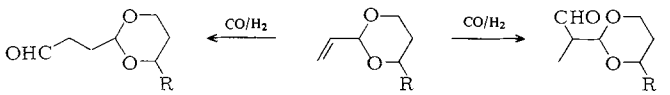
Furancarboxylic acid derivatives are of great industrial importance in seed disinfection[24] and in wood preservation[25].



(34) *(35)*, X = NR_2 *(37)*, X = OR *(36)*, X = NR_2 *(38)*, X = OR

5.2. Pyrimidines *via* Methylmalonaldehyde Monoacetals

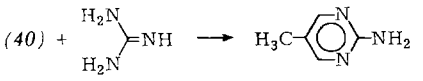
Depending on the reaction conditions hydroformylation of the cyclic acetals of acrylaldehyde *(39)* leads either to the methylmalonaldehyde monoacetals *(40)* or succinaldehyde monoacetals *(41)*.



(41) *(39)* *(40)*

When the reaction is carried out at 600 bar CO/H_2 and 80 °C in the absence of complexing agents, *(41)* and *(40)* are obtained in the ratio 25:75[26]. At 20 bar CO/H_2 and 140 °C in the presence of more than a fiftyfold excess of triphenylphosphane (referred to rhodium) the reaction product contains 70% *(41)* and 30% *(40)*. Compound *(41)* is a possible intermediate for the synthesis of 1,4-butanediol[27].

5-Methyl-2-pyrimidinylamine *(42)*, which is used as starting material for the synthesis of sulfonamides, can be readily prepared by reaction of the methylmalonaldehyde monoacetal *(40)* with guanidine.

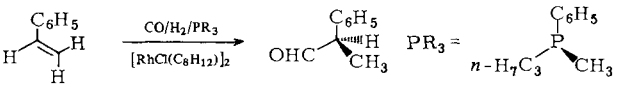


(42)

6. Asymmetric Hydroformylation with Chiral Rhodium Complexes

Horner was the first to point out that an asymmetric hydrogen transfer should be possible[29] by reaction of an optically active phosphane as ligand with one of the rhodium complexes previously found by *Wilkinson et al.*[28] to be effective catalysts in hydrogenation. Following the subsequent independent confirmation of this prediction by *Knowles* and *Sabacky*[30] and by *Horner et al.*[31], Monsanto started using this novel synthetic method on an industrial scale. *Knowles et al.* developed a method for the preparation of L-dopa by asymmetric hydrogenation of an appropriately substituted α-(*N*-acylamino)cinnamic acid[32].

Reaction of styrene *(43)* with carbon monoxide and hydrogen in the presence of *(S)*-(+)methyl(phenyl)-*n*-propylphosphane, *(S)*-*(44)*[33], and rhodium complex catalyst affords optically active (*R*)-(−)-phenylpropanol *(R)*-*(45)*[34].



(43) *(R)*-(−)-*(45)* *(S)*-(+)-*(44)*

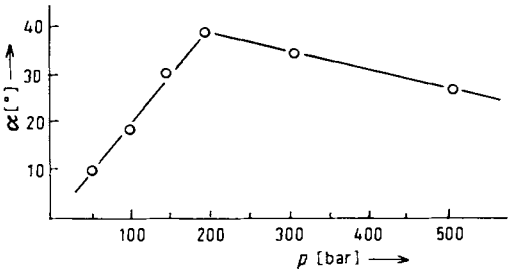
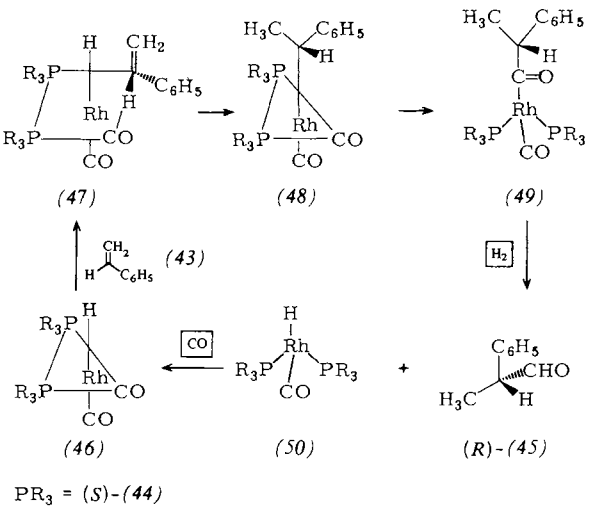


Fig. 1. Dependence of optical induction on pressure in the hydroformylation of styrene *(43)* to *(R)*-(−)-2-phenylpropanol *(R)*-*(45)* with di-μ-chlorobis(η-1,5-cyclooctadiene)dirhodium and *(S)*-(+)-methyl(phenyl)-*n*-propylphosphane *(S)*-*(44)*.

As shown in Figure 1 a noticeable enantioselective synthesis can be observed at 500 bar CO/H_2—a proof that carbon monoxide does not completely displace the chiral phosphane from the carbonylrhodium complex, even at high pressure. In order to establish its absolute configuration, the prepared (−)-2-phenylpropanol *(45)* was oxidized by various methods to 2-phenylpropionic acid. In each case this had *R*-configuration; accordingly, *(45)* is likewise *R*-configurated. This enantionselective synthesis can best be explained in terms of the mechanism proposed by *Wilkinson et al.*[35] for the hydroformylation of olefins with $HRhCO(PPh_3)_3$ or $HRh(CO)_2(PPh_3)_2$.



(47) *(48)* *(49)* *(43)* *(46)* *(50)* *(R)*-*(45)*

PR_3 = *(S)*-*(44)*

Similarly to an enzyme, the chiral catalyst *(46)* can differentiate between the enantiotopic sides of the prochiral olefin. In the case of *(S)*-(+)-*(44)* as ligand PR_3 of the coordinative unsaturated complex *(46)*, styrene *(43)* preferably adds at the side unshielded by the phenyl group. A Rh-π-complex *(47)* is formed and is rapidly converted into a complex *(48)* containing a Rh-alkyl bond. The absolute configuration of the 2-

phenylpropanal is thus established, since CO is inserted in the *cis* position [*(48)*→*(49)*]. The rate determining step of the reaction is cleavage of the acylrhodium complex *(49)* by hydrogen: *(R)*-(−)-*(45)* and the tetrahedral hydrido complex *(50)* are formed, which after uptake of CO to give the complex *(46)* can further add styrene.

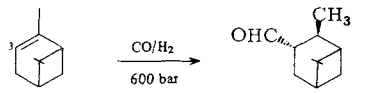
A mechanism involving replacement of one of the two chiral phosphane groups by a carbonyl group in the reaction *(46)*→*(50)* leads to the same result.

With *(S)*-phosphanes, the *(R)*-aldehyde is formed. It is immediately apparent that the arrangement of the groups in the chiral 2-phenylpropanol *(45)* pre-images to a certain extent the groups in the chiral phosphane. With *(S)*-(+)-*(44)* or the corresponding isopropyl compound as complex ligand the enantiomeric purity of the products is *ca.* 20% and 30%, respectively.

The asymmetric hydroformylation of prochiral olefins has so far found no use in industry. One reason for this is the low enantiomeric purity—also observed by other authors[36–39]—of the products obtained from the substrates hitherto examined. Hence, this method is at the moment considered impracticable for the industrial production of optically active intermediates which could be used for optical resolution or asymmetric syntheses.

7. Optically Active Intermediates *via* Hydroformylation of Unsaturated Chiral Natural Products

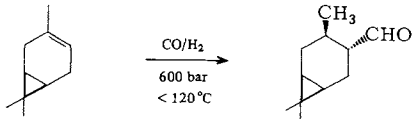
(−)-α-Pinene *(51)*, which is available in large amounts from the cluster pine *(Pinus Pinaster* Sol.), is hydroformylated with rhodium catalysts in a diastereoselective synthesis to (+)-3-pinanecarbaldehyde *(52)*[45]. (+)-α-Pinene from the Aleppo pine (*Pinus Pinaster* Mill.) affords (−)-3-pinanecarbaldehyde[40].



(−)-*(51)* (+)-*(52)*

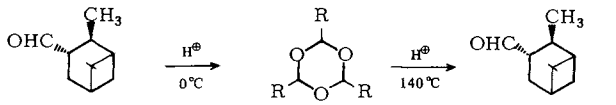
The formation of the reaction products can be explained by the fact that the intermediary alkylrhodium complex evades as far as possible steric hindrance by the isopropylidene bridge and the methyl group. The least hindered position is the equatorial one on the carbon atom 3 of the α-pinene *(51)*. The *cis* addition of CO and H_2 then forces the methyl and formyl group likewise to take up an equatorial position in the 3-pinanecarbaldehyde *(52)*. Depending on the reaction conditions the selectivities are up to 85%. The most important by-products are isomeric aldehydes, which are derived from the β-pinene formed during the reaction by isomerization of the double bond. In the analogous hydroformylation of (+)-3-carene, (+)-*(53)*, the reaction proceeds with a selectivity of only 60–65% to the (+)-2-caranecarbaldehyde (+)-*(54)*[41] owing to comparably little steric hindrance by the isopropylidene bridge.

The enantiomeric purity of the (−)- or (+)-3-pinanecarbaldehyde *(52)* corresponds to that of the α-pinene employed (70–85%). Enantiomerically pure 3-pinanecarbaldehyde is obtained by acid-catalyzed trimerization in the presence of



(+)-*(53)* (+)-*(54)*

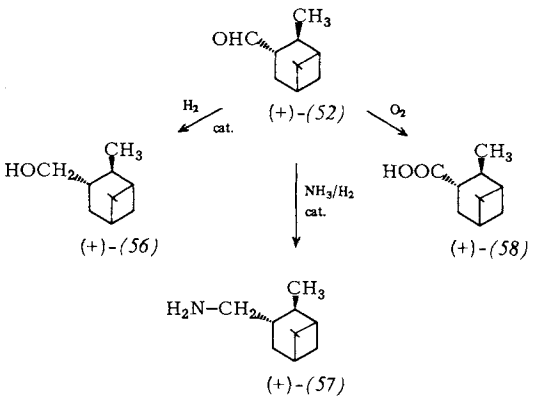
solvents[42]; only one enantiomer is thereby preferentially trimerized to the crystalline compound *(55)*. This is isolated and then cleaved again in the presence of acids to 3-pinanecarbaldehyde.



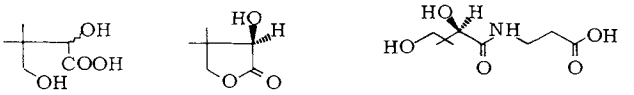
enantiomeric purity 70–85% *(55)* enantiomeric purity ≈100%

R = (+)-3Pinanyl

The optically active pinanecarbaldehydes are very stable against racemization. They can be hydrogenated, aminohydrogenated, or oxidized with retention of configuration by the usual industrial methods.



(+)-3-Pinanylmethanol *(56)*, (+)-3-(pinanylmethyl)amine *(57)*, and (+)-3-pinanecarboxylic acid *(58)* are configurationally stable, optically active intermediates which can be used for enantiomerization and asymmetric syntheses. For example, the amine (+)-*(57)* forms very easily separable diastereomeric salts with DL-pantoic acid *(59)*.



(59) *(60)* *(61)*

Thus, D-(−)-pantolactone *(60)*, a precursos of D-pantothenic acid *(61)*, is obtained in 90% yield and in very high enantiomeric purity[43,44].

8. Outlook

The rhodium-catalyzed hydroformylation of special olefins for the production of aldehydes is a versatile method for unconventional solutions of problematic syntheses in the fine chemicals industry. The possibilities of this method range from simple aliphatic aldehydes to chiral compounds. A dis-

advantage, however, is that not all of the necessary starting olefins are avilable on an industrial scale and that, with higher concentrations of catalyst, the expensive and relatively scarce rhodium must be recycled. However, in spite of these problems still further new syntheses with rhodium-catalyzed hydroformylation intermediates are to be expected in the future.

We thank all our colleagues and co-workers for their most invaluable teamwork and assistance, and Dr. Hohenschutz, Dr. Pape, and Prof. Dr. Reif for their kind support of this work.

Received: December 4, 1979 [A 310 IE]
German version: Angew. Chem. 92, 182 (1980)

[1] *J. Falbe:* Carbon Monoxide in Organic Synthesis. Springer, Berlin 1970.
[2] *W. Himmele, H. Siegel,* DOS 2235466 (1972), BASF; Chem. Abstr. *81,* 3593 (1974); *W. Himmele, H. Siegel, W. Aquila,* DOS 2219168 (1972), BASF; Chem. Abstr. *80,* 14740 (1974).
[3] *W. Himmele, H. Siegel, W. Aquila, H. Fröhlich,* DOS 2301940 (1973), BASF; Chem. Abstr. *81,* 120222 (1974).
[4] *W. Aquila, W. Hoffmann, W. Himmele, H. Siegel,* DOS 2340812 (1973), BASF; Chem. Abstr. *82,* 170377 (1975).
[5] *W. Himmele, W. Aquila,* DBP 2053736 (1970), BASF; Chem. Abstr. *77,* 34198 (1972).
[6] *W. Himmele, W. Aquila,* DBP 2064279 (1970), BASF; Chem. Abstr. *77,* 114126 (1972).
[7] *W. Himmele, W. Aquila, H. Siegel, A. Amann, H. Giertz,* DOS 2137276 (1971), BASF; Chem. Abstr. *78,* 111003 (1973).
[8] *W. Himmele, W. Aquila, H. Siegel, A. Amann, H. Giertz,* DOS 2157454 (1971), BASF; Chem. Abstr. *81,* 37429 (1979).
[9] *H. Pommer, W. Sarnecki,* DBP 1059900 (1957), BASF; Chem. Abstr. *55,* 14511 (1961).
[10] *H. Pasedach, M. Seefelder,* DBP 1081883 (1958), BASF; Chem. Abstr. *56,* 10000 (1962).
[11] *W. Sarnecki, H. Pommer,* DBP 1060386 (1957), BASF; Chem. Abstr. *55,* 4577 (1961).
[12] *W. Himmele, W. Aquila,* DOS 1945479 (1969), BASF; Chem. Abstr. *74,* 111589 (1971).
[13] *W. Himmele, W. Aquila,* DOS 1941632 (1969), BASF; Chem. Abstr. *75,* 23258 (1971).
[14] *L. Schuster, J. Paust, H. Siegel,* DOS 2513999 (1976), BASF; Chem. Abstr. *86,* 71885 (1977).
[15] *W. Rebafka, H. Siegel,* unpublished results.
[16] *M. Seefelder, J. Speck,* DBP 1082237 (1960), BASF; Chem. Abstr. *55,* 27217 (1961).
[17] *W. Hoffmann, H. Siegel,* Tetrahedron Lett. *1975,* 533.
[18] *W. Hoffmann, H. Siegel,* unpublished results.
[19] *W. Aquila, W. Himmele, W. Hoffmann,* DOS 2050677 (1970), BASF; Chem. Abstr. *77,* 19184 (1972).
[20] *W. Himmele, W. Hoffmann, H. Pasedach, W. Aquila,* DOS 1964962 (1969), BASF; Chem. Abstr. *75,* 63130 (1971).
[21] *W. Aquila, H. Siegel,* unpublished results.
[22] *H.-R. Merkle, H. Siegel,* DOS 2227547 (1972), BASF; Chem. Abstr. *80,* 70681 (1974).
[23] *H.-R. Merkle, H. Siegel,* DOS 2207098 (1972), BASF; Chem. Abstr. *79,* 146374 (1973).
[24] *H. Distler, R. Widder, E. Pommer,* DOS 2019535 (1970), BASF; Chem. Abstr. *76,* 46068 (1972).
[25] *B. Zeeh, F. Linhart, E. H. Pommer,* DBP 2455082 (1974), BASF; Chem. Abstr. *85,* 142972 (1976).
[26] *W. Himmele, W. Aquila,* DOS 2111116 (1971), BASF; Chem. Abstr. *77,* 152153 (1972).
[27] *R. Kummer,* U.S.-Pat. 4017550 (1977), BASF; Chem. Abstr. *83,* 178295 (1975).
[28] *J. A. Osborn, F. H. Jardine, J. F. Young, G. Wilkinson,* J. Chem. Soc. *A, 1966,* 1711.
[29] *L. Horner, H. Büthe, H. Siegel,* Tetrahedron Lett. *1968,* 4023.
[30] *W. S. Knowles, M. J. Sabacky,* Chem. Commun. *1968,* 1945.
[31] *L. Horner, H. Siegel, H. Büthe,* Angew. Chem. *80,* 1034 (1968); Angew. Chem. Int. Ed. Engl. *9,* 942 (1968).
[32] *W. S. Knowles, M. J. Sabacky, B. D. Vineyard,* Chemtech. *1972,* 590.
[33] *L. Horner, H. Winkler, A. Rapp, H. Mentrup, H. Hoffmann, P. Beck,* Tetrahedron Lett. *1961,* 161.
[34] *W. Himmele, H. Siegel, W. Aquila, F. J. Müller,* DBP 2132314 (1971), BASF; Chem. Abstr. *78,* 97328 (1973).
[35] *D. Evans, J. A. Osborn, G. Wilkinson,* J. Chem. Soc. *A 1968,* 3133.
[36] *C. Botteghi, G. Consiglio, P. Pino,* Chimia *26,* 141 (1972).
[37] *C. Salomon, G. Consiglio, C. Botteghi, P. Pino,* Chimia *27,* 245 (1973).
[38] *M. Tanaka, Y. Watanabe, T. Mitsudo, K. Yamamoto, Y. Takegami,* Chem. Lett. *1972,* 483.
[39] *I. Ogata, Y. Ikeda,* Chem. Lett. *1972,* 487.
[40] *W. Himmele, H. Siegel, S. Pfohl, J. Paust, W. Hoffmann, K. v. Fraunberg,* DOS 2404306 (1974), BASF; Chem. Abstr. *84,* 59781 (1976).
[41] *W. Himmele, H. Siegel,* unpublished results.
[42] *W. Himmele, H. Siegel,* DOS 2452804 (1974), BASF; Chem. Abstr. *85,* 78229 (1976).
[43] *S. Pfohl, J. Paust, H. Siegel, W. Himmele, W. Hoffmann, K. v. Fraunberg,* DOS 2404305 (1974), BASF; *83,* 205780 (1975).
[44] *W. Hoffmann, W. Himmele, J. Paust, K. v. Fraunberg, H. Siegel, S. Pfohl,* DOS 2453283 (1974), BASF; Chem. Abstr. *84,* 121637 (1976).
[45] *W. Himmele, H. Siegel,* Tetrahedron Lett. *1976,* 907.

3-Phenylpropylamines, A New Class of Systemic Fungicides

By Walter Himmele and Ernst-Heinrich Pommer[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The biological activity of 3-phenylpropylamines is not exclusively determined by their structure. It could be demonstrated that the fungicidal activity of partially hydrogenated compounds of this class of substances is also substantially influenced by the conformation. An optimization of the conformational criteria—illustrated by many examples, yet constituting only a small number of those actually examined—afforded compounds with excellent properties, *e.g.* *N*-[3-(4-*tert*-butyl-1-cyclohexenyl)-2-methylpropyl]-*cis*-2,6-dimethylmorpholine.

1. Introduction: Importance of Fungicides for Crop Growth

Amines such as *N*-tridecyl-2,6-dimethylmorpholine *(Tridemorph)* and *N*-cyclododecyl-2,6-dimethylmorpholine *(Dodemorph)* are active in crops against special types of fungi. Also other 2,6-dimethylmorpholines with suitable substituents on nitrogen and on the heterocycle have very good fungicidal properties, especially toward powdery mildew[1].

Today in intensive crop cultivation, besides a well-balanced fertilization, directed plant protection measures are of importance. First of all, the emphasis for assuring and improving crop yields lay in the area of weed-control. But in the last 10–15 years, besides seed desinfection, the use of fungicides in combatting foot rot and leaf and ear diseases has been recognized as an important factor as well. In 1971 in the fight against mildew in barley a breakthrough was made by the introduction of the systemic fungicide Tridemorph; depending upon the type of disease a 10% or substantially greater increase in produce could be achieved. This fungicide is also very active toward wheat mildew, but we have observed in the case of some wheat species and under unfavorable application conditions that the tolerance of the plant is unsatisfactory. The search for new biologically active substances without this shortcoming, and at the same time which are active against other important plant pathogenic fungi, *e.g.* wheat rust fungi, formed the starting point for the work described in this paper.

The most important parasites which cause leaf diseases in crops are the powdery mildew fungi from the species Erysiphe and the rust fungi from the species Puccinia. It is estimated that alone in Europe a crop cultivation area of more than six million hectares is endangered. For economic reasons the farmer would like to use the smallest possible amounts of plant protection substances and therefore he prefers fungicides having a broad activity spectrum, thus making the use of specifically active products unnecessary. The activity of the conventional fungicides, *e.g.* dithiocarbamates, is restricted because essentially they protect the plant surface only through direct contact with the fungi spores. Such fungicides are directly exposed to rain, air, wind, light *etc.* and cannot give protection to many parts of a plant during rapid growth. From a systemic fungicide however, one expects the following properties:

1. easy uptake through leaves and roots, independent of the plant type;
2. rapid transport and rapid distribution throughout the entire plant, independent of whether one year old or ligneous plants (trees) are involved;
3. broad spectrum of fungicidal activity;
4. well tolerated, even after attaining the fungitoxic concentration in the plant tissue; persisting activity also after "dilution" of the fungicide by new growth;
5. degradation of the biologically active fungicide to harmless metabolites within a definite time period between the last application and harvest.

The fungicidally active 3-phenylpropylamines so far investigated showed systemic properties. Representatives from the species of powdery mildew fungi and of grain rust fungi were chosen since our aim was to find biologically active substances exhibiting the above mentioned range of activity. Wheat, barley and oats were chosen as the cultivated plants.

The compounds mentioned in this article were synthesized by the usual preparative methods. Stereoisomers could be separated using laboratory columns with forty to eighty plates. Assignment of configuration was achieved by means of ^{1}H- and ^{13}C-NMR spectroscopy[*].

2. 3-Phenylpropylamines with Optimized Fungicidal Activity

2.1. Discovery of this Class of Compounds

Instead of morpholine derivatives (tetrahydro-1,4-oxazines), derivatives of other cyclic amines can be used for the investigation. The fungicidal activities of 2,6-dimethylmorpholines[1,2] and of 3,5-dimethyl-4-piperidones[3,4], in both cases with the same substituent on the nitrogen, are about the

[*] Dr. Himmele
Central Laboratory, BASF Aktiengesellschaft
D-6700 Ludwigshafen (Germany)

Dr. Pommer
Agricultural Experimental Station, BASF Aktiengesellschaft
D-6703 Limburgerhof (Germany)

[*] We thank Dr. *W. Bremser* and Herr *A. Hardt*, BASF, Central Laboratory, for the NMR spectra.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0184 $ 02.50/0

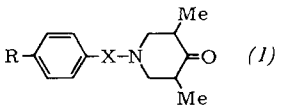
same. In the following investigations, both classes of compounds are examined.

Aryloxyalkylamines[1a], in which the nitrogen is part of a morpholine ring, are also satisfactorily effective against barley mildew, though their activity against wheat mildew is not strong enough. In many cases also the tolerence in wheat does not meet with market requirements.

2.2. Significance of the Alkylene Chain for Fungicidal Activity

3,5-Dimethyl-4-piperidones[2b] with a suitable arylalkyl substituent on the nitrogen atom show fungicidal activity against wheat mildew, barley mildew and brown rust of wheat[3,4]. The phytotoxicity of this class of compounds is relatively low.

Table 1. Dependence of the fungicidal activity on the alkylene chain between the aromatic ring and the heterocycle. BM = barley mildew, WM = wheat mildew, CRO = crown rust of oats. See text for concentration of the active compound and the biological assessment.



(1)

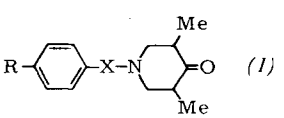
Cpd.	R	X	BM	WM	CRO
(1a)	H	CH_2	5		
(1b)	H	CHMe CH_2	2		
(1c)	H	CH_2 CHMe	2	2	5
(1d)	OCH_3	CHMe CH_2	2	0	
(1e)	H	CHMe CH_2 CH_2	2	0	5

The biologically active solution is prepared by dissolving the substance in acetone, adding a wetting agent and diluting with water. The concentration of the substance is 0.05 weight percent (Tables 1–13).

The fungicidal activities listed in the tables are assessed as follows: 0 = complete destruction of fungi, graded to 5 = no significant attack against the fungi. A = trace, B = intermediate and C = intense damage to the leaves; no remark = no crop damage.

A clear dependence of the activity on the size of the alkylene chain can be seen for the compounds listed in Table 1. The activity against barley mildew increases with increasing length of the chain between the aromatic ring and the cycloamine. The benzyl derivative *(1a)* has no activity against mildew fungi. A clearly defined activity is seen in compounds such as *(1b)*–*(1d)* which have a β-phenylethyl moiety attached to the nitrogen.

Table 2. Dependence of the fungicidal activity on the alkylene chain between the aromatic ring and the heterocycle. BM = barley mildew, WM = wheat mildew, CRO = crown rust of oats.

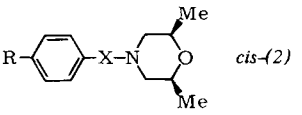


(1)

Cpd.	R	X	BM	WM	CRO
(1f)	H	CH_2 CH_2 CH_2	2	3	5
(1e)	H	CHMe CH_2 CH_2	2	0	5
(1g)	H	CHMe CH_2 CHMe CH_2	0	5	5
(1h)	H	CH_2 CH_2 CHEt CH_2	0C	3	5
(1i)	H	CHMe CH_2 CHEt CH_2	2	3A	5A
(1j)	H	$(CH_2)_3$ CHMe CH_2	0	5	

3-Phenylpropylamines[4–9] are found to be quite active against both mildew species (see Table 2). While *(1f)*, with an unsubstituted chain, has relatively good activity against barley mildew, it shows only moderate activity against wheat mildew. The activity level changes if the trimethylene chain is substituted. Thus, compound *(1e)*, which has a methyl group α to the phenyl group, has a very good activity against wheat mildew. Generally, a good activity against barley mildew but a strongly reduced activity against wheat mildew is observed if the chain is lengthened to 4–5 carbon atoms and at the same time substituted with lower alkyl groups.

Table 3. Dependence of fungicidal activity on the alkylene chain between the aromatic ring and the heterocycle. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



cis-(2)

Cpd.	R	X	BM	WM	BRW
cis-(2a)	H	CH_2 CHEt $(CH_2)_2$	0	5	5
cis-(2b)	H	$(CH_2)_2$ CHEt $(CH_2)_2$	0	0	5
cis-(2c)	H	CHMe CH_2 CHMe CH_2	0	5	5

The same structure-activity relation holds true for *cis*-2,6-dimethylmorpholines in which the nitrogen atom is substituted by an arylalkyl moiety. An alkylene chain with more than three members appears to decrease the activity against wheat mildew and brown rust of wheat (Table 3).

An optimization of the activity against crop-damaging fungi for the compounds discussed here is obtained by a chain containing three (substituted) methylene groups. These results motivated continuation of our work based on the model shown in Figure 1.

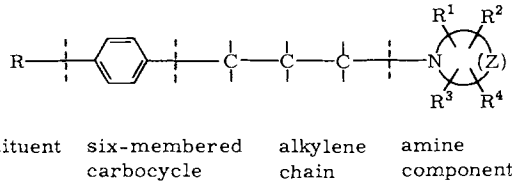
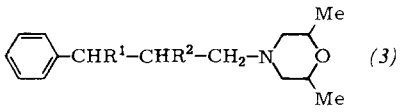


Fig. 1. Molecular model for illustrating the working hypothesis.

The substitution pattern of the alkylene chain is important for the activity. A methyl group α to the nitrogen usually causes a decrease in the activity against barley mildew while the activity against brown rust of wheat is almost completely lost [see *(1l)*, Table 6]. Introduction of methyl groups in the corresponding β-phenylethylamine derivatives [see *(1c)*] also results in a strong decrease in activity. Hence, the effect of alkyl groups attached to the middle carbon atom and at the γ-carbon atom of the chain was primarily studied.

Compounds of type *(3)*, which are alkyl-substituted at the middle carbon atom and/or at the γ-carbon atom of the trimethylene chain, generally have a low activity level (Table

Table 4. Dependence of fungicidal activity on the alkylene chain between the aromatic ring and the heterocycle. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.

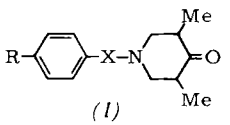


(3)

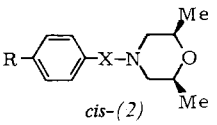
Cpd.	R^1	R^2	BM	WM	BRW
(3a)	Me	H	2		5
(3b)	H	Me	2		5
(3c)	Et	Me	5	5	5
(3d)	*n*-Pr	Et	5	5	5
(3e)	*n*-Bu	*n*-Pr	2	3	3

4). However, the activity of these compounds can be strongly increased by substitution of the phenyl group (see Tables 6 and 7).

Table 5. Dependence of the fungicidal activity on the heteroatoms in the alkylene chain between the aromatic ring and the heterocycle. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



(1)



cis-(2)

Cpd.	R	X	BM	WM	BRW
(1e)	H	CHMe CH_2 CH_2	2	0	5 [a]
(1k)	H	O CHMe CH_2	3		
(1l)	H	CH_2 CH_2 CHMe	2	3	5
(1m)	H	NMe CH_2 CHMe	2	5	5
cis-(2d)	H	O CHMe CH_2	5	3	5
cis-(2e)	*t*-Bu	O CHMe CH_2	3	3	3
cis-(2f)	*c*-Hex	O CHMe CH_2	0		

[a] Crown rust of oats.

The extent to which the activity is changed on replacing a carbon atom by a heteroatom in the alkylene chain can be deduced from Table 5.

If the carbon atom α to the aromatic ring is replaced by an oxygen atom, the fungicidal activity decreases. The same effect is observed on replacement of this atom by a methylamino group. The comparison *(1e)/(1k)*, however, is not exact since the chain is differently substituted; the same holds true for a comparison of *(3b)* (mixture of stereoisomers; see Table 4) and *cis-(2d)*.

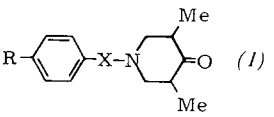
2.3. Influence of the Substituents of the Aromatic Ring on the Fungicidal Activity

A marked increase in the activity can be achieved by *para*-substitution of the aromatic ring.

Table 6 shows that an isopropyl group in the *para* position of the phenyl group increases the activity. A *tert*-butyl group in the same position causes an even clearer increase in the activity. This holds true for barley and wheat mildew as well as for brown rust of wheat.

Introduction of a methyl group in the trimethylene chain and at the same time *para*-substitution of the aromatic ring leads to a very good level of fungicidal activity over the entire spectrum (see Table 7). A decisive increase in the fungicidal activity, and with it the breakthrough for utilization in wheat cultures, was brought about by an introduction of a methyl group at the middle carbon of the trimethylene chain.

Table 6. Change in fungicidal activity on simultaneous variation of the substituents on the aromatic ring and of the position of the methyl group in the trimethylene chain. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.

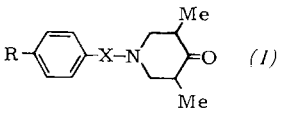


(1)

Cpd.	R	X	BM	WM	BRW
(1e)	H	CHMe CH_2 CH_2	2	0	5 [a]
(1f)	H	CH_2 CH_2 CH_2	2	3	5 [a]
(1l)	H	CH_2 CH_2 CHMe	2	3	5
(1n)	*i*-Pr	CHMe CH_2 CH_2	0A	3	3
(1o)	*t*-Bu	CHMe CH_2 CH_2	0	2	2

[a] Crown rust of oats.

Table 7. Dependence of the fungicidal activity on substitution of the aromatic ring and the trimethylene chain. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



(1)

Cpd.	R	X	BM	WM	BRW
(1f)	H	CH_2 CH_2 CH_2	2	3	5 [a]
(1e)	H	CHMe CH_2 CH_2	2	0	5 [a]
(1n)	*i*-Pr	CHMe CH_2 CH_2	0A	3	3
(1o)	*t*-Bu	CHMe CH_2 CH_2	0A	2	2
(1p)	*i*-Pr	CH_2 CHMe CH_2	0	0	0
(1q)	*t*-Bu	CH_2 CHMe CH_2	0	0	0

[a] Crown rust of oats.

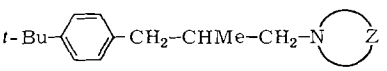
At the test concentrations chosen here (0.05 wt-%), the isopropyl group as substituent on the aromatic ring leads to the same activity as the *tert*-butyl group. If more dilute solutions are used, the *tert*-butyl compound *(1q)* is clearly more active than the corresponding isopropyl compound *(1p)*.

2.4. Significance of the Cycloamine Component for the Fungicidal Activity

As can be seen from Table 7, from the point of view of composition and structure the 3-(*p-tert*-butylphenyl)-2-methylpropyl group is the "optimum arylalkyl residue". Cycloamines with this group substituted on the nitrogen generally show a very good activity against barley mildew, wheat mildew and brown rust of wheat.

The differences in activity of the cycloamine derivatives *(4)* examined (Table 8), which were used here in concentrations of 0.05 weight-%, first become noticeable at low concentrations. In general, piperidine derivatives such as *(4b)* show very good activities. The C-4 atom of the piperidine ring can also be replaced by a heteroatom such as oxygen

Table 8. Dependence of the fungicidal activity on variation of the "optimally substituted arylalkyl moiety" on the cycloamine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



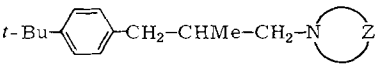
(4)

Cpd.	Z	BM	WM	BRW
(4a)	$(CH_2)_4$	0	0	0
(4b) [a]	$(CH_2)_5$	0	0	0
(4c)	$(CH_2)_6$	0	0	0
(4d)	$(CH_2)_2$ O $(CH_2)_2$	0	0	0
(4e)	$(CH_2)_2$ NMe $(CH_2)_2$	0	0	0
(4f)	CH_2 CHMe S CHMe CH_2	0	0	0

[a] Fenpropidin.

[*(4d)*], sulfur [*(4f)*] or nitrogen [*(4e)*]. A particularly good activity is obtained by methyl group substitution in the 3- and 5-position of the six-membered amine ring [see *e.g.* *(4f)*] (see also Tables 12 and 13).

Table 9. Dependence of the fungicidal activity on variation of the "optimally substituted arylalkyl moiety" on the cycloamine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



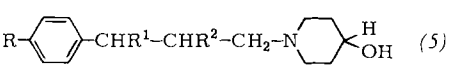
(4)

Cpd.	Z	BM	WM	BRW
(4g)	CH_2 $CH(CH_2OH)$ $(CH_2)_3$	0	0	0
(4h)	$(CH_2)_2$ CHOAc $(CH_2)_2$	0	0	0
(4i)	CH_2 CHMe $(CH_2)_3$	0	0	0
(4j)	CH_2 CHMe CH_2 CHMe CH_2	0	0	0
(4k)	CH_2 $C(Me)_2$ $(CH_2)_3$	0	0	0
(4l)		0	0	0

Table 9 shows that there is just as little decrease in activity on substitution of the six-membered amine ring with alkyl groups or hydroxymethyl groups as on benzoannelation.

The dependence of the fungicidal activity on the substitution has also been examined in the case of the six-membered ring amine 4-hydroxypiperidine, whose polarity is completely different from that of the cycloamines used previously (Table 10). The dependence was found to be the same in the case of the piperidones (Table 7). The "optimum arylalkyl residue" proves to be the best also in compounds *(5)*.

Table 10. Dependence of the fungicidal activity on the arylalkyl moiety substituted on the nitrogen atom of 4-hydroxypiperidine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.

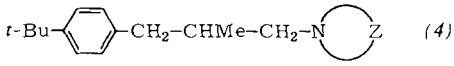


(5)

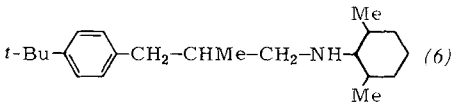
Cpd.	R	R^1	R^2	BM	WM	BRW
(5a)	*i*-Pr	Me	H	0	2	5
(5a) · HCl				3	2	5
(5b)	*t*-Bu	Me	H	0	2	5
(5b) · HCl				0	2	5
(5c)	*i*-Pr	H	Me	0	2	5
(5c) · HCl				0	2	2
(5d)	*t*-Bu	H	Me	0	0	0
(5d) · HCl				0	0	0

While slight deviations from the optimum composition and structure in all the variations studied (Tables 7 and 10) initially decrease the activity against brown rust of wheat, further modification of the otherwise promising type of compounds bearing six-membered cycloamines can lead to a completely different behavior (Table 11).

Table 11. Dependence of the fungicidal activity on variation of the "optimally substituted arylalkyl moiety" on the cycloamine or amine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



(4)



(6)

Cpd.	Z	BM	WM	BRW
(4m)	CH_2 $C(Me)_2$ CH_2 CHMe CH_2	0	3	0
(4n)	CHMe CH_2 CHMe $(CH_2)_2$	0	3	0
(4o)	CHMe $(CH_2)_2$ CHMe CH_2	3		0
(4p)		0	5	0
(6)	see above	0	3	0

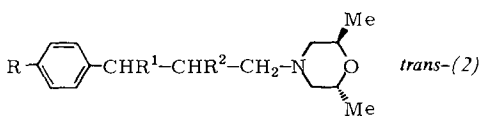
Although the activity against brown rust of wheat is retained on alkyl substitution of such a cycloamine (cf. Table 8), the activity against wheat mildew is decreased to a very low level.

3. Significance of the Configuration for the Fungicidal Activity

3.1. Influence of the Configurational Features of the Cycloamine Component

The specificity of the activity against fungi, which is brought about by configurational features of the cycloamine component, can be seen in Tables 12 and 13.

Table 12. Dependence of the fungicidal activity on the arylalkyl moiety on the nitrogen atom of *trans*-2,6-dimethylmorpholine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.

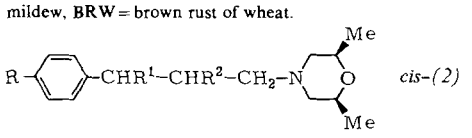


trans-(2)

Cpd.	R	R^1	R^2	BM	WM	BRW
trans-(2g)	*i*-Pr	Me	H	3	2	5
trans-(2g) · HCl				3	2	5
trans-(2h)	*t*-Bu	Me	H	2	0	5
trans-(2h) · HCl				0	0	5
trans-(2i)	*i*-Pr	H	Me	0	0	3
trans-(2i) · HCl				0	0	0
trans-(2j)	*t*-Bu	H	Me	0	0	0
trans-(2j) · HCl				0	0	0

Compounds *cis-(2g)* to *cis-(2j)* have a much more favorable activity than their *trans* analogues. Here also it is quite evident that small deviations from the optimum structure

Table 13. Dependence of the fungicidal activity on the arylalkyl moiety on the nitrogen atom of *cis*-2,6-dimethylmorpholine. BM = barley mildew, WM = wheat mildew, BRW = brown rust of wheat.



cis-(2)

Cpd.	R	R^1	R^2	BM	WM	BRW
cis-(2g)	*i*-Pr	Me	H	0	0	5
cis-(2g) · HCl				0	0	3
cis-(2h)	*t*-Bu	Me	H	0	0	3
cis-(2h) · HCl				0	0	3
cis-(2i)	*i*-Pr	H	Me	0	0	0
cis-(2i) · HCl				0	0	0
cis-(2j)	*t*-Bu	H	Me	0	0	0
cis-(2j) · HCl				0	0	0

and configuration cause a decrease in the activity towards brown rust of wheat. Generally, for a decrease in activity against wheat mildew, more drastic deviations from these optimal conditions are necessary.

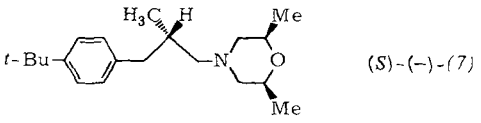
Since the *cis*-2,6-dimethylmorpholine derivative *cis-(2j)* has far better fungicidal properties than *trans-(2j)*, conversion of the *trans*-derivative into the *cis*-derivative was investigated. This isomerization can be accomplished using palladium catalysts at elevated temperatures[10]. The two stereoisomeric forms can be separated without difficulty by fractionation, thus making it possible to use the more effective isomer *cis-(2j)* in a purity of more than 98%.

N-[3-(*p-tert*-Butylphenyl)-2-methylpropyl]-*cis*-2,6-dimethylmorpholine [*cis-(2j)*], which was chosen for further development, has a favorable LD_{50}; for rats (p.o.) it is 3515 mg/kg. From experience so far, 500–750 g substance per hectare is enough to keep the crop free of mildew and rust for at least three to four weeks[2].

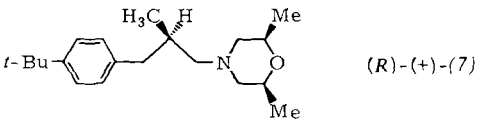
3.2. Influence of the Chiral Center in the 2-Methyltrimethylene Chain

A chiral center exists at the middle of the trimethylene chain owing to the presence of the methyl substituent. Separation of the two enantiomeric forms of the compound *cis-(2j)* was achieved by the classical method using camphorsulfonic acid[11]. A distinct difference in the activity of the two enantiomers (−)-*(7)* and (+)-*(7)* against crop damaging fungi was observed (Table 14).

Table 14. The difference in activity of the enantiomers with different arrangement at the chiral center in the 2-methyltrimethylene chain.



(S)-(−)-*(7)*



(R)-(+)-*(7)*

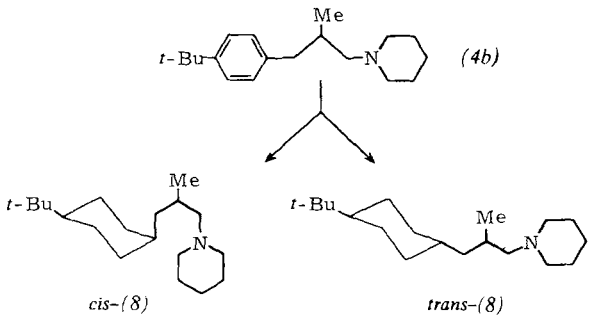
Cpd.	*c* [%]	Wheat mildew	Brown rust of wheat
(S)-(−)-*(7)*	0.012	0	0
	0.006	0	0
	0.003	0	0
(R)-(+)-*(7)*	0.012	0	2
	0.006	2	3
	0.003	3	3
Control	—	4	4

Whereas the (−)-enantiomer is very active against both wheat mildew and brown rust of wheat, the (+)-enantiomer displays only moderate activity against wheat mildew and is practically inactive against brown rust of wheat.

An X-ray structure analysis[*] of the hydrochloride of the levorotatory form showed it to be the *(S)*-enantiomer [*(S)*-(−)-*(7)* · HCl].

3.3. Configurational Features which Influence the Fungicidal Activity of 3-(4-*Tert*-Butylcyclohexyl)-2-methylpropylamine Derivatives

When 3-(*p-tert*-butylphenyl)-2-methylpropylamine, in which the nitrogen atom is part of a cycloamine, is catalytically hydrogenated to the cyclohexane derivative, two isomers are obtained which differ in their stereochemistry at the C-1 and C-4 positions of the cyclohexane ring[12].



(4b)

cis-(8) *trans-(8)*

Tests carried out against crop fungi (see Table 15) clearly showed that the 1,4-*trans* product has the stronger activity.

Table 15. The difference in activity of the two stereoisomers of perhydrogenated Fenpropidin.

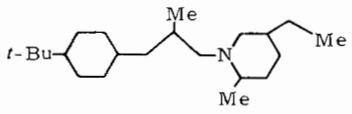
Cpd.	*c* [%]	Wheat mildew	Brown rust of wheat
cis-(8)	0.025	0	3
	0.012	0	3
	0.006		3
	0.003	0	3
	0.0015	0	4
	0.00075	1	5
trans-(8)	0.003	0	0
	0.0015	0	3
	0.00075	0	4

Although the *cis-(8)* and *trans-(8)* derivatives show very little difference in activity toward wheat mildew, only the *trans*-form exhibits very good activity against brown rust of wheat. Other amine derivatives behave in a similar fashion.

If 5-ethyl-2-methylpiperidine is chosen as amine component of the perhydrogenated compound [*(9)*], three fractions

[*] We thank Dr. *E. Hädicke*, BASF/Ammonia Laboratory, for the X-ray structural analysis.

can be obtained by distillation. The lowest boiling fraction I is inactive against wheat mildew and brown rust of wheat. Fraction II shows a good activity against wheat mildew but no activity against brown rust of wheat. The highest boiling fraction III is very active against both fungi.



(9)

3.4. Fungicidal Activity of *N*-[3-(4-*tert*-butyl-1-cyclohexenyl)-2-methylpropyl]-*cis*-2,6-dimethylmorpholine *(11)*

If cycloamines of type *(10)*, bearing a 3-(4-*tert*-butylcyclohexyl)-2-methylpropyl residue on the nitrogen are prepared by hydrogenation of the aromatic precursers and if the hydrogenation is interrupted when about half of the starting material has disappeared, the product contains besides starting material and the two cyclohexane compounds yet another 1-cyclohexenyl derivative. By several fractionations it is possible to enrich the cyclohexenyl derivative, *e.g. (11)*, to more than 85% (see Fig. 2).

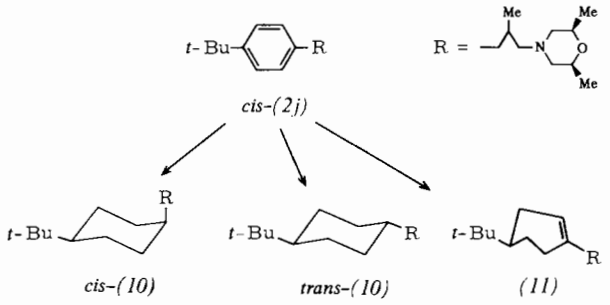
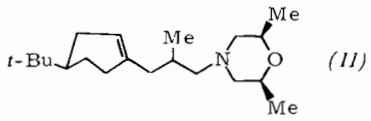


Fig. 2. Partial hydrogenation of *cis-(2j)* to *(11)*.

Table 16. Fungicidal activity of the cyclohexenyl derivative *(11)*.



(11)

Wheat mildew *c* [%]		Brown rust of wheat *c* [%]	
0.025	0B	0.025	0
0.012	0	0.012	0
0.006	0	0.006	0
Systemic activity against wheat mildew			
0.003	0/2 [a]		
0.0015	2/3 [a]		

[a] Mildew attack on untreated fresh foliage.

As shown in Table 16, the activity of compound *(11)* against wheat mildew and brown rust of wheat can be designated as very good. Compound *(11)* has a substantially better activity than the 1,4-*cis*-cyclohexane compound *cis-(10)*.

The conformation of *(11)* is similar to that of the educt *cis-(2j)* and to that of the very active 1,4-*trans*-cyclohexane compound *trans-(10)*. It would seem that the conformation of this class of compound plays a very important role regarding the fungicidal activity.

4. Conclusion

It has been shown in this article that the fungicidal activity of 3-phenylpropylamines is primarily determined by the conformation of the molecule. If a molecule contains several chiral centers it is also worth while making an optimization with regard to the configurational features. The effort spent in doing this is amply rewarded in the form of a better fungicidal activity and thus in a lowering of the amount of fungicide required. The productivity is improved to the same extent by this small amount of substance as by a larger amount of the stereoisomeric mixture. The crop culture is far less burdened on using a substance having an optimum molecular structure.

Received: December 17, 1979 [A 306 IE]
German version: Angew. Chem. *92*, 176 (1980)

[1] a) *K. H. König, E. H. Pommer, W. Sanne*, Angew. Chem. *77*, 327 (1965); Angew. Chem. Int. Ed. Engl. *4*, 336 (1965); b) *K. H. Büchel:* Pflanzenschutz und Schädlingsbekämpfung. Thieme, Stuttgart 1977, p. 149; c) *R. Wegler:* Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel. Springer, Berlin 1970, p. 123.

[2] a) *K. Bohnen, S. Pfiffner:* Fenpropimorph, a new systemic fungicide to combat powdery mildew and rust diseases in crop growth. International Symposium on Plant Protection, Gent (May 8, 1979). b) *E. H. Pommer, W. Himmele:* Combatting Important Crop Diseases with Fenpropemorph, a New Morpholine Derivative. International Symposium on Plant Protection, Gent (May 8, 1979).

[3] *W. Himmele, K. H. König, N. Götz, B. Zeeh*, DOS 2720612 (1978), BASF; Chem. Abstr. *90*, 121425j (1979).

[4] *N. Götz, W. Himmele, B. Zeeh, E. H. Pommer*, DOS 2753278 (1979), BASF; Chem. Abstr. *91*, 107899f (1979).

[5] *W. Himmele, E. H. Pommer, N. Götz*, DOS 2656747 (1976), BASF; Chem. Abstr. *89*, 109522k (1978).

[6] *W. Himmele, E. H. Pommer, N. Götz, B. Zeeh*, DOS 2727482 (1977), BASF; Chem. Abstr. *90*, 159004a (1979).

[7] *A. Pfiffner, K. Bohnen*, DOS 2752096 (1977), Hoffmann-La Roche; Austrian priority: A 866076 (1976); Chem. Abstr. *89*, 129409g (1978).

[8] *A. Pfiffner, K. Bohnen*, DOS 2752135 (1977), Hoffmann-La Roche; Austrian priority: A 866076 (1976); Chem. Abstr. *89*, 197339j (1978).

[9] *E. Buschmann, B. Zeeh, N. Götz*, unpublished work; Dtsch. Pat.-Anm. P 2830127 (1978), BASF.

[10] *N. Götz, W. Himmele, L. Hupfer*, unpublished work; Dtsch. Pat.-Anm. P 2830998 (1978), BASF.

[11] *W. Himmele, H. Siegel, E. H. Pommer*, unpublished work; Dtsch. Pat.-Anm. P 2907614 (1979), BASF.

[12] *W. Himmele, E. H. Pommer*, unpublished work; Dtsch. Pat.-Anm. P 2921131 (1979), BASF.

Developments in the Field of Inorganic Pigments[**]

By Knut Bittler and Werner Ostertag[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The specific properties of inorganic pigments result from an interplay of solid-state properties, particle size, and particle shape. However, phenomena occurring at the pigment interfaces also have implications for the use of the pigment. The interrelations for individual classes of pigments are indicated, and two selected examples, namely transparent colored pigments and magnetic pigments, are subsequently discussed with particular attention being paid to industrial developments.

1. Introduction

Inorganic pigments have been known for a very long time. They are found in prehistoric cave drawings, for example the drawings in the Pech-Merle caves in the South of France.



Fig. 1. a) Detail from a cave drawing in Pech-Merle (France). b) Antique Grecian vase, from the 5th century BC.

Figure 1a shows a detail from these cave drawings, believed to be about 17000 years old.

Another example of the use of inorganic colored pigments is to be found in antique pottery, such as the antique Grecian vase in Figure 1b which dates from the 5th century BC.

An appreciation of the artistic value of the pigments was soon followed by an appreciation of their commercial importance, and in this respect inorganic pigments have meanwhile lost none of their attractiveness. Today, with world sales running at about 10 billion DM per annum they are an important economic factor.

The beginnings of the pigment industry date back to the 18th century when colored pigments such as Berlin blue, $Fe[Fe_2(CN)_6]_3$, cobalt blue, $CoAl_2O_4$, Scheele's green, $Cu(AsO_2)_2 \cdot Cu(OH)_2$, and chrome yellow, $PbCrO_4$, were discovered and produced on a large scale.

The real commercial upswing, however, only occurred in the present century thanks to more modern means of production and more refined methods of scientific investigation. New applications were also discovered.

Nowadays, pigments are classified under the following headings:

Colorants; magnetic pigments; rustproofing pigments; and fillers.

Pigments are small solid particles roughly within the size range from 0.1 to 1 μm[*], and of greatly varying shape. They furthermore have a narrow particle size distribution and conform to a number of stability criteria, such as heat resistance, insolubility in solvents and binders, fastness to weathering, and stability to ultraviolet light.

The specific properties of a pigment, which determine its use as a colorant, magnetic pigment, rustproofing pigment or filler, essentially result from the interplay of the solid state properties, particle size, and particle morphology of the pigment. In addition, there are numerous phase boundary phenomena occurring between the pigment and the binder.

Typical solid state properties, *i. e.* properties resulting from the chemical composition and structure of the solid, include the color, the refractive index, and the magnetic order.

Pigment properties which are determined by, or affected by, the particle size and particle shape include the hue, the light scattering and the magnetic coercive field strength.

Phase boundary phenomena occurring between the pigment and the binder in the main play a part in the dispersibility of a pigment and the stability of the dispersion, but also in other specific effects, which will be referred to later. Pigments are always employed in dispersed form, because only in this form do the properties other than purely solids properties of the pigments come into play. At the same time, dispersions are technically easy to apply.

2. Properties of Pigment Categories

2.1. Colorants

Colorants are classified into white pigments and colored pigments[**].

White pigments show no absorption in the visible range; colored pigments absorb certain wavelengths of visible light. The reasons for the color reside in the molecule itself or in

[*] Dr. Knut Bittler, Dr. Werner Ostertag
BASF Aktiengesellschaft, Hauptlaboratorium
D-6700 Ludwigshafen (Germany)

[**] Based on a plenary lecture read at the General Meeting of the GDCh at Berlin on September 12, 1979.

[*] The size range is not precisely defined: there are pigments of 0.01 μm particle size and also pigments of 10 μm particle size.

[**] In this classification, black pigments are regarded as colored pigments.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0190 $ 02.50/0 Angew. Chem. Int. Ed. Engl. 19, 190-196 (1980)

the type of lattice. Various absorption mechanisms may be involved[1].

The following are some characteristic examples: The color of yellow lead chromate $PbCrO_4$ is attributable to charge transfer in the chromate anion. This electronic transition from oxygen to chromium is caused by the blue region of visible light.

The color of the blue cobalt aluminum spinel $CoAl_2O_4$ is due to the ligand field of the O^{2-} tetrahedra of the spinel lattice. This ligand field splits the originally equivalent d-levels of the Co^{2+} and permits electron transitions between the split energy levels as a result of light absorption in the visible range.

In the case of the red pigment Cd(SeS), the color is caused by the absorption of light of short wavelengths, which triggers electron transitions between the valency band and the conduction band of the solid.

Finally, the color of pigments can also be due to the presence of different valencies of one and the same element in the lattice, and to non-stoichiometric compositions. Examples are black iron oxide Fe_3O_4, and molybdenum blue MoO_{3-x}, a non-stoichiometric molybdenum oxide.

Whilst the color of a colored pigment is due to the light absorption *per se,* the shape of the absorption spectrum is responsible for the purity of hue.

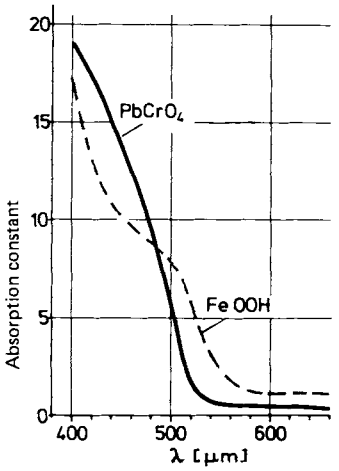


Fig. 2. Absorption spectra of chrome yellow, $PbCrO_4$, and yellow iron oxide, FeOOH, in the 400–660 µm range [2].

Figure 2 shows the absorption spectra of chrome yellow and yellow iron oxide[2]. The sharper, *i.e.* the steeper, the absorption edge, and the fewer additional absorption bands present in the visible range, the purer the hue of a colorant. The sharper rise in absorption in the case of chrome yellow is responsible for its exceptional brilliance. In the case of yellow iron oxide, the absorption curve is overall not so steep and therefore the color is distinctly duller.

Color and purity of hue are, however, not the only requirements which a colorant has to meet; it must also possess good tinctorial strength[*] and hiding power.

[*] In practice, the tinctorial strength is determined as the relative tinctorial strength according to DIN 53254 and DIN 55943; it results from the particular absorption characteristics *and* scattering characteristics of the pigment in question.

The hiding power of a colorant depends primarily on the light scattering which occurs at the pigment particles in the dispersion. This phenomenon is shown diagrammatically in Figure 3.

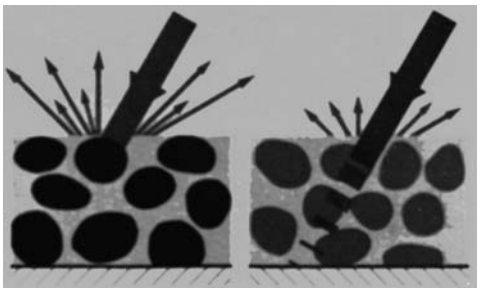


Fig. 3. Diagrammatic representation of light scattering at pigment particles in a dispersion; particles of high refractive index on the left; particles of low refractive index on the right. The gray background represents the binder.

The light scattering is seen to be more pronounced, the greater the difference in refractive indices of the pigment and the binder.

However, the scattering power also depends on the particle size of the pigment; this dependence is shown in Figure 4 for a rutile dispersion in oil[3].

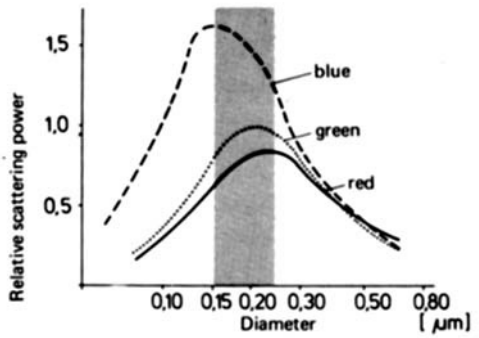


Fig. 4. Dependence of the relative scattering power of a rutile/oil dispersion on the type of light and the particle size [3].

It will be seen that optimum light scattering requires a very specific particle size for each wavelength. For the white pigment TiO_2, the particle sizes corresponding to this optimum are in the range from 0.15 to 0.25 µm. This is because, for TiO_2, the scattering maxima for the wavelengths of white light lie in this range.

2.2. Magnetic Pigments

The most important requirement for a magnetic pigment is ferromagnetism or ferrimagnetism. As is well known, this magnetism depends on the crystalline state of the material and is due to the parallel orientation of the spin moments of greater or lesser domains of the crystal lattice.

Examples of ferromagnetic materials are iron and CrO_2, and examples of ferrimagnetic materials are certain iron oxides, *e.g.* γ-Fe_2O_3, or ferrites, *e.g.* $CoFe_2O_4$. Both categories of materials are equally suitable for the production of magnetic pigments.

The first field of use for magnetic pigments was in sound-recording tapes. At the present time, magnetic tapes are used extensively not only in the entertainments industry but in information and data processing. Figure 5 shows, in a greatly simplified form, the principle of magnetic recording[4]. The magnetic tape is led past the gap of a horseshoe-shaped iron or ferrite core, which is wound with a coil and referred to as the magnetic head. The information to be stored is first converted into an electrical alternating voltage. This alternating voltage is used to generate, *via* the coil and the iron or ferrite core, a magnetic leakage field at the gap. This leakage field orients the initially random magnetic domains of the pigment coating on the tape. This orientation is retained after the magnetization, *i. e.* after leaving the leakage field.

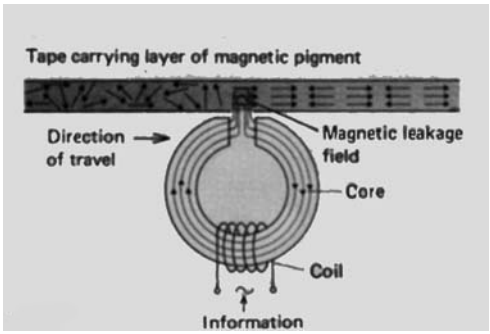


Fig. 5. Principle of magnetic recording. The arrows represent the magnetic domains of the pigment coating. The core may be iron or ferrite.

The intensity and durability of the magnetic recording is essentially dependent on three parameters: the Curie temperature, the residual induction, and the coercive field strength. The Curie temperature indicates the temperature at which the pigment loses its magnetization due to thermal motion of the spins, and becomes paramagnetic. Hence, for practical applications the Curie temperature should be as high as possible. The residual induction and coercive field strength are characteristic parameters of the magnetization behavior of a pigment. The magnetization behavior is represented in the form of a hysteresis loop (Fig. 6a). The residual induction M_r is the magnetization which remains after magnetically saturating the pigment by means of the external magnetic field (M_s = saturation magnetization) and then switching off the field. The coercive field strength H_c of a pigment is the magnetic field needed in order completely to demagnetize the magnetic pigment again. The coercive field strength can also be regarded as a measure of the ability of the pigment to resist demagnetization, *i. e.* a measure of its ability to retain information once accepted. The hysteresis curve has a characteristic appearance for each pigment.

In general, pigments of high residual induction are desirable, since they exhibit powerful recording signals and hence permit production of very thin magnetic coatings. On the other hand, the coercive field strength must not be too low or too high. If it is too low, the tape can be demagnetized too easily, and loses its information. If it is too high, the tape can no longer be erased.

However, the residual induction and coercive field strength of a magnetic tape are not merely characteristics of the particular solid-state material used. The shape of the pigment particles also greatly influences the magnetic tape characteristics. This effect was recognized at an early stage, and it was found that acicular particles give higher coercive field strengths than compact particles. Moreover, acicular pigment particles also prove advantageous in other respects. This is because, the pigment particles in the flowing dispersion can be oriented parallel to the tape surface and tape direction by means of a permanent magnet. This orientation widens the hysteresis curve and thus further increases the coercive field strength and produces a not insubstantial gain in residual induction[5] (see Fig. 6b).

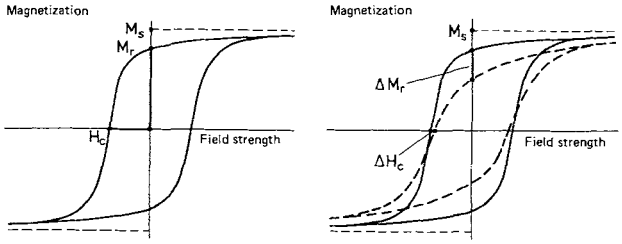


Fig. 6. a) Magnetization behavior of a magnetic pigment. Ordinate: Magnetization of the pigment. Abscissa: Field strength of an externally applied magnetic field. M_s = saturation magnetization, M_r = residual induction, H_c = coercive field strength. b) Effect of the orientation of acicular pigment particles. Broken curve without orientation; solid curve with orientation. ΔM_r = gain in residual induction, ΔH_c = gain in coercive field strength.

2.3. Rustproofing Pigments

The effect of a rustproofing pigment is attributable to diverse physical and chemical phenomena occurring at the surface of the pigment particle. The physical protective action may be illustrated with reference to micaceous iron ore, which is a rustproofing pigment[6] (Fig. 7).

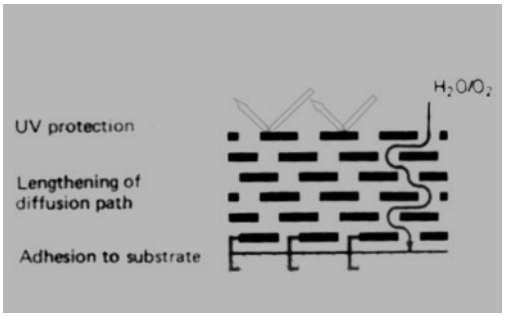


Fig. 7. Diagrammatic representation of physical rustproofing action illustrated for micaceous iron ore [6].

The black bars in the figure represent the flake-like micaceous iron ore particles. The binder — indicated in gray — is

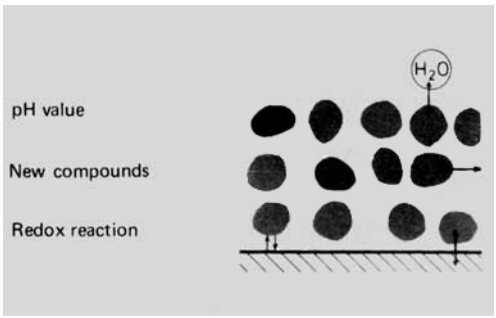


Fig. 8. Diagrammatic representation of chemical rustproofing action.

located between the particles. It is found in practice that pigmented finishes show better adhesion to the substrate than non-pigmented finishes. This adhesion is symbolized by brackets. In addition, the overlapping flakes form a kind of labyrinth for any penetrating air and moisture, and thus lengthen their diffusion path to the surface to be protected.

Further protection results from the fact that the pigment screens the organic binder against UV rays, both by absorption and by reflection.

As is shown diagrammatically in Figure 8, the chemical protective action of pigments is based on chemical interactions in the interfacial region between the pigment and the substrate, the pigment and the binder, and the pigment and any moisture which has penetrated. For example, redox reactions occur, new protective compounds are formed or a certain pH results in the vicinity of the pigment particles.

In the case of red lead it is known[7] that the redox reaction between tetravalent lead and the iron substrate results in the formation of insoluble protective layers containing Pb^{2+} and Fe^{3+} ions. In addition, the reaction of the red lead with the fatty acids of the binder leads to the formation of "lead soaps", which also act as a protective film. Hydrolysis finally gives $Pb(OH)_2$, which produces a basic pH in the vicinity of the particles and hence additionally retards corrosion.

It follows from what has been said above that the ideal rustproofing pigment must perform a large number of functions. The problem of rusting would in principle be solved if it were possible to produce coatings which cannot be damaged mechanically, adhere firmly, and are impermeable to water and to air. However, this has not hitherto proved possible. Hence, pigments remain the best solution to the problem of corrosion.

2.4. Fillers[*]

Fillers serve as diluents, for extending and improving pigment dispersions[8]. For example, fillers can be used to adjust the flow characteristics of finishes and dispersions, and to improve their processability. Moreover, the hardness, and adhesion to the substrate, of a pigment dispersion can also often be optimized by adding fillers. Fillers can also be used to render surfaces hydrophilic or hydrophobic. In some cases, fillers are used in order to fix dyes. Well-known fillers include pyrogenic silica, SiO_2, and Blanc fixe, $BaSO_4$.

3. Recent Developments

3.1. Transparent Colored Pigments

The relatively recent field of transparent colored pigments has become commercially interesting in the last 10 years, because they make possible particular optical effects. Figure 9a shows a photograph covered with two lacquer film strips pigmented with iron oxide. Both strips contain the same amount of iron oxide and are of equal thickness. Nevertheless, the left-hand strip is opaque and the right-hand strip transparent. The phenomenon is readily explained when the particle size of the particular pigments is considered. The opaque dispersion layer has a particle size of about 0.5 μm whilst the particles in the transparent layer are substantially smaller.

The hiding power of a pigmented lacquer film depends — as indicated in Section 2.1 — on the particle size of the pigment used. The larger particles show high light scattering and hence good hiding power. On the other hand, the substantially smaller particles have largely lost the ability to scatter light; the corresponding lacquer film is transparent. However, the light absorption, and hence the color, persists also in the case of the small particles. As a result, interesting effects can be achieved with transparent pigments. For example, it is possible to pigment articles without masking and hence losing the structure of the substrate. This effect is shown in Figure 9b on three samples of wood treated with transparent pigment dispersions.

What pigments are suitable for transparent lacquers and glazes? In principle, all colored pigments, provided their process of manufacture allows them to be obtained in a sufficiently finely divided form.

Table 1. Transparent inorganic colorants.

FeOOH	Iron oxide yellow
Fe_2O_3	Iron oxide red
$Cr_4O_3(OH)_6$	Hydrated chromium oxide green
Cr_2O_3/SiO_2	Chromium oxide green
$CoAl_2O_4$	Cobalt blue

Table 1 shows compounds with which it has hitherto proved possible to produce transparent colorations. Essentially, they are transition metal oxides.

Of these pigments, it is especially the iron oxide pigments which are commercially important. The reasons include their good pigmenting power and the ability of iron oxide to absorb UV radiation and hence to protect the organic dispersants against rapid degradation. Among the transparent iron oxides, iron oxide red, which is particularly heat-stable, has found the widest use. Transparent iron oxide red pigments are manufactured industrially by two processes, a wet chemical precipitation process and a pyrolytic process.

The precipitation process[9] involves three steps:

$$\text{Precipitation } Fe^{2+} + 2OH^- \rightarrow Fe(OH)_2$$
$$\text{Oxidation } Fe(OH)_2 + \text{air} \rightarrow FeOOH$$
$$\text{Dehydration } FeOOH \rightarrow Fe_2O_3$$

Pigments prepared by this method have the typical acicular appearance shown in Figure 10a. The average particle size is about 0.1 μm. Due to the method of preparation, iron oxide pigments obtained by precipitation are difficult to disperse. The user must frequently subject the finely divided oxide, which tends to agglomerate, to a very lengthy deagglomeration treatment because the optical effect of agglomerates is similar to that of larger particles, *i. e.* agglomerates reduce the transparency.

[*] The classification of fillers and pigments overlapped for a long time. According to the definition in a German standards specification (DIN 55943) and an international standards specification (ISO standard 3262), white powders with refractive indices greater than 1.7 are regarded as pigments and those with refractive indices of less than 1.7 as fillers.

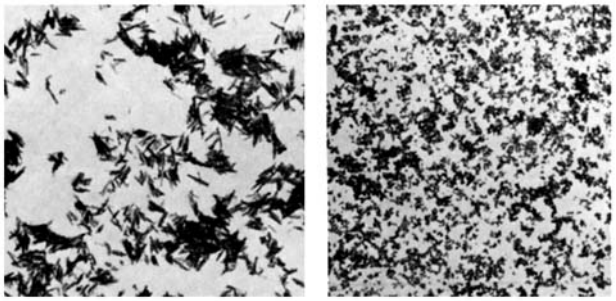


Fig. 9. a) Photograph with two lacquer strips pigmented with iron oxide (the amounts of iron oxide and the thickness of the lacquer film being the same for both strips). The left-hand lacquer film is opaque and the right-hand strip transparent. b) Samples of wood treated with various transparent pigment dispersions.

A more easily dispersible finely divided pigment is obtained by the pyrolytic process[10]:

$$Fe(CO)_5 + air \xrightarrow{600\,^{\circ}C} Fe_2O_3 + CO_2$$

The essential point in this process is to avoid sintering. The particles of pyrogenic iron oxide red pigments are smaller by about a factor of ten than the particles of the products obtained by precipitation. This can be seen very clearly in the electron micrographs in Figure 10. In contrast to the acicular precipitated product, the pyrolytically produced particles have a round shape.



a) b)

Fig. 10. Electron micrographs of transparent iron oxide red pigments. a) Pigment obtained by the wet precipitation process. 15 mm in the figure correspond to 1 μm. b) Pigment obtained by the pyrolytic process.

Table 2 compares further properties of the pyrolysis product with the corresponding properties of the precipitated product. The very finely divided nature of the pyrolysis product manifests itself in its larger specific surface area and in a more yellowish hue. The smaller particles give better transparency but as a result a lower tinctorial strength. A factor particularly important in practice is the excellent dispersibility of the pyrolytically prepared pigment, as shown by the short dispersing time needed to develop the full depth of color.

Table 2. Comparison of some properties of transparent Fe_2O_3 pigments.

Product	Surface area, BET method [m^2/g]	Hue	Relative tinctorial strength [%]	Dispersing time [min]
Pyrolysis product	160	yellowish red	85	5
Precipitation product	100	red	100	40

Transparent iron oxides are in the main used in high-grade metallic-effect finishes in the automotive industry. Other fields of use are in tinting wood, in printing of packaging materials, and in coloring plastics and leather.

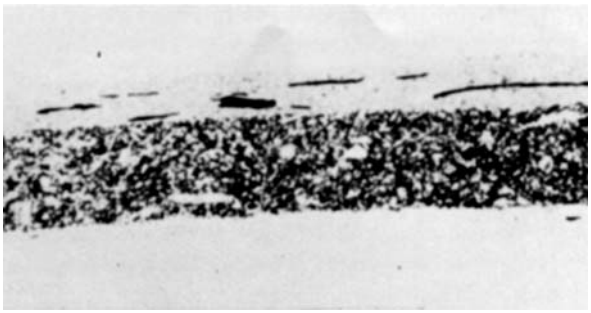


Fig. 11. Microscopic section through a metallic-effect finish. Bottom: primer layer. Top: pigmented finish containing aluminum flakes: 12.5 mm correspond to 25 μm.

Figure 11 shows a microscopic section through a metallic-effect finish. The lacquer layer, pigmented with transparent iron oxide red, lies on top of the dark primer layer. This lacquer layer additionally contains aluminum flakes, about 10–50 μm in size, which in the electron micrograph appear as thin black lines in the lacquer layer. These aluminum flakes act as miniature mirrors and produce the well-known metallic effect. They also allow the surface of the automobile to show a pronounced light-dark visual effect (cf. Fig. 12a). Such light-dark effects can only be achieved with particularly finely divided pigments.



Fig. 12. a) Light-dark effect in metal-effect finishes. b) Light-dark effect as a function of the particle size of the pigment used. Left: lacquer film strip containing high-hiding pigment (larger particles); right: lacquer film strip containing transparent pigment (very small particles); between these: two lacquer film strips containing semi-transparent pigments.

This effect is demonstrated for a slightly curved aluminum foil in Figure 12b. Four different lacquer film strips are applied to this foil; one containing a high-hiding pigment is shown on the extreme left, followed by two containing semi-transparent pigments and, finally, one containing a transparent pigment on the extreme right. The light-dark change in brightness is very pronounced only in the case of the right-hand strip. In the case of the semi-transparent strips the change in brightness is just still discernible, while in the case of the high-hiding film the brightness differences have disappeared.

3.2. Advances in Magnetic Pigments

The very rapid development of radio, television, and not least electronic data processing is ultimately attributable to magnetic pigments. This development started in the early 1930's and resulted from the cooperation between AEG and the Ludwigshafen Research Department of what was at that time IG Farben.

Subsequently, four important types of pigment have come to the forefront. Table 3 shows their characteristic parameters[11].

Table 3. Types of magnetic pigment and some of their characteristic data. Curie temperature, coercive field strength (H_c), saturation magnetization (M_s), and residual induction (M_r). The values (average values) shown apply to acicular pigments.

Pigment	Curie temp. [°C]	H_c [Oe]	M_s [gauss cm³/g]	M_r
γ-Fe_2O_3	600	340	76	60
CrO_2	120	570	100	75
$Co_xFe_{3-x}O_4$ [a]	580	630	90	70
Fe (Co, Ni) [b]	800	1000	217	160

[a] Average values for a pigment containing 10% of cobalt. [b] The magnetic values apply to an iron pigment.

The classical product among these pigments is γ-Fe_2O_3. The manufacture of acicular γ-Fe_2O_3 pigments requires a complicated multi-stage process leading *via* iron oxide hydrate, FeOOH, and magnetite, Fe_3O_4[5,12]. The key product is FeOOH which is easily obtained in an acicular form and to which the shape of the pigment ultimately obtained is attributable.

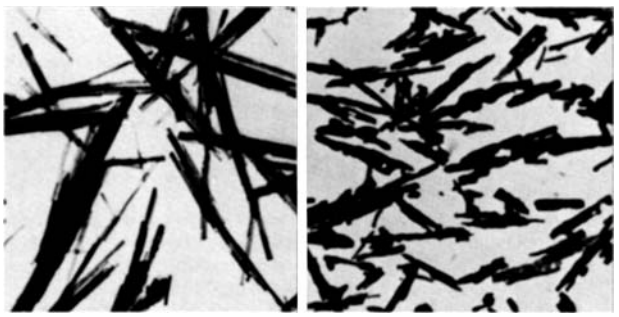


Fig. 13. Electron micrographs of iron oxide pigments. a) an FeOOH pigment; b) the γ-Fe_2O_3 pigment prepared therefrom. 16 mm in the figure correspond to 1 μm.

Figure 13a shows an electron micrograph of FeOOH needles. The needles shown in Figure 13b are the γ-Fe_2O_3 pigment prepared from the FeOOH needles. It will be seen that whilst the acicular shape suffers considerably as a result of the intermediate conversion stages, it is nevertheless basically retained, and this is the vital factor.

The particular advantage of γ-Fe_2O_3 pigments resides in their chemical stability and heat stability, and in the low temperature-dependence of the magnetic properties. The magnetic properties of γ-Fe_2O_3 shown in Table 3 allow γ-Fe_2O_3 pigments to be used for all applications, for example computer tapes, video tapes, and radio tapes. Hence, it is not surprising that this pigment enjoyed a monopoly position for a long time. However, in the mid-1960's miniaturization in the audio and video industry started and the age of the cassette began.

In order to achieve the desired playing time of several hours in small handy cassettes it is necessary for space reasons to make better use of the tapes in these cassettes, *i. e.* to write more closely on the tapes. The high recording density of the cassette tapes is nowadays achieved, *inter alia*, by a drastic reduction in the speed at which the tape is led past the recording head or playback head. The high recording densities required for this technology can, however, not be achieved with conventional γ-Fe_2O_3 pigments without sacrificing some quality; pigments with higher coercive field strengths are required.

As may be seen from Table 3, the other three pigments show the requisite higher coercive field strengths.

Chromium dioxide pigment was first introduced in the early 1970's. Chromium dioxide is chemically metastable; it contains tetravalent chromium. Nevertheless, it can be handled industrially since it releases substantial amounts of oxygen only at elevated temperatures.

Chromium dioxide magnetic pigments can be prepared by two methods[13]:

$$CrO_3 \rightarrow CrO_2 + 0.5\ O_2$$
$$CrO_3 + Cr_2O_3 \rightarrow 3\,CrO_2$$

Both reactions must be carried out under hydrothermal conditions.



Fig. 14. Electron micrograph of a CrO_2 pigment. 14 mm in the figure corresponds to 1 μm.

Figure 14 shows an electron micrograph of a chromium dioxide pigment. The extreme uniformity of the particles is discernible; they are essentially single crystals.

A conspicuous feature is the low Curie temperature of CrO_2, which is about 120 °C. However, this has not proved of disadvantage in practice. On the contrary, a particularly interesting use for CrO_2 pigments results from this very prop-

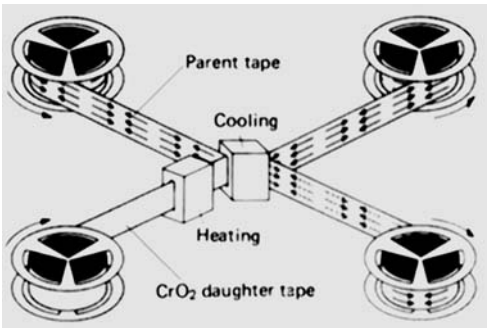


Fig. 15. Diagram illustrating thermoremanent copying.

erty: the low Curie temperature of CrO_2 and the substantial stability of the magnetization up to the Curie temperature make thermoremanent copying feasible. This process, which is only feasible with chromium dioxide pigments, is illustrated in greatly simplified form in Figure 15.

The parent (or mother) tape corresponds to a printing plate, carrying information in mirror image form. The parent tape is brought into intimate contact with the daughter (or slave) tape, which has been heated to just above the Curie temperature. On cooling, the magnetic domains of the pigment of the daughter tape undergo orientation corresponding to the parent tape, and pick up the information of the latter.

In audio cassettes and video cassettes, however, chromium dioxide soon encountered competition from cobalt-modified iron oxides, which show magnetic properties similar to those of CrO_2. It has been known since about the mid-1950's that the coercive field strength of Fe_3O_4 pigments is greatly increased by modifying the pigments with cobalt[14]. Originally, the modification was effected by replacing part of the Fe^{2+} in the octahedral lattice positions in the magnetite randomly by Co^{2+} so that the modification extends over the entire lattice.

With this type of modification, however, the heat stability of the magnetic recording diminishes considerably with increasing cobalt content. Hence, the magnetic tapes produced with such modified iron oxide pigments did not prove satisfactory.

A breakthrough was only achieved when a different type of modification was used, namely surface modification[15]. The principle in shown in Figure 16.

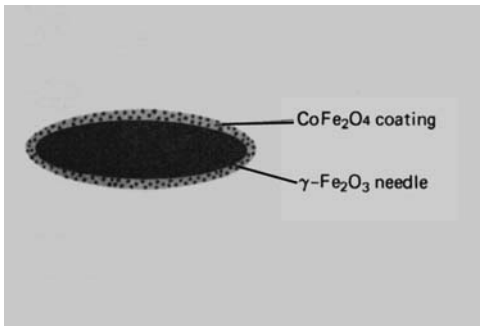


Fig. 16. Principle of surface modification.

In this process, a coating of, say, cobalt ferrite is applied, *e.g.*, to acicular γ-Fe_2O_3 pigments. In this way, the advantages of both types of pigment are exploited: the γ-Fe_2O_3 core gives heat-stable magnetic properties while the Co-containing coating at the same time confers a high coercive field strength upon the pigment.

The ultimate objective of magnetic pigment research has always been to obtain suitable metallic pigments, since metals have attractive magnetic properties. The fact that metal pigments have not long been in use is due to the difficulty of preparing stable, elongate—preferably acicular—metallic pigment particles. Only very recently has this been achieved.

The preferred element for the production of metallic pigments is iron, mainly because of its residual induction.

However, the preparation of metallic iron pigments[16] yields pyrophoric particles, which raises substantial problems. Not only must the particles be protected against oxidation during the manufacturing process; it is also necessary, in particular, to ensure that the pigment subsequently remains stable in the tape.

Looking at the magnetic properties of metallic pigments (Table 3), it is clear that they are the pigments of the future. However, how rapidly metallic pigment tapes will be able to gain a foothold in magnetic recording technology, and how wide their use will be, depends not least on the equipment manufacturers and on the success of their endeavors to modify the equipment to give optimum results with such pigments.

The tape manufacturers have already offered the first metallic pigment tapes to the public—for the first time in 1978 at the "Consumers Electronic Show" in Chicago, and more recently at the 1979 Radio Exhibition in Berlin.

4. Future Prospects

The present-day importance of inorganic pigments is attributable, to a not insignificant degree, to the constantly refined methods of investigation and preparative techniques available in the field of solid-state compounds. The likely future advances in the physics and chemistry of surfaces and solids may therefore be expected also to lead to new fields of use, and to maintain the momentum of the inorganic pigment sector.

Received: December 19, 1979 [A 311 IE]
German version: Angew. Chem. *92*, 187 (1980)

[1] *W. Feitknecht:* The Theory of the Color of Inorganic Substances. Pigments—An Introduction to their Physical Chemistry. Elsevier, Amsterdam 1967.
[2] *P. Hauser*, BASF Aktiengesellschaft, unpublished data.
[3] Ullmanns Encyklopädie der technischen Chemie, 3rd. Edit., Vol. 13. Urban & Schwarzenberg, Munich 1962, p. 740; 4th Edit., Vol. 18, Verlag Chemie, Weinheim 1979, p. 554; *R. J. Brühlman, L. W. Thomas, E. Gonick*, Off. Dig. Fed. Paint Varn. Prod. Clubs *43*, 252 (1961).
[4] *E. A. Sobotta:* Die Hysterese und andere Grundbegriffe des Magnetismus zum Verständnis der magnetischen Speicherung. Die BASF—A publication reporting the work of Badische Anilin- & Soda-Fabrik AG *21* (October 1977), p. 65; *E. Köster*, Grundlagen der magnetischen Datenaufzeichnung. NTG-Fachberichte, Vol. 58, VDE-Verlag, Berlin 1977.
[5] BASF brochure: Tonband, Herstellung und Eigenschaften, pp. 5–7 (Order No. M. 0582682).
[6] *G. v. Pokorny*, DEFAZET Dtsch. Farben-Z. *12*, 588 (1973).
[7] *J. Ruff:* Korrosion/Schutz durch Lacke + Pigmente. Verlag W. A. Colomb, Stuttgart 1972, pp. 76 *et seq.*
[8] *D. Hunkar*, DEFAZET Dtsch. Farben-Z. *20*, 39 (1966).
[9] *T. C. Patton*, Pigment Handbook, Vol. I. Wiley & Sons, New York 1973, p. 343; *G. C. Marcot, W. J. Cauwenberg, S. A. Lamanna*, U. S. Pat. 2558302 (1951) American Cyanamid.
[10] *F. L. Ebenhöch, K. P. Hansen, H. Stark* DBP 2210279 (1977), BASF; *W. Ostertag, F. L. Ebenhöch, G. Wunsch, D. Werner, G. Bock, K. Opp.* DOS 2344196 (1973), BASF.
[11] *E. Köster*, BASF, unpublished data.
[12] *C. D. Mee:* Physics of Magnetic Recording. Vol. II. North Holland, Amsterdam 1964, p. 180.
[13] *T. J. Swoboda, P. Arthur, N. L. Cox, J. N. Ingraham, A. L. Oppegard, M. S. Sadler*, J. Appl. Phys. *32*, 374 (1961); *W. Ostertag, W. Stumpfi, R. Falk, M. Ohlinger*, Elektroanzeiger *4* No. 11, p. 225 (1972).
[14] British Pat. 717269 (1954), Agfa; *J. C. Jeschke*, U. S. Pat. 3243375 (1966), Minnesota Mining.
[15] *S. Umeki, T. Uebori, M. Motegi*, DBP 2410517 (1979), TDK-Electronic Tokyo; *H. J. Becker, Chr. Jäckh, E. Köster, W. Löser, M. Ohlinger, W. Steck*, DOS 2705967 (1978), BASF.
[16] See [12], pp. 197 *et seq.*

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Ultratrace Analysis: Determination of Cr, Fe, and Co in the ppb and ppt Range for Checking the Preparation of High-Purity Niobium[**]

By *Werner G. Faix, Viliam Krivan,* and *Klaus Schulze*[*]

Interest in high-purity niobium has increased tremendously in recent years owing to its scientifically and technologically important properties and its possible application in nuclear and superconductor technology, fusion research, and other fields[1]. Many interesting properties of niobium can be influenced by mere trace of impurities[2]. Hence, the development of highly efficient methods for preparation and analysis are of decisive importance.

We have now been able for the first time to prepare extremely pure niobium and to carry out a reliable analytical characterization. The contents of the elements investigated Cr, Fe, Co, Ta and W lie in the ppb to ppt range. Other highly purified high-melting metals of this type are unknown.

The research group in Stuttgart has developed a three-step purification method. 1. Commercially available pure niobium is subjected to refining electrolysis in a ternary alkali-metal fluoride melt containing Nb^{4+} at $T=750\,^{\circ}C$ with simultaneous cathodic separation as single crystals. 2. The single crystals are purified by zone refining in an ultravacuum according to the "floating-zone method". 3. Immediately after zone refining, the samples are heated in the same apparatus by direct current to temperatures slightly below the melting point of niobium, decarburized in a stream of oxygen at $p_{O_2}=10^{-6}$ mbar, and finally annealed for 48 h until a pressure of 10^{-10} mbar is reached.

Of interest in assessing the purification method are: i) the content of major impurities Ta and W, which can be determined by instrumental neutron activation analysis, and ii) the content of a few other trace elements such as Cr, Fe, and Co, whose overall concentration is relatively high so that contamination can even take place during the purification process.

Since the detection limits and accuracy in non-activation methods are essentially determined by the blank values it appeared more meaningful to us to use neutron activation analysis, which offers unique advantages with respect to the blank[3]. The research group at Ulm has worked out the following analytical procedure: Sample and standard are activated by prolonged irradiation in a medium or high-flux reactor (in our case: 42 days' irradiation in the FR-2 at the Nuclear Research Center in Karlsruhe, with a thermal neutron flux of 8×10^{13} n cm^{-2} s^{-1}). After irradiation and surface decontamination of the niobium sample, 2 mg each of Cr, Fe and Co are added as carriers and the sample dissolved in HF/HNO_3. The matrix and major impurities, and the radionuclides formed from them are separated (based on work given in[4]) on a strongly basic anion exchanger (Dowex 1, X4, 50/100 mesh) in fluoride form. The eluate (50 ml 2N HF) after this separation contains the indicator radionuclides (IRN) of the investigated elements ^{51}Cr, ^{59}Fe, and ^{60}Co and can be used for their quantitative determination by gamma-ray spectroscopy. For specific separation of the IRN (based on work given in[5]) the sample solution is transferred in hydrochloric acid medium (*ca.* 8 N) onto a strongly basic anion exchanger in chloride form and eluted with HCl of different concentrations (50 ml 8 N HCl→Cr; 50 ml 4N HCl→Co; 50 ml 0.1N HCl/0.1% N_2H_4→Fe). The fractions containing each of the elements are then counted using a 3 × 3″ NaI well-type detector in an 11 cm-thick shielding of low-activity lead.

For a sample weight of *ca.* 100 mg, detection limits down to 10 ppt for Cr, 1.5 ppb for Fe and 4.0 ppt for Co can be achieved.

Using this analysis technique, the concentrations of Cr, Fe, and Co in several high-purity niobium samples were determined. The results for these elements as well as for Ta and W (determined by instrumental neutron activation analysis) are given in Table 1.

Table 1. Contents of Cr, Fe, Co, Ta and W determined in niobium (for the description of samples and purification methods see text).

Element	Sample		
	Nb-WCT [a]	R-Nb-1 [b]	R-Nb-2 [b]
Cr	1.7 ± 0.5 ppb	3.6–16.7 ppb	10 – 24.7 ppt
Fe	15.5 ± 3.0 ppb	0.6– 1.8 ppm	2 – 6.6 ppb
Co	53.9 ± 2.0 ppt	0.2– 1.6 ppb	4 – 19.0 ppt
Ta	163 ppm	0.1– 6.0 ppm	0.1– 6.0 ppm
W	7.5 ppm	2 –60 ppb	2 –100 ppb

[a] Averages from three determinations with average deviations.
[b] Content ranges of five separately purified samples.

As starting material for the high-purity niobium samples we used Nb-WCT (Teledyne Wah Chang, Albany, Oregon [USA]), which was remelted under vacuum in an electron beam furnace. The lower melting metals Cr, Fe, Co evapo-

[*] Prof. Dr. V. Krivan, Dipl.-Chem. W. G. Faix
Sektion Analytik und Höchstreinigung der Unversität
Oberer Eselsberg N 26, D-7900 Ulm (Germany)

Dr. K. Schulze
Laboratorium für Reinststoffe, Max-Planck-Institut für Metallforschung
Seestrasse 92, D-7000 Stuttgart 1 (Germany)

[**] This work was supported by the Bundesministerium für Forschung und Technologie.

rate with high vapor pressure at $T > 2500\,^{\circ}C$, thus accounting for their low content; the high melting impurities Ta and W, on the other hand, remain in the niobium. The samples R-Nb-1 were electrolyzed; the major impurities Ta and W are thus removed, but metals such as Cr, Fe, and Co are apparently involved by contamination. The samples R-Nb-2 were additionally zone refined and annealed, which leads to a marked decrease in the Cr, Fe, and Co content.

The niobium thus obtained can be additionally characterized by its specific electrical resistivity of ϱ (4.2 K) $= 6 \times 10^{-10}\ \Omega$ cm in the normal state; the total content of non-metals is about 100 ppb. These findings show that niobium of particularly high purity and structural perfection can be prepared by the above method. The analytical method developed here for the determination of Cr, Fe, and Co is characterized by its extremely high sensitivity and freedom from error regarding contamination and losses.

Received: August 27, 1979 [Z 392 IE]
supplemented: January 21, 1980
German version: Angew. Chem. 92, 194 (1980)

CAS Registry numbers:
Nb, 7440-03-1; Cr, 7440-47-3; Fe, 7439-89-6; Co, 7440-48-4; Ta, 7440-25-7; W, 7440-33-7

[1] *C. Lieser:* Vanadium, Niob, Tantal – ihre Verarbeitung und ihre Einsatzgebiete. Vortragsveranstaltung „Sonder-Werkstoffe", Essen 1979; *W. H. Taylor:* Some studies of the $^{93}Nb(n,n)^{93m}Nb$ reaction; *F. Aegedüs:* Fast neutron dosimetry by the reaction $^{93}Nb(n,n)^{93m}Nb$. Both lectures 2nd ASTM-EURATOM Symposium on Reactor Dosimetry, Palo Alto (USA) 1977; *J. A. Martin, R. Braun, H. Stockert,* Radiochem. Radioanal. Lett. *28,* 59 (1977).

[2] *T. O. Niinikowski et al.,* Hyperfine Interactions *6,* 229 (1979); *P. Kneisel, O. Stolz, J. Halbritter,* J. Appl. Phys. *45,* 2296 (1974); *A. Das Gupta, W. Gey, J. Halbritter, H. Knüpfer, J. A. Yasaitis, ibid. 47,* 2146 (1976); *R. Krevet, W. Schauer, K. Schulze,* Appl. Phys. Let., in press.

[3] *V. Krivan,* Angew. Chem. *91,* 132 (1979); Angew. Chem. Int. Ed. Engl. *18,* 123 (1979).

[4] *G. Auboin, F. Dugain, J. Laverlochere,* Bull. Soc. Chim. Fr. *1965,* 547; *J. I. Kim, H. Lagally, H.-J. Born,* Anal. Chim. Acta *64,* 29 (1973).

[5] *K. A. Kraus, G. E. Morre,* J. Am. Chem. Soc. *75,* 1460 (1953).

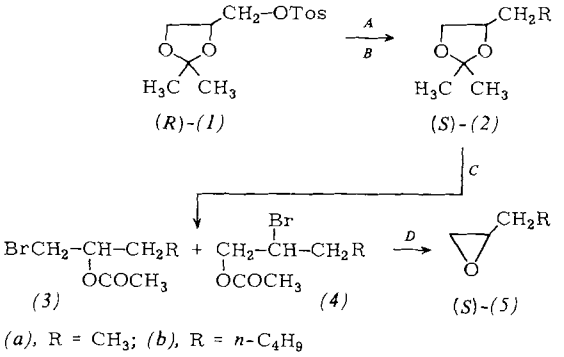
Synthesis of Monosubstituted (*S*)-Oxiranes in High Optical Purity

By *Ulrich Schmidt, Jörg Talbiersky, Frank Bartkowiak,* and *Jochen Wild*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Epoxides are cleaved regioselectively and stereoselectively by nucleophiles. Optically active epoxides are therefore useful building blocks for the synthesis of complicated chiral natural products. We have found that the optically active 2,2-dimethyl-1,3-dioxolan-4-ylmethyl *p*-toluenesulfonate (2,3-isopropylideneglycerol 1-tosylate) *(1)* reacts stereoselectively with alkylmetal compounds to give the dioxolanes *(2)*, in which the toluenesulfonyloxy group of *(1)* is replaced by an alkyl group. (*S*)-*(2)* gives oxiranes *(5)* of high optical purity having the *S* configuration.

The reactant (*R*)-*(1)* is readily accessible on a 100 g-scale from diisopropylidenemannitol, whose preparation[1] could be improved. The 1,2-butanediol derivative *(2a)* obtained from *(1)* and methyllithium/copper(I) iodide was transformed by treatment with hydrogen bromide/glacial acetic acid[2] into a mixture of bromoalkyl acetates *(3a)/(4a)*, from which 1,2-epoxybutane *(5a)* resulted by elimination. The rotatory power of *(5a)* agreed with the value reported[3]



Scheme 1. (*R*)-*(1)*→(*S*)-*(2a)*, variant *A*: CH_3Li/CuI; (*R*)-*(1)*→(*S*)-*(2b)*: variant *A*: n-C_4H_9Li/CuI; variant *B*: $(n\text{-}C_4H_9)_2Mg/Li_2CuCl_4$; *C*: CH_3COOH/HBr [2]; *D*: n-$C_5H_{11}OH/n$-$C_5H_{11}OK$ [2].

for optically pure (*S*)-*(5a)*. Optically pure (*S*)-1,2-epoxyheptane *(5b)* is produced analogously[4]. Variant *B*[5] gave a higher yield (67%) in step *(1)*→*(2b)* than did variant *A* (43%) (Scheme 1).

Procedure

Diisopropylidenemannitol: Anhydrous zinc chloride (544 g, not fused) is dissolved in acetone (2800 ml). The solution is allowed to stand for 3 d over a 3-Å molecular sieve (200 ml), D-mannitol (340 g) is added, and the mixture is stirred for 2 h at room temperature, whereupon the mannitol dissolves. After filtering off the molecular sieve, the mixture is rapidly stirred into a solution of potassium carbonate (680 g) in water (700 ml) covered with ether (2000 ml). After 30 min, zinc carbonate is decanted off and the precipitate washed with ether/acetone (1:1). The combined organic phases are evaporated down *in vacuo* and the residue recrystallized from water; yield 470 g of moist crude product of sufficient purity for further work.

(R)-(1): Diisopropylidenemannitol is cleaved according to ref.[6] with sodium periodate and the resulting aldehyde reduced directly with $NaBH_4$. The optically active isopropylideneglycerol which—contrary to the statement in ref.[6]—can be distilled without racemization (b. p. 33 °C/0.1 torr; $\alpha_D^{20} = +15.59°$ (neat), is treated with *p*-toluenesulfonyl chloride to give *(R)-(1)*; m. p. of crude product: 20–25 °C.

(S)-(5a): A solution of *(1)* (7.25 g) in ether (35 ml) is added at −35 °C to a solution prepared from CuI (6.79 g) in ether (15 ml) and CH_3Li (71.3 mmol) in ether (40 ml) according to ref.[7]. The mixture is warmed to 0 °C within 1 h and stirring continued for 12 h. After hydrolysis with saturated NH_4Cl solution, it is extracted several times with ether, and the ethereal solution is dried and distilled; yield 2.31 g (70%), *(2a)*, $\alpha_D^{25} = +19.2°$ ($c = 0.8$ g/100 ml, methanol).—HBr/glacial acetic acid (saturated) (11.6 g) is added dropwise to *(2a)* (2.12 g) at 0 °C within 5 min. After 30 min the mixture is diluted with H_2O (100 ml), neutralized with Na_2CO_3, and extracted repeatedly with ether and the ethereal phase distilled; yield 2.6 g (82%) of *(3a)/(4a)*, b. p. 72 °C/16 torr.—Elimination according to ref.[2] in *n*-pentanol with potassium pentyl oxide afforded 0.93 g of (*S*)-*(5a)*, yield 96%, $\alpha_D^{16} = -12.25°$ ($c = 6$ g/100 ml, dioxane); ref.[3]: $\alpha_D^{16} = -12.4°$.

Received: August 1, 1979 [Z 394 IE]
German version: Angew. Chem. 92, 201 (1980)
Publication delayed at authors' request

[*] Prof. Dr. U. Schmidt, Dr. J. Talbiersky, F. Bartkowiak, J. Wild
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

CAS Registry numbers:
(1), 23788-74-1; *(2a)*, 72952-75-1; *(2b)*, 61228-99-7; *(3a)*, 72952-76-2; *(3b)*, 61229-02-5; *(4a)*, 72952-77-3; *(5a)*, 30608-62-9; *(5b)*, 61229-03-6; diisopropylidene-D-mannitol, 1707-77-3; D-mannitol, 69-65-8; acetone, 67-64-1

[1] *E. Baer*, Biochem. Prep. *2*, 31 (1952).
[2] Cleavage and elimination were performed under the same conditions as the reaction of glycols to give epoxides: *B. T. Golding, D. R. Hall, S. Sakrikar*, J. Chem. Soc. Perkin Trans. I, *1973*, 1214.
[3] *J. L. Coke, R. S. Shue*, J. Org. Chem. *38*, 2210 (1973).
[4] The *(S)-(5b)* ($\alpha = -14°$) obtained by *K. Mori*, Agric. Biol. Chem. *40*, 1617 (1976), afforded in the completely stereoselective synthesis of *(S)*-massiolactone the enantiomer of the natural product in 90.5% optical purity. Assuming the reactant *(S)-(5b)* to have the same optical purity, then $\alpha = -15.5°$ can be calculated for optically pure *(S)*-1,2-epoxyheptane *(S)-(5b)*; a value of $\alpha_{21}^{D} = -15.6°$ ($c = 1.8\%$, ethanol) was measured.
[5] Reaction conditions corresponding to *G. Fouquet, M. Schlosser*, Angew. Chem. *86*, 50 (1974); Angew. Chem. Int. Ed. Engl. *13*, 82 (1974); and references cited therein.
[6] *J. J. Baldwin, A. W. Raab, K. Mensler, B. H. Arison, D. E. McClure*, J. Org. Chem. *43*, 4876 (1978).
[7] *C. R. Johnson, G. A. Dutra*, J. Am. Chem. Soc. *95*, 7777 (1973).

Rearrangement of Cyclopropyl Ketone Oximes to 5,6-Dihydro-4*H*-1,2-oxazines

By *C. N. Rentzea*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Cyclopropyl 4-methylstyryl ketone oxime *(2a)*, R = *p*-tolyl, was obtained by reaction of the *trans*-ketone *(1a)*[1] with $NH_2OH \cdot HCl$ in ethanol at 40 °C as a *Z/E* mixture[2]; m. p. 118 °C, yield 14% and m. p. 135 °C, yield 57%, respectively. Both the ketone *(1a)* and the oxime *(2a)* led, under more drastic conditions[3] (8 h reflux in ethanol; *(1a)* or *(2a)*: $NH_2OH \cdot HCl = 1:1.5$), to the same *trans*-3-(4-methylstyryl)-5,6-dihydro-4*H*-1,2-oxazine *(5a)*[2] in 41% yield. Further examples are to be found in Table 1.

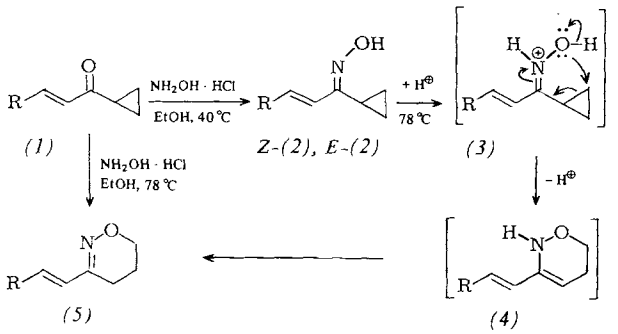


Table 1. Physical data of the compounds *(5a-k)*[2] obtained from the ketones *(1a-k)*[1]. IR in KBr, ^{1}H-NMR in $CDCl_3$, TMS as internal standard.

(5a), m. p. 199 °C (from acetone); IR: 1545, 1225, 960, 800 cm^{-1}; ^{1}H-NMR: $\delta = 2.06-2.2$ (m, 2H), 2.33 (s, 3H), 2.84–2.95 (t, 2H), 4.0–4.11 (t, 2H), 6.77–6.86 (d, 1H), 7.11–7.2 (d, 2H), 7.31–7.42 (d, 1H), 7.37–7.46 (d, 2H); ^{13}C-NMR ($CDCl_3$): $\delta = 143.63$, 139.42, 136.58, 133.50, 129.63 (×2), 127.36 (×2), 115.07, 62.71, 28.45, 21.28, 16.96

(5b), R = C_6H_5; m. p. 164 °C (from acetone); yield 42%; ^{1}H-NMR: $\delta = 2.0-2.36$ (m, 2H), 2.83–3.1 (t, 2H), 4.0–4.25 (t, 2H), 6.8–7.02 (d, 1H), 7.3–7.7 (m, 6H)

(5c), R = 4-$(C_6H_5)C_6H_4$; m. p. 196 °C (from acetonitrile); yield 45%; ^{1}H-NMR: $\delta = 1.88-2.33$ (m, 2H), 2.55–2.96 (t, 2H), 3.70–4.10 (t, 2H), 6.52–6.38 (d, 1H), 7.05–7.55 (m, 10H)

(5d), R = 1-$C_{10}H_7$; m. p. 153 °C (from acetic acid); yield 41%; IR: 1540, 1225, 962, 778 cm^{-1}; ^{1}H-NMR: $\delta = 2.13-2.26$ (m, 2H), 3.0–3.08 (t, 2H), 4.08–4.17 (t, 2H), 7.42–7.57 (m, 4H), 7.62–7.75 (d, 1H), 7.77–7.91 (m, 3H), 8.06–8.15 (d, 1H)

(5e), R = 4-ClC_6H_4; m. p. 171 °C (from acetone); yield 30%; IR: 1540, 1232, 960, 805 cm^{-1}; ^{1}H-NMR: $\delta = 1.95-2.4$ (m, 2H), 2.73–3.1 (t, 2H), 3.88–4.25 (t, 2H), 6.55–6.9 (d, 1H), 7.10–7.50 (m, 5H)

(5f), R = 4-BrC_6H_4; m. p. 192 °C (from acetone); yield 40%; IR: 1542, 1230, 963, 802 cm^{-1}; ^{1}H-NMR: $\delta = 2.0-2.42$ (m, 2H), 2.75–3.1 (t, 2H), 3.84–4.18 (t, 2H), 6.48–6.82 (d, 1H), 7.10–7.45 (m, 5H)

(5g), R = 2,4-$Cl_2C_6H_3$; m. p. 150 °C (from acetone); yield 40%; IR: 1550, 1220, 960, 810 cm^{-1}; ^{1}H-NMR: $\delta = 1.95-2.5$ (m, 2H), 2.80–3.20 (t, 2H), 3.9–4.35 (t, 2H), 6.9–7.48 (m, 4H), 7.55–7.85 (d, 1H)

(5h), R = 3,4-$Cl_2C_6H_3$; m. p. 175 °C (from acetonitrile); yield 47%; ^{1}H-NMR: $\delta = 2.0-2.58$ (m, 2H), 2.81–3.18 (t, 2H), 3.98–4.38 (t, 2H), 6.62–7.0 (d, 1H), 7.22–7.76 (m, 4H)

(5i), R = 4-$(F_3C)C_6H_4$; m. p. 196 °C (from acetone); yield 47%; ^{1}H-NMR: $\delta = 1.86-2.35$ (m, 2H), 2.54–2.96 (t, 2H), 3.7–4.16 (t, 2H), 6.51–6.9 (d, 1H), 7.12–7.52 (d, 5H)

(5j), R = 4-$(O_2N)C_6H_4$; m. p. 216 °C (from acetic acid); yield 40%; IR: 1532, 1340, 975, 833 cm^{-1}; ^{1}H-NMR: $\delta = 2.0-2.48$ (m, 2H), 2.7–3.1 (t, 2H), 3.84–4.2 (t, 2H), 6.52–6.92 (d, 1H), 7.19–7.4 (d, 1H), 7.5–7.6 (d, 2H), 7.88–8.15 (d, 2H)

(5k), R = 4-$(CH_3O)C_6H_4$; m. p. 169 °C (from acetone) yield 29%; ^{1}H-NMR: $\delta = 1.95-2.45$ (m, 2H), 2.7–3.12 (t, 2H), 3.78 (s, 3H), 3.85–4.28 (t, 2H), 6.76–7.64 (m, 6H)

Like the Cloke rearrangement[4] of *(6)* to *(7)*, this novel rearrangement of cyclopropyl ketone oxime *(2)* to oxazines *(5)* appears to involve protonation of the nitrogen atom.



The cyclization of *(3)* to *(4)* is probably an example of 6-*endo-tet* ring closure rarely observed so far.

Received: November 6, 1979 [Z 395 IE]
German version: Angew. Chem. *92*, 195 (1980)

CAS Registry numbers:
(1a), 72881-67-5; *(1b)*, 63261-41-6; *(1c)*, 72881-68-6; *(1d)*, 72881-69-7; *(1e)*, 72881-70-0; *(1f)*, 72881-71-1; *(1g)*, 72881-72-2; *(1h)*, 72881-73-3; *(1i)*, 72881-74-4; *(1j)*, 63261-42-7; *(1k)*, 72881-75-5; (E)-*(2a)*, 72881-76-6; (Z)-*(2a)*, 72881-77-7; (E)-*(2b)*, 72881-78-8; (Z)-*(2b)*, 72881-79-9; (E)-*(2c)*, 72881-80-2; (Z)-*(2c)*, 72881-81-3; (E)-*(2d)*, 72881-82-4; (Z)-*(2d)*, 72881-83-5; (E)-*(2e)*, 72881-84-6; (Z)-*(2e)*, 72881-85-7; (E)-*(2f)*, 72881-86-8; (Z)-*(2f)*, 72881-87-9; (E)-*(2g)*, 72881-88-0; (Z)-*(2g)*, 72881-89-1; (E)-*(2h)*, 72881-90-4; (Z)-*(2h)*, 72881-91-5; (E)-*(2i)*, 72881-92-6; (Z)-*(2i)*, 72881-93-7; (E)-*(2j)*, 72881-94-8; (Z)-*(2j)*, 72881-95-9; (E)-*(2k)*, 72881-96-0; (Z)-*(2k)*, 72881-97-1; *(5a)*, 72881-98-2; *(5b)*, 72881-99-3; *(5c)*, 72882-00-9; *(5d)*, 72882-01-0; *(5e)*, 72882-02-1; *(5f)*, 72882-03-2; *(5g)*, 72882-04-3; *(5h)*, 72882-05-4; *(5i)*, 72882-06-5; *(5j)*, 72882-07-6; *(5k)*, 72882-08-7

[1] *S. C. Bunce, H. J. Dorsman, F. D. Popp*, J. Chem. Soc. *1963*, 303; *G. D. Diana, U. J. Salvador, E. S. Zalay, R. E. Johnson, J. C. Collins, D. Johnson, W. B. Hinshaw, R. R. Lorenz, W. H. Thielking, F. Pancic*, J. Med. Chem. *20*, 750 (1977).
[2] All the new compounds gave correct analytical values and molecular weights.
[3] *K. v. Auwers*, Ber. Dtsch. Chem. Ges. *62*, 1320 (1929); *K. v. Auwers, H. Brink*, Justus Liebigs Ann. Chem. *493*, 218 (1932).
[4] *J. B. Cloke*, J. Am. Chem. Soc. *51*, 1174 (1929); *R. V. Stevens, M. C. Ellis, M. P. Westland, ibid. 90*, 5576 (1968).
[5] *J. E. Baldwin*, J. Chem. Soc. Chem. Commun. *1976*, 734; *P. A. Wade*, J. Org. Chem. *43*, 2020 (1978).

Synthesis of Carbocyclic and Heterocyclic π-Electron Systems with Pentafulvenoid Chloroformamidinium Chlorides

By *Klaus Hafner* and *Hans-Peter Krimmer*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

In 1960, *Eilingsfeld, Seefelder*, and *Weidinger*[1] first reported the preparation and reactions of "carbamide chlorides" (chloroformamidinium chlorides) which have proved

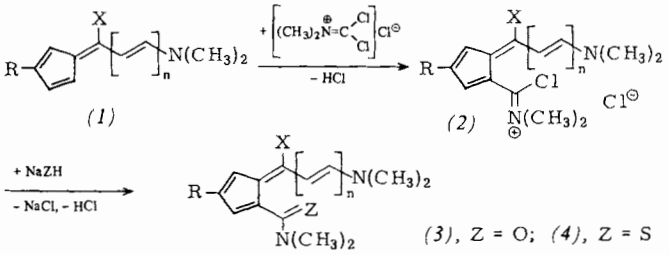
[*] Dr. C. N. Rentzea
BASF-Aktiengesellschaft, Hauptlaboratorium
D-6700 Ludwigshafen (Germany)

[*] Prof. Dr. K. Hafner, Dipl.-Ing. H.-P. Krimmer
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

their value as reactive synthons in the past two decades[2]. We have now found a facile method for the preparation of pentafulvenoid chloroformamidinium chlorides, which permit surprisingly easy syntheses of interesting carbo- and heterocyclic π-electron systems.

By analogy with the formylation of dialkylaminofulvenes of type *(1)*[3], their reaction with dichloromethylene(dimethyl)ammonium chloride[2] gives the cyclically vinylogous chloroformamidinium chlorides *(2)* (yellow hygroscopic crystals; yield 50–70%), which display pronounced reactivity towards numerous nucleophilic partners. Structural proof comes, *inter alia*, from their hydrolysis or reaction with sodium hydrogen sulfide to give amides of carboxylic and thiocarboxylic acids *(3)* and *(4)* (yellow crystals; yield 35–90%).

The 1,4- and 1,6-bifunctional fulvenes *(2)* react with suitable nucleophiles *via* cyclization thus *(2d)* reacts with ammonia to give 5-*tert*-butyl-1,3-bis(dimethylamino)-2-azapentalene *(5)*[4] in 31% yield (blue-violet needles), while 6-*tert*-butyl-1,4-bis(dimethylamino)-2*H*-cyclopenta[*d*]pyridazine *(6)* (dark green needles, yield 51%) is formed with hydrazine. The reaction of *(2d)* with sodium cyclopentadienide and its *tert*-butyl derivative gives the 4,8-bis(dimethylamino)-*s*-indacenes *(7a)* and *(7b)* (green and golden yellow platelets with metallic sheen; 30 and 38% yield, respectively) as heat- and



	R	X	*n*
a	H	H	0
b	$(CH_3)_3C$	H	0
c	H	$(CH_3)_2N$	0
d	$(CH_3)_3C$	$(CH_3)_2N$	0
e	H	H	1

air-stable derivatives of the parent compound so far detected only in solution at low temperature[5].

Like *(2d)*, compound *(2e)* also reacts with ammonia to give the stable 4-(dimethylamino)-5-azaazulene *(8)* (blood red platelets; yield 54%)[6].

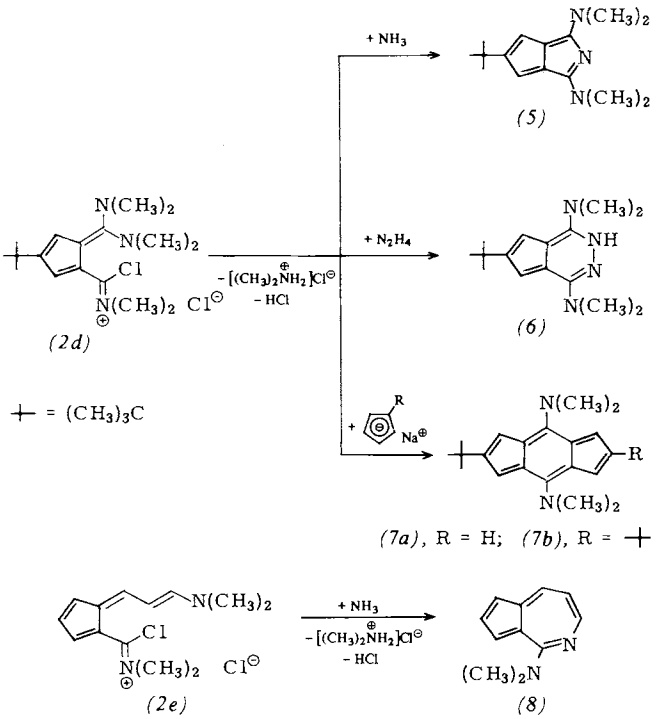
Table 1 lists physical data of some new compounds.

Table 1. Selected physical data of compounds *(2a)*, *(3a–d)*, *(4a)*, *(5)*, *(6)*, *(7a)*, *(7b)*, and *(8)*.

Cpd.	M.p. [°C]	UV (Dioxane) λ [nm] (log ε)	^{1}H-NMR($CDCl_3$), δ-values
(2a)	173	284 (4.18) 386 (4.66) [a]	3.66 (s, 3H, 6-N CH_3), 3.72 (s, 3H, 6-N CH_3), 3.87 (s, 6H, CCl $N(CH_3)_2$), 6.90 (m, 2H, H-3,4), 7.73 (m, 1H, H-2), 8.42 (s, 1H, H-6) [d]
(3a)	122	239 (3.99) 340 (4.44)	3.13 (s, 6H, 6-$N(CH_3)_2$), 3.27 (s, 6H, CO $N(CH_3)_2$), 6.38 (dd, J_1 = 4.8 Hz, J_2 = 3.2 Hz, 1H, H-3), 6.52 (dd, J_1 = 3.2 Hz, J_2 = 1.6 Hz, 1H, H-2), 6.71 (dd, J_1 = 4.8 Hz, J_2 = 1.6 Hz, 1H, H-4), 8.02 (s, 1H, H-6)
(3b)	91	243 (4.06) 342 (4.41)	1.23 (s, 9H, $C(CH_3)_3$), 3.13 (s, 6H, 6-$N(CH_3)_2$), 3.26 (s, 6H, CO $N(CH_3)_2$), 6.43 (d, J = 1.6 Hz, 1H, H-4), 6.51 (d, J = 1.6 Hz, 1H, H-2), 7.82 (s, 1H, H-6)
(3c)	121	253 (4.14) 356 (4.27)	3.03 (s, 12H, 6-$N(CH_3)_2$), 3.16 (s, 6H, CO $N(CH_3)_2$), 6.14 (dd, J_1 = 4.0 Hz, J_2 = 3.1 Hz, 1H, H-3), 6.28 (dd, J_1 = 4.0 Hz, J_2 = 1.9 Hz, 1H, H-4), 6.52 (dd, J_1 = 3.1 Hz, J_2 = 1.9 Hz, 1H, H-2)
(3d)	236	255 (4.18) 363 (4.25)	1.23 (s, 9H, $C(CH_3)_3$), 2.98 (s, 12H, 6-$N(CH_3)_2$), 3.10 (s, 6H, CO $N(CH_3)_2$), 6.03 (d, J = 2.3 Hz, 1H, H-4), 6.43 (d, J = 2.3 Hz, 1H, H-2)
(4a)	124	265 (4.24) 304 (4.38) 417 (3.47)	3.27 (s, 6H, 6-$N(CH_3)_2$), 3.30–3.60 (broad s, 6H, CS $N(CH_3)_2$), 6.26 (dd, J_1 = 3.1 Hz, J_2 = 1.7 Hz, 1H, H-2), 6.32 (dd, J_1 = 4.6 Hz, J_2 = 3.1 Hz, 1H, H-3), 6.69 (dd, J_1 = 4.6 Hz, J_2 = 1.7 Hz, 1H, H-4), 8.04 (s, 1H, H-6)
(5)	229	225 (4.35) 298 (4.32) 308 (4.32) 388 (3.11) 563 (2.71) [b]	1.29 (s, 9H, $C(CH_3)_3$), 3.17 (s, 6H, 1,3-N CH_3), 3.29 (s, 6H, 1,3-N CH_3), 5.98 (s, 2H, H-4,6)
(6)	152	249 (4.49) 298sh (3.90) 592 (1.08) [b]	1.31 (s, 9H, $C(CH_3)_3$), 3.11 (s, 12H, 1,4-$N(CH_3)_2$), 6.43 (s, 2H, H-5,7), 11.35 (s, 1H, NH, vanishes with D_2O)
(7a)	199	284 (4.63) 410 (4.28) 471 (4.21) 693 (2.46)	1.20 (s, 9H, $C(CH_3)_3$), 3.40 (s, 12H, 4,8-$N(CH_3)_2$), 5.93 (t, J = 4.0 Hz, 1H, H-6), 6.36 (s, 2H, H-1,3), 6.45 (d, J = 4.0 Hz, 2H, H-5,7)
(7b)	265	288 (4.34) 412 (4.00) 476 (3.91) 720 (2.12)	1.18 (s, 18H, 2,6-$C(CH_3)_3$), 3.36 (s, 12H, 4,8-$N(CH_3)_2$), 6.27 (s, 4H, H-1,3,5,7)
(8)	73	221 (3.99) 267 (4.28) 306 (4.29) 396 (3.34) 410 (3.31) 492 (3.16) [c]	3.42 (s, 6H,$N(CH_3)_2$), 6.30 (dd, J_1 = 7.7 Hz, J_2 = 6.2 Hz; 1H, H-7), 7.04 (dd, J_1 = 3.8 Hz, J_2 = 1.7 Hz, 1H, H-3), 7.10 (m, 1H, H-1), 7.27 (dd, J_1 = 4.0 Hz, J_2 = 3.8 Hz, 1H, H-2), 7.90 (d, J = 7.7 Hz, 1H, H-8), 8.04 (dd, J_1 = 6.2 Hz, J_2 = 1.7 Hz, 1H, H-6)

[a] In CH_3CN. [b] In CH_2Cl_2. [c] In *n*-hexane. [d] In [D_6]-acetone.

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0303-0200 $ 02.50/0



Procedure

(2d): A suspension of dichloromethylene(dimethyl)ammonium chloride in CH_2Cl_2 (20 ml) is added dropwise to a stirred solution of *(1d)*[7] (2.2 g, 20 mmol) and triethylamine (2.0 g, 20 mmol) in CH_2Cl_2 (100 ml) at 0 °C. The mixture is then refluxed for 2 h. After cooling to room temperature the solution can be used directly for preparation of *(5)*, *(6)*, and *(7)*. Compound *(2d)* can be isolated as perchlorate.

(5): A slow stream of dry ammonia is passed into the solution of *(2d)* at 0 °C for 30 min. After 2 h, saturated aqueous NH_4Cl solution (200 ml) is added and the mixture extracted with CH_2Cl_2 (3 × 50 ml). On removal of the solvent the residue is chromatographed on Al_2O_3 B IV with ethyl acetate; 770 mg (31%) of *(5)* is isolated from the first violet zone.

(6): Anhydrous hydrazine (320 mg, 10 mmol) is added at room temperature to a solution of *(2d)* and the mixture refluxed for 2 h and worked up as *(5)*. The first green zone gives 1.33 g (51%) of *(6)*.

(7a) and *(7b):* A 2.69 M solution of sodium cyclopentadienide (3.7 ml, 10 mmol) in tetrahydrofuran is added dropwise to a solution of *(2d)*. After refluxing for 2 h the product is worked up as *(5)*. Yield 880 mg (30%) *(7a)*. Compound *(7b)* is obtained analogously with sodium *tert*-butylcyclopentadienide.

(8): A suspension of dichloromethylene(dimethyl)ammonium chloride (1.6 g, 10 mmol) in CH_2Cl_2 (20 ml) is added dropwise to a stirred solution of *(1e)*[3] (1.5 g, 10 mmol) and triethylamine (2.0 g, 20 mmol) in CH_2Cl_2 (100 ml) at 0 °C under N_2. After stirring for 2 h at 0 °C, dry ammonia is passed into the mixture for 30 min and the product is worked up as *(5)*; eluent: hexane/ether (4:1). The first red zone affords 930 mg (54%) of *(8)*.

Received: November 29, 1979 [Z 396 IE]
German version: Angew. Chem. *92*, 202 (1980)

CAS Registry numbers:
(1a), 696-68-4; *(1b)*, 72866-30-9; *(1c)*, 703-24-2; *(1d)*, 72866-31-0; *(1e)*, 2481-72-3; *(2a)*, 72866-32-1; *(2b)*, 72866-33-2; *(2c)*, 72866-34-3; *(2d)*, 72866-36-5; *(2e)*, 72866-37-6; *(3a)*, 72866-38-7; *(3b)*, 72866-39-8; *(3c)*, 72866-40-1; *(3d)*, 72881-43-7; *(4a)*, 72866-41-2; *(5)*, 72866-42-3; *(6)*, 72866-43-4; *(7a)*, 72866-44-5; *(7b)*, 72881-44-8; *(8)*, 72866-45-6; ammonia, 7664-41-7; hydrazine, 302-01-2; sodium-cyclopentadienide, 4984-82-1; sodium *tert*-butylcyclopentadienide, 55562-84-0.

[1] *H. Eilingsfeld, M. Seefelder, H. Weidinger,* Angew. Chem. *72*, 836 (1960); *H. Eilingsfeld, G. Neubauer, M. Seefelder, H. Weidinger,* Chem. Ber. *97*, 1232 (1964).

[2] See *H. G. Viehe, Z. Janousek,* Angew. Chem. *85*, 837 (1973); Angew. Chem. Int. Ed. Engl. *12*, 806 (1973); *Z. Janousek, H. G. Viehe* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry. Part I. Wiley, New York 1976, p. 343.

[3] *K. Hafner, K. H. Häfner, C. König, M. Kreuder, G. Ploss, G. Schulz, E. Sturm, K. H. Vöpel,* Angew. Chem. *75*, 35 (1963); Angew. Chem. Int. Ed. Engl. *2*, 123 (1963); *K. Hafner,* Pure Appl. Chem., Suppl. *2*, 1 (1971), and further references cited therein.

[4] *K. Hafner, H.-G. Kläs, M. C. Böhm,* Tetrahedron Lett. *1980*, 41; *(5)* can also be prepared in 75% yield from lithium *tert*-butylcyclopentadienide and 1,3-dichloro-*N,N,N',N'*-tetramethyl-2-azatrimethinecyanine chloride; *H.-G. Kläs,* Diplomarbeit, Technische Hochschule Darmstadt 1979; cf. also *H.-J. Gais, K. Hafner,* Tetrahedron Lett. *1974*, 771.

[5] *K. Hafner,* Angew. Chem. *75*, 1041 (1963); Angew. Chem. Int. Ed. Engl. *3*, 165 (1964); *E. Sturm,* Dissertation, Universität München 1965.

[6] *(8)* is obtained in 28% yield by reaction of the 5-azaazulen-4-one/phosphoryl chloride complex with dimethylamine; *M. Gold,* Dissertation, Technische Hochschule Darmstadt 1979.

[7] *(1d)* is obtained from lithium *tert*-butylcyclopentadienide by analogy with 6,6-bis(dimethylamino)fulvene (*K. Hafner, G. Schulz, K. Wagner,* Justus Liebigs Ann. Chem. *678*, 39 (1964)).

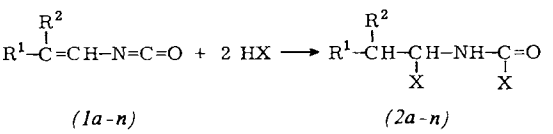
Synthesis of α-Haloalkylcarbamoyl Halides

By *Karl-Heinz König, Christian Reitel,* and *Karl-Heinz Feuerherd*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Ever since vinyl isocyanate[1] was first synthesized there have been repeated reports on the polymerizability of α,β-unsaturated isocyanates and their sensitivity to moisture, acids, and bases[2]. Since these compounds are readily accessible on an industrial scale[3] we have been engaged in a detailed examination of their chemical properties.

We have found that α,β-unsaturated isocyanates *(1)* can react with hydrogen halides at low temperature without polymerization to give α-haloalkylcarbamoyl halides in very good yields (Method A; Table 1)[4]. Remarkably, some of these compounds can be stored for several weeks with cooling.



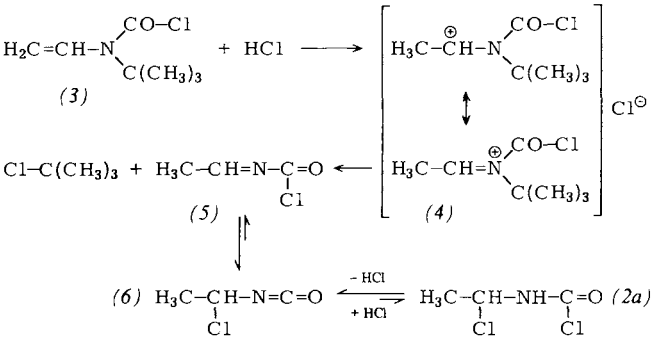
(1a-n) *(2a-n)*

Table 1. Overview of the α-haloalkylcarbamoyl halides *(2)*.

	R^1	R^2	X
a, b, c	H	H	Cl, Br, I
d, e, f	CH_3	H	Cl, Br, I
g, h, i	C_2H_5	H	Cl, Br, I
j	C_2H_5	CH_3	Br
k	$CH(CH_3)_2$	H	Cl
l	*n*-C_6H_{13}	H	Br
m	$(CH_2)_5$		Cl
n	C_6H_5	CH_3	Br

[*] Dr. K.-H. König [+], Dr. Ch. Reitel, Dr. K.-H. Feuerherd
BASF Aktiengesellschaft, Hauptlaboratorium, WHW
D-6700 Ludwigshafen (Germany)
[+] Author to whom correspondence should be addressed.

Moreover, we have found a further entry to *(2)* (Method B) which avoids dealing with isocyanates *(1)*. Hydrogen chloride is allowed to react with *N*-(1-alkenyl)-*N*-alkylcarbamoyl chlorides[5] of type *(3)*. Thus, for example, *N-tert*-butyl-*N*-vinylcarbamoyl chloride *(3)* reacts with hydrogen chloride at 0 °C with elimination of *tert*-butyl chloride to give α-chloroethylcarbamoyl chloride *(2a)*[6].



That the reaction involves attack by hydrogen chloride at the vinyl group with intermediary formation of *(4)* follows from the observation that *N-tert*-buyl-*N*-chloromethylcarbamoyl chloride is not cleaved. The driving force would appear to lie in the cleavage of *tert*-butyl chloride with intermediary formation of *N*-ethylidenechloroformamide *(5)*, which should be present in equilibrium[7] with α-chloroethyl isocyanate *(6)*. Both *(5)* as well as *(6)* can form the end product *(2a)* with hydrogen chloride.

On storage at room temperature some of the solid derivatives *(2)* eventually lose hydrogen chloride and begin to liquefy without any appreciable amount of polymeric products being formed. Other than in the case of the well-known alkylcarbamoyl chlorides, the equilibrium between *(2a)* and *(6)* already lies well on the side of *(6)* at room temperature. The form *(5)*, already postulated in the case of α-chlorobenzyl isocyanates[7c], could be detected in small amounts in equilibrium with *(6)* by IR spectroscopy.

The new α-haloalkylcarbamoyl halides *(2)* and α-haloalkyl isocyanates *(6)* are highly reactive bifunctional synthetic building blocks. Their structure was confirmed by IR and NMR spectroscopy.

Procedure[4a,6]

(2a), Method A: A mixture of *(1a)* (69 g, 1 mol) and CCl_4 (400 ml) is treated with 73 g (2 mol) of hydrogen chloride at −20 °C. After an additional 15 minutes' stirring the crystalline product is filtered off under N_2; yield 137 g *(2a)* (96%); m. p. 21 °C (dec.); ^{1}H-NMR (CCl_4): $\delta = 1.8$ (3H, d), 5.8 (1H, q), 7.5 (1H, broad).

(2a), Method B: *(3)* (161.5 g, 1 mol) is treated with 75 g (2.05 mol) of hydrogen chloride within 1 h at 0 °C. The mixture is stirred for a further 15 minutes, excess hydrogen chloride is removed by passage of N_2, *tert*-butyl chloride is drawn off at reduced pressure, and the residue is crystallized from CCl_4; yield 135 g *(2a)* (95%); m. p. 20–21 °C (dec.).

Received: December 11, 1979 [Z 398 IE]
German version: Angew. Chem. *92*, 197 (1980)

CAS Registry numbers:
(1a), 3555-94-0; *(1d)*, 4737-18-2; *(1g)*, 40352-23-6; *(1j)*, 69668-39-9; *(1k)*, 69668-36-6; *(1l)*, 69668-38-8; *(1m)*, 69668-42-4; *(1n)*, 69668-44-6; *(2a)*, 70008-75-2; *(2b)*, 72866-46-7; *(2c)*, 72866-47-8; *(2d)*, 72866-48-9; *(2e)*, 72866-49-0; *(2f)*, 72866-50-3; *(2g)*, 72866-51-4; *(2h)*, 72866-52-5; *(2i)*, 72866-53-6; *(2j)*, 72866-54-7; *(2k)*, 72866-55-8; *(2l)*, 72866-56-9; *(2m)*, 72866-57-0; *(2n)*, 72866-58-1; *(3)*, 28705-47-7; *(5)*, 72866-59-2; *(6)*, 72866-60-5; *tert*-butyl chloride, 507-20-0

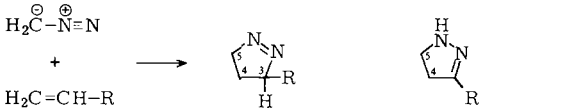
[1] *D. D. Coffman*, US-Pat. 2334476 (1943).
[2] a) *R. Hart*, Bull. Soc. Chim. Belg. *65*, 291 (1956); b) *K.-H. König, H. Pommer*, DBP 1232951 (1967), BASF.
[3] *K.-H. König, Ch. Reitel, D. Mangold, K.-H. Feuerherd, H.-G. Oeser*, Angew. Chem. *91*, 334 (1979); Angew. Chem. Int. Ed. Engl. *18*, 319 (1979).
[4] a) *K.-H. König, Ch. Reitel*, DOS 2732284 (1979), BASF; b) *K.-H. König, K.-H. Feuerherd*, DOS 2830969 (1980), BASF.
[5] *H. Kiefer*, Synthesis *1972*, 39.
[6] *K.-H. König, Ch. Reitel, D. Mangold*, DOS 2741980 (1979), BASF.
[7] a) *L. J. Samaraj, O. W. Wischnewskij, G. J. Derkatsch*, Angew. Chem. *80*, 620 (1968); Angew. Chem. Int. Ed. Engl. *7*, 621 (1968); b) *L. J. Samaraj et al.*, Zh. Org. Khim. *12*, 547 (1976); c) *H. Holtschmidt*, Angew. Chem. *74*, 848 (1962); Angew. Chem. Int. Ed. Engl. *1*, 632 (1962).

Cycloadditions of Diazoalkanes to 1-Alkenes

By *Rolf Huisgen, Johannes Koszinowski, Akihiro Ohta,* and *Reinhard Schiffer*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The successful MO perturbation treatment of the reactivity and regioselectivity of concerted cycloadditions bestows special importance on simple models. Disregarding angularly strained cycloalkenes and bicycloalkenes, very little has been reported about 1,3-dipolar cycloadditions of diazoalkanes to non-conjugated alkenes; the reasons are the slow rate of reaction and the sensitivity of the adducts. The report that 4-substituted pyrazolines are formed on reaction of diazomethane and 1-alkenes[1] is incorrect.



(1), R = H
(2), R = C_4H_9
(3), R = $CH_2C_6H_5$
(4), R = C_4H_9
(5), R = $CH_2C_6H_5$

Azzarello[2] obtained *ca.* 10% crude pyrazoline on passing ethylene into an ethereal solution of diazomethane. We allowed ethylene to react (at a pressure of 50 at) with 0.29 M diazomethane in ether for 24 h at 20 °C in a glass vessel in an autoclave; after removal of ether, GC analysis (anisole as standard) showed 95% 1-pyrazoline *(1)*. This method provides the best access to *(1)*, which can be obtained in pure form on subsequent distillation[3].

1-Hexene reacts ninety times slower than ethylene with diazomethane at 25 °C[4]. A solution of diazomethane (0.63 M) in 1-hexene turned colorless after 24 days at 5 °C and yielded after distillation 50% *(2)*; the area ratio of the downfield and upfield multiplets in the ^{1}H-NMR spectrum approaches 3:11, whereas the isomeric 4-butyl-1-pyrazoline would require 4:10. On treatment with hydrochloric acid, *(2)* was tautomerized to the 2-pyrazolines *(4)* and *(6)*, which were dehydrogenated by sulfur at 175 °C to give 3-butylpyrazole *(12)* in 85% yield. *(12)* was identified by its ^{1}H-NMR spectrum (Table 1) and by permanganate oxidation to 3-pyrazolecarboxylic acid.

[*] Prof. Dr. R. Huisgen, Dipl.-Chem. J. Koszinowski
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

Prof. Dr. A. Ohta
Tokyo College of Pharmacy
1432-1 Horinouchi, Hachioji, Tokyo 192-03 (Japan)

Dr. R. Schiffer
BASF Aktiengesellschaft, D-6700 Ludwigshafen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0202 $ 02.50/0

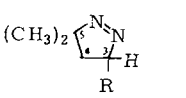
Table 1. Some physical data of the pyrazolines (^{1}H-NMR spectra in $CDCl_3$, δ values).

(1), b. p. 61 °C/80 torr; IR: (N=N) 1545 cm^{-1}; $n_D^{25} = 1.4380$
(2), b. p. 77 °C/9 torr; NMR: 0.7–2.3 (m, 11 H), 4.05–4.65 (m, 3H)
(3), IR: (N=N) 1545 cm^{-1}; NMR: 0.7–2.5 (m, 4-H_2), 2.81 and 3.25 (AB of C_6H_5-CH_2, $J_{gem} = 14.0$ Hz, split by 3-H with $J = 7.5$ and 6.0 Hz), 4.0–4.9 (m, 3-H and 5-H_2), 7.17 (s, C_6H_5)
(5)·HCl, NMR: 2.98 and 3.68 (AA'BB' in 2 pseudo-t with $J = 7.5$ Hz, 4- and 5-H_2), 3.82 (s, benzyl-CH_2), 7.83 (s, C_6H_5)
(6), b. p. 95 °C/11 torr; IR: (NH) 3290 cm^{-1}; NMR: 4.80 (s, broad, NH), 6.73 (s, 3-H); in a mixture with *(4)*
(7)·HCl, m. p. 146–147 °C; IR: (H-N$^{\oplus}$) 2498, (C=N) 1519 cm^{-1}; NMR (pyridine): 7.59 and 7.44 (dd, $J_{gem} = 4.0$ Hz, $J_{4,5} = 1.8$ and 1.5 Hz, 4-H_2), 7.16 (center of the AB of the benzyl protons)
(8), m. p. −10 °C; IR: (N=N) 1605 cm^{-1}; NMR: 0.92 and 1.50 (2 dd, AB of the 4-H_2 with $J_{gem} = 12.0$ Hz and $J_{3,4} = 8.0$ Hz), 1.07 and 1.23 (2 s, 5-$(CH_3)_2$), 2.77 and 3.30 (2 dd, AB of the benzyl-CH_2, $J_{gem} = 14.0$ Hz, $J_{A,3} = 7.5$ Hz, $J_{B,3} = 5.5$ Hz), 4.47 (m, 3-H)
(9), b. p. 30 °C/0.02 torr; NMR: 0.90 and 1.50 (2 dd, AB of the benzyl-CH_2, $J_{gem} = 12.5$ Hz, $J_{3,4} = 8.0$ Hz), 1.21 and 1.48 (2 s, 5-$(CH_3)_2$).
(10)·HCl, b. p. 151–153 °C; IR: (H-N$^{\oplus}$) 2500, (C=N) 1625 cm^{-1}; NMR: 1.62 (s, 5-$(CH_3)_2$), 2.85 (s, 4-H_2), 3.88 (s, benzyl-CH_2), 7.26 (s, C_6H_5)
(11), b. p. 130 °C/0.001 torr; IR: (NH) 3330, 3380; (C=O) 1700 cm^{-1}; NMR: 6.38 (s, NH)
(12), 127 °C/10 torr, IR: (NH) 3170 cm^{-1}; NMR: 6.08 and 7.47 (2 d, $J = 1.7$ Hz, 4-H and 5-H), 12.66 (s, NH)
(13), b. p. 112 °C/0.001 torr; IR: (NH) 3090, 3140, 3170; (C=O) 1715 cm^{-1}; NMR: 6.60 (s, 4-H), 12.38 (s, NH)

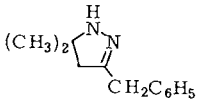
A 0.90 M solution of diazomethane in allylbenzene afforded 91% *(3)* within four days at 5 °C. The diastereotopy of the α-benzyl protons and the ratio of the ring protons in the ^{1}H-NMR spectrum (Table 1) confirm substitution in position 3. On treatment with hydrogen chloride in $CHCl_3$, *(3)* is converted into the hydrochlorides of the 2-pyrazolines *(5)* and *(7)*; in *(5)* the benzyl protons are isochronous, in *(7)* anisochronous.



(6), R = C_4H_9
(7), R = $CH_2C_6H_5$



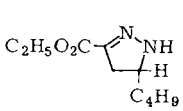
(8), R = $CH_2C_6H_5$
(9), R = CH_3



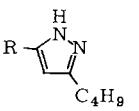
(10)

In the reaction with allylbenzene *ca.* 10% of the structurally isomeric cycloadduct could have eluded detection—in the reaction with 1-hexene even more. On the other hand, the fully resolved ^{1}H-NMR spectrum of the adduct *(8)* from 2-diazopropane and allylbenzene (red solution decolorized after 4 h at 5 °C) guaranteed freedom from isomers within more narrow limits. The anisochronism of the protons of the 5-methyl groups, of the methylene protons at C-4, and of the α-benzyl protons (Table 1) confirms the 3-position of the benzyl. The hydrochloride of the 2-pyrazoline *(10)* obtained in quantitative yield on treatment of *(8)* with HCl shows the expected symmetry by exhibiting singlets in the NMR spectrum.

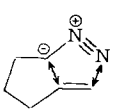
2-Diazopropane was condensed onto propene; decolorization occurred after 3 h at 5 °C. The trimethyl-1-pyrazoline *(9)* could not be completely separated from the acetone azine; the latter arose from the competing decomposition of 2-diazopropane. The NMR spectrum unequivocally confirmed the structure *(9)*.



(11)



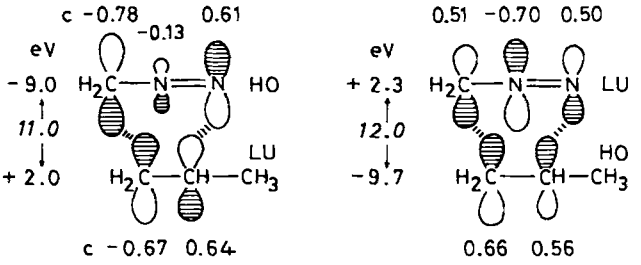
(12), R = H
(13), R = $CO_2C_2H_5$



(14)

The same direction of addition is observed in the case of ethyl diazoacetate. After 30 days' heating with 1-hexene at 70 °C the oily 2-pyrazoline *(11)* could be isolated in 56% yield and was aromatized with chloranil to *(13)*; the structure and composition was confirmed by the NMR spectrum and by oxidation to 3,5-pyrazoledicarboxylic acid.

As in many concerted cycloadditions the orientation rules are not rigid. The intramolecular reaction in *(14)* (as those producing larger rings) is effected in the opposite direction[5] compared with the above examples; the electronically "normal" addition would lead to a strained ring in the case of *(14)*.



Scheme 1

Scheme 1 contains atomic orbital coefficients calculated by CNDO/2 as well as values for HOMO and LUMO energies which are based on ionization potentials and electron affinities[6]. The MO perturbation treatment of the frontier orbital interaction of diazomethane and propene shows that the formation of 3-methyl-1-pyrazoline is slightly favored. The switchover from 3- to 4-substitution is presumably in the region of the enol ethers (and alkoxyacetylenes) for diazomethane and diazoacetic acid ester[7]. In the case of ethyl diazoacetate, which cycloadds to enamines[7] and ynamines[8] to give 4-aminopyrazolines and pyrazoles, respectively, the bidirectionality has been established more convincingly than in the case of diazomethane.

Received: December 17, 1979 [Z 399 IE]
German version: Angew. Chem. *92*, 198 (1980)

CAS Registry numbers:
(1), 2721-43-9; *(2)*, 72893-91-5; *(3)*, 72893-92-6; *(4)*, 72893-93-7; *(5)*, 72893-94-8; *(6)*, 72893-95-9; *(7)*, 72893-96-0; *(8)*, 72893-97-1; *(9)*, 2721-30-4; *(10)*, 72893-98-7; *(11)*, 72893-99-3; *(12)*, 28998-67-6; *(13)*, 72894-00-9; diazomethane, 334-88-3; ethylene, 74-85-1; 1-hexene, 592-41-6; allylbenzene, 300-57-2; 2-diazopropane, 2684-60-8

[1] *A. Padwa, Hao Ku*, Tetrahedron Lett. *1979*, 4425.
[2] *E. Azzarello*, Gazz. Chim. Ital. *36*, I, 618 (1906).
[3] Previously, oxidation of pyrazolidine with Ag_2O: *R. J. Crawford, R. J. Dummel, A. Mishra*, J. Am. Chem. Soc. *87*, 3023 (1965).
[4] *J. Geittner, R. Huisgen, R. Sustmann*, Tetrahedron Lett. *1977*, 881.
[5] *W. Kirmse, D. Grassmann*, Chem. Ber. *99*, 1746 (1966).
[6] *H.-U. Reissig*, Dissertation, Universität München 1978, S. 131–133.
[7] *R. Huisgen, H.-U. Reissig*, Angew. Chem. *91*, 346 (1979); Angew. Chem. Int. Ed. Engl. *18*, 330 (1979).
[8] *R. Huisgen, H.-U. Reissig, H. Huber*, J. Am. Chem. Soc. *101*, 3647 (1979).

Perfluoro- and Perchlorodisulfenes[**]

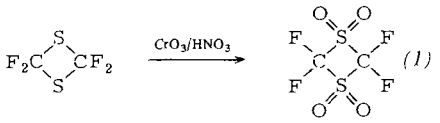
By *Rolf Seelinger* and *Wolfgang Sundermeyer*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

While 1,3-dithietane 1,1,3,3-tetraoxide ("disulfene"), first synthesized by dehydrohalogenation of mesyl chloride with

[*] Prof. Dr. W. Sundermeyer, Dipl.-Chem. R. Seelinger
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

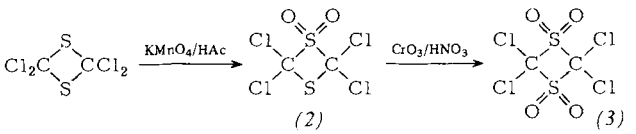
trimethylamine, has long been known[1], all attempts to prepare the corresponding prefluoro compound *(1)*, as the smallest perfluorinated cyclic disulfone, have so far failed[2]. Following unsuccessful attempts to electrofluorinate disulfene[3] we have now been able to prepare 2,2,4,4-tetrafluoro-1,3-dithietane 1,1,3,3-tetraoxide *(1)* by reaction of tetrafluoro-1,3-thietane with excess chromium trioxide in boiling fuming nitric acid.



(1)

The white crystalline oxidation product (m. p. 134 °C, subl.) isolable by sublimation has a peculiar moldy smell. The unusually high symmetry of the molecule *(1)* (planar ring, F and O atoms each in a plane vertical to each other and to the ring plane) was determined by X-ray structure analysis[4] and explained the high vapor pressure. Elemental analysis, mass spectrum ($m/e = 228$, M^+, 5%), ^{19}F-NMR (singlet at $\delta = 95.9$ rel. $CFCl_3$ int.), and IR data (1401 vs, 1255 vs, 1201 vs, 1174 vs, 853 vs, 718 vs, 522 vs, 510 m, and 482 cm^{-1} s) confirm the structure and composition of the compound, which is sensitive to hydrolysis and is soluble in tetrachloromethane, glacial acetic acid and acetonitrile. As by-product in the synthesis of *(1)* we also obtained 2,2,4,4-tetrafluoro-1,3-dithietane 1,1-dioxide[2].

The analogous reaction of tetrachloro-1,3-dithietane (dimeric thiophosgene) using this method fails, owing to rapid hydrolysis; however, the reaction with potassium permanganate in glacial acetic acid affords white crystalline 2,2,4,4-tetrachloro-1,3-dithietane 1,1-dioxide *(2)* (m. p. 89.5 °C) in 60% yield, which is likewise sublimable and can be recrystallized from petroleum ether.



(2) *(3)*

Above 120 °C, the 1,1-dioxide *(2)* [X-ray structure[4]; IR: 1372 vs (sulfone group), 1180 vs, 873 m, 820 vs, 696 vs, 558 vs, 535 vs, 398 m, and 355 cm^{-1} m] loses tetrachloroethylene. On prolonged standing, formation of a small amount of the isomeric 1,3-dioxide can be detected (mass spectrum; IR band at 1255 cm^{-1}), which, however, could not yet be isolated in pure form. The non-halogenated 1,3-dithietane 1,3-dioxide is well known[5].

(2) is soluble in fuming nitric acid, in which it reacts with CrO_3 to give the 2,2,4,4-tetrachloro-1,3-dithietane 1,1,3,3-tetraoxide *(3)*, a white, crystalline (from petroleum ether), readily sublimable substance (m. p. 200 °C, b. p. 215 °C). The structure of the perchloro compound is also confirmed by the IR spectrum (1383 vs, 1156 vs, 1050 m, 712 vs, 710 s, 569 vs, 480 vs, 404 m, and 333 cm^{-1} s) and X-ray structure analysis[4]. On oxidation of tetrabromo-1,3-dithietane[6] with $KMnO_4$ in glacial acetic acid we obtained the 1,1-dioxide homologous to *(2)* in 45% yield [IR: 1370 vs, 1162 vs, 740 m, 676 s, 550 s and 500 cm^{-1} s]; 2,2-dibromo-4-oxo-1,3-dithietane[6] and CBr_4 occur as impurities. — *(4)* can be further oxidized, analogously to *(2)*→*(3)*, to the already well-known 2,2,4,4-tetrabromo-1,3-diethietane 1,1,3,3-tetraoxide[1].

Procedure

(1): $(F_2CS)_2$ (8.3 g) is added dropwise within 2 h to a stirred solution of dry CrO_3 (15 g) in fuming HNO_3 (40 ml) (reflux condenser: −15 °C). After one hour's refluxing, the solution is evaporated down in a high vacuum. *(1)* is separated from the residue by sublimation and purified; yield 15%.

(2): Pulverized $(Cl_2CS)_2$ (11.4 g) is added portionwise to a solution of $KMnO_4$ (15.8 g) in glacial acetic acid (80 ml) such that the reaction temperature does not exceed 40 °C. After one hour's stirring at room temperature, the mixture is poured onto ice and the precipitate recrystallized from petroleum ether; yield 60%.

(3): (2) (6.5 g) is added within 1.5 h to a stirred solution of CrO_3 (10 g) in fuming HNO_3 (50 ml). Stirring is continued for a further 1 h and the temperature not allowed to exceed 40 °C. The reaction solution is then poured onto ice and the precipitate is recrystallized from petroleum ether; yield 27%.

Received: August 9, 1979 [Z 411 IE]
supplemented: November 2, 1979
German version: Angew. Chem. *92*, 223 (1980)

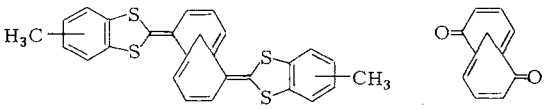
[1] *G. Opitz, H. R. Mohl*, Angew. Chem. *81*, 36 (1969); Angew. Chem. Int. Ed. Engl. *8*, 73 (1969).
[2] *R. A. Carboni, J. C. Kauer*, US-Pat. 3058993 (1962); Chem. Abstr. *58*, 5696e (1963).
[3] *W. Sundermeyer, R. Seelinger*, unpublished.
[4] *M. Ziegler, K. Weidenhammer, B. Balbach*, unpublished.
[5] *E. Block, E. R. Corey, R. E. Penn, T. L. Renken, P. F. Sherwin*, J. Am. Chem. Soc. *98*, 5715 (1976).
[6] *G. Diderrich, A. Haas, M. Yazdanbakhsch*, Chem. Ber. *110*, 916 (1977).

Synthesis of a Homologous Tetrathiafulvalene with Central Bicyclo[4.4.1]undeca-1(10),3,5,8-tetraene-2,7-diylidene Group[**]

By *Richard Neidlein* and *Hartmut Zeiner*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

We now report the synthesis of dimethyl-2,2′-bicyclo[4.4.1]undeca-1(10),3,5,8-tetraene-2,7-diylidenedi(1,3-benzodithiol) *(1)*. This compound contains structural units of a tetrathiafulvalene and a quinodimethane and is of interest as a potential donor component. Although the dione *(2)*[1] derived from the central bicycle is stable and to be regarded as a quinone on the basis of its physicochemical properties[1], it does not open a preparative entry to *(1)*.



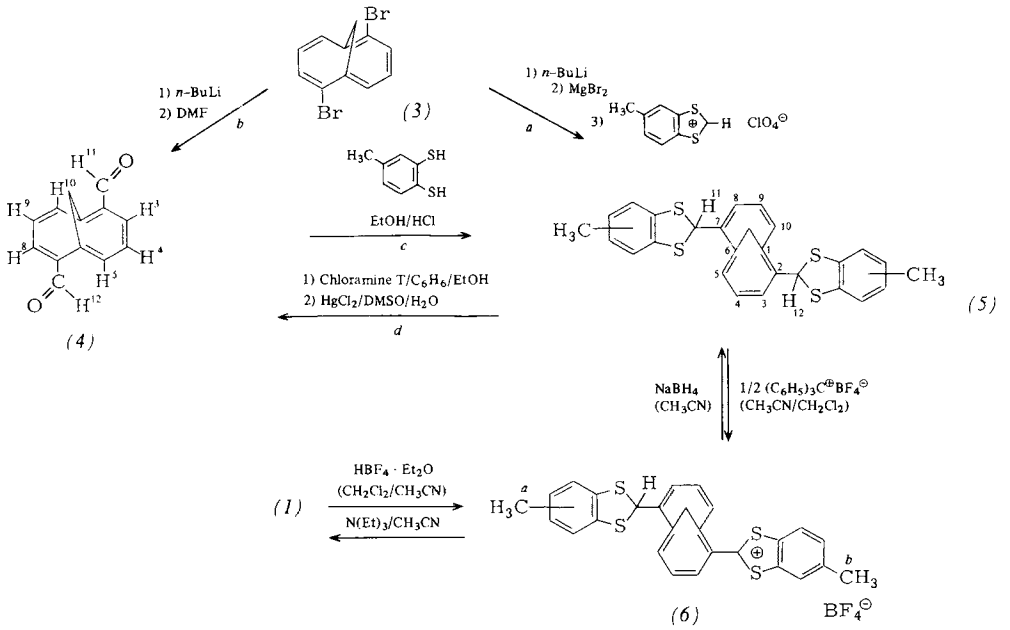
(1) *(2)*

Such an entry is provided by the key compound *(5)* which we have prepared by two pathways (see Scheme 1).

Reaction a: (3) was transformed by *n*-butyllithium into the dilithium compound (anhydrous Et_2O, −20 to 0 °C, N_2) according to *Vogel et al.*[1-3]; metal exchange with anhydrous $MgBr_2$ then affords the bifunctional Grignard compound. Reaction with freshly prepared 5-methyl-1,3-dithiolium perchlorate[4] at 0 °C, followed by 1 hour's stirring at room temperature, addition of NH_4Cl, and chromatography on silica gel (CH_2Cl_2) gives the pale yellow *(5)* as a mixture of diastereomers.

Reactions b and c: The dialdehyde *(4)* was obtained from *(3)* by metalation with *n*-butyllithium (anhydrous ether, −20

[*] Prof. Dr. R. Neidlein, Dipl.-Chem. H. Zeiner
Pharmazeutisch-chemisches Institut der Universität
Im Neuenheimer Feld 364, D-6900 Heidelberg (Germany)
[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.



Scheme 1

to 0 °C, N_2) and subsequent reaction with an excess of dimethyl-formamide (DMF). Thioacetalization of *(4)* with 4-methyl-1,2-benzenedithiol in HCl-saturated ethanol (0 °C, 45 min) led to *(5)* in 72% yield.

Reaction d: Subsequent thioacetal cleavage of *(5)* with Chloramine T and $HgCl_2$[5] gave almost pure *(4)* in 78% yield. Abstraction of a hydride ion from *(5)* with triphenylmethyl tetrafluoroborate (2 h, 60 °C, 12 h, room temperature) furnished the monocation *(6)* which could be transformed into *(1)* by elimination of a proton with triethylamine in CH_2Cl_2/CH_3CN. Compound *(1)* forms brick-red crystallites which can be stored for about one day but are air- and acid-sensitive; addition of $HBF_4 \cdot Et_2O$ to *(1)* regenerates the monocation *(6)*. Reduction with $NaBH_4$ in CH_3CN transforms *(6)* into *(5)*.

Structural proof of *(1)* was accomplished by spectroscopic methods (cf. Table 1); the reaction *(1)*→*(6)* also shows that *(1)* contains the molecular skeleton of *(6)*. The ^{1}H-NMR spectrum of *(1)* clearly indicates that de-aromatization of the 1,6-methanocyclodecapentaene group occurs on deprotonation of *(6)*. The question whether *(1)* has C_2 symmetry and thus exists as an enantiomeric pair and not as a mixture of diastereomers cannot be answered with absolute certainty, although some supporting evidence is available (^{1}H-NMR, TLC). Thus the protons of the two CH_3 groups appear as a singlet ($\delta = 2.30$, 6H); however, diastereotopic CH_3 groups can also exhibit accidental isochronism, or differences in chemical shifts may avoid detection at the measurement frequency.

Table 1. Selected physical properties of compounds *(4)*, *(5)*, and *(6)*.

(1): m. p. 166–168 °C; yield 95% based on *(6)*; ^{1}H-NMR (90 MHz, $CDCl_3$): $\delta = 1.29$ (s, 2H, CH_2), 2.30 (s, 6H, CH_3), 6.0–6.36, 6.87–7.21 (2 m, 12H, 2 identical ABC systems for 6 olefinic H, 2 ABX systems for 6 aromatic H); UV (CH_2Cl_2): $\lambda_{max} = 234$ nm ($\varepsilon = 43495$), 271 (21345, sh), 316 (9263, sh), 494 (17720); MS (70 eV): $m/e = 472$ (63%, M^+)

(4): m. p. 107 °C; yield 48% (based on *(3)*); ^{1}H-NMR (90 MHz, $CDCl_3$): $\delta = -0.13$ (s, 2H, CH_2), 7.30–8.60 (m, 6H, $H_3 - H_{10}$; simple ABC system: 8.56 (d, 2H, H_3, H_8, $J_{3,4} = J_{8,9} = 8.6$ Hz), 7.74 (d, 2H, H_5, H_{10}, $J_{4,5} = J_{9,10} = 9.1$ Hz), 7.40 (t, 2H, H_4, H_9 because $J_{3,4} \approx J_{4,5}$), 10.15 (s, 2H, H_{11}, H_{12}); UV (CH_3CN): $\lambda_{max} = 202$ nm ($\varepsilon = 18376$), 222 (15390), 268 (28138), 352 (13093), 400 (5283, sh), 408 (5053, sh), 424 (3675, sh); MS (70 eV): $m/e = 198$ (46%, M^+); IR (KBr): 2730 cm^{-1} (w, C H-aldehydic proton), 1670 (C=O)

(5): m. p. 77–79 °C (dec.); yield 60% (path *a*); ^{1}H-NMR (90 MHz, $CDCl_3$): $\delta = -0.5$ (s, 2H, CH_2), 2.26 (s, 3H) and 2.28 (s, 3H) for diastereotopic CH_3, 6.83 (s, 2H, H-11, H-12), 6.89–7.84 (m, 12H: 2 identical ABC systems of annulene-H and ABC systems of the benzo-aromatic H); UV (CH_2Cl_2): $\lambda_{max} = 234$ nm ($\varepsilon = 42902$), 268 (58313), 318 (14578), 330 (13747, sh); (CH_3CN): $\lambda_{max} = 231$ nm (44645), 265 (61269), 315 (14486), 327 (13774, sh); MS (70 eV): $m/e = 474$ (26%, M^+)

(6): m. p. 212 °C (dec.); yield 82%; ^{1}H-NMR (90 MHz, CD_3CN): $\delta = 0.01$ (B part: H_{anti}) [6], 0.09 (A part of AB system: H_{syn}; 2H, $J_{AB} = 10.7$ Hz, A part as triplet owing to long range coupling doublet of doublets $J \approx 1$ Hz, CH_2), 2.23, 2.28 (2s, 3H, CH_3-a), 2.63 (s, 3H, CH_3-b), 6.90 (s, 1H), 6.94–8.45 (m, 12 aromatic H); UV (CH_3CN): $\lambda_{max} = 207$ ($\varepsilon = 36089$), 237 (29389), 264 (20690 sh), 324 (7053), 430 (7523, sh); (CH_2Cl_2): $\lambda_{max} = 233$ (38635), 250 (33734, sh), 320 (7496, sh), 340 (6631, sh), 453 (7352, sh), 521 (9659); IR (KBr): 1050 cm^{-1} (s, $BF_4^\ominus$)

Received: December 20, 1979 [Z 402 IE]
German version: Angew. Chem. *92*, 199 (1980)

CAS Registry numbers:
(1), 72952-78-4; *(3)*, 15825-93-1; *(4)*, 72939-26-5; *(5)*, 72952-81-9; *(6)*, 72952-80-8; 5-methyl-1,3-dithiolylium perchlorate, 72939-27-6; dimethylformamide, 68-12-2; 4-methyl-1,2-benzodithiol, 496-74-2.

[1] *E. Vogel, W. A. Böll, E. Lohmar*, Angew. Chem. *83*, 403 (1971); Angew. Chem. Int. Ed. Engl. *10*, 399 (1971).

[2] *E. Vogel, W. A. Böll*, Angew. Chem. *76*, 784 (1964); Angew. Chem. Int. Ed. Engl. *3*, 642 (1964); *E. Vogel, W. A. Böll, M. Biskup*, Tetrahedron Lett. *1966*, 1569.

[3] *W. A. Böll*, Angew. Chem. *78*, 755 (1966); Angew. Chem. Int. Ed. Engl. *5*, 744 (1966); *E. Vogel*, in: Aromaticity. Spec. Publ. Chem. Soc. No. 21, London 1967, p. 113.

[4] *L. Soder, R. Wizinger*, Helv. Chim. Acta *42*, 1733 (1959).

[5] *R. Fochi, I. Degani*, J. Chem. Soc. Perkin Trans. 1, *1976*, 1886; Synthesis *1976*, 759.

[6] In this case, "*syn*" means turned to the charged side.

Double Addition of a Nucleophile to Carbyne and Carbonyl C-Atom: *S*-Phenyl 2-Phenyl-2-(phenylthio)thioacetate from *trans*-Bromotetracarbonyl(phenylcarbyne)chromium and Thiophenolate[1]

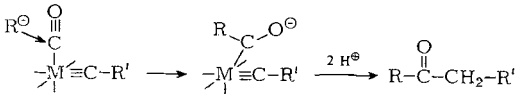
By *Ernst Otto Fischer* and *Werner Röll*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

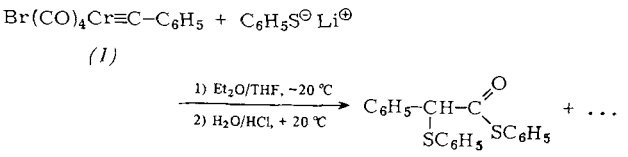
Neutral *trans*-halotetracarbonyl-carbyne complexes react with nucleophiles such as $I^\ominus$[2], Li-cyclopentadienide[3], or

[*] Prof. Dr. E. O. Fischer, Dipl.-Chem. W. Röll
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

carbonylmetalate ions[4] with replacement of the halogen ligand. Anions such as $C_6H_5^{\ominus}$, $OH^{\ominus}$, $OR^{\ominus}$, on the other hand, attack the positively polarized C atom of a carbonyl ligand[5]; the next reaction step is probably transfer of the resulting "acylate group" onto the carbyne carbon atom, followed by reductive elimination of the entire organic ligand on protonation by acid:

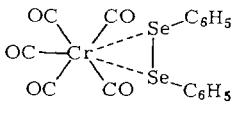


We have surprisingly obtained the hitherto unknown *S*-phenyl-2-phenyl-2-(phenylthio)thioacetate *(2)* on reaction of *trans*-bromotetracarbonyl(phenylcarbyne)chromium *(1)* with Li-thiophenolate and subsequent protonation with hydrochlorid acid:

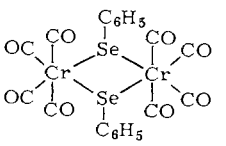


(1) *(2)*

This result can be explained in terms of double attack by the thiophenolate ions on a carbonyl and on the carbyne carbon atom and differs from the reaction of *(1)* with $C_6H_5O^{\ominus}$, which affords the expected phenyl phenylacetate in poor yield. The analogous reaction with selenophenolate does not lead to a corresponding ester but, *inter alia,* to (diphenyl diselenide)pentacarbonylchromium *(3)* and di-μ-phenylselenobis(tetracarbonylchromium) *(4)*.



(3)



(4)

The IR spectrum (KBr) of *(2)* exhibits the strong CO band of the thioester at 1690 (vs) cm^{-1} and typical phenyl absorptions (980 s, 750 vs, 725 s, 690 s cm^{-1}). In the ^{1}H-NMR spectrum (CCl_4) one finds a multiplet at $\delta = 7.2$ for the three phenyl groups and a singlet at $\delta = 5.0$ for the methine proton.

In addition to the multiplets of the ring carbon atoms in the range $\delta = 128.38$ to 134.62, the ^{13}C-NMR spectrum ($CDCl_3$) exhibits the two singlets of the α-C atom ($\delta = 63.88$) and the CO groups ($\delta = 195.32$).

Procedure

Methyllithium (10 mmol) is added to thiophenol (1.1 g, 10 mmol) in tetrahydrofuran (25 ml) and the resulting thiophenolate solution is added dropwise at −20 °C to a stirred solution of *(1)* (3.3 g, 10 mmol) in ether (150 ml). After 2 h, the solvent is removed at 20 °C and the brown residue is stirred in ether (100 ml) for 15 min with 4N HCl (25 ml). The ether phase is separated off, deacidified with $NaHCO_3$ solution, dried over Na_2SO_4, and evaporated down. Chromatography of the crude product on silica gel with ether/pentane (1:10) and twofold recrystallization from pentane gives *(2)* as analytically pure colorless needles, m. p. 70 °C. Yield 18%.

Received: December 17, 1979 [Z 405 IE]
German version: Angew. Chem. *92*, 206 (1980)

CAS Registry numbers:
(1), 50701-13-8; *(2)*, 72985-60-5; $C_6H_5Si^-L^+$, 2973-86-6

[1] Transition Metal-Carbyne Complexes, Part 57. — Part 56: *O. Orama, U. Schubert, F. R. Kreißl, E. O. Fischer,* Z. Naturforsch. *B 35*, 82 (1980).
[2] *E. O. Fischer, T. L. Lindner, F. R. Kreissl, P. Braunstein,* Chem. Ber. *110*, 3139 (1977).
[3] *E. O. Fischer, T. L. Lindner, F. R. Kreissl,* J. Organomet. Chem. *112*, C27 (1976).
[4] *E. O. Fischer, G. Huttner, T. L. Lindner, A. Frank, F. R. Kreissl,* Angew. Chem. *88*, 163 (1976); Angew. Chem. Int. Ed. Engl. *15*, 157 (1976).
[5] *E. O. Fischer, T. L. Lindner,* Z. Naturforsch. *B 32*, 713 (1977).

Correlation between Radical Reactivities and Copolymerization Parameters[**]

By *Bernd Giese* and *Jürgen Meixner*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Radical copolymerizations are directed by the rates k_{ij} of addition of the polymeric radicals $R_i^{\ominus}$ to the competing monomeric alkenes M_j[1]. *Alfrey* and *Price*[2] described the substituent influence of the alkenes in terms of Q_j and e_j values, which can be determined from the copolymerization parameters r_1 and r_2[1,3] [eq. (a)–(c)]. P_i and e_i values characterize the properties of the radicals.

$$M_1 \rightarrow R_1^{\ominus} \xrightarrow[M_2]{k_{12}} ; \quad r_1 = \frac{k_{11}}{k_{12}}$$

$$M_2 \rightarrow R_2^{\ominus} \xrightarrow[M_1]{k_{21}} ; \quad r_2 = \frac{k_{22}}{k_{21}}$$

$$k_{ij} = P_i \cdot Q_j \cdot e^{-e_i \cdot e_j} \qquad \text{(a)}$$

$$r_1 = \frac{Q_1}{Q_2} e^{-e_1(e_1 - e_2)} \qquad \text{(b)}$$

$$r_1 \cdot r_2 = e^{-(e_1 - e_2)^2} \qquad \text{(c)}$$

We have now *directly* measured the substituent effect on the rate of addition of the alkyl radical *(1)* to the polymerizable alkenes *(2)*–*(17)* and hence the chain propagation step of the radical copolymerization; the rate constants determined by the "mercury method"[4] are listed in Table 1.

If the experimental values k_{rel} of radical addition are inserted into eq. (a) and P_i and e_i are kept constant, then the *Q,e* scheme can be checked according to eq. (d).

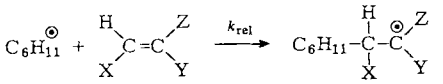
$$\log k_{rel} - \log Q_j = \text{const} - \frac{e_i}{2.303} e_j \qquad \text{(d)}$$

A straight line is indeed obtained on graphical evaluation of eq. (d) (Fig. 1).

The linear relationship between the parameters of copolymerization and the reactivities of the radical *(1)* is surprisingly good (correlation coefficient = 0.95), particularly since the relative rate constants for the mono-, di-, and trisubstituted

[*] Prof. Dr. B. Giese, Dipl.-Chem. J. Meixner
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0206 $ 02.50/0



(1) (2)-(17)

Table 1. Relative rate constants (k_{rel}) [a] for the addition of the cyclohexyl radical (1) to the alkenes (2)-(17) at 293 K in dichloromethane (experimental error ± 10%).

Alkene	X	Y	Z	k_{rel}
(2)	CH_3	H	CO_2CH_3	0.067
(3)	H	H	p-$CH_3OC_6H_4$	0.53
(4)	H	H	p-$CH_3C_6H_4$	0.84
(5)	H	H	C_6H_5	≡1.00
(6)	H	Cl	Cl	1.2
(7)	H	H	p-ClC_6H_4	1.6
(8)	$CO_2C_2H_5$	$CO_2C_2H_5$	H	3.3
(9)	H	CH_3	CO_2CH_3	5.0
(10)	H	H	CO_2CH_3	6.7
(11)	H	CH_3	CN	13
(12)	H	H	CN	24
(13)	$CO_2C_2H_5$	H	$CO_2C_2H_5$	30
(14)	Methylmaleic anhydride			140
(15)	H	Cl	CN	200
(16)	H	$CO_2C_2H_5$	$CO_2C_2H_5$	270
(17)	CN	H	CN	310

[a] The k_{rel} values are the rate constants per vinylic C atom attacked.

alkenes (2)-(17) extend over five orders of magnitude. The slope of the straight line in Figure 1 affords an e_j value of −1.9 for the cyclohexyl radical. Because e parameters characterize the influence of polar effects[1,5], the negative e value once again proves the nucleophilic[6] properties of alkyl radicals.

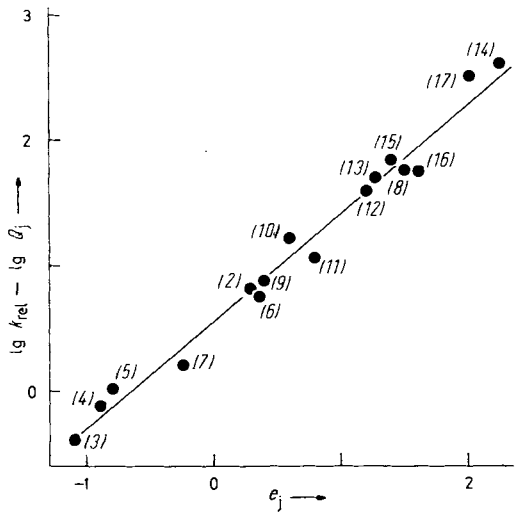


Fig. 1. Correlation between the relative reactivities (log k_{rel}) of the cyclohexyl radical (1) and Q_j, e_j values of the alkenes (2)-(17).

Such reactivity measurements permit a simple determination of the Q_j and e_j values of new alkenes and thus facilitate prediction of optimum conditions for their copolymerization.

Received: July 24, 1979 [Z 407 IE]
German version: Angew. Chem. 92, 215 (1980)
Publication delayed at authors' request

CAS Registry numbers:
(1), 623-43-8; (2), 18707-60-3; (3), 637-69-4; (4), 622-97-9; (5), 100-42-5; (6), 75-35-4; (7), 1073-67-2; (8), 141-05-9; (9), 80-62-6; (10), 96-33-3; (11), 126-98-7; (12), 107-13-1; (13), 623-91-6; (14), 616-02-4; (15), 920-37-6; (16), 3377-20-6; (17), 764-42-1

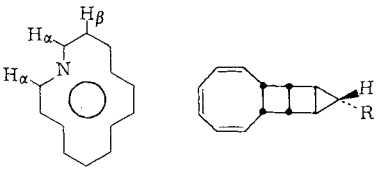
[1] A. D. Jenkins, in A. D. Jenkins, A. Ledwith: Reactivity, Mechanism and Structure in Polymer Chemistry. Wiley, London 1974, p. 117.
[2] T. Alfrey, C. C. Price, J. Polym. Sci. 2, 101 (1947); H. Mark, Angew. Chem. 61, 313 (1949).
[3] A compilation of Q_j and e_j values can be found in L. J. Young, J. Polym. Sci. 54, 411 (1961).
[4] B. Giese, J. Meixner, Angew. Chem. 91, 167 (1979); Angew. Chem. Int. Ed. Engl. 18, 154 (1979); and references cited therein.
[5] G. Fleischer, Plaste Kautsch. 20, 10 (1973).
[6] F. Minisci, Top. Curr. Chem. 62, 1 (1976); T. Caronna, A. Citterio, F. Minisci, O. Porta, J. Am. Chem. Soc. 99, 7960 (1977); B. Giese, J. Meister, Angew. Chem. 89, 178 (1977); Angew. Chem. Int. Ed. Engl. 16, 178 (1977).

Aza[14]annulenes[**]

By *Herbert Röttele* and *Gerhard Schröder*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Monocyclic vinylogs of benzene, furan, and pyrrole containing $(4n+2)$ π electrons have already been well documented[1]. We recently reported on aza[18]annulene[2], the first monocyclic vinylog of pyridine containing $(4n+2)$ π electrons. In this communication we describe the synthesis and some properties of the aromatic and conformationally mobile aza[14]annulene (1).



(1)

(2), R = $COOC_2H_5$
(3), R = COOH
(4), R = CON_3
(5), R = $NH-CONH_2$
(6), R = N_3

Reaction of tricyclo[6.4.0.0^{9,12}]dodeca-2,4,6,10-tetraene[3] with ethyl diazoacetate in the presence of copper powder affords three structurally isomeric monoadducts, of which (2) is the main product[4]. The carboxylic acid (3)[4] is converted by reaction with triethylamine, ethyl chloroformate and aqueous sodium azide into the acid azide (4) (92%). On heating for 3 h in benzene, (4) is converted into the isocyanate (not isolated), which reacts with NH_3 to give the urea derivative (5) (90%). The incompletely characterized N-nitrosourea [obtained by reaction of (5) with N_2O_4 in ether] reacts with lithium azide in methanol to give the 11-azidotetracyclo[6.5.0.0^{9,13}.0^{10,12}]trideca-2,4,6-triene (6), which after column chromatography (SiO_2, pentane/ether = 9:1) is obtained, still in impure form, as a colorless oil [*ca.* 10% (6) based on (5)][5]. The reaction path described here for transformation of an acid azide into an azide has already proven successful in other cases[2,6]. Photolysis of (6) in pentane (*ca.* 10^{-4} M) at −70 °C with a Hg low-pressure lamp affords, dark-violet crystalline aza[14]annulene (1) (≥50%).

The temperature-dependent ^{1}H-NMR spectra of (1) (see Table 1) provide confirmation of structure. The low-temperature ^{1}H-NMR spectrum (−70 °C) provides the following information: the difference between the centroids of the resonance signals of the three inner (Hi) and ten outer protons (Ha) amounts to *ca.* 9.5. (1), like [14]annulene[8], is distinctly diatropic. Both doublets of the two outer protons are caused by the protons (H_α) situated in the α-position to the nitrogen and having non-identical chemical shifts. The coupling constants prove the *cis* arrangement of H_α and H_β; hence the ni-

[*] Prof. Dr. G. Schröder, Dr. H. Röttele
Institut für Organische Chemie der Universität
Richard-Willstätter-Allee 2, D-7500 Karlsruhe 1 (Germany)

[**] This work was supported by BASF AG, Ludwigshafen.

Table 1. Selected physical data of compounds *(1)-(6)*.

(1): m. p. *ca.* 135 °C (dec., from pentane); ^{1}H-NMR (90 MHz, −70 °C, CD_2Cl_2): $\delta = -1.28$ (t, $J = 14.1$ Hz, 1Hi), −1.12 and −0.58 (one t each, $J = 13.7$ Hz, 2Hi), 7.73 (d, d, $J = 6.2$, 8.0 Hz, $1Ha = 1H_\beta$), 7.90–9.10 (m, 7Ha), 9.60 (d, $J = 4.4$ Hz, $1Ha = 1H_\alpha$), 9.69 (d, $J = 6.2$ Hz, $1Ha = 1H_\alpha$); ^{1}H-NMR (90 MHz, 30 °C, CD_2Cl_2): $\delta = -0.51$ (pseudo-t, J ca. 13.0 Hz, 1Hi), 2.0–6.4 (very broad unstructured absorption which hardly rises above the base line, 2Hi + 2Ha), 7.70–8.80 (m, *ca.* 6Ha), 9.55 (d, $J = 5.3$ Hz, $2Ha = 2H_\alpha$); ^{1}H-NMR (90 MHz, 80 °C, [D$_6$]-DMSO) [7]: $\delta = -0.50$ (m, 1Hi), 4.00 (two overlapping br. m., 2Hi + 2Ha), 7.70–8.70 (m, *ca.* 6Ha), 9.47 (d, $J = 5.3$ Hz, $2Ha = 2H_\alpha$); UV (dioxane): $\lambda_{max} = 323$ ($\varepsilon = 76700$), 398 (7200), 420 (sh, 4760), 435 (sh, 3460), 499 (420), 512 (494), 544 (531), 561 (593), 580 (sh, 642), 599 (1685), 620 nm (1760)

(2): colorless oil, ^{1}H-NMR (60 MHz, 35 °C, CCl_4): $\delta = 1.23$ (t, $J = 7$ Hz, 3H), 1.53 (pseudo-s, 1H), 2.27 (m, 2H), 2.58 (m, 2H), 3.60 (m, 2H), 4.09 (q, $J = 7$ Hz, 2H), 5.90 (m, 6H); UV (cyclohexane): $\lambda = 250$ nm (sh, $\varepsilon = 1700$)

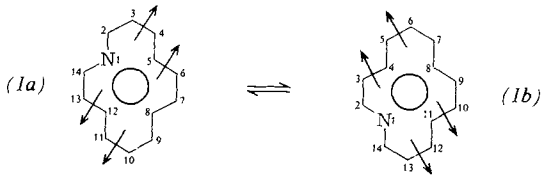
(3): m. p. 222 °C (dec.); ^{1}H-NMR (100 MHz, 26 °C, [D$_5$]-pyridine): $\delta = 1.82$ (pseudo-s, 1H), 2.50 (narrow m, 4H), 3.56 (narrow m, 2H), 5.80 (s, 2H), 6.02 (AB system 4H); UV (methanol): $\lambda_{max} = 253$ nm ($\varepsilon = 1600$)

(4): m. p. 91 °C (dec.); ^{1}H-NMR (90 MHz, 28 °C, $CDCl_3$): $\delta = 1.64$ (pseudo-s, 1H), 2.52 (narrow m, 4H), 3.62 (narrow m, 2H), 5.80 (s, 2H), 6.00 (AB system, 4H); UV (dioxane): $\lambda = 258$ nm (sh, $\varepsilon = 1900$)

(5): m. p. 196 °C (dec.); ^{1}H-NMR (90 MHz, 28 °C, $CDCl_3$): $\delta = 2.10$ (d, $J = 3$ Hz, 2H), 2.53 (narrow m, 3H), 3.62 (narrow m, 2H), 4.77 (br. s, 2H, NH_2), 4.93 (br.s, 1H, NH), 5.80 (s, 2H), 6.00 (AB system, 4H); UV (dioxane): $\lambda = 250$ nm (sh, $\varepsilon = 1700$)

(6): colorless oil, ^{1}H-NMR (90 MHz, 28 °C, $CDCl_3$): $\delta = 2.06$ (d, $J = 3$ Hz, 2H), 2.53 (narrow m, 2H), 2.92 (pseudo-s, 1H), 3.60 (narrow m, 2H), 5.80 (s, 2H), 6.0 (AB system, 4H); IR (CCl_4): 2100 cm^{-1}

trogen in the aza[14]annulene *(1)*, like that in the aza[18]annulene[2], occupies an inner position. In the ^{1}H-NMR spectrum of *(1)*, one H_β can be located by double resonance experiments. Its two vicinal protons are *cis* oriented.



(1a) ⇌ *(1b)*

The characteristic temperature-dependent ^{1}H-NMR spectra demonstrate a pairwise mixing of proton resonance signals. The degenerate equilibrium *(1a)*⇌*(1b)* describes the conformational mobility of the aromatic aza[14]annulene *(1)*. The following protons change places pairwise: outer protons (Ha): H-2/H-14, H-3/H-13, H-6/H-10, H-7/H-9; inner (Hi) *and* outer protons (Ha): H-4/H-12, H-5/H-11; only the inner proton H-8 remains unchanged. Particularly striking in the ^{1}H-NMR spectrum at 80 °C are the doublet for the two H_α and the 4H signal resulting around $\delta = 4.00$ by averaging.

Received: December 19, 1979 [Z 400 IE]
German version: Angew. Chem. *92*, 204 (1980)

CAS Registry numbers:
(1), 295-18-1; *(2)*, 72881-62-0; *(3)*, 72881-63-1; *(4)*, 72881-64-2; *(5)*, 72881-65-3; *(6)*, 72881-66-4; tricyclo[6.4.0.0^{9,12}]dodeca-2,4,6,10-tetraene, 5020-35-9; diazoacetic ester, 503-68-4

[1] *G. Schröder*, Pure Appl. Chem. *44*, 925 (1975), and references cited therein; *G. Frank, G. Schröder*, Chem. Ber. *108*, 3736 (1975); *W. Henne, G. Plinke, G. Schröder, ibid. 108*, 3753 (1975); *H. Röttele, G. Heil, G. Schröder, ibid. 111*, 84 (1978); *G. Schröder, G. Plinke, J. F. M. Oth, ibid. 111*, 99 (1978).

[2] *W. Gilb, G. Schröder*, Angew. Chem. *91*, 332 (1979); Angew. Chem. Int. Ed. Engl. *18*, 312 (1979).

[3] *G. Schröder, W. Martin*, Angew. Chem. *78*, 117 (1966); Angew. Chem. Int. Ed. Engl. *5*, 130 (1966).

[4] *G. Frank*, Dissertation, Universität Karlsruhe 1974, first described *(2)*, a structural isomer of *(2)* and the carboxylic acid *(3)*.

[5] Preliminary work involved in the preparation of compounds *(4)-(6)* was performed by *K. Wesch*.

[6] *W. Kirmse, H. Schütte*, Chem. Ber. *101*, 1674 (1968).

[7] We assign absorption signals around $\delta = 10.0$ (d, $J = 7.3$ Hz) and 5.5 (br. m) to an isomeric aza[14]annulene of still unknown structure whose concentration amounts to 20% max. The doublet around $\delta = 10.0$ appears also in the spectra at 30 and −70 °C. In the case of [14]annulene two isomers are also detected in solution [8].

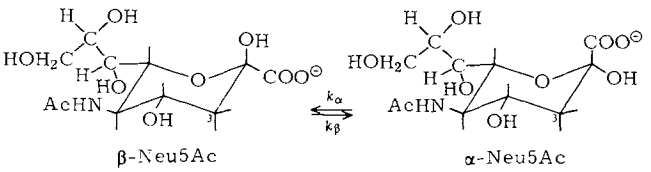
[8] *R. C. Haddon, V. R. Haddon, L. M. Jackman*, Fortschr. Chem. Forsch. *16*, 103 (1971), and references cited therein.

^{1}H-NMR Investigations on the Mutarotation of *N*-Acetyl-D-neuraminic Acid[**]

By *Horst Friebolin, Martin Supp, Reinhard Brossmer, Gunda Keilich*, and *Dietmar Ziegler*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Numerous oligosaccharides, glycoproteins, glycolipids, and gangliosides contain *N*-acetyl-D-neuraminic acid (Neu5Ac[1]) with α-ketosidic bonding as terminal sugar. From the optical properties, however, it was deduced that free Neu5Ac is present exclusively in the β-configuration in aqueous solution. It was shown by X-ray structure analysis that Neu5Ac also crystallizes in the β-configuration[2]. The anomer, α-Neu5Ac, could only recently be detected; *Friebolin et al.*[3] showed by ^{1}H-NMR spectroscopy that free Neu5Ac is an anomeric mixture in aqueous solution. In agreement with ^{13}C-NMR measurements[4] 5–8% α-Neu5Ac was found besides 95–92% β-Neu5Ac; accordingly a mutarotation equilibrium should exist for Neu5Ac, as for other sugars.



β-Neu5Ac ⇌ α-Neu5Ac

Moreover, the detection of separate signals for α- and β-Neu5Ac in the NMR spectra points to a slow kinetic process on the NMR time scale. Owing to the unfavorable position of this equilibrium, however, determination of the kinetic data of the mutarotation is impossible, either NMR spectroscopically or polarimetrically.

In investigations on the specificity of neuraminidases we have now succeeded for the first time in demonstrating by means of ^{1}H-NMR spectroscopy that α-Neu5Ac is liberated as primary fragment from a α-ketoside of Neu5Ac[5]. This finding contradicts previously held views[6].

For this experiment we used an incubation solution (0.5 ml) of 20 mM Neu5Acα2→3Galβ1→4Glc (II^{3}Neu5Ac-Lac) in 50 mM Na/K phosphate buffer in D_2O (pD = 5.4) and 800 mU neuraminidase from *Clostridium perfringens*[7]. Hydrolysis was carried out in the spectrometer, and spectra were recorded at various intervals. We specifically observed the region of the signals of the axial and equatorial protons on C-3 (cf.[3]). Initially, we found only the characteristic signals of α-Neu5Ac together with those of the substrate. Then, in the further course of reaction, the additional signals of β-Neu5Ac were observed. This β-Neu5Ac can only be formed by mutarotation from α-Neu5Ac. As long as α-Neu5Ac is still being liberated from the substrate, determination of

[*] Prof. Dr. H. Friebolin [+]
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg (Germany)

Dr. M. Supp, Prof. Dr. R. Brossmer, Dr. G. Keilich, Dr. D. Ziegler
Institut für Biochemie II der Universität
Im Neuenheimer Feld 328, D-6900 Heidelberg (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We thank Dr. *P. Kunzelmann* for his help in recording the ^{1}H-NMR spectra.

quantitative data on the kinetics of the mutarotation is problematic. In our experiment, no more substrate was detectable after 168 min. At this point the concentration of α-Neu5Ac was *ca.* 40%, and that of β-Neu5Ac was *ca.* 60% (Table 1).

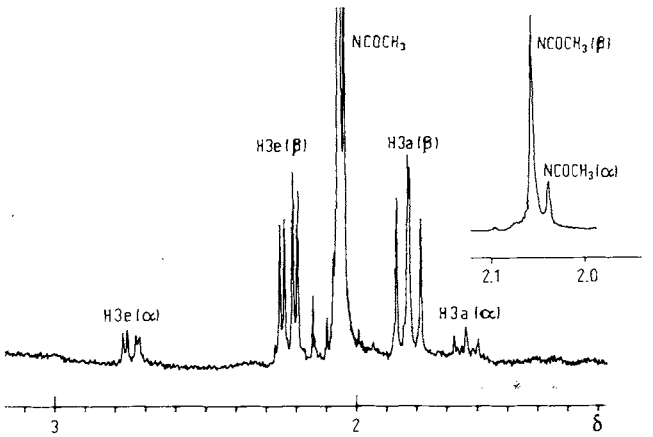


Fig. 1. Part of the 300-MHz ^{1}H-NMR spectrum of the anomeric mixture of α- and β-Neu5Ac, recorded 294 min after beginning the cleavage experiment (see text). Small diagram: Signals of the *N*-acetyl protons. Spectrometer: Bruker Physik WH 300, solvent D_2O, phosphate buffer (pD = 5.4), internal standard δ [$(CH_3)_3SiCD_2CD_2COONa$] = 0, T = 30 °C, number of pulses 830, 8 K data points (duration of measurement *ca.* 15 min).

Table 1. Ratio of the amounts of II^{3}Neu5Ac-Lac (substrate) and α- and β-Neu5Ac determined during the cleavage reaction. Up to t = 138 min the signals of the protons on C-3 and on the *N*-acetyl group were measured, thereafter only the *N*-acetyl signals were integrated. The numerical data are mean values for the time required to record the spectrum (*ca.* 10–20 min).

t [min]	α [%]	β [%]	II^{3}Neu5Ac-Lac [%]
18	43	8	49
58	42	25	33
108	41	41	18
138	38	53	9
168	38	62	<5
194	33	67	
251	23	77	
280	19	81	
294	17	83	
317	17	83	
340	16	84	
368	13	87	
900	8	92	

This ratio deviates so markedly from the equilibrium (8% α-Neu5Ac: 92% β-Neu5Ac) that it is possible for the first time to follow its course. In order to determine the amounts of α- and β-Neu5Ac as a function of time we integrated the well resolved signals of the *N*-acetyl protons of the two anomers (Fig. 1, Table 1).

The following data could be calculated[8] for the mutarotation equilibrium and the kinetics:

$$\alpha\text{-Neu5Ac} \underset{k_\beta}{\overset{k_\alpha}{\rightleftharpoons}} \beta\text{-Neu5Ac}$$

$$K = [\beta]/[\alpha] = 11.5$$

$$\Delta G(\alpha) - \Delta G(\beta) = 6.1 \text{ kJ/mol } (= 1.55 \text{ kcal/mol})$$

$$k_\alpha = 1.3 \times 10^{-4} \text{ s}^{-1};\ k_\beta = 1.1 \times 10^{-5} \text{ s}^{-1}$$

$$t_{0.5} = 80 \pm 10 \text{ min}$$

From these investigations we could show that establishment of the equilibrium of mutarotation of Neu5Ac in 50 mM Na/K phosphate buffer in D_2O (pD = 5.4) is unexpectedly slow (half-life = $t_{0.5}$).

Received: December 20, 1979 [Z 401 IE]
German version: Angew. Chem. *92*, 200 (1980)

CAS Registry numbers:
N-Acetyl-α-neuraminic acid, 21646-00-4; *N*-acetyl-β-neuraminic acid, 19342-33-7

[1] Neu5Ac: nomenclature suggested for *N*-acetyl-D-neuraminic acid at the Vth International Symposium on Glycoconjugates, Kiel, September 1979.
[2] *J. L. Flippen*, Acta Crystallogr. *B 29*, 1881 (1973).
[3] *U. Dabrowski, H. Friebolin, R. Brossmer, M. Supp*, Tetrahedron Lett. *1979*, 4637.
[4] *L. W. Jaques, E. B. Brown, J. M. Barret, W. S. Brey, W. Weltner, Jr.*, J. Biol. Chem. *252*, 4533 (1977).
[5] *H. Friebolin, R. Brossmer, G. Keilich, D. Ziegler, M. Supp*, Hoppe Seylers Z. Physiol. Chem. (1980), in press.
[6] *L. Holmquist, B. Östmann*, FEBS Lett. *60*, 327 (1975).
[7] 1 m unit (mU) corresponds to the liberation of 1 nmol Neu5Ac/min in 50 mM Na acetate buffer (pH = 5.0) at 37 °C with 2.5 mM II^{3}Neu5Ac-Lac as substrate.
[8] *A. Mannschreck, A. Mattheus, G. Rissmann*, J. Mol. Spectrosc. *23*, 15 (1967).

Structural Changes on Oxidation: Flattening of the C_4-Cluster of Tetrahedrane[1]

By *Hans Bock, Bernhard Roth,* and *Günther Maier*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Oxidation or reduction of molecules M generally leads to structural modifications[2] which can be advantageously investigated by ESR spectroscopy of radical ions $M^{\bullet\oplus}$ or $M^{\bullet\ominus}$[1]. In clusters, the number of electrons is most important: in the case of electron-deficient compounds such as boranes or carbaboranes, oxidation effects progressive "encapsulation" *hypho* → *arachno* → *nido* → *closo*[3], whereas in the case of electron-excess compounds cage-opening can occur, *e.g.* S_4N_4 yields the planar dication $S_4N_4^{2\oplus}$[2,3]. Little is known about the oxidation and reduction behavior of clusters with a "balanced" number of electrons such as tetrahedranes $(CX)_4$: the tetrahedral structure of the systems with 12 electrons in the C_4 skeleton corresponds to *Euler*'s formula for convex polyhedra[4]: number of faces = number of edges − number of vertices + 2 = 6 − 4 + 2 = 4. The tetrakis(*tert*-butyl) derivative is formed photochemically from its cyclobutadiene valence isomer with assistance from the "corset effect" of the bulky alkyl groups[5]; the delicate balance of charge distribution is underlined by the possibility of thermal reconversion to starting material at the melting temperature of 135 °C[6].

As a saturated alkane, tetra-*tert*-butyltetrahedrane exhibits the unusually low ionization energy of only 7.50 eV[7] and is therefore oxidized to the radical cation by $AlCl_3/CH_2Cl_2$[1]. The ESR spectrum of $[C_4(C(CH_3)_3)_4]^{\bullet\oplus}$ shows the equidistant signals of the proton 37-tet (Fig. 1).

Heating of tetrahedrane to 140 °C for 1 h in the evacuated ESR capillary and subsequent $AlCl_3/CH_2Cl_2$ oxidation of the resulting tetra-*tert*-butylcyclobutadiene [which is even easier to ionize at IE_1 = 6.35 eV[7]] affords an identical ESR spectrum (Fig. 1).

[*] Prof. Dr. H. Bock, Dipl.-Chem. B. Roth
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. G. Maier
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0303-0209 $ 02.50/0*

In order to discuss the unexpected result that both valence isomers of $C_4(C(CH_3)_3)_4$ give the same radical on $AlCl_3/CH_2Cl_2$ oxidation, sections are calculated through the energy

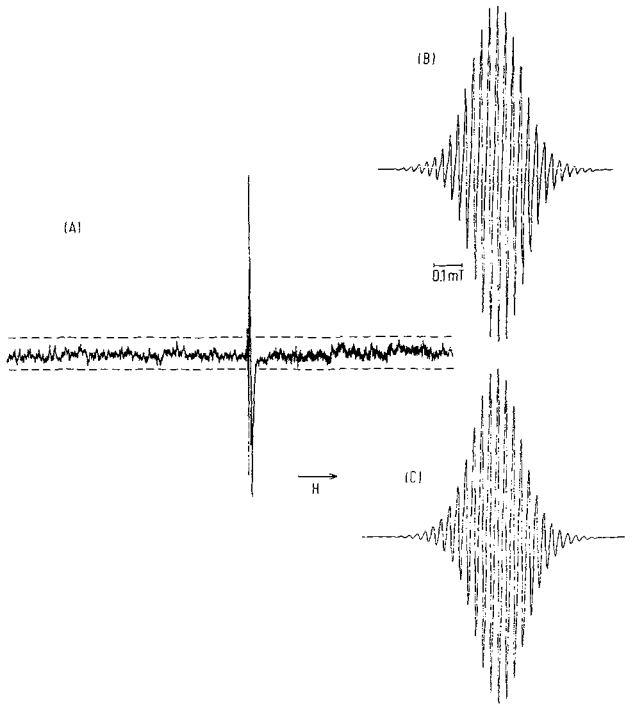
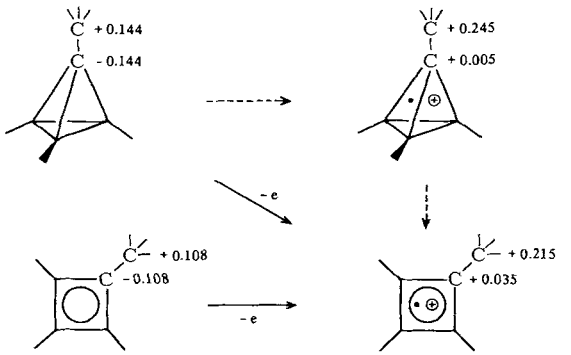


Fig. 1. ESR spectrum of the radical cation generated from tetra-*tert*-butyl tetrahedrane by treatment with $AlCl_3/CH_2Cl_2$, recorded at 180 K: (A) entire range (20 mT, 10 × amplification), in which ^{13}C satellites (1:4, 1.1% natural abundance) cannot be detected within the given intensity range (----); (B) highly resolved center line with simulation; (C) for the 37-tet of the protons the coupling constant amounts to $a_H = 0.027$ mT and the intensity ratio of the outside line: center line = 1:9.075135298. The same ESR spectrum is observed on oxidation of the valence isomeric tetra-*tert*-butylcyclobutadiene; in both cases the radical cation generated is stable up to about 200 K and exhibits a g factor of 2.0024.

hypersurfaces along the isomerization valleys for the sterically unconstrained tetramethyltetrahedrane and its radical cation (Fig. 2).

Spontaneous isomerization of the C_4 cluster on electron removal (Fig. 2) can be explained on the basis of the calculated charge distributions[8].



The positive charge can be better distributed on participation of the cyclobutadiene π-system; greater stabilization of the $M^{\bullet\oplus}$ ground state is also suggested by the ionization energy of 6.35 eV, which is lower than that of tetrahedrane by 1.15 eV[7]. While the neutral C_4 cluster can exist with support from substituents, oxidation leads to its planarization as in the case of $S_4N_4^{2\oplus}$.

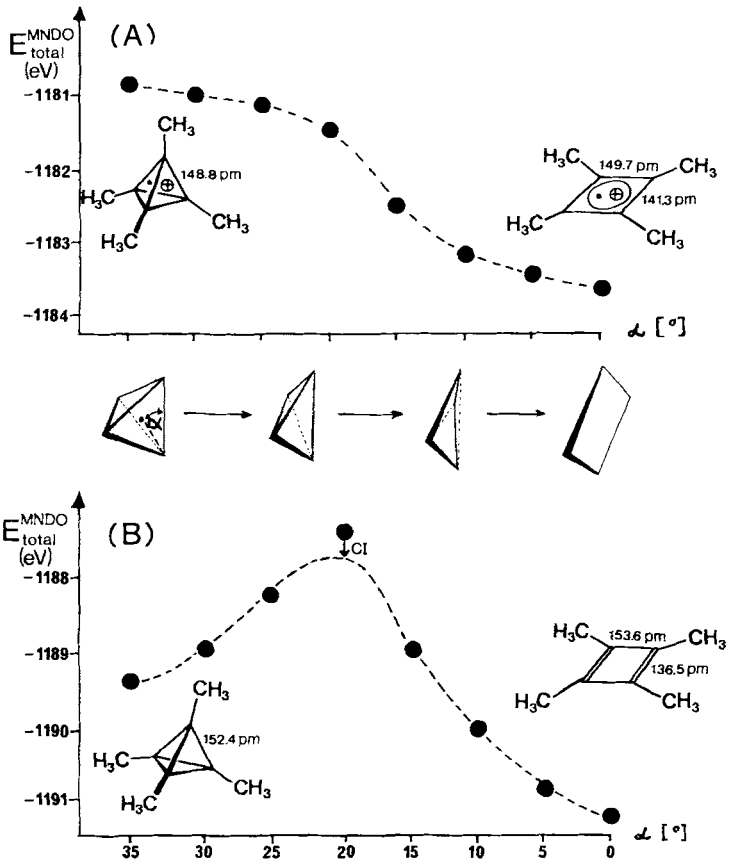


Fig. 2. Tetrahedrane ⇄ cyclobutadiene valence isomerization is advantageously described by an angular coordinate: if α is made smaller then two opposite tetrahedral edges approach each other. Calculation of the individual points along the isomerization section through the hypersurface is performed with open shell (A) and closed shell (B) MNDO [8], with structure optimization in each case, *i.e.* the CC distances and the CCC angles are determined afresh each time. An isomerization barrier of 170 kJ/mol [6] is approximately calculated (without CI) for going from tetramethyltetrahedrane to he energetically more favorable tetramethylcyclobutadiene. However, the radical cation does not lie in a local minimum and the C_4 cluster should therefore undergo spontaneous isomerization on electron removal.

Received: October 22, 1979 [Z 404a IE]
German version: Angew. Chem. *92*, 213 (1980)

CAS Registry numbers:
Tetra-*tert*-butyltetrahedrane, 66809-06-1; tetra-*tert*-butyltetrahedrane radical cation, 72952-85-3; tetra-*tert*-butylcyclobutadiene, 66809-05-0; tetra-*tert*-butylcyclobutadiene radical cation, 72952-86-4.

[1] Radical Ions, Part 39. Part of Diplomarbeit *B. Roth*, Universität Frankfurt 1979.—Part 38: *H. Bock, G. Brähler, W. Kaim, M. Kira, B. Roth, A. Semkow, U. Stein, A. Tabatabai* in *J. S. Bargon:* Computational Methods in Chemistry. Plenum Press, New York, in press.

[2] Cf. *H. Bock*, Angew. Chem. *89*, 631 (1977); Angew. Chem. Int. Ed. Engl. *16*, 613 (1977) and references cited therein; for S_4N_4: *R. Gleiter*, J. Chem. Soc. *A 1970*, 3174.

[3] Cf. *K. Wade*, Adv. Inorg. Chem. Radiochem. *18*, 1 (1976); *K. F. Purcell, J. C. Kotz:* Inorganic Chemistry. Saunders, Philadelphia 1977, pp. 980ff. and relevant references cited. A clear brief account is given by *R. W. Rudolph, W. R. Pretzer*, Inorg. Chem. *11*, 1974 (1972).

[4] Cf. *N. L. Biggs, E. K. Lloyd, R. J. Wilson:* Graph Theory 1736—1936. Clarendon Press, Oxford 1976, pp. 74ff.

[5] *G. Maier, S. Pfriem, U. Schäfer, R. Matusch*, Angew. Chem. *90*, 552 (1978); Angew. Chem. Int. Ed. Engl. *17*, 520 (1978).

[6] The barrier was determined as $\Delta E = 113$ kJ/mol by kinetic methods (*G. Maier, H.-O. Kalinowski, K.-D. Malsch*, unpublished). *A. Schweig* and *W. Thiel*, J. Am. Chem. Soc. *101*, 4742 (1979), calculated about 80 kJ/mol by MNDO/CI; the effect of the *tert*-butyl substituents was estimated as about 20 kJ/mol.

[7] *E. Heilbronner, T. B. Jones, A. Krebs, G. Maier, K.-D. Malsch, J. Pocklington, A. Schmelzer*, J. Am. Chem. Soc. *102*, 564 (1980).

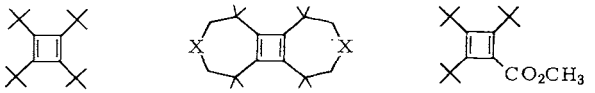
[8] *M. J. S. Dewar, G. P. Ford*, J. Am. Chem. Soc. *101*, 5558 (1979). We thank Prof. *Dewar* for kindly providing the MNDO program.

Structure of Tetra-*tert*-butylcyclobutadiene[**]

By *Hermann Irngartinger, Norbert Riegler, Klaus-Dieter Malsch, Klaus-Albert Schneider,* and *Günther Maier*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The results of X-ray structure analysis[1] of tetra-*tert*-butylcyclobutadiene *(1)*[2], the first kinetically stabilized cyclobutadiene having four identical substituents, are surprising: the molecule lies on a crystallographic twofold axis which runs through the center of the two long bonds of the four-membered ring (Fig. 1). Long [1.482(2), 1.484(2) Å] and short bonds [1.464.(2) Å] occur in the ring; although they differ significantly, they do not alternate nearly so pronouncedly as in the derivatives *(2)* (1.344 and 1.600 Å)[3a], *(3)* (1.339 and 1.597 Å)[3b], or *(4)*[3c].



(1) *(2)*, X = S; *(3)*, X = CH_2 *(4)*

The quaternary C-atoms of the *tert*-butyl substituents of *(1)* deviate alternately by 0.37 Å above and below the plane through the ring atoms. The four-membered ring is not planar but possesses a folded conformation with a dihedral angle of 170.2°.

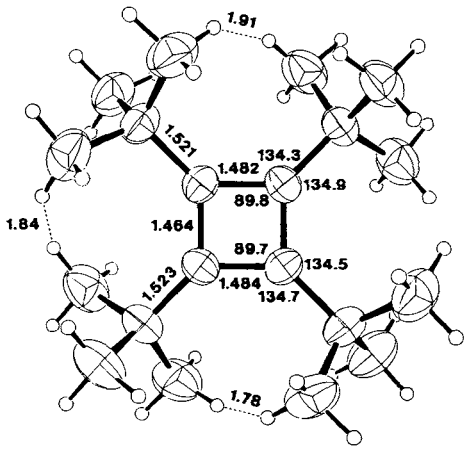


Fig. 1. Selected bond lengths [Å], angles [°], and intramolecular distances [Å] of *(1)* in the crystal, standard deviations 0.002–0.003 Å and 0.1°. The $C(sp^3)$-$C(sp^3)$ bonds have an average length of 1.533 ± 0.004 Å.

The pronounced lengthening of the double bond in *(1)* from a standard value of 1.34 Å to 1.464 Å can be attributed to two reasons: steric interaction between the *tert*-butyl groups imposes a torsional angle of 28.1° on the double bond (Fig. 2), leading to weakening of the bond. Comparison with other twisted double bond compounds shows[4] that this

[*] Prof. Dr. H. Irngartinger [+], N. Riegler
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
Prof. Dr. G. Maier, Dipl.-Chem. K.-D. Malsch,
Dipl.-Chem. K.-A. Schneider
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen 1 (Germany)
[+] To whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

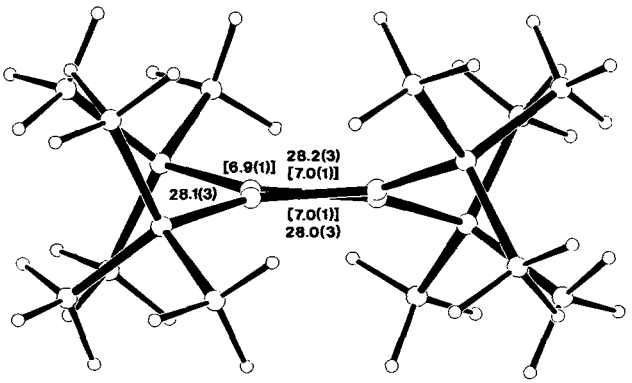


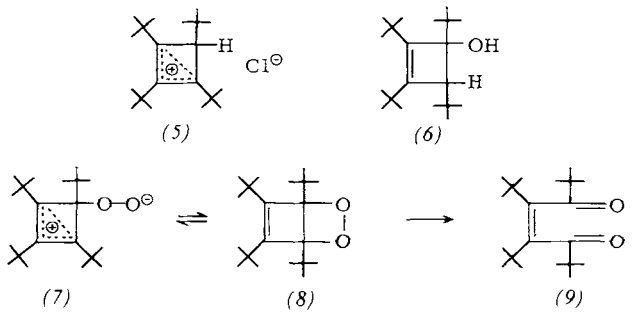
Fig. 2. Side view of *(1)* looking along the twofold axis. The numbers given are torsional angles [°]. The values in square brackets are the torsional angles in the four-membered ring.

alone does not suffice to explain the extent of bond lengthening, particularly since the torsion on the "inside" is only 6.9° owing to fixation in the ring system. Moreover, in spite of the deviation of the substituents from the plane of the four membered ring (Fig. 2), additional repulsive interactions — the H ... H distance in *(1)* is still extremely small at 1.84 Å — lead to further lengthening of the weakened double bond.

The $C(sp^2)$-$C(sp^2)$ single bond in *(1)* is considerably shorter, compared with *(2)*–*(4)*, and lies in the usual range for such bonds in four-membered rings[5]. Thus in *(2)* and *(3)* the single bond is stretched, and in *(1)* the double bond. Almost four-fold symmetry is established in this way for *(1)*.

Such a geometry raises the question of the spin multiplicity of *(1)*. The chemical properties do not permit any decision, since by analogy with tri-*tert*-butylcyclobutadiene[6a] *(1)* shows both basic and "diradical-type" behavior. Addition of hydrogen chloride in dichloromethane affords the homocyclopropenylium salt *(5)*, which reacts with water to give cyclobutenol *(6)* [colorless crystals, m. p. 74 °C; IR (CCl_4): 3650 cm^{-1} (OH); MS: $m/e = 294$ (M^+)]. The same alcohol is also formed without acid catalysis on direct action of water on *(1)*. On the other hand, the cyclobutadiene is very sensitive to oxygen; the primary oxidation product is the dioxetane *(8)*. In a polar medium (CD_2Cl_2) this molecule shows broadening between 0 and 30 °C and coalescence of the ^1H- and ^{13}C-NMR signals of the two kinds of *tert*-butyl groups[6b]. This result suggests that in the temperature interval specified the peroxide bridge in *(8)* migrates around the carbon ring in a kind of merry-go-round rearrangement *via* intermediates of type *(7)*. In a competing process, *(8)* undergoes a slow (half-life *ca.* 2 h at room temperature) irreversible cleavage to the diketone *(9)* [colorless crystals, m. p. 93 °C; IR (CCl_4): 1680 cm^{-1}; MS: $m/e = 308$ (M^+)].

Now that *(1)* has been shown to have a folded structure, which is undoubtedly due to the four bulky substituents and which explains the ready valence isomerization to tetrahe-



(5) *(6)* *(7)* *(8)* *(9)*

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0303-0211 $ 02.50/0*

Table 1. NMR data (δ, rel. to TMS) of compounds *(5)*, *(6)*, *(8)*, and *(9)*.

	^{1}H-NMR	^{13}C-NMR (p = primary, q = quaternary)
(5)	(CD_2Cl_2, *RT*): 4.05 (1H), 1.59 (9H), 1.47 (18H), 1.14 (9H)	(CD_2Cl_2, −60 °C): 159.42 (C-2), 156.00 (C-1, C-3), 78.48 (C-4; not decoupled: d), 37.74 (q), 36.63 (q), 35.90 (q), 30.33 (p, 1 *t*Bu), 29.80 (p, 3 *t*Bu)
(6)	($CDCl_3$, *RT*): 2.57 (1H), 1.56 (OH), 1.24 (9H), 1.20 (9H), 1.04 (9H), 0.98 (9H)	($CDCl_3$, *RT*): 151.58 (olefinic), 151.06 (olefinic), 84.85 (C-O), 60.42 (allylic, ring), 38.46 (q), 33.63 (q), 32.80 (q), 32.55 (q), 31.06 (p), 30.76 (p), 30.33 (p), 27.81 (p)
(8)	(CD_2Cl_2, −60 °C): 1.38 (18H), 1.22 (18H)	(CD_2Cl_2, −60 °C): 161.44 (olefinic), 108.73 (C-O), 34.48 (q), 34.04 (q), 31.77 (p), 28.93 (p)
(9)	(CD_2Cl_2, *RT*): 1.32 (18H), 1.14 (18H)	(CD_2Cl_2, *RT*): 218.12 (C=O), 146.67 (olefinic), 45.15 (q), 35.43 (q), 33.13 (p), 28.53 (p)

RT = room temperature.

drane[2], it nevertheless remains to be examined whether this kind of stabilization [transition from the more energetic D_{4h} to D_{2d} (or D_2) instead of D_{2h} symmetry[7]] might also be significant in other cases too, possibly even in the unsubstituted parent compound.

Received: July 11, 1979;
revised: November 2, 1979 [Z 404 b IE]
German version: Angew. Chem. *92*, 214 (1980)

[1] Room temperature, $Mo_{K\alpha}$ radiation, Siemens AED, graphite monochromator, $\sin\Theta/\lambda \leq 0.664$ Å^{-1}, 2267 independent reflections (of which 662 were unobserved); crystallographic data: $a = 17.749(4)$, $b = 9.271(2)$, $c = 11.870(2)$ Å, $\beta = 106.90(2)°$; monoclinic space group C2/c, $Z = 4$; $\varrho_{calc.} = 0.98$ g cm^{-3}.

[2] *G. Maier, S. Pfriem, U. Schäfer, R. Matusch*, Angew. Chem. *90*, 552 (1978); Angew. Chem. Int. Ed. Engl. *17*, 520 (1978).

[3] a) *H. Irngartinger, H. Rodewald*, Angew. Chem. *86*, 783 (1974); Angew. Chem. Int. Ed. Engl. *13*, 740 (1974); b) *A. Krebs, J. Pocklington, H. Schmalstieg, H. Irngartinger, N. Riegler*, Israel J. Chem., in press; c) *L. T. J. Delbaere, M. N. G. James, N. Nakamura, S. Masamune*, J. Am. Chem. Soc. *97*, 1973 (1975).

[4] Review: *T. T. Tidwell*, Tetrahedron *34*, 1855 (1978).

[5] Review: *D. Seebach* in *Houben/Weyl*: Methoden der organischen Chemie. Thieme, Stuttgart 1971, Vol. IV/4, p. 11, Table 4.

[6] a) *G. Maier, W. Sauer*, Angew. Chem. *87*, 675 (1975); *89*, 49 (1977); Angew. Chem. Int. Ed. Engl. *14*, 648 (1975); *16*, 51 (1977); b) this phenomenon does not occur in cyclosilane: *K. D. Malsch, K. A. Schneider, G. Maier, H.-O. Kalinowski*, unpublished.

[7] In the latest calculations too [8] only planar arrangements are considered. It should also be mentioned that the same number (7) of active vibrations is to be expected in the IR spectrum [9] of unsubstituted cyclobutadiene whether in a folded (D_{2d}) or rectangular geometry.

[8] *H. Kollmar, V. Staemmler*, J. Am. Chem. Soc. *99*, 3583 (1977); *W. T. Borden, E. R. Davidson, P. Hart, ibid. 100*, 388 (1978); *J. A. Jafri, M. D. Newton, ibid. 100*, 5012 (1978).

[9] Experiment: *S. Masamune, F. A. Souto-Bachiller, T. Machiguchi, J. E. Bertie*, J. Am. Chem. Soc. *100*, 4889 (1978); theory: *H. Kollmar, V. Staemmler, ibid. 100*, 4304 (1978); *L. J. Schaad, B. A. Hess, C. S. Ewig, ibid. 101*, 2281 (1979).

Enantioselective Synthesis of α-Methylserines[**]

By *Ulrich Schöllkopf, Wolfgang Hartwig*, and *Ulrich Groth*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Optically active synthetic amino acids are gaining increasing importance in research and practice, *e.g.* as enzyme inhibitors or as pharmaceuticals.

We recently reported on the enantioselective synthesis of α-methylamino acids by base-induced alkylation of (3*S*,6*S*)-(+)-2,5-dimethoxy-3,6-dimethyl-3,6-dihydropyrazine *(1)*, which is obtainable by reaction of cyclo(L-Ala-L-Ala) with trimethyloxonium tetrafluoroborate[1]. We have now found that lithiated lactim ethers *(2)* also react with carbonyl compounds *(3)* — in tetrahydrofuran (THF) or (better) dimethoxyethane — with, in some cases very high, induction at C-3 (cf. Table 1). With aldehydes or unsymmetric ketones, a chirality center is also established at C-7 of the product *(4)*. The induction is somewhat lower in this case, being 41–78% (cf. Table 1).

The configuration and degree of induction at C-3 of *(4)* can — if R^1 or R^2 is aryl — be determined ^{1}H-NMR spectroscopically from the signal of the C-6 methyl protons. This appears at relatively high field in the case of the isomer formed in lower yield because the methyl group is situated in the shielding anisotropic region of the aryl group, which might lie π-complex-like over the heterocycle[2]. Accordingly, the carbonyl compound adds to *(2)* preferably in the *trans*-position to the C-6 methyl group, so that an *R*-configuration is induced at C-3 of *(4)*. This also applies in the case of formaldehyde, since (*R*)-(−)-α-methylserine[3] is obtained on hydrolysis of *(4a)*. Acid hydrolysis of the adduct *(4)* leads to α-methylserine esters *(5)*. Their enantiomeric purity at the α-carbon atom corresponds to the asymmetric induction, when optically pure *(1)* is used as starting material[4].

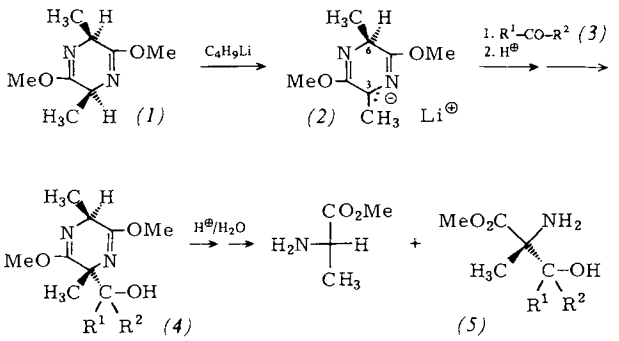


Table 1. Adducts *(4)* synthesized from the metalated lactim ethers *(2)* and carbonyl compounds *(3)*.

(4)	R^1	R^2	M.p. [°C] B.p. [°C/torr]	Yield [%]	Asymm. induction at C-3	Induced configuration	Asymm. induction at C-7	Induced configuration
a	H	H	50–55; 60/0.1	70	85–90 [a, c]	*R*		
b	CH_3	CH_3	95–105/15	80	80 [a, d] 85 [b]	*R*		
c	C_6H_5	C_6H_5	99	89	>95 [a]	*R*		
d	C_6H_5	CH_3	95–100/0.2	70	86 [a] >95 [b]	*R*	41 [a]	*R*
e	C_6H_5	H	105–110/0.1	72	76 [a] 82 [b]	*R*	21 [a] 52 [b]	*R*
f	4-$CH_3OC_6H_4$	H	115–120/0.1	69	73 [a] 85 [b]	*R*	48 [a] 74 [b]	*R*

[a] In THF. [b] In dimethoxyethane. [c] Determined with Eu(tfc)$_3$ on *(4a)*. [d] Determined with Eu(tfc)$_3$ on *(5b)*.

[*] Prof. Dr. U. Schöllkopf, Dr. W. Hartwig, Dipl.-Chem. U. Groth
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Asymmetric syntheses *via* Heterocyclic Intermediates, Part 3. — Part 2: [1].

A retroaldol reaction can occur during the hydrolysis. Thus, *(4c)* readily decomposes to benzophenone and *(1)*, whereas the hydrolysis of *(4a)* or *(4b)* is straightforward. The diastereomers of *(4e)* (separated by HPLC) primarily afford (2*R*,3*R*)-α-methyl-β-phenylserine methyl esters, which decompose *via* retroaldol reaction on distillation[5], while the (2*R*,3*S*)-diastereomer is thermostable[5].

Lactim ethers of type *(1)*, which are differently substituted on C-3 and C-6, also react with carbonyl compounds with high asymmetric induction; *e.g.*, in the reaction of (3*S*)-6-lithio-2,5-dimethoxy-3-(3,4-dimethoxybenzyl)-3-methyl-3,6-dihydropyrazine with acetone it is ≈93%[6].

Procedure

(1)→(4): Butyllithium (11 mmol, 7 ml of a 1.55 N solution in hexane) is added to a solution of *(1)*[7] (1.7 g, 10 mmol) in *ca.* 20 ml of THF or (better) dimethoxyethane at −70 °C. A solution of the carbonyl compound *(3)* (10 mmol) in *ca.* 20 ml THF or dimethoxyethane, precooled to −70 °C, is then added dropwise to the mixture. In the case of formaldehyde a suspension of 20 mmol of paraformaldehyde in 20 ml of THF is added. After stirring for 6–10 h (20 h in the case of *(4a)*) at −70 °C the mixture is treated with 0.66 g of glacial acetic acid in *ca.* 5 ml of THF and the temperature allowed to come to room temperature. After removal of solvent *in vacuo* the residue is shaken with 30 ml of ether and 50 ml of phosphate buffer solution (pH = 7); the aqueous solution is then extracted twice more with 20 ml ether and the combined ether extracts are dried over sodium sulfate. After removal of ether, *(4)* is distilled in a bulb-to-bulb apparatus.

(4b)→(5b): A mixture of *(4b)* (0.23 g, 1 mmol) and 0.13 N HCl (16 ml) is stirred for 15 min at room temperature. After removal of solvent in a vacuum (bath temp. 40 °C) the remaining mixture is covered with a layer of ether (5 ml). The vigorously stirred mixture is then treated with dilute ammonia solution until the pH = 8. The ether phase is saturated with sodium chloride and extracted a further five times with ether. The combined ether extracts are dried over sodium sulfate and, after removal of ether, distilled (slight decomposition); yield 0.11 g (72%) (*R*)-(—)-α,β,β-trimethylserine methyl ester, b. p. 100–110 °C/0.1 torr, enantiomeric purity 71% (determined with Eu(hfc)$_3$), corresponding to an asymmetric induction in the case of *(4b)* of *ca.* 80%. — ^{1}H-NMR ($CDCl_3$): δ = 1.26 and 1.40 (s, $CH_3$9H), 1.49 (s, $NH_2$2H), 3.75 (s, OCH_3, 3H); 8.3 (br., OH); $[\alpha]_D^{20} = -64.1°$ (*c* = 1.1 in ethanol).

Received: January 2, 1980 [Z 403 IE]
German version: Angew. Chem. *92*, 205 (1980)

CAS Registry numbers:
(1), 72953-31-2; *(2)*, 72953-32-3; *(3a)*, 50-00-0; *(3b)*, 67-64-1; *(3c)*, 119-61-9; *(3d)*, 98-86-2; *(3e)*, 100-52-7; *(3f)*, 123-11-5; *(4a)*, 72953-33-4; *(4b)*, 72968-03-7; *(4c)*, 71785-63-2; *(4d)*, 72953-34-5; *(4e)*, 72953-35-6; *(4f)*, 72953-36-7; *(5a)*, 72953-37-8; *(5b)*, 72953-38-9; *(5c)*, 71785-69-8; *(5d)*, 72953-39-0; *(5e)*, 73035-89-9; *(5f)*, 72953-40-3

[1] *U. Schöllkopf, W. Hartwig, U. Groth*, Angew. Chem. *91*, 922 (1979); Angew. Chem. Int. Ed. Engl. *18*, 863 (1979).
[2] Such preferred conformations (folded conformations) have been demonstrated on a number of occasions with benzyl-substituted heterocycles; cf. *A. K. Bose, M. S. Manhas, R. V. Tavates, J. M. van der Veen, H. Fujiwara*, Heterocycles *7*, 1227 (1977).
[3] *N. Takamura, S. Terashima, K. Achiwa, S. Yamada*, Chem. Pharm. Bull. *15*, 1776 (1967).
[4] The compound *(1)* described in [1] is 93–95% optically pure. — Triethyloxonium tetrafluoroborate reacts more rapidly than trimethyloxonium tetrafluoroborate with *cyclo*-(L-Ala-L-Ala). In the case of the ethyl lactim ethers — OEt instead of OMe in *(1)* — the asymmetric inductions are just as high as in the case of *(1)*, but the ^{1}H-NMR spectra are less informative.
[5] Cf. *U. Groth*, Diplomarbeit, Universität Göttingen 1979.
[6] Cf. *H. Kehne*, Dissertation, Universität Göttingen 1980.
[7] Synthesized as in [1]; b. p. 75 °C/8–10 torr, $[\alpha]_D^{20} = +82.6°$ (*c* = 1.0, ethanol).

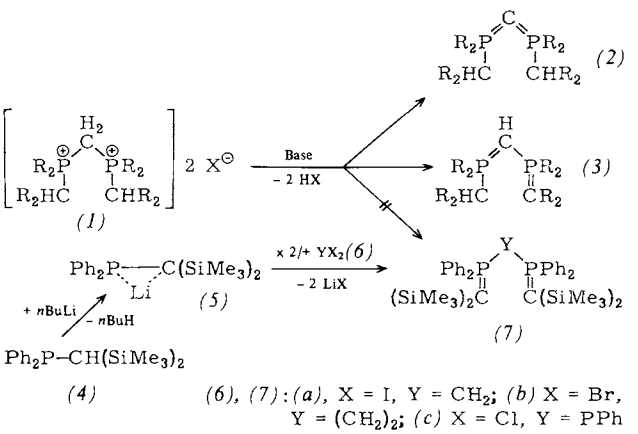
Lithium [Bis(trimethylsilyl)methylene]diphenylphosphoranide, a Building Block for the Synthesis of Bis(methylenephosphoranes)[1]

By *Rolf Appel* and *Gerhard Haubrich*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Previous studies have shown that the deprotonation of methylene-bridged bisphosphonium salts *(1)* always takes place at the central C-atom. Either carbodiphosphoranes *(2)* or double ylides *(3)* containing a conjugated P=C–P bond system are obtained[2]. The formation of isomeric bis(methylenephosphoranes) of type *(7)* containing two terminal ylide functions, which are of interest as potential chelating agents, has hitherto not been observed[2].

We have now found that the salt *(5)*, *i.e.* the title compound, which is obtainable from [bis(trimethylsilyl)methyl]diphenylphosphane *(4)* and *n*-butyllithium, permits the synthesis of the novel double ylides *(7a)*–*(7c)*. From the smooth reaction of *(5)* with diiodomethane *(6a)*, 1,2-dibromoethane *(6b)* and dichloro(phenyl)phosphane *(6c)* it can be concluded that the species originally deprotonated at the α-C-atom reacts ambivalently as "Li-phosphoranide" with the difunctional halogen compounds.



Only the reaction with diiodomethane yields *(7a)*; dichloromethane is dehydrochlorinated by *(5)*, while reaction with dibromomethane leads to *(4)* together with three further still unidentified products.

The structure and composition of the double ylides are confirmed by elemental analysis, characteristic fragmentation pattern in the mass spectrum[3], and above all by the po-

NMR spectroscopic data of the bis(methylenephosphoranes)[4]
(7a): $^{31}P\{^1H\}$-NMR: δ = 18.7 (s); ^{1}H-NMR: δ = 0.05 (s, $SiCH_3$), 0.31 (s, $SiCH_3$), 1.20 (t, ^2J(PCH) = 12.0 Hz, CH_2), 7.45 (m, C_6H_5); $^{13}C\{^1H\}$-NMR: δ = 3.0 (d, ^3J(PCSiC) = 1.4 Hz, SiC), 7.1 (pseudo-t, ^3J(PCSiC) + ^5J(PCPCSiC) = 3.6 Hz, SiC), 13.8 (t, J(PC) = 53.6 Hz, CH_2), 128.6 (d, ^3J(PC-3) = 23.8 Hz, C-3), 131.6 (s, C-4), 133.8 (pseudo-dd, ^2J(PC-2) + ^4J(PCPC-2) = 10.2 Hz, C-2), 139.8 (pseudo-dd, J(PC-1) + ^3J(PCPC-1) = 87.4 Hz, C-1).
(7b): $^{31}P\{^1H\}$-NMR: δ = 16.1 (s); ^{1}H-NMR: δ = 0.22 (s, $SiCH_3$), 2.80 (m, CH_2), 7.35 (m, C_6H_5); $^{13}C\{^1H\}$-NMR: δ = 6.5 (s, SiC), 27.5 (pseudo-t, J(PC) + ^2J(PCC) = 50.6 Hz, CH_2), 128.6 (pseudo-t, ^3J(PC-3) + ^6J(PCCPC-3) = 10.4 Hz, C-3), 131.1 (s, C-4), 132.5 (pseudo-t, ^2J(PC-2) + ^5J(PCCPC-2) = 11.2 Hz, C-2), 136.4 (dd, J(PC-1) = 39.5 Hz, ^4J(PCCPC-1) = 1.2 Hz, C-1).
(7c): $^{31}P\{^1H\}$-NMR: δ = 35.2 (Ph_2P), 8.1 (PhP, A_2B system mit J(AB) = 441.2 Hz); ^{1}H-NMR: δ = 0.20 (s, $SiCH_3$), 7.25 (m, C_6H_5); $^{13}C\{^1H\}$-NMR: δ = 5.9 (d, ^3J(PCSiC) = 1.1 Hz, SiC), the complex aromatic region could not be assigned

[*] Prof. Dr. R. Appel, Dipl.-Chem. G. Haubrich
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

sition—and the coupling pattern in the case of *(7c)*—of the methylenephosphorane signal in the $^{31}P\{^1H\}$-NMR spectrum. The chemical non-equivalence of the *exo*- and *endo*-silyl groups in *(7a)* and the ^{1}H-NMR triplet for the methylene bridge preclude a prototropic carbodiphosphorane structure. We ascribe the surprising stability with regard to a 1,3-proton shift from the methylene bridge to the ylide center to the influence of the silyl substitution.

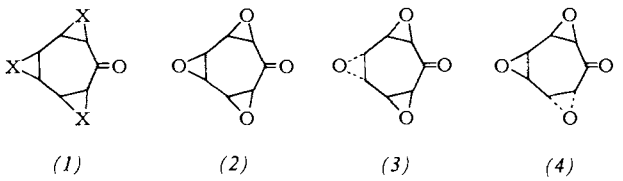
Procedure

A 15% solution of *n*-butyllithium (125 ml, 200 mmol) in *n*-hexane is added rapidly to a magnetically stirred solution of *(4)*[5] (13.8 g, 40 mmol) in ethylene glycol dimethyl ether (80 ml). After cooling, the suspension is filtered in the absence of moisture and the yellow precipitate is taken up in 200 ml of *n*-hexane and added dropwise within 2 h to a solution of *(6)* (20 mmol) in benzene (100 ml). After *ca.* 12 h the lithium halide that is formed is separated off, the solvent removed in a vacuum, and *(7)* recrystallized from *n*-hexane.—*(7a):* yellow crystals, m. p. 76 °C (dec.), yield 46%. *(7b):* anthracite colored crystals, m. p. 113 °C, yield 61%. *(7c):* minium-colored crystals, m. p. 123–125 °C (dec.), yield 56%.

Received: December 21, 1979 [Z 406 IE]
German version: Angew. Chem. *92*, 206 (1980)

CAS Registry numbers:
(4), 70530-40-4; *(5)*, 72985-32-1; *(6a)*, 75-11-6; *(6b)*, 74-95-3; *(6c)*, 644-97-3; *(7a)*, 72985-33-2; *(7b)*, 72985-34-3; *(7c)*, 72985-35-4

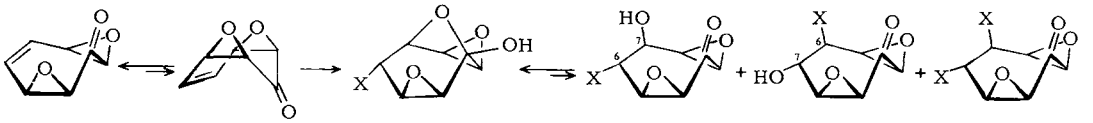
[1] Phosphorus-Carbon-Halogen Compounds, Part 21.—Part 20: *R. Appel, U. Baumeister, Z.* Naturforsch. *B*, in press.
[2] *H. Schmidbaur, A. Wohlleben-Hammer*, Chem. Ber. *112*, 510 (1979) and earlier communications in the series "Double Ylides".
[3] $[M^+ - Ph_2PC(SiMe_3)_2]$ ions of higher relative intensity.
[4] The ^{1}H- (Bruker WH 90, 90.0 MHz, TMS int.), $^{31}P\{^1H\}$-(Varian CFT 20, 30.2 MHz, H_3PO_4 ext.) and $^{13}C\{^1H\}$-NMR spectra (Bruker WH 90, 22.6 MHz, TMS int.) were measured in concentrated C_6D_6 solutions.
[5] *R. Appel, J. Peters*, unpublished.



(1) *(2)* *(3)* *(4)*

The starting compound for *(2)* and *(3)* is the *cis*-diepoxide *(5)*[2], which is readily accessible from tropone. *(5)* preferably exists as the "open" tub configuration and is only difficultly amenable to electrophilic attack at the C=C double bond. Consequently, a direct epoxidation succeeds only to a very limited extent (<5%)[3], even under drastic conditions. On the other hand, *(5)* smoothly adds the components of HOX (X = Br, Cl): with *N*-bromosuccinimide in water/dioxane (1:1, 0 °C) the overall yield is good, but the (β-OH) selectivity is poor. Besides *ca.* 10% dibromide *(9a)* (m. p. 145 °C (dec.), ν_{CO} = 1688 cm^{-1}), 40% and 27%—not optimized—of 6α,7β-*(7a)* and 6β,7α-bromohydrin *(8a)* (oil), respectively, are also formed, *(7a)* as the semiacetal *(6a)* (m. p. 175 °C (dec.)). High α-OH selectivity is attained with *tert*-butyl hypochlorite in water/acetone (1:1, 0 °C): in addition to the 6α,7β-isomer *(7b)*, isolated as *(6b)* (5%, m. p. 185 °C (dec.)), 80–85% of the oily 6β,7α-chlorohydrin *(8b)* (urethane: m. p. 244 °C (dec.)) is obtained, with traces of *(9b)* possibly escaping detection.

Semiketal formation and the open boat conformation also determine the result of the reaction of *(6a)*⇄*(7a)* with 5% methanolic KOH solution (60 °C). Without epoxide formation to give *(2)* being detectable (TLC, ^{1}H-NMR), transannular substitution takes place almost exclusively—*via (11)*—to give *(10)* (84–88%, m. p. 117 °C). However, on using diazabicyclononene (DBN) or -undecene (DBU) in aprotic media (CH_3CN, 60 °C)[4], only the desired "α,α,α"-trioxaketone *(2)* is isolated (provisionally 70–75%; m. p. 245 °C, ν_{CO} = 1731 cm^{-1}; see Table 1).



(5) *(6)* *(7)* *(8)* *(9)*

(a), X = Br 40% 27% 10%
(b), X = Cl 5% 80–85%

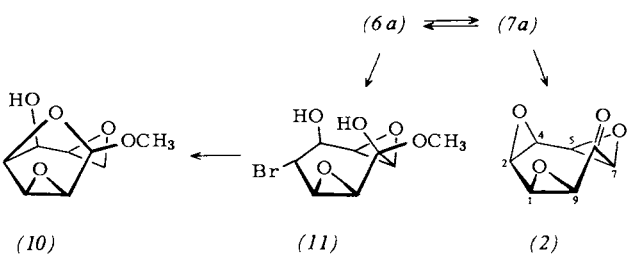
"α,α,α"-, "α,β,α"- and "α,α,β"-Trioxa-tris-σ-homotropone[**]

By *Wolfgang Seppelt, Hans Fritz, Christoph Rücker,* and *Horst Prinzbach*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The tris-σ-homotropones *(1)* (X = CH_2, O, NR) are of interest to us in connection with theoretical and preparative objectives already reported in a previous communication[1]. We have now synthesized the stereoisomeric trioxa-compounds *(2)*–*(4)*.

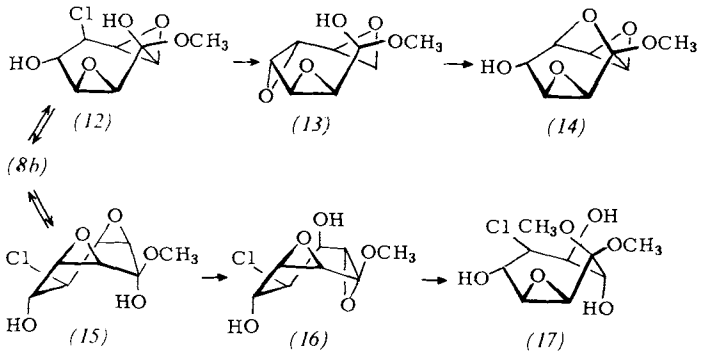
Semiketal formation, transannular substitution, and, in addition, epoxide migration[5] are the dominant competing processes in the reaction of *(8a)*/*(8b)* with KOH/methanol (1.5 equiv.). Plausible intermediates in the reactions leading to *(14)* (m. p. 144 °C) and *(17)* (m. p. 189 °C), obtained from *(8b)* and isolated in 47 and 42% yield, respectively, are the compounds *(12)* and *(13)* and *(15)* and *(16)*, respectively. In



(10) *(11)* *(2)*

[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. W. Seppelt, Prof. Dr. H. Fritz, Dr. Ch. Rücker
Lehrstuhl für Organische Chemie der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

favor of *(13)* is the observation that *(3)* smoothly yields *(14)* under the same conditions. Unexpected—and so far inexplicable—is the behavior towards the bases, which have already been successfully employed in the case of *(6a)*⇄*(7a)*. Thus, even at 0 °C *(8a)*/*(8b)* react with DBN or DBU or KOH/tBuOH or tBuOK/tBuOH almost spontaneously to give a dark polymer. The supposition that the quasi-antiperiplanar arrangement of the X/O pair, as in previous cases[4], is



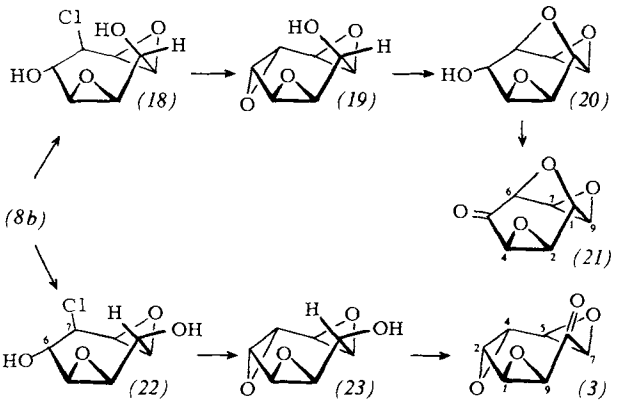
hindered by electrostatic interactions between halogen atom and epoxide oxygen atom(s), and epoxide formation is rendered relatively difficult, is, in view of the ease of polymerization and the smooth cyclization *(22)*→*(23)*, wholly unsatisfactory.

The complications arising from CO in *(8a)*/*(8b)* are avoidable by the circuitous route *via* the alcohols. On reaction with $NaBH_4$ (ethanol, 0 °C) a *ca.* 1:1 mixture of the diols *(18)* and *(22)* (m. p. 183 and 181 °C, respectively; overall yield provisionally 70%) is obtained from *(8b)*. Treatment of this mixture with 5% KOH/methanol (1.5 equiv., 60 °C, 20 min) affords *(20)* and *(30)* in quantitative yield. A control experiment confirms that *(19)*—prepared from *(3)*—is wholly converted into *(20)* under these conditions. *(20)* (m. p. 135 °C) and *(23)* (m. p. 159 °C) can be separated chromatographically (silica gel, ethyl acetate) and oxidized conventionally (CrO_3/pyridine/CH_2Cl_2) to *(21)* (55–60%, m. p. 150 °C, $\nu_{CO}=1735\ cm^{-1}$; see Table 1) and to the "α,β,α"-trioxaketone *(3)*, respectively (65–70%, m. p. 169, $\nu_{CO}=1728\ cm^{-1}$; see Table 1). The extent to which the reduction of *(8b)* can be more selectively controlled has still to be checked.

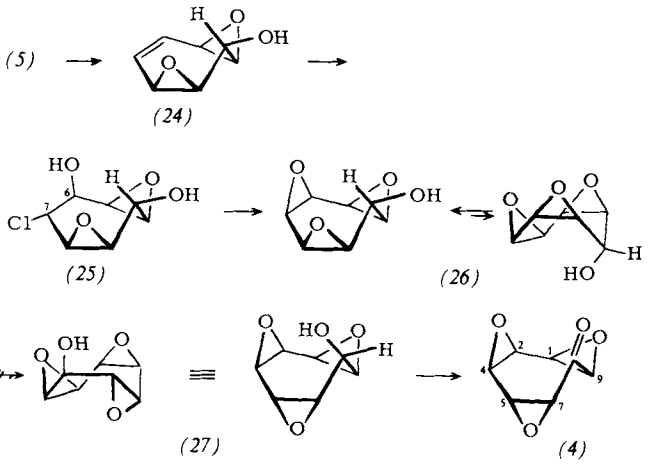
Table 1. ^{1}H- and ^{13}C-NMR data (δ values, *J* [Hz]) of the ketones *(2)*, *(3)*, *(4)*, and *(21)*.

	^{1}H-NMR	^{13}C-NMR
(2)	3.72 (7(9)-H), 3.69 (2(4)-H), 3.61 (1(5)-H); $[J_{1,2}+J_{1,4}]\approx 1$, $J_{1,9}=4.5$	194.9, 55.1, 54.1, 50.5
(3)	3.73 (7(9)-H), 3.53 (2(4)-H), 3.67 (1(5)-H); $[J_{1,2}+J_{1,4}]\approx 1$, $J_{1,9}=4.5$	200.5, 58.0, 54.6, 52.8
(4)	3.75, 3.69, 3.56, 3.52, 3.48, 3.42; *J* = 1.5, 1.7, 2.4, 3.5, 4.8, 4.8	199.6, 58.4, 55.9, 53.7, 52.9, 52.8, 52.2
(21)	4.59 (6-H), 4.27 (1-H), 3.96 (7-H), 3.63 (9-H), 3.62 (4-H), 3.17 (2-H); $J_{1,2}=1$, $J_{2,4}=4.0$, $J_{4,6}=1.5$, $J_{7,9}=3.0$, $J_{1,9}=J_{6,7}=0$	200.6, 79.9, 70.7, 54.1, 52.6, 52.0, 51.5

The "α,α,β"-isomer *(4)* was originally sought *via* an epoxide migration[5] in the α-alcohol *(26)* to give *(27)*. *(26)* is obtained in high yield from *(5)*, since reduction ($NaBH_4$, ethanol, 0 °C, 95% *(24)*, 5% β-alcohol) and addition of HOCl (conditions as in the case of *(5)*; besides 15% dichloride (m. p. 135 °C), 65% 6β,7α-chlorohydrin *(25)* (acetate m. p. 125 °C), possibly traces of 6α,7β-isomer *(22)*) can be carried



out stereoselectively and the subsequent cyclization (5% KOH/methanol, 60 °C, 15 min) is unproblematic (85–90%, m. p. 200 °C)[6]. However, under a large variety of conditions *(26)* does not isomerize to *(27)*. Apparently the transition into the "closed" conformation necessary for this isomerization is energetically unattainable. Hence, *(4)* (m. p. 104 °C, $\nu_{CO}=1727\ cm^{-1}$; see Table 1) was prepared by oxidation (RuO_2, $NaIO_4$, CH_2Cl_2, H_2O, K_2CO_3, 20 °C, 90%) of *(27)*[1] generated *via* an alternative route[7].



Received: November 28, 1979 [Z 408 IE]
German version: Angew. Chem. *92*, 216 (1980)

CAS Registry numbers:
(2), 72985-61-6; *(3)*, 73037-30-6; *(4)*, 73037-31-7; *(5)*, 61520-91-0; *(6a)*, 72985-62-7; *(6b)*, 72985-63-8; *(7a)*, 73037-32-8; *(7b)*, 72985-41-2; *(8a)*, 72985-42-3; *(8b)*, 73037-17-9; *(9a)*, 72985-43-4; *(10)*, 72985-44-5; *(14)*, 73037-18-0; *(17)*, 72985-45-6; *(18)*, 73037-19-1; *(19)*, 73037-20-4; *(20)*, 72985-46-7; *(21)*, 72985-47-8; *(22)*, 73037-21-5; *(23)*, 73037-22-6; *(24)*, 61463-45-4; *(25)* acetate, 72968-05-9; *(25)* dichloro analogue, 72985-48-9; *(26)*, 73037-23-7; *(27)*, 67650-78-6

[1] *H. Prinzbach, Ch. Rücker, H. Fritz*, Angew. Chem. *91*, 646 (1979); Angew. Chem. Int. Ed. Engl. *18*, 611 (1979).
[2] *H. Prinzbach, W. Seppelt, H. Fritz*, Angew. Chem. *89*, 174 (1977); Angew. Chem. Int. Ed. Engl. *16*, 198 (1977). The equilibrium formulated there for *(5)* [there *(3)*] with its *trans*-isomer has proved to be in error; hence the exclusive formation of *cis*-derivatives is explainable. This *trans*-isomer has in the meantime been prepared *via* an independent route: ^{1}H-NMR ($CDCl_3$): δ = 6.01 (6(7)-H), 3.74 (1(3)-H), 3.57 (5(8)-H); ^{13}C-NMR ($CDCl_3$): δ = 200.0 (C-2), 128.9 (C-6(7)), 59.3 (C-1(3)), 50.5 (C-5(8); *W. Seppelt* Dissertation, Universität Freiburg 1980.
[3] *H. Prinzbach, Ch. Rücker*, Angew. Chem. *88*, 611 (1976); Angew. Chem. Int. Ed. Engl. *15*, 559 (1976).
[4] *R. Keller, R. Schwesinger, W. Fritsche, H.-W. Schneider, D. Hunkler, H. Prinzbach*, Chem. Ber. *112*, 3347 (1979), and references cited therein.
[5] *S. J. Angyal, P. T. Gilham*, J. Chem. Soc. *1957*, 3691.
[6] The circuitous route *via (26)* is worthwhile for the preparation of *(2)*, since the oxidation proceeds in 80% yield.
[7] The new compounds gave correct analyses and characteristic spectra; the NMR data given in Table 1 for the ketones *(2)*–*(4)* and *(21)* also substantiate the difficulty of spectroscopic differentiation in the case of *(2)*/*(3)*.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0303-0215 $ 02.50/0*

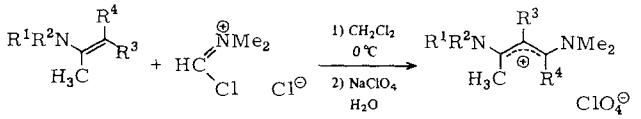
1,3-Bis(dialkylamino)-1,3-butadiene from 1-Methylvinamidinium Salts[**]

By *Rudolf Gompper* and *Ulrich Heinemann*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Vinamidinium salts [vinylogous amidinium salts, see *(1)*] are able to react as ambifunctional systems with bases and nucleophiles[1,2]. With 2-ethoxy-1,1-dimethoxy-4-(dimethylamino)-1,3-butadiene and 1,1-dimethoxy-2,4-bis(dimethylamino)-1,3-butadiene as examples we have shown that "electron-rich" butadienes can be prepared by deprotonation of the corresponding 1-(dimethoxymethyl)allylium salts with NaH[2]. Independently of us, *Oppolzer et al.*[3] and *Ghosez et al.*[4] have found that 1-aminobutadienes can be obtained from 1-amino-3-methylallylium salts. 1-(Dialkylamino)butadiene derivatives have been formulated as intermediates also in polysubstitutions of olefins and ketones with dimethylformamide/phosphorus oxide chloride[5] and in thio-Claisen rearrangements[6].

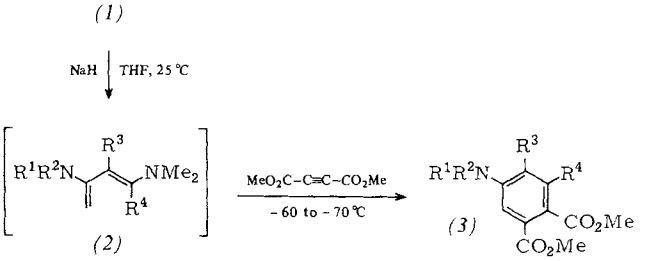
Since only relatively few 1-alkylvinamidinium salts such as *(1e,f)* (Table 1)[7,8] have been described, we have prepared a few others *(1a–d)* from β-aminocrotonic esters and dimethylformamidoyl chloride derivative (Table 1).



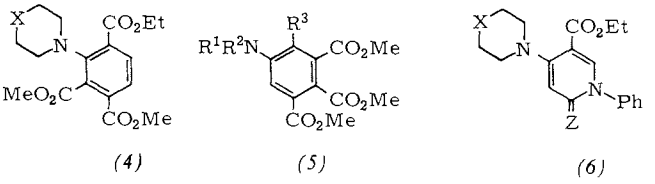
R^3 = CO_2R, R^4 = H

(1a–d)

fact that besides *(3c,d)* small amounts of *(4c,d)* are found, which derive from [2+2]-cycloadditions. Furthermore, on



reaction of *(1a–c)* with two equivalents of dimethyl acetylenedicarboxylate, the tetracarboxylates *(5)* (Table 1) are also obtained besides *(3)* and *(4)*.



(4) *(5)* *(6)*

If heterocumulenes such as phenyl isocyanate or isothiocyanate are used as trapping reagents for *(2)*, the α-pyridones and α-thiopyridones *(6)*, respectively, can be isolated (Table 1).

Received: November 30, 1979 [Z 409a IE]
German version: Angew. Chem. *92*, 207 (1980)

Table 1. Vinamidinium salts *(1)* and trapping products of the intermediary 1,3-diamino-1,3-butadienes *(2)*.

					(1)		*(3)*		*(5)*	
	R^1	R^2	R^3	R^4	M.p. [°C]	Yield [%]	M.p. [°C]	Yield [%]	M.p. [°C]	Yield [%]
a	Me	Me	CO_2Et	H	72–73	71	70–72	49	148	23
b	Me	Me	CO_2Me	H	93–95	64	88–90 [a]	48	201–203 [d]	18
c	$(CH_2)_5$		CO_2Et	H	95–97	63	[b]	37	81–82	6
d	$(CH_2)_2O(CH_2)_2$		CO_2Et	H	107–108•	69	81–83	27		
e	Me	Me	H	H	[8]		58–59 [c]	43		
f	Me	Me	H	Ph	[8]		89–90	48		

	(4)			*(6)*	
	X	M.p. [°C]	Yield [%]	Z	M.p. [°C]	Yield [%]
a	CH_2			O	149	67
b	O			O	136–138 (dec.)	56
c	CH_2	57–59	12	S	145–146 (dec.)	61
d	O	105–106	18	S	161–163	85

[a] M. p. 79–81 °C [9]. [b] B. p. 250 °C/0.01 mbar. [c] M. p. 59 °C [9]. [d] M. p. 202–203 °C [9].

The 1,3-bis(dialkylamino)-1,3-butadienes *(2)* are generated by action of sodium hydride on *(1)* (tetrahydrofuran, room temperature). Attempts to isolate them have so far met without success; they are best handled in solution. If, after evolution of hydrogen has ceased, the solution is cooled to −60 to −70 °C and then treated with one equivalent of dimethyl acetylenedicarboxylate, one obtains the phthalates *(3)* (Table 1).

Presumably *(3)* is formed by a [4+2]-cycloaddition involving dipolar intermediates. This is supported, *inter alia*, by the

[*] Prof. Dr. R. Gompper, Dipl.-Chem. U. Heinemann
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

CAS Registry numbers:
(1a), 72952-93-3; *(1b)*, 72952-95-5; *(1c)*, 72952-97-7; *(1d)*, 72952-99-9; *(1e)*, 72953-01-6; *(1f)*, 7099-64-1; *(3a)*, 72953-02-7; *(3b)*, 52251-20-4; *(3c)*, 72953-03-8; *(3d)*, 72953-04-9; *(3e)*, 39617-05-5; *(3f)*, 72953-05-0; *(4c)*, 72953-06-1; *(4d)*, 72953-07-2; *(5a)*, 72953-08-3; *(5b)*, 52251-21-5; *(5c)*, 72953-09-4; *(6a)*, 72953-10-7; *(6b)*, 72953-11-8; *(6c)*, 72953-12-9; *(6d)*, 72953-13-0; ethyl 3-(dimethylamino)-2-butenoate, 14205-42-6; methyl 3-(dimethylamino)-2-butenoate, 15895-69-9; ethyl 3-(1-piperidiryl)-2-butenoate, 36276-69-4; ethyl 3-(4-morpholinyl)-2-butenoate, 36277-32-4; *N,N*-dimethyl-1-propen-2-amine, 22499-75-8; *N,N*-dimethyl-1-phenyl-1-propen-2-amine, 2618-46-4; *N*-(chloromethylene)-*N*-methylmethanaminium chloride, 3724-43-4

[1] *R. Gompper, R. Sobotta*, Angew. Chem. *90*, 808, 810 (1978); Angew. Chem. Int. Ed. Engl. *17*, 760, 762 (1978); *H. G. Viehe, Z. Janousek, R. Gompper, D. Lach, ibid. 85*, 581 (1973) and *12*, 566 (1973); *R. Gompper, C. S. Schneider*, Synthesis *1979*, 213, 215.
[2] *R. Gompper, R. Sobotta*, Tetrahedron Lett. *1979*, 921.
[3] *W. Oppolzer, L. Bieber, E. Francotte*, Tetrahedron Lett. *1979*, 981

[4] *M. Gillard, C. T'Kint, E. Sonveaux, L. Ghosez*, J. Am. Chem. Soc. *101*, 5837 (1979).
[5] *C. Jutz* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry. Part 1. Wiley, New York 1976, pp. 250–253, 289–294.
[6] *Y. Tamaru, T. Harada, Z. Yoshida*, Tetrahedron Lett. *1978*, 2167.
[7] *C. Jutz, R. Kirchlechner, H.-J. Seidel*, Chem. Ber. *102*, 2301 (1969).
[8] *Z. Arnold, A. Holý*, Collect. Czech. Chem. Commun. *28*, 2040 (1963).
[9] *H. Neunhoeffer, G. Werner*, Justus Liebigs Ann. Chem. *1973*, 1955.

1,3-Bis(dimethylamino)-2-aza-1,3-butadienes from 1-Alkyl-2-azavinamidinium Salts[**]

By *Rudolf Gompper* and *Ulrich Heinemann*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Numerous aspects of the chemistry of 2-aza-1,3-butadienes have been investigated over the past ten years. In connection with investigations on the application of the allopolarization principle[1] to 2-azaallyl anions we found simple methods for the synthesis of 4-(dimethylamino)- and 4,4-bis(methylthio)-2-aza-1,3-butadienes[2]. The conversion of 1-methylvinamidinium salts into 1,3-bis(dialkylamino)-1,3-butadienes[3] now also opens a route to 1,3-bis(dimethylamino)-2-azabutadienes *(2)*.

The 1-alkyl-2-azavinamidinium salts *(1)* required as starting substances (cf. also [4]) can be obtained by reaction of amidines or guanidines[5] with carboxamide/dimethyl sulfate adducts[6] (see Table 1). Reaction of *(1)* with sodium hydride

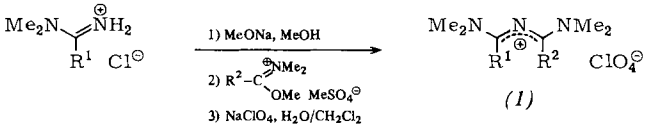
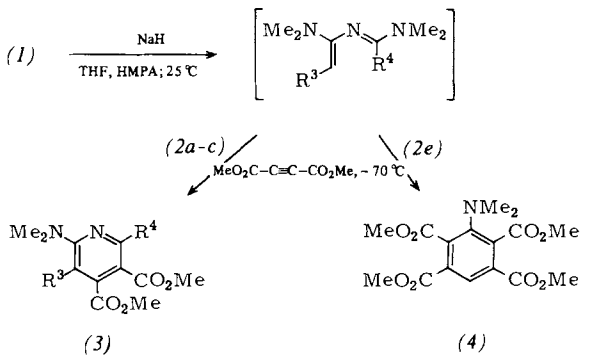


Table 1. 2-Azavinamidinium salts *(1)* and trapping products of the intermediary 1,3-diamino-2-aza-1,3-butadienes *(2)*.

	Product	R^1	R^2	M.p. [°C]	Yield [%]
	(1a)	Me	H	94–95	79
	(1b)	$PhCH_2$	H	129–131	61
	(1c)	Ph	Me	111–112	73
	(1d)	Me	Me	185–187	70
	(1e)	Me_2N	Me	88–89	74
Reaction	Product	R^3	R^4	M.p. [°C]	Yield [%]
(1a)→*(2a)*→*(3a)*		H	H	111–112	16
(1b)→*(2b)*→*(3b)*		Ph	H	113–114	50
(1c)→*(2c)*→*(3c)*		H	Ph	91–92	28
(1e)→*(2e)*→*(4)*				173	12
				173 [7]	

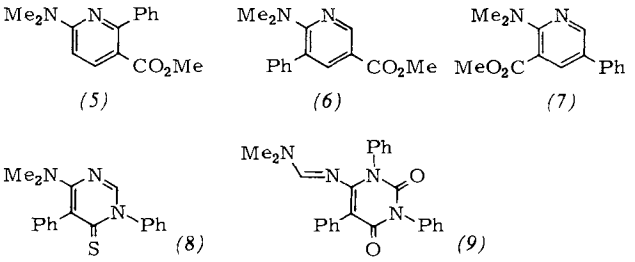
in tetrahydrofuran (THF) or—in the case of *(1b,c)*—hexamethylphosphoric triamide (HMPA) affords the azabutadienes *(2)*, which can be identified by their reactions; so far, they have not been isolated. On addition of dimethyl acetylenedicarboxylate to solutions of *(2a–c)* at −70 °C, the 6-(dimethylamino)-3,4-pyridinedicarboxylates *(3)* are obtained (see Table 1).

Reaction of *(2e)* with dimethyl acetylenedicarboxylate surprisingly leads—*via* a [2+2]-cycloadduct—to the aminobenzenetetracarboxylates *(4)*.



(2a), $R^3 = R^4 = H$; *(2b)*, $R^3 = Ph$, $R^4 = H$;
(2c), $R^3 = H$, $R^4 = Ph$; *(2e)*, $R^3 = H$, $R^4 = NMe_2$

On reaction of *(2c)* with methyl propiolate, the pyridinecarboxylate *(5)* is obtained (yield 12%, m. p. 46–48 °C). The corresponding reaction of *(2b)* yields, besides the 6-dimethylamino-3-pyridine-carboxylates *(6)* ([4+2]-cycloaddition), the 2-(dimethylamino)-derivative *(7)* ([2+2]-cycloaddition) (yields 29 and 14%, m. p. 66 °C and b. p. 230 °C/0.01 mbar, respectively).



Reaction of *(2b)* with phenyl isothiocyanate leads to the expected pyrimidinethione *(8)* (yield 36%, m. p. 203–204 °C), whereas reaction with phenyl isocyanate, however, gives the aminouracil derivative *(9)* (yield 30%, m. p. 254–255 °C). A 1,3,5-triazocinedione structure for *(9)*, also likely on the basis of its ^{1}H-NMR spectrum ($\delta = 2.49$, s, 6H), could be ruled out because acid hydrolysis of *(9)* leads to the well-known triphenylbarbituric acid[8].

Received: November 30, 1979 [Z 409b IE]
German version: Angew. Chem. *92*, 208 (1980)

CAS Registry numbers:
(1a), 72953-15-2; *(1b)*, 72953-17-4; *(1c)*, 72953-19-6; *(1d)*, 72953-21-0; *(1e)*, 72953-23-2; *(2a)*, 72953-24-3; *(2b)*, 72953-25-4; *(2c)*, 72953-26-5; *(2e)*, 72953-27-6; *(3a)*, 72953-28-7; *(3b)*, 72953-29-8; *(3c)*, 72953-30-1; *(4)*, 56873-67-7; *N,N*-dimethylethanimidamide · HCl, 2909-15-1; *N,N*-dimethylbenzenethanimidamide · HCl, 41890-15-7; *N,N*-dimethylbenzenecarbonimidamide · HCl, 41890-12-4; *N,N,N',N'*-tetramethylguaridine · HCl, 1729-17-5; *N*-(methoxymethylene)-*N*-methylmethanaminium methyl sulfate, 21511-55-7; *N*-(methoxyethylidene)-*N*-methylmethanaminium methylsulfate, 920-98-9; dimethyl acetylenedicarboxylate, 762-42-5

[*] Prof. Dr. R. Gompper, Dipl.-Chem. U. Heinemann
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)
[**] This work was supported by the Fonds der Chemischen Industrie.

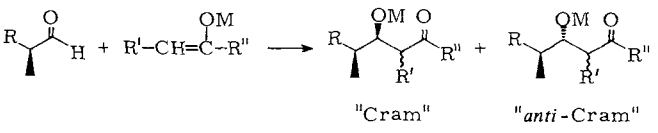
[1] *R. Gompper, H.-U. Wagner*, Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976).
[2] *R. Gompper, U. Heinemann*, Dtsch. Pat.-Anm. P 2919891.2 (May 17, 1979).
[3] *R. Gompper, U. Heinemann*, Angew. Chem. *92*, 207 (1980); Angew. Chem. Int. Ed. Engl. *19*, 216 (1980).
[4] *J. C. Meslin, A. Reliquet, F. Reliquet, C. TeaGokou*, C. R. Acad. Sci. *C 286*, 397 (1978).
[5] Experiments in collaboration with *R. Sobotta* (1978).
[6] *W. Kantlehner* in *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry. Part 2. Wiley, New York 1979, p. 194.
[7] *H. Neunhoeffer, B. Lehmann*, Justus Liebigs Ann. Chem. *1975*, 1113.
[8] *S. Senda, H. Fujimura, H. Izumi*, Jap. Pat. 7907 ('65) 1965) Takeda Chem. Ind.; Chem. Abstr. *64*, P 12694c (1966).

Enhancement of 1,2-Asymmetric Induction on C—C Linkage by Use of Chiral 2-Butenylboronic Esters[**]

By *Reinhard W. Hoffmann* and *Hans-Joachim Zeiss*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The formation of β-methylalkanols by aldol-type C—C linkage is of cardinal importance in the synthesis of macrolides and related structures[1]. This raises the problem of 1,2-asymmetric induction associated with the Cram rule[2]:



The diastereoselectivities achieved so far lie mainly in the range of 0.8–4:1[3]. These results should be open to improvement by use of a chiral reagent instead of an achiral one in the reaction with the optically active aldehyde normally used[4]. We have therefore examined the effect of modifying the chirality[5] on the reaction of 2-methylbutyraldehyde *(4)* with 2-butenylboronic esters[6].

1-Methylallylboronic bis(dimethylamide) *(1)* was isomerized[7] by heating with 10 wt. % of $ZnCl_2$ at 150 °C for 80 h, giving a 7:3 mixture of 2-butenylboronic bis(dimethylamides) *(2)* (b. p. 98.3 °C/100 torr) and *(3)* (b. p. 101 °C/100 torr). After separation over a 1-m spinning band column, compounds *(2)* and *(3)* were transformed quantitatively into the chiral reagents (−)-*(5)* and (−)-*(8)* by treatment with (+)-2-*exo*,3-*exo*-dihydroxy-3-*endo*-phenylbornane[5]. The reaction of racemic 2-methylbutyraldehde *(4)* with the (*E*)-butenylboronic ester *(5)* afforded (as in ref.[5]) the two isomers *(6)* and *(7)* of 3,5-dimethyl-1-hepten-4-ol in 95% yield; the ratio of the isomers was determined by gas chromatography. Both isomers must have a *threo* configuration with respect to C-3/C-4[6]. Assignment of the relative configuration of C-4/C-5 was accomplished, after hydrogenation of the double bond, on the basis of the ^{13}C-NMR spectra since the hydrogenation product of *(7)* shows a symmetry plane. The *erythro* products *(9)* and *(10)* arising from *(4)* and *(8)* were determined and assigned in corresponding manner.

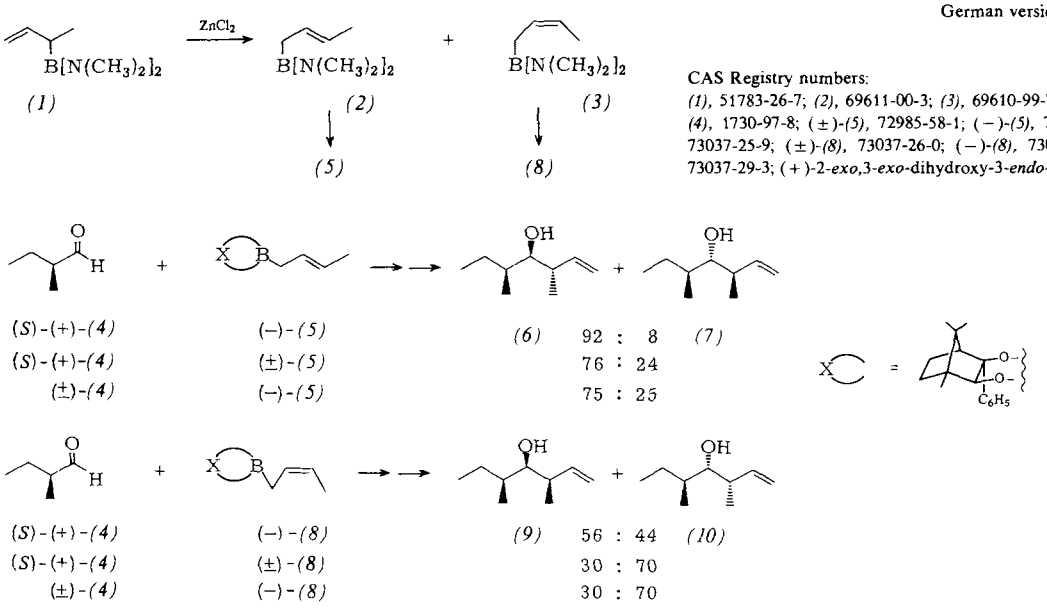
Reaction of racemic *(5)* with the (*S*)-(+)-aldehyde *(4)*[8] gave the isomeric alcohols in the ratio of 3:1, with the "Cram" product *(6)* predominating. On use of chiral *(5)*, the diastereoselectivity rose to *ca.* 11:1 because the tendency towards preferential formation of the Cram product and the tendency of the reagent to form an alcohol with (*R*) configuration at C-4[5] now cooperate. This result demonstrates the enhancement of diastereoselectivity which can be effected by a chiral reagent. It can be deduced from the diastereomeric ratio of 3:1 found for the reaction of the racemic aldehyde with the chiral reagent *(5)* that the (*R*)-(−)-aldehyde yields the enantiomers of *(6)* and *(7)* in the ratio of 1.4:1 because the Cram preference and chiral control by the reagent now oppose each other.

On reaction of the racemic (*Z*)-2-butenylboronic ester *(8)* with the (*S*)-(+)-aldehyde *(4)*, the anti-Cram product *(10)* predominated in the ratio 2.3:1. Although the amount of *(9)* could be increased by the chiral ragent *(8)*, it was not possible to overcompensate the anti-Cram preference. On the other hand, the anti-Cram preference and chiral control should again reinforce each other in the reaction of (*R*)-(−)-2-methylbutyraldehyde with *(8)*. Indeed, the data obtained for the reaction of racemic *(4)* with chiral *(8)* indicate a corresponding selectivity of 20:1! It can be seen that the selectivity could so far only be adequately enhanced in favor of one out of two possible diastereomers.

The anti-Cram preference in the reaction of *(8)* with *(4)* is also remarkable: such preference has so far only been observed in the addition of (*Z*)-enol borinates[3d], but not in that of lithium (*Z*)-enolates[3a]. This could be a result of the more compact cyclic transition states encountered with the boron reagents[10]; molecular models show that the anti-Cram transition state is less hindered in the case of *(8)*, and the Cram transition state less hindered in the case of *(5)*.

Received: December 13, 1979 [Z 410 IE]
German version: Angew. Chem. *92*, 218 (1980)

CAS Registry numbers:
(1), 51783-26-7; *(2)*, 69611-00-3; *(3)*, 69610-99-7; (±)-*(4)*, 57456-98-1; (*S*)-(+)-*(4)*, 1730-97-8; (±)-*(5)*, 72985-58-1; (−)-*(5)*, 73037-24-8; *(6)*, 72985-59-2; *(7)*, 73037-25-9; (±)-*(8)*, 73037-26-0; (−)-*(8)*, 73037-27-1; *(9)*, 73037-28-2; *(10)*, 73037-29-3; (+)-2-*exo*,3-*exo*-dihydroxy-3-*endo*-phenylbornane, 17957-90-3



[*] Prof. Dr. R. W. Hoffmann, Dipl.-Chem. H.-J. Zeiss
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *C. Masamune, G. S. Bates, J. W. Corcoran*, Angew. Chem. *89*, 602 (1977); Angew. Chem. Int. Ed. Engl. *16*, 585 (1977).
[2] Cf. also: *N. Trong-Anh, O. Eisenstein*, Nouveau J. Chim. *1*, 61 (1977), further references cited therein.
[3] a) *C. T. Buse, C. H. Heathcock*, J. Am. Chem. Soc. *99*, 8109 (1977); b) *G.*

Schmid, T. Fukuyama, K. Akasaka, Y. Kishi, ibid. 101, 259 (1979), ref. 15 therein; c) *A. I. Meyers, D. M. Roland, D. L. Comins, R. Henning, M. P. Fleming, K. Shimizu, ibid. 101,* 4732 (1979); d) *M. Hirama, D. S. Garvey, L. D.-L. Lu, S. Masamune,* Tetrahedron Lett. *1979,* 3937.

[4] The principle of double stereodifferentiation (*Y. Izumi, A. Tai:* Stereodifferentiating Reactions. Academic Press, New York 1977, p. 247) was recently applied to a similar problem: *C. H. Heathcock, C. T. White,* J. Am. Chem. Soc. *101,* 7076 (1979).

[5] *T. Herold, R. W. Hoffmann,* Angew. Chem. *90,* 822 (1978); Angew. Chem. Int. Ed. Engl. *17,* 768 (1978); *R. W. Hoffmann, W. Ladner,* Tetrahedron Lett. *1979,* 4653.

[6] *R. W. Hoffmann, H. J. Zeiss,* Angew. Chem. *91,* 329 (1979); Angew. Chem. Int. Ed. Engl. *18,* 306 (1979).

[7] *K. G. Hancock, J. D. Kramer,* J. Organomet. Chem. *64,* C 29 (1974).

[8] The aldehyde prepared according to ref. [9] from enantiomerically pure (Mosher determination [9b]) (*S*)-(−)-methylbutanol ($[\alpha]_D^{25} = -5.76°$ (neat)) showed a rotation of $[\alpha]_D^{25} = +32.5°$ (neat) (34.5° [9a]). Reduction with BH_3/THF [9c] regenerated the enantiomerically pure alcohol.

[9] a) *W. Kirmse, H. Arold,* Chem. Ber. *104,* 1800 (1971); b) *J. A. Dale, H. S. Mosher,* J. Am. Chem. Soc. *95,* 512 (1973); c) *D. Enders, H. Eichenauer,* Chem. Ber. *112,* 2933 (1979).

[10] *D. A. Evans, E. Vogel, J. V. Nelson,* J. Am. Chem. Soc. *101,* 6120 (1979).

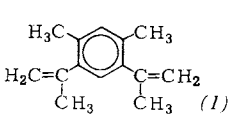
1,3-Bis(1-lithio-3-methyl-1-phenylpentyl)benzene, an Organodilithium Compound Soluble in Aromatic Hydrocarbons[**]

By *Günther Schulz* and *Hartwig Höcker*[*]

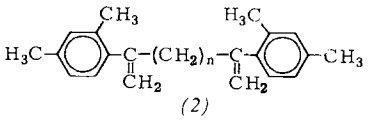
Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Some vinyl compounds, such as 1,1-diphenylethylene[1], α-isopropenylnaphthalene, and 1-isopropenyl-2,4-dimethylbenzene[2] cannot be anionically homopolymerized. On electron transfer from alkali metals (in polar solvents, *e.g.* tetrahydrofuran) they form monomeric radical anions, which combine to give dimeric dianions.

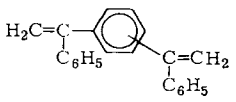
In the presence of electron transfer agents the corresponding divinyl compounds undergo polycombination reactions, which—depending on the structure of the divinyl compound—can proceed either exclusively inter- or inter- and intramolecularly. Some of the polyanions thus obtained are suitable as initiators for anionic polymerization (*e.g.* of styrene and butadiene). The divinyl compounds *(1)* and *(2)* tend to undergo side-reactions (*e.g.* proton abstraction)[4a], while *(3a)* and *(3b)* give uniform products[3]. Particularly noteworthy is the high tendency of *(3b)* to undergo cyclodimerization in the presence of electron transfer agents[5], which leads to the tetraanion.



(1)



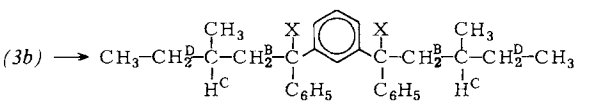
(2)



(3a), p-
(3b), m-

The reaction of anionically non-homopolymerizable divinyl compounds with butyllithium should lead to organodilithium compounds. If these dissolve in apolar solvents (benzene, toluene) they offer the possibility of initiating the anionic bifunctional 1,4-polymerization of 1,3-dienes. Since all previously known organodilithium compounds are scarcely soluble in such solvents owing to association, either polar substances such as ethers or amines have to be added, or they must be treated with small amounts of monomer (diene) to give oligomers (seeding technique). Disadvantages are the higher 1,2-content of the polymers and the heterogeneity of the initiator[6].

The compounds *(1)* and *(2)* react only to a negligibly small extent within 24 h even with excess *sec*-BuLi in toluene or benzene at 65 °C. *(3a)* is preferably monolithiated by BuLi. Reaction of *(3b)* with *sec*-BuLi (molar ratio 1:2) in toluene at room temperature, however, leads within 2 h quantitatively to the diadduct *(4)*, which is protonated to 1,3-bis(3-methyl-1-phenylpentyl)benzene *(5)*[4].



(4), X = Li; *(5)*, X = H^A; *(6)*, X = COOH

The starting compound *(3b)* can no longer be detected in the gas- and gel-chromatograms of *(5)*; on the basis of the gel chromatogram, higher adducts are ruled out. The IR spectrum shows no absorption at 900 cm^{-1} characteristic for the double bonds in *(3b)*. Proof of the structure is provided by the ^{1}H-NMR spectrum [δ = 7.11 and 7.00 (14 aromatic H), 3.94 (t, 2H^A, J_{AB} = 7 Hz), 1.8 (broad, 4H^B), 1.2 (m, 2 H^C + 4 H^D), 0.6–1.0 (m, 12 H, CH_3)] and the mass spectrum (70 eV) [*m/e* = 398 (M^+), 327 ($M^+ - C_5H_{11}$), 179 ($327 - C_5H_{11} - C_6H_5$)]. In addition, the fragment with *m/e* = 257 is formed by McLafferty rearrangement and elimination of isopentene.

The initially formed dilithium compound *(4)* is soluble in benzene and toluene up to a concentration of 0.1 mol/l. Clouding of the solution does not occur, even after 10 weeks' storage in a refrigerator.

The bifunctionality of the initiator *(4)* was checked by chemical methods on 0.1 M solutions in toluene.

1. Double titration by the method of *Gilman*[7] gave 95% of the calculated content of active organolithium groups.

2. The product obtained on reaction with solid CO_2 was isolated by extraction with aqueous NaOH. The IR spectrum of the carboxylic acid obtained on acidification is consistent with the expected structure *(6)*; the ^{1}H-NMR spectrum confirms the presence of a dicarboxylic acid quantitatively: δ = 0.3–1.6 (18 methyl-, methylene-, methine-H), 2.26 (4H^B), 7.15 (14 aromatic H), 12.07 (2 carboxylic H).

3. The dilithium compound *(4)* is suitable as bifunctional initiator for the anionic 1,4-polymerization of 1,3-butadiene and for the preparation of block copolymers (*e.g.* with styrene) of type ABA[8].

Procedure

To 40 ml of toluene or benzene, previously boiled for several days over potassium in an argon atmosphere, is added a small amount of *sec*-BuLi and the solution distilled directly into a reaction vessel containing 1.412 g (0.005 mol) *(3b)*. When *(3b)* (at 20 °C) has dissolved, a 1 M solution of *sec*-BuLi (10.0 ml) is added to the mixture. After one hour's standing at 20 °C the 0.1 M solution of the dilithium compound is ready for use; it can be stored for several weeks at −20 °C.

Received: December 21, 1979 [Z 413 IE]
German version: Angew. Chem. *92,* 212 (1980)

[*] Prof. Dr. H. Höcker, Dipl.-Chem. G. Schulz
Lehrstuhl für Makromolekulare Chemie I der Universität
Universitätsstrasse 30, D-8580 Bayreuth (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *G. Spach, H. Monteiro, M. Levy, M. Szwarc,* Trans. Faraday Soc. *58,* 1809 (1962); *J. Jagur, M. Levy, M. Feld, M. Szwarc, ibid. 58, 2168 (1962); J. Jagur,*

H. Monteiro, M. Szwarc, ibid. 59, 1353 (1963); M. Matsuda, J. Jagur-Grodzinski, M. Szwarc, Proc. Roy. Soc. (London) *A 288,* 212 (1965); *J. Jagur-Grodzinski, M. Szwarc, ibid. A 288,* 224 (1965).
[2] *H. Hopff, H. Lüssi,* Makromol. Chem. *62,* 31 (1963).
[3] *G. Lattermann, H. Höcker,* Makromol. Chem. *175,* 2865 (1974); *H. Höcker, G. Lattermann,* J. Polym. Sci., Symp. *54,* 361 (1976).
[4] a) *G. Schulz,* Dissertation, Universität Mainz 1979; b) *H. Höcker, G. Schulz,* Dtsch. Pat.-Anm. (September 25, 1979), BASF.
[5] *G. G. H. Schulz, H. Höcker,* Makromol. Chem. *178,* 2589 (1977).
[6] *R. P. Foss, H. W. Jacobson, W. H. Sharkey,* Macromolecules *10,* 287 (1977); *G. Beinert, P. Lutz, E. Franta, P. Rempp,* Makromol. Chem. *179,* 551 (1978); *L. J. Fetters, C. W. Kamienski, R. C. Morrison, R. N. Young,* Macromolecules *12,* 344 (1979).
[7] *H. Gilman, F. K. Cartledge,* Organomet. Chem. *2,* 447 (1974).
[8] *G. Schulz, H. Höcker,* unpublished.

$(AsPh_4)_2[W_2NCl_{10}]$, a μ-Nitrido Complex Containing Tungsten(V) and Tungsten(VI)

By *Frank Weller, Wolfgang Liebelt,* and *Kurt Dehnicke*[*]

The only dinuclear μ-nitrido complexes of transition metals hitherto reported in the literature were those of ruthenium(IV)[1,2] and of osmium(IV)[1,3]. We have found during attempts to synthesize the previously described $AsPh_4[WNCl_4]$ complex[4] in acetonitrile that dark brown single crystals of the composition $(AsPh_4)_2[W_2NCl_{10}]$ *(1)* are formed in a slow side reaction. As follows from elemental analysis, IR spectrum and a crystal structure determination[5], *(1)* is the first dinuclear μ-nitrido complex of tungsten containing two tungsten atoms in different oxidation states.

In the anion of *(1)* (Fig. 1) the WNW bridge is linear. The centrosymmetric space group $P2_1/n$ precludes any definite decision between a symmetric or asymmetric position of the N atom between the W atoms since disorder of the crystal might create the impression that the former applies. Under this assumption the refinement affords the two WN distances of 165.7 and 207.2 pm. Also in agreement with this is the IR spectrum, in which two WN stretching vibrations are observed at 1015 and 944 cm^{-1}.

A comparison with the WN bond lengths of the tetrameric $[WNCl_3 \cdot POCl_3]_4 \cdot 2POCl_3$[6] *(2)*, linked *via* stretched W≡N—W bridges, shows that also the long WN bond in *(1)* profits from a $d_\pi p_\pi$ overlapping. This multiple bonding also manifests itself in the *eclipsed* position of the four equatorial Cl atoms: The W atoms utilize the two d orbitals d_{xz} and d_{yz} at right angles to each other for bond strengthening. As a result of the sterically demanding WN multiple bonds the equatorial Cl atoms are shifted outwards a little (on average 7 pm), along the WNW axis. The W...W distance of 372.9 pm in *(1)* is markedly shorter than in *(2)* (386.0 pm)[6], corresponding to a Jahn-Teller stabilization of the tungsten(V). An analogous W...W distance of 372.8 pm was found in the complex $(HNMe_3)_2[W_4O_8Cl_8(OH_2)_4] \cdot 2H_2O$, in which tungsten(V) and tungsten(VI) are likewise coupled *via* linear WOW bridges[7].

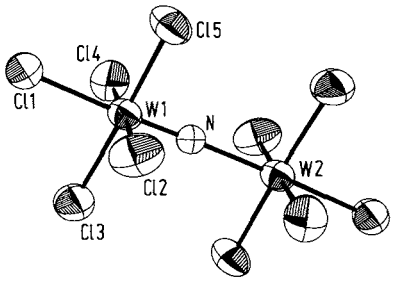


Fig. 1. Structure of the $[W_2NCl_{10}]^{2-}$ ions with ellipsoids of thermal vibration (at 21 °C; 50% probability).

Bond lengths [pm]		Bond angles [°]	
W1-N	165.7(71)	Cl2-W-Cl1	87.6(2)
W2-N	207.2(72)	Cl3-W-Cl1	85.8(2)
W-Cl1	242.6(6)	Cl4-W-Cl1	90.2(2)
W-Cl2	233.3(6)	Cl4-W-Cl2	177.2(3)
W-Cl3	228.0(6)	Cl4-W-Cl3	94.2(2)
W-Cl4	230.5(8)	Cl5-W-Cl1	89.5(2)
W-Cl5	232.5(6)	Cl5-W-Cl2	87.4(2)
		Cl5-W-Cl3	173.1(3)
		Cl5-W-Cl4	90.8(3)
		N-W-Cl1	176.7(18)
		N-W-Cl2	95.2(18)
		N-W-Cl3	92.5(17)
		N-W-Cl4	87.0(18)
		N-W-Cl5	92.5(17)

[*] Dr. W. Liebelt, Prof. Dr. K. Dehnicke, Dr. F. Weller
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

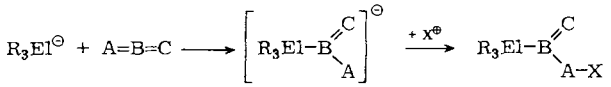
Received: August 6, 1979 [Z 415 IE]
German version: Angew. Chem. *92,* 211 (1980)

[1] *W. P. Griffith,* Coord. Chem. Rev. *8,* 369 (1972); and references cited therein.
[2] *M. Ciechanowicz, A. C. Skapski,* J. Chem. Soc. *A 1971,* 1792; *R. J. D. Gee, H. M. Powell, ibid. A 1971,* 1795.
[3] *K. W. Given, L. H. Pignolet,* Inorg. Chem. *16,* 2982 (1977).
[4] *K. Dehnicke, W. Kolitsch,* Z. Naturforsch. *B 32,* 1485 (1977).
[5] Crystal data: monoclinic, space group $P2_1/n$, $a = 1063$, $b = 1230$, $c = 2013$ pm, $\beta = 97°$, $Z = 2$. Single crystal diffractometer CAD 4 (Enraf-Nonius, Delft), $Mo_{K\alpha}$ radiation, graphite monochromator ω scan, $\vartheta = 3$–22°, 1461 observed independent reflections, Patterson methods, $R = 4.9\%$.
[6] *W. Musterle, J. Strähle, W. Liebelt, K. Dehnicke,* Z. Naturforsch. *B 34,* 942 (1979).
[7] *Y. Yeannin, J.-P. Launnay, J. Livage, A. Nel,* Inorg. Chem. *17,* 377 (1978).

Nucleophilic Addition of Triphenylstannyllithium to Carbon Disulfide

By *Paul-Reiner Bolz, Udo Kunze,* and *Werner Winter*[*]

Triorganoelement anions of Group IVb elements, R_3El^- (R = Ph, Me; El = Si, Ge, Sn, Pb), are strong nucleophiles and therefore should react readily with electrophilic heteroallenes such as CO_2, COS, CS_2, R'NCO, and R'NCS according to



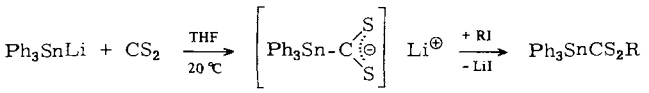
to give element-functional ligand systems which can be stabilized with Lewis acids ($X^\oplus$). Almost all such attempts have hitherto failed, since formation of the stable di-element compounds, $R_3El—ElR_3$, with reduction of the heteroallene predominates[1]. On the other hand, the reactions of carbonylmetalate ions[2] and diorganophosphides[3] with carbon disulfide (and other heteroallenes) demonstrate that the proposed reaction route is fundamentally possible.

[*] Doz. Dr. U. Kunze [+], Dipl.-Chem. P.-R. Bolz
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

Doz. Dr. W. Winter [++]
Institut für Organische Chemie der Universität Tübingen (Germany)

[+] Author to whom correspondence should be addressed.
[++] X-ray structure analysis.

We have now been able to show that a nucleophilic addition takes place on reaction of triphenylstannyllithium with carbon disulfide. The initial product *(1)* can be trapped by alkylation with methyl or ethyl iodide in tetrahydrofuran (THF).



(1) *(2a)*, R = Me; *(2b)*, R = Et

After separation by column chromatography, the products *(2a)* and *(2b)* can be crystallized from petroleum ether as air-stable violet needles of m. p. 128–129 °C and 47–48 °C, respectively, with the given composition.

With aryl halides such as iodobenzene or *p*-bromotoluene, however, no substitution products could be detected, but only bis(triphenyltin) sulfide in small amounts. Attempted nucleophilic addition of trimethylstannyllithium also failed; apparently stabilization of the electron-rich initial product by mesomerizable groups attached to tin is essential.

Table 1. Spectroscopic data of the substitution products *(2a)* and *(2b)*.

Method	*(2a)*	*(2b)*
IR (KBr) [cm^{-1}]	(C=S), 1048 s	(C=S), 1060 m
^{1}H-NMR ($CDCl_3$)	2.74 (s, 3 H, CH_3), 7.25–7.69 (mc, 15 H, C_6H_5)	1.28 (t, 3 H, CH_3), 3.42 (q, 2 H, CH_2), 7.24–7.72 (mc, 15 H, C_6H_5)
MS [a] (^{120}Sn) [m/e]	442 $[M]^{+\cdot}$ [b], 427 $[M-Me]^+$, 398 $[M-CS]^{+\cdot}$, 351 $[Ph_3Sn]^+$	456 $[M]^{+\cdot}$, 427 $[M-Et]^+$, 412 $[M-CS]^{+\cdot}$, 351 $[Ph_3Sn]^+$
UV ($CHCl_3$) λ_{max} [nm] (ε)	313 (5070), 532 (126)	314 (5000)

[a] 70 eV, direct inlet. [b] Molecular mass, calc. 441.3, exp. 439 (osmometric in benzene).

It cannot be definitely decided from the spectroscopic data (Table 1) whether the stannyl-substituted dithioformate (*A*) or the isomeric dithiocarboxylate complex (*B*) is formed.



Dithiocarboxylates of the structural type (*B*) are indeed known[4] (not of course, for R = Me, Et), but they differ very little from the substitution products *A* in their physical properties. Therefore an X-ray structure analysis of *(2a)* was carried out[5], which confirmed the structural type *A*.

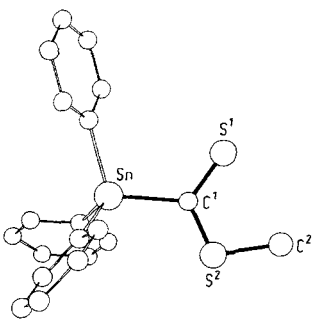
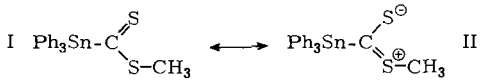


Fig. 1. Molecular structure of *(2a)*; Sn—C^1 = 214 ± 0.8, C^1—S^1 = 164 ± 2, C^1—S^2 = 162 ± 2, C^2—S^2 = 184 ± 4 pm; angles around C^1: 120 ± 1°, C^1—S^2—C^2 = 106 ± 1.5° [5].

Crystallographically, *(2a)* has a tetraphenyltin structure exhibiting "ordered disorder"[6] in which the phenyl groups with a population factor of 0.25 are replaced by methylthiothiocarbonyl ligands. An outstanding feature of this completely planar structural unit[7] is that the S—C^1 bonds are, within the limits of error, of equal length, thus suggesting participation of the mesomeric resonance hybrid II:



Procedure

Double the stoichiometric amount of CS_2 is added dropwise to a stirred solution of Ph_3SnLi[8] (16 mmol) in THF (50 ml), whereupon the solution becomes warm and turns reddish-brown in color. After cooling, MeI or EtI is added in excess. Column chromatographic separation (silica gel, THF) of the violet solution affords a red fraction and a dark brown fraction. After removal of solvent and double recrystallization from petroleum ether the red fraction gives pure *(2a)* (yield 60%) and *(2b)* (yield *ca.* 5%), respectively.

Received: July 16, 1979 [Z 418 IE]
German version: Angew. Chem. *92*, 227 (1980)

[1] *C. Tamborski, F. E. Ford, E. J. Soloski*, J. Org. Chem. *28*, 181 (1963); *28*, 237 (1963); cf. [9].
[2] *J. E. Ellis, R. W. Fennel, E. A. Flom*, Inorg. Chem. *15*, 2031 (1976).
[3] *J. Kopf, R. Lenck, S. N. Olafsson, R. Kramolowsky*, Angew. Chem. *88*, 811 (1976); Angew. Chem. Int. Ed. Engl. *15*, 768 (1976).
[4] *S. Kato, T. Kato, T. Yamauchi, Y. Shibahashi, E. Kakuda, M. Mizuta, Y. Ishii*, J. Organomet. Chem. *76*, 215 (1974).
[5] Tetragonal, space group $P\bar{4}2_1c$ ($Z = 2$); $a = 1184$, $b = 677$ pm; 1200 reflections with $F \geq 3\sigma(F)$, NONIUS CAD-4 ($Mo_{K\alpha}$, graphite monochromator); refinement: $R = 0.0487$ (isotropic, SHELX).
[6] *P. C. Chieh, J. Trotter*, J. Chem. Soc. *A 1970*, 911.
[7] *I. S. Butler, A. E. Fenster*, J. Organomet. Chem. *66*, 161 (1974).
[8] *H. Schumann, K. F. Thom, M. Schmidt*, J. Organomet. Chem. *1*, 167 (1963).
[9] *Note added in proof*: The only reaction that has been reported is the addition of carbon dioxide to triorganosilyl- and germyl anions: *A. G. Brook, H. Gilman*, J. Am. Chem. Soc. *76*, 77 (1954); *77*, 2322 (1955).

Photooxidation of the Ligands of Bis(*o*-semiquinonediimine)nickel(II) and -platinum(II)[**]

By *Arnd Vogler* and *Horst Kunkely*[*]

All the photoredox reactions of transition metal complexes examined so far involve direct participation of the metal[1]. We now report a photoreaction in which the ligands are oxidized while the oxidation state of the metal remains unchanged.

o-Hydroquinones and *o*-quinones[2], as well as *o*-phenylenediamine and *o*-quinonediimine[3] form transition metal complexes which can undergo mutual interconversion by several reversible one-electron redox reactions *via* stable semiquinone and semiquinonediimine species, respectively. The complexes $M[o\text{-}C_6H_4(NH_2)]_2^z$ having M = Ni, Pd, and Pt then occur with charges $z = -2, +1, 0, -1$, and -2[3]. The end members with $z = +2$ and -2 contain the ligands *o*-qui-

[*] Prof. Dr. A. Vogler, Dr. H. Kunkely
Institut für Chemie der Universität
Postfach, D-8400 Regensburg (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

nonediimine o-$C_6H_4(NH)_2$ and o-phenylenediamide o-$C_6H_4(NH)_2^{2-}$. The most stable members of these redox series are the uncharged diamagnetic and deep-blue complexes $M[o\text{-}C_6H_4(NH)_2]_2$ having two mutually coupled o-semiquinonediimine ligands. One-electron oxidation of the neutral complexes leads to the cations $M[o\text{-}C_6H_4(NH)_2]_2^+$, with loss of one ligand electron. This can be deduced, *inter alia*, from the fact that the potentials of the oxidation are almost independent of the metal and the unpaired electron of the cations is localized on the ligands[3]. We observed that this ligand oxidation also occurs as a photochemical reaction. The complexes of Ni and Pt were studied in detail.

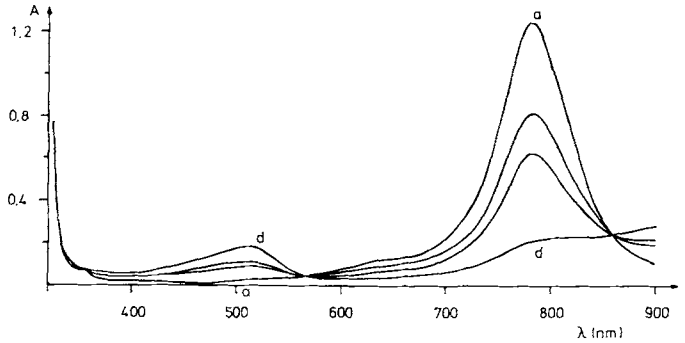


Fig. 1. Change in the absorption spectrum during the photolysis of $Ni[o\text{-}C_6H_4(NH_2)]_2$ (2.29×10^{-5} mol/l) in $CHCl_3$ in a 1-cm cell. Excitation with light of $\lambda > 330$ nm; duration of irradiation: a = 0, d = 3 min.

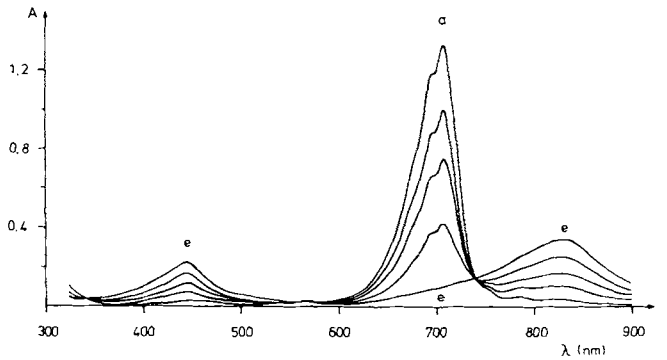


Fig. 2. Change in the absorption spectrum during the photolysis of $Pt[o\text{-}C_6H_4(NH)_2]_2$ (1.37×10^{-5} mol/l) in $CHCl_3$ in a 1-cm cell. Excitation with light of $\lambda > 330$ nm; duration of irradiation a = 0, e = 4 min.

Irradiation of the complexes $M[o\text{-}C_6H_4(NH)_2]_2$ (M = Ni and Pt) dissolved in $CHCl_3$ with light of wavelength $\lambda < 350$ nm led, with decoloration of the blue solutions in a smooth reaction (Figures 1 and 2), to formation of the cations $M[o\text{-}C_6H_4(NH)_2]_2^+$ which could once again be reduced completely to the neutral complexes (*e.g.* with $NaBH_4$). The solvent $CHCl_3$ serves as electron scavenger[4] during the photooxidation. The quantum yields were $\phi = 0.28$ (Ni) and 0.33 (Pt) on excitation at $\lambda = 313$ nm.

It is assumed that the photooxidation is initiated by an excited intraligand state since the excitation wavelength ($\lambda < 350$ nm) is independent of the metal. It is remarkable that light absorption by the intense long-wave bands (Fig. 1 and 2), which are also assigned to intraligand transitions, did not lead to a photoreaction.

Received: September 12, 1979 [Z 419 IE]
German version: Angew. Chem. *92*, 228 (1980)

[1] *A. W. Adamson, P. D. Fleischauer:* Concepts of Inorganic Photochemistry. Wiley, New York 1975; *V. Balzani, V. Carassiti:* Photochemistry of Coordination Compounds. Academic Press, New York 1970.

[2] *H. H. Downs, R. M. Buchanan, C. G. Pierpont,* Inorg. Chem. *18*, 1736 (1979), and references cited therein.

[3] *A. L. Balch, R. H. Holm,* J. Am. Chem. Soc. *88*, 5201 (1966).

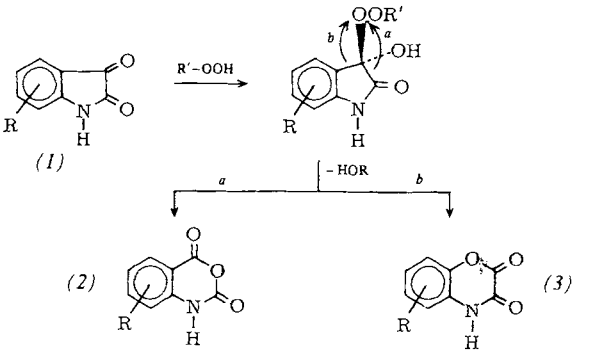
[4] *A. Vogler, W. Losse, H. Kunkely,* J. Chem. Soc. Chem. Commun. *1979*, 187.

Oxidation of Isatins to Isatoic Anhydrides and 2,3-Dioxo-1,4-benzoxazines

By *Gernot Reissenweber* and *Dietrich Mangold*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Isatoic anhydrides[1], which are of interest as intermediates for the synthesis of numerous heterocycles, can be obtained by oxidation of isatins with chromium trioxide in glacial acetic acid or acetic anhydride[2]. With the aim of using a less toxic oxidizing agent than chromium trioxide we have further investigated the Baeyer-Villiger oxidation of isatins, for it is well known that *N*-phenyl-substituted isatins can be converted by peracids into the corresponding isatoic anhydrides[3].



In a Baeyer-Villiger oxidation of isatins *(1)* two reaction products are possible on attack of peroxide at C^3: Rearrangement of the initially formed Criegee adduct yields isatoic anhydride *(2) via* route *a* and the isomeric 2,3-dioxo-1,4-benzoxazines *(3) via* route *b*.

Depending upon the reaction conditions and the oxidizing agent we have been able to carry out a regioselective synthesis of isatoic anhydrides *(2)* or 2,3-dioxo-1,4-benzoxazines *(3)* from *(1)*; Table 1 shows some examples.

On addition of an equimolar amount or slight excess of 30% aqueous hydrogen peroxide to a suspension of isatin in glacial acetic acid at 25–35 °C, a slightly exothermic reaction ensues after a short period of time; the suspension goes into solution and after a few minutes the isatoic anhydride *(2)* begins to precipitate from the warm solution. As a rule the compounds *(2)* are free of isomers.

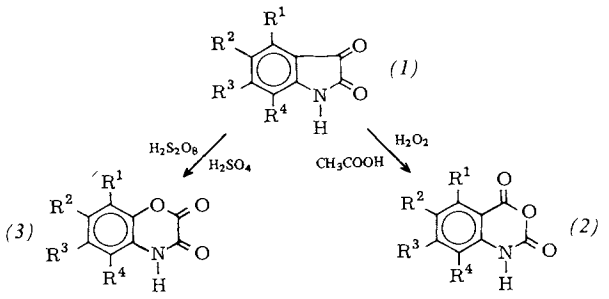
The reaction is accelerated by catalytic amounts of sulfuric acid, phosphoric acid, or *p*-toluenesulfonic acid. Use of formic acid as solvent or use of larger amounts of sulfuric acid leads to lower overall yields of *(2)*, and the crude product is contaminated with varying amounts of *(3)*.

In contrast, the oxidation of isatins *(1)* with potassium peroxodisulfate in sulfuric acid at room temperature or below affords 2,3-dioxo-1,4-benzoxazines *(3)* in high yields in

[*] Dr. G. Reissenweber [+], Dr. D. Mangold
BASF Aktiengesellschaft, Hauptlaboratorium, WHW
D-6700 Ludwigshafen (Germany)

[+] Author to whom correspondence should be addressed.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0222 $ 02.50/0



CAS Registry numbers:
(1a), 91-56-5; *(1b)*, 1127-59-9; *(1c)*, 391-12-8; *(1d)*, 6374-92-1; *(1e)*, 87-48-9; *(1f)*, 611-09-6; *(1g)*, 7477-63-6; *(1h)*, 72985-49-0; *(1i)*, 443-69-6; *(1j)*, 324-03-8; *(1k)*, 20205-43-0; *(2a)*, 118-48-9; *(2b)*, 66176-17-8; *(2c)*, 72985-50-3; *(2d)*, 4693-00-9; *(2e)*, 24088-82-2; *(2f)*, 4693-02-1; *(2g)*, 63497-60-9; *(2h)*, 72985-51-4; *(2i)*, 321-69-7; *(2j)*, 321-50-6; *(3a)*, 3597-63-5; *(3b)*, 72985-52-5; *(3c)*, 72985-53-6; *(3d)*, 72985-29-6; *(3e)*, 72985-30-9; *(3k)*, 72985-31-0.

[1] *G. M. Coppola, G. E. Hardtmann, O. R. Pfister,* J. Org. Chem. *41,* 825 (1976); *G. M. Coppola, G. E. Hardtmann,* J. Heterocycl. Chem. *16,* 829 (1979).
[2] *H. Kolbe,* J. Prakt. Chem. [2] *30,* 467 (1884); *R. Dorsch, ibid.* [2] *33,* 32 (1886); *D. G. O'Sullivan, P. W. Sadler,* J. Chem. Soc. *1957,* 2916.
[3] *R. A. Scherrer, A. Arbor,* US-Pat. 3238201 (1966).

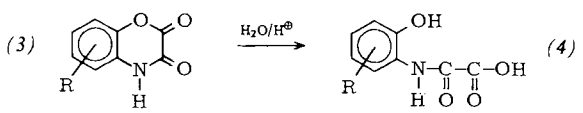
Table 1. Isatoic anhydrides *(2)* from isatins *(1)* with H_2O_2 in acetic acid; 2,3-dioxo-1,4-benzoxazines *(3)* from isatins *(1)* with $H_2S_2O_8$ in sulfuric acid [a].

	R^1	R^2	R^3	R^4	*(2)* Yield [%]	*(2)* M.p. [°C] (dec.)	*(2)* M.p. [°C] in [2]	*(3)* Yield [%]	*(3)* M.p. [°C] (dec.)
a	H	H	H	H	79	252–253	233–235 dec.	95	285 [b]
b	H	H	H	CH_3	75	237–239	277	89	247–249
c	H	H	H	CF_3	81	184–186		82	207–210
d	H	Cl	H	Cl	90	252–256	254–256 dec.	95	255–257
e	H	Br	H	H	83	270–275	270–275 dec.	95	318–320
f	H	NO_2	H	H	80	224–232	220–230 dec.		
g	H	H	H	Cl	85	210–215			
h	CH_3	H	H	OCH_3	70	235–242			
i	H	F	H	H	83	265–268	260		
j	H	H	F	H	84	229–231	241		
k	H	H	CH_3	CH_3				90	278–284

[a] All compounds gave correct analyses and characteristic IR and NMR spectra. [b] M. p. 275–276 °C (dec.) [4].

an exothermic reaction. Isatoic anhydrides do not occur as by-products.

Some of the compounds prepared, *e.g. (3c)* and *(3d)*, are very sensitive to hydrolysis even in weakly acid solution at room temperature, so that mixtures of benzoxazine *(3)* and *N*-(2-hydroxyphenyl)oxamidic acid *(4)* are sometimes obtained on work-up.



Compared with the synthesis of 2,3-dioxo-1,4-benzoxazines *(3)* from *o*-aminophenols and oxalyl chloride[4], the synthesis from isatins *(1)* offers advantages, particularly for the directed synthesis of derivatives substituted at the benzene ring. Thus, for example, preparation of the *o*-aminophenols required for the synthesis of *(3b)* or *(3c)* is tedious and not without difficulty, whereas the corresponding isatins are readily accessible[5].

The isomers *(2)* and *(3)* can be easily and unequivocally distinguished by mass spectrometry.

Procedure[6]

(2): A suspension of *(1)* (1 mol) in glacial acetic acid (*ca.* 1000 ml) and conc. sulfuric acid (5 ml) is heated to *ca.* 30 °C. It is then treated dropwise within 20 min with 1.1 mol hydrogen peroxide as a 30% aqueous solution and the reaction temperature kept at 60–70 °C by gentle cooling. After 2 hours' stirring and cooling to room temperature the precipitate is filtered off and washed with water.

(3): 1 mol of *(1)* is added to a solution of $K_2S_2O_8$ (1–1.5 mol) in *ca.* 1000 ml 85–95% sulfuric acid at 0 to 10 °C. After stirring for a few minutes the solution is poured onto ice. The precipitate is filtered off and washed with water.

Received: December 11, 1979 [Z 397 IE]
German version: Angew. Chem. *92,* 196 (1980)

[4] *K. Dickoré, K. Sasse, K.-D. Bode,* Justus Liebigs Ann. Chem. *733,* 70 (1970).
[5] Houben-Weyl: Methoden der organischen Chemie. Vol. 7/4. Thieme, Stuttgart 1968, p. 5.
[6] *G. Reissenweber,* DOS 2925175 (1979), BASF; *G. Reissenweber, D. Mangold,* DOS 2944696 (1979), BASF.

Influence of Isomerism of Alkanes on the Thermodynamic Properties of Cyclohexane/Alkane Mixtures

By *Andreas Heintz, Rüdiger N. Lichtenthaler,* and *Klaus Schäfer*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The various chemical structures of isomeric hydrocarbons also lead to differences in thermodynamic behavior of the pure isomers and of their mixtures with other compounds. Owing to the industrial importance of such mixtures in isolation procedures, a knowledge of the so-called excess quantities ΔZ_M is important. For binary mixtures it holds that:

$$\Delta Z_M = Z_M - x_1 Z_1 - x_2 Z_2 \qquad (1)$$

The quantity Z may be, *e.g.* the enthalpy H, the entropy S, the free energy G, or the volume V. ΔZ_M represents the difference between Z in the mixture (subscript M) and the contributions of the pure components 1 and 2; x_1 and x_2 are the mole fractions.

As examples of our studies, Figure 1 shows the experimentally determined molar enthalpies of mixing ΔH_M for mixtures of cyclohexane (*c*-C_6) with *n*-octane (*n*-C_8), 2,2,4-trimethylpentane (*i*-C_8), *n*-hexadecane (*n*-C_{16}), and 2,2,4,4,6,8,8-heptamethylnonane (*i*-C_{16}).

[*] Prof. Dr. K. Schäfer, Dr. A. Heintz, Prof. Dr. R. N. Lichtenthaler
Physikalisch-Chemisches Institut der Universität
Im Neuenheimer Feld 253, D-6900 Heidelberg (Germany)

The data were obtained with an isothermal flow calorimeter which has been described on a previous occasion[1]. Figure 2 shows experimental results for the equimolar entropy

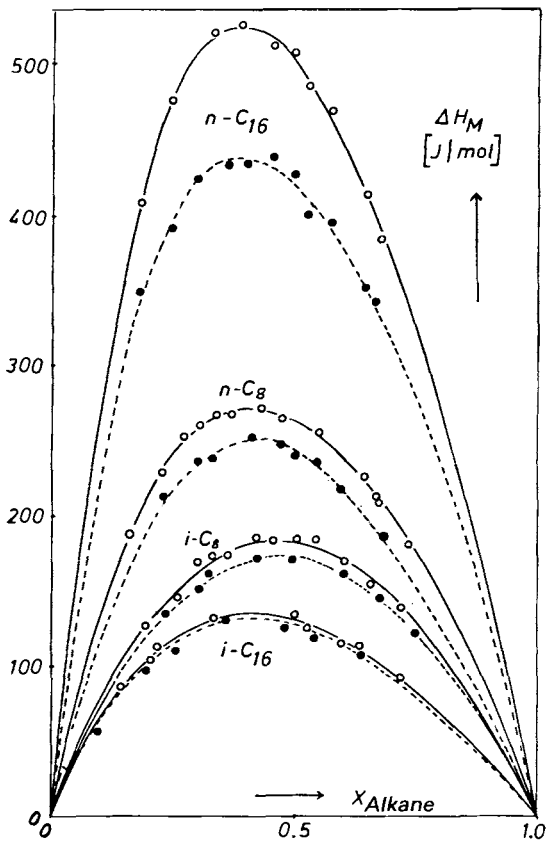


Fig. 1. Experimental molar enthalpies of mixing ΔH_M for mixtures of cyclohexane with isomeric alkanes as a function of the mole fraction x_{alkane} at 298.15 K/1 bar (—○) and 313.15 K/1 bar (---●).

of mixing ΔS_M of various isomeric alkanes + c-C_6 as a function of the number of carbon atoms n. These data were obtained from measurements of the vapor pressure of the mixtures with a recently described vapor pressure apparatus[2], from which ΔG_M was initially determined. The entropy of mixing ΔS_M could then be calculated with the aid of the calorimetrically determined ΔH_M values.

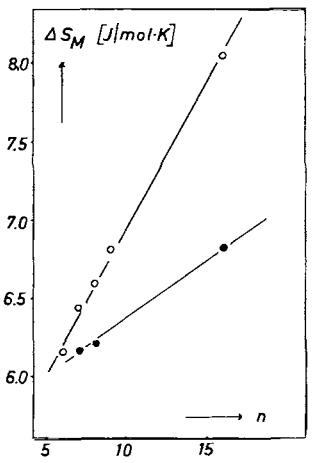


Fig. 2. Experimental equimolar entropies of mixing ΔS_M for mixtures of cyclohexane with isomeric alkanes at 298.15 K as a function of the number of carbon atoms n. ○ points for n-alkanes, ● points for branched alkanes (i-C_7=2,2-dimethylpentane; i-C_8, i-C_{16}, see text).

It is seen that ΔH_M and ΔS_M are considerably higher for the n-alkane/c-C_6 systems than ΔH_M and ΔS_M for the systems with branched isomers. It is seen from Figure 1 that ΔH_M decreases significantly with increasing temperature, which is not the case with the branched isomers. Theoretical rationalization of this difference in behavior is not only of interest from the standpoint of molecular physics but is also important in practice in order to predict the excess quantities over large ranges of temperature and pressure.

A theory suitable for treating mixtures of molecules of different sizes is that of *Flory et al.*[3]. This theory employs experimental quantities of state of the pure components and requires for calculation of the excess quantities just a single adjustable parameter X_{12} which contains the difference between the segmental intermolecular interaction parameters η_{ij} of identical and different molecules of the mixture. It holds that

$$X_{12} \triangleq (\eta_{11} + \eta_{22} - 2\eta_{12}) \qquad (2)$$

Adjustment of the theoretical expression for ΔH_M to the experimental data leads to widely differing X_{12} values for mixtures of the isomers with c-C_6; *e.g.* $X_{12}(i\text{-}C_{16} + c\text{-}C_6) = 5.1$ J cm^{-3} and $X_{12}(n\text{-}C_{16} + c\text{-}C_6) = 16.5$ J cm^{-3} at 298.15 K. Moreover, the temperature dependence of ΔH_M in the n-alkane/c-C_6 mixtures cannot be described with a constant value of X_{12}; instead, lower X_{12} values are required at higher temperature. For example $X_{12}(n\text{-}C_{16} + c\text{-}C_6) = 16.5$ J cm^{-3} at 298.15 K and 14.1 J cm^{-3} at 313.15 K. This does not agree with the simple Flory theory which stipulates that X_{12} should be constant as a molecular parameter. Nor can the large differences in X_{12} of the isomeric pairs be explained by the differing numbers of CH_3, CH_2, and CH group increments since the differences in interaction energy are slight[4]. Experimental results obtained on depolarized Rayleigh light scattering showed that some degree of close range order exists in the pure n-alkanes, probably sterically favored partial parallel orientations of molecular chain segments which are also energetically stabilized[5].

On mixing with a globular molecule such as c-C_6 these ordered structures are destroyed, depending upon the mixing ratio; this is associated with an endothermic contribution to ΔH_M. Thus ΔH_M is considerably greater for n-alkanes than for branched isomers which have practically no such ordered structures. This also explains the higher ΔS_M values of n-alkane/c-C_6 mixtures since the entropy of the pure n-alkane is smaller than for the corresponding branched isomer owing to the ordered structure.

Application of a theory of rotational transformation of simple molecules[6] to chain segments permits derivation of expressions for a orientation-dependent component of the segmental interaction energies so that an effectively temperature dependent component must also be considered in addition to the expression valid for η (n-alkane) in eq. (2). It then follows[1]:

$$X_{12} = X_{12}^{\infty} \cdot T/(T - T_0) \quad (T > T_0) \qquad (3)$$

X_{12}^{∞} is the value of X_{12} when T approaches infinity; the second factor in eq. (3) is temperature dependent and includes the "orientational component" of X_{12}. T_0 has the formal significance of a transition temperature for orientation of the chain segments. T_0 and X_{12}^{∞} in eq. (3) can be determined from the temperature dependence of X_{12}. X_{12}^{∞} has an approximately constant value of 3.5 J cm^{-3} for n-alkane/c-C_6 mixtures, while T_0 lies about 10–30 K below the melting point of the particular n-alkane. In fact, transition phenom-

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0224 $ 02.50/0

ena have already been observed for alkanes in the solid state[7].

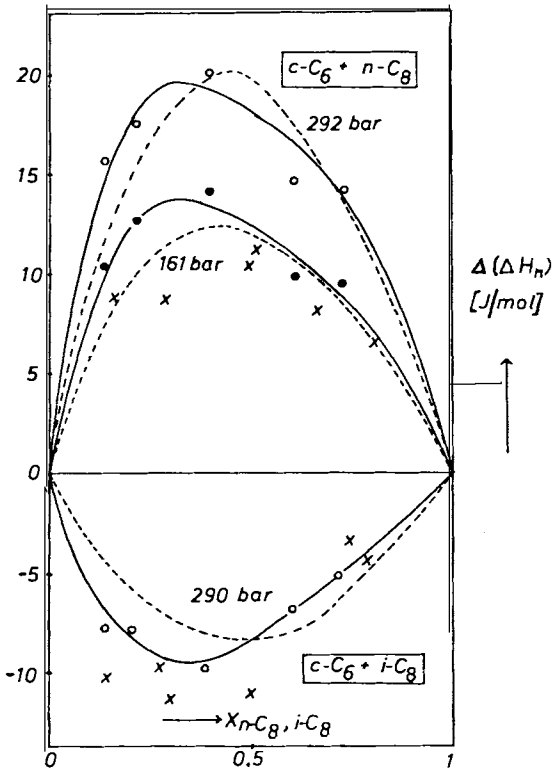


Fig. 3. Pressure dependence of enthalpy of mixing $\Delta(\Delta H_M)$ for n-C_8 + cyclohexane and i-C_8 + cyclohexane at 298.15 K. (—○) calorimetric data, × indirect data obtained from ΔV_M. --- curves calculated with adjusted X_{12} values.

In order to study the temperature dependence of the ordered structures, ΔH_M of several alkane/c-C_6 mixtures at high pressure was determined in a modified flow calorimeter. A recent report[8] concerns this apparatus. Figure 3 shows

$$\Delta(\Delta H_M) = \Delta H_M \text{ (high pressure)} - \Delta H_M \text{ (1 bar)}$$

for n-C_8 + c-C_6 and i-C_8 + c-C_6. In addition to directly determined calorimetric experimental values, indirectly determined ones are also given, which were obtained from measurements of the excess volume ΔV_M and its temperature dependence according to the following thermodynamic identity:

$$\Delta(\Delta H_M) = (\Delta V_M - T \cdot [\Delta(\Delta V_M)/\Delta T])\Delta p \qquad (4)$$

The excess volumes were established from density measurements of the mixtures and the pure components by a proven new method[9]. The broken curves in Figure 3 have been calculated with adjusted X_{12} values. For i-C_8, X_{12} remains pressure-constant (7.2 J cm^{-3}), while for the n-C_8 mixture X_{12} increases from 9.7 J cm^{-3} at 1 bar to 10.7 J cm^{-3} at 290 bar. According to eq. (3), an increase of X_{12} means an increase in T_0 with pressure. This is to be expected since T_0 is shown in ref.[6] to be proportional to the energy required to bring about the transition. This energy is all the greater, the higher the pressure (*i.e.* the density) since steric and energetic hindrance of the transition are all the greater at higher density.

The extended Flory theory thus permits a consistent description of the excess quantities for mixtures of isomeric alkanes with cyclohexane. They provide not only an accurate picture of the systems under study in terms of molecular physics but also allow prediction of excess quantities in other ranges of temperature and pressure.

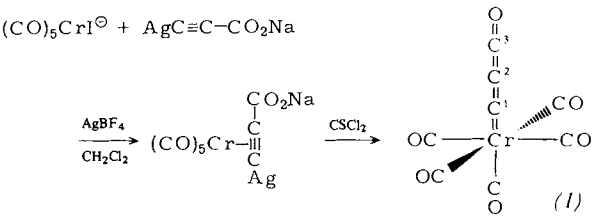
Received: December 6, 1979 [Z 412 IE]
German version: Angew. Chem. *92*, 209 (1980)

[1] *A. Heintz, R. N. Lichtenthaler*, Ber. Bunsenges. Phys. Chem. *81*, 921 (1977).
[2] *D. Meixner, R. N. Lichtenthaler*, Ber. Bunsenges. Phys. Chem. *83*, 567 (1979).
[3] *P. J. Flory, R. A. Orwoll, A. Vrij*, J. Am. Chem. Soc. *86*, 3507 (1964).
[4] *V. Te Lam, P. Picker, D. Patterson, P. Tancrède*, J. Chem. Soc. Faraday Trans. II, *70*, 1465 (1974).
[5] *P. Tancrède, P. Bothorel, P. de St. Romain, D. Patterson*, J. Chem. Soc. Faraday Trans. II, *73*, 15, 20 (1977).
[6] *K. Schäfer*, Z. Phys. Chem. *B 44*, 127 (1939).
[7] *H. L. Finke, M. E. Gross, G. Waddington, H. M. Huffman*, J. Am. Chem. Soc. *76*, 333 (1954).
[8] *A. Heintz, R. N. Lichtenthaler*, Ber. Bunsenges. Phys. Chem. *83*, 853 (1979).
[9] *A. Heintz*, Ber. Bunsenges. Phys. Chem. *83*, 155 (1979).

Complex Stabilization of 3-Oxopropadienylidene (C_3O) with Pentacarbonylchromium(0)[**]

By *Heinz Berke* and *Peter Härter*[*]

A facile entry to metal complexes containing carbene-analogous cumulene ligands is possible *via* propiolic acid derivatives[1]. We have now been able to synthesize pentacarbonyl(3-oxopropadienylidene)chromium(0) *(1)*.



On using the method of *Connor et al.*[2] with pentacarbonyliodochromate and the silver acetylide derivative of sodium propiolate as starting substances, presumably a π-complex is initially formed (IR spectroscopic detection), which we did not isolate but allowed to react further with thiophosgene. Chromatographic separation of the product mixture afforded *(1)* in *ca.* 35% yield. Losses on purification due to the high volatility of this black-violet compound (dec. pt. 32 °C), which is stable for some time in the crystalline and pure state at room temperature, can hardly be avoided. The structure of *(1)* follows from spectroscopic findings and chemical characterization.

In the IR spectrum (solution in n-hexane) the absorptions of the carbonyl ligands correspond to C_{4v} symmetry [2074 w (A_1), 1977 s (E), 1971 cm^{-1} m (A_1)]. A further band at 2028 cm^{-1} (s) is assigned to the vibration in the complex *(1)* which is equivalent to the ν_1 vibration of free C_3O[3], appearing, as expected, at a lower wavelength. In the gas phase, two absorptions of weak intensity are observed [2005 m (A_1), 2001 cm^{-1} s (E)]. No band, which could be assigned to the ν_2-vibration of the C_3O ligand, has been observed so far. Even in investigations on free C_3O[3] and on carbonylmethyl compounds[4] no such band has ever been found.

The ^{13}C-NMR data of *(1)* are listed in Table 1.

[*] Dr. H. Berke, Dipl.-Chem. P. Härter
Fakultät für Chemie der Universität
Postfach 5560, D-7750 Konstanz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by Research Facilities of the Universität Konstanz.

Table 1. Chemical shifts in the ^{13}C-NMR spectrum of *(1)* at −40 °C in diethyl ether rel. to TMS.

	CO_{cis}	CO_{trans}	C-1	C-2	C-3
δ	212.8	224.0	440.6	—	389.9

The value of δCO_{cis} and δCO_{trans}, as well as their difference, are normal for a pentacarbonylchromium compound[5]. The tentative assignment of the two extreme resonances to C-1 and C-3 is supported by the charge distribution obtained for C_3O in *(1)* from MO calculations by the extended Hückel method[6].

The mass spectrum of *(1)* shows the successive fragmentation of three CO groups (m/e=244 $[M^+]$, 216 $[M-CO]^+$, 188 $[M-2\ CO]^+$, 160 $[M-3\,CO]^+$). A further fragmentation path is indicated by the appearance of $Cr(CO)_6^+ = [M-C_2]^+$ and its CO-fragmentation series. The intensity of the pure organic fragment ion m/e=76 $[C_5O]^+$ depends on the temperature of the ion source; it successively loses carbon atoms.

In *n*-hexane solution, *(1)* undergoes detectable decomposition with decoloration, even at 0 °C. The metal-containing product $Cr(CO)_6$ is apparently formed by loss of a C_2 fragment, from which highly unsaturated organic species (acetylenic and cumulenic IR bands) can be formed *via* well-known reaction steps[7].

Oxidation of *(1)* by the method of *Casey et al.*[8] and methanolysis leads to dimethyl malonate (GC/MS analysis).

$$(CO)_5CrC_3O \xrightarrow{DMSO} [C_3O_2] \xrightarrow{MeOH} CH_2(CO_2Me)_2$$

Our findings show that C_3O, a "cumulog"[9] of the CO molecule is stable as ligand. The complex *(1)* can thus be included in the series of coordination compounds in which particles otherwise detectable only in low-temperature matrices are considerably stabilized.

Procedure

$[n\mathrm{Bu_4N}][(CO)_5CrI]$ (1.4 g, 2.5 mmol) is dissolved in CH_2Cl_2 (90 ml) and ether (10 ml) at −60 °C. $AgBF_4$ (700 mg) is added and the mixture allowed to warm to −20 °C. AgC≡C—CO_2Na (for preparation see below) is added in slight excess and the mixture homogenized in an ultrasonic bath with cooling to *ca.* −30 °C. After 1 hour's stirring at −10 °C, 0.5 ml of thiophosgene is added, whereupon the color of the mixture turns violet. At substantially shorter reaction times a mixture is obtained containing the thiophosgene complex $(CO)_5Cr(Cl_2CS)$, which cannot be separated on work-up. After filtration over kieselguhr the solvent is removed below −10 °C. The residue is taken up in *n*-pentane and chromatographed on silica gel (l=20 cm) at −50 to −60 °C. The eluate of the deep-violet zone is evaporated down at −20 °C. For further purification the residue is sublimed onto a cold finger (−20 °C) at 0 °C. Yield: 220 mg of *(1)* (36%).

AgC≡C–CO_2Na is prepared by a combination of the two procedures by *Bayer*[10a] and *Wille et al.*[10b] from the Na-salt of the propiolic acid in sodium carbonate solution by addition of $AgNO_3$. The acetylide separates out as a yellow precipitate. The precipitate is filtered off and washed several times with water, ethanol, and ether. Since the acetylide is sensitive to light, and readily detonates on aging, it cannot be stored.

Received: July 11, 1979 [Z 414 IE]
German version: Angew. Chem. 92, 224 (1980)

[1] *H. Berke*, Angew. Chem. *88*, 684 (1976); Angew. Chem. Int. Ed. Engl. *15*, 624 (1976).
[2] *J. A. Connor, E. M. Jones, G. K. McEwen*, J. Organomet. Chem. *43*, 357 (1972).
[3] *R. L. DeKock* and *W. Weltner Jr.*, J. Am. Chem. Soc. *93*, 7106 (1971).
[4] *R. F. C. Brown, F. W. Eastwood, K. J. Harrington*, Aust. J. Chem. *27*, 2393 (1974); *R. F. C. Brown, G. L. McMullen, ibid. 27*, 2385 (1974).
[5] *L. J. Todd, J. R. Wilkinson*, J. Organomet. Chem. *77*, 1 (1974).
[6] *R. Hoffmann*, J. Chem. Phys. *39*, 1397 (1963); *R. Hoffmann, W. N. Lipscomb, ibid. 36*, 2179, 3489 (1962); *37*, 2872 (1962).
[7] *P. S. Skell, J. J. Havel, M. J. McGlinchey*, Acc. Chem. Res. *6*, 97 (1973).
[8] *C. P. Casey, T. J. Burkhardt, Ch. A. Bunnel, J. C. Calabrese*, J. Am. Chem. Soc. *99*, 2127 (1977).
[9] Cf. *M. Parmantier, J. Galloy, M. van Meersche, H. G. Viehe*, Angew. Chem. *87*, 33 (1975) Angew. Chem. Int. Ed. Engl. *14*, 53 (1975).
[10] *A. v. Bayer*, Ber. Dtsch. Chem. Ges. *18*, 2274 (1885); *F. Wille, W. Schwab*, Z. Naturforsch. B *32*, 733 (1977).

First Fixation of the Unstable Species Sulfur Monoxide in a Cluster: Synthesis and Structure of $Fe_3(CO)_9(S)SO$

By *László Markó, Bernadett Markó-Monostory, Thomas Madach*, and *Heinrich Vahrenkamp*[*]

It has long been known that acidification of aqueous solutions containing tetracarbonylferrate and sulfite leads to polynuclear iron carbonyl sulfides $Fe_3(CO)_9S_2$ *(1)* and $Fe_2(CO)_6S_2$[1]. The course of this complex reaction has not yet been elucidated; however, it may be assumed that $Fe(CO)_4H_2$ is involved as a strong reducing agent. In addition to the products mentioned, we have now also found a more strongly polar compound *(2)* which can be prepared in good yield from $Fe_3(CO)_{11}H^-$, which in turn arises on partial oxidation of $Fe(CO)_4^{2-}$.

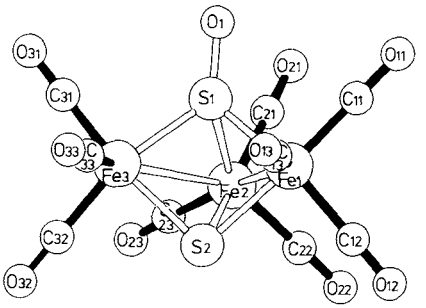


Fig. 1. Molecular structure of complex *(2)* in the crystal.

Cluster bond lengths [pm]			
Fe1–Fe2	262.3(1)	Fe2–Fe3	264.7(1)
Fe1–S1	214.0(1)	Fe1–S2	226.9(1)
Fe2–S1	222.2(1)	Fe2–S2	223.0(1)
Fe3–S1	213.9(1)	Fe3–S2	226.3(1)
S1–O1	147.1(2)		

(2) proved to be the novel cluster $Fe_3(CO)_9(S)SO$; its composition is confirmed by elemental analysis and EI mass spectrum. The IR spectrum (in hexane: 2070 vs, 2052 vs,

[*] Prof. Dr. L. Markó
Institute of Organic Chemistry
University of Chemical Engineering
Schönherz Z. u. 12,
H-8200 Veszprém (Hungary)

Dr. B. Markó-Monostory
Hungarian Petroleum and Natural Gas Research Institute
H-8200 Veszprém (Hungary)

Prof. Dr. H. Vahrenkamp, Dipl.-Chem. T. Madach
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

2035 s, 2026 m, 2017 w, 1992 cm^{-1} w, br) closely resembles that of *(1)* shifted to higher wave numbers by 7–20 cm^{-1}. Moreover, *(2)* shows a strong band at 1107 cm^{-1} (in KBr) which can be assigned to the SO stretching vibration.

The structure of *(2)* was determined by X-ray methods[2] (cf. Fig. 1); this provided the first proof of the existence of an SO ligand[3]. The S—O bond length is 147 pm and corresponds to that in free SO (148 pm)[4a] and many other S=O double bonds[4b]. The Fe—S bonds to the SO group are significantly shorter than those to the S atom, probably due to the radius contraction of the sulfur by the electronegative oxygen. This shift of the SO group towards the center of the molecule leads to an S···S contact of only 272 pm, which is considerably shorter than the sum of the van der Waals radii (2×185 pm). In analogy with some complexes of the $Fe_2(CO)_6(\mu_2\text{-}X)_2$ type[5], a partially bonding S—S interaction must therefore be assumed in this case.

The fact that *(2)*, like *(1)*[6], contains an open triangle of iron atoms, *i.e.* only two metal-metal bonds, leads to the conclusion that the SO molecule is a 4-electron ligand like the S atom. This is also supported by the close relationship observed between the structures of *(1)* and *(2)*.

The extensive similarity between the two complexes also justifies our viewing *(2)* as the product of addition of a Lewis-acid O atom to *(1)*, with only minor modification of the bonding in the skeleton of *(1)*. The sufficient basicity of a μ_3-bonded sulfur atom in M_3S cluster units has already been detected: the 16-electron fragment $Cr(CO)_5$ can be added[8] to the $SFeCo_2(CO)_9$ cluster[7], again with hardly any structural change. Complex *(2)* can also be regarded as an intermediate of reduction of sulfite to sulfide by iron carbonyl hydrides [$Fe_3(CO)_{11}H_2$ is a less powerful reducing agent than $Fe(CO)_4H_2$!].

In contrast to its formation, the bonding and the structure of *(2)* are not unusual. This suggests that further SO clusters might be accessible.

Procedure

First H_2O_2 (16.7 mmol; 1.7 ml of a 30% aqueous solution) and then $Na_2SO_3 \cdot 7H_2O$ (7.5 g, 30 mmol; dissolved in water (20 ml)) are added to a solution obtained by basic reaction of $Fe(CO)_5$ (4.9 g, 25 mmol) and NaOH (4.0 g, 100 mmol) in H_2O/CH_3OH (1:2) (30 ml). After 10 min, the reaction mixture is acidified with dilute hydrochloric acid, the dark precipitate filtered off, washed with water, and chromatographed in benzene on a silica gel column. Elution with hexane gives *(1)* (24% yield) and with benzene gives *(2)* (yield 10%). *(2)* can be recrystallized from toluene (+25/−78 °C), affording 0.28 g (0.56 mmol; 6.7%) of dark red-brown, air-stable crystals. The compound decomposes without melting at 125–128 °C.

Received: August 6, 1979 [Z 416 IE]
German version: Angew. Chem. *92*, 225 (1980)

[1] *W. Hieber, J. Gruber*, Z. Anorg. Allg. Chem. *296*, 91 (1958).
[2] Triclinic, P1, $Z=2$; $a=951.4(1)$, $b=1032.0(1)$, $c=906.5(4)$ pm, $\alpha=91.38(2)$, $\beta=116.97(2)$, $\gamma=97.06(1)°$; 2930 independent reflections, $R=0.023$.
[3] Cf. *G. Schmid, G. Ritter*, Chem. Ber. *108*, 3008 (1975).
[4] a) *F. X. Powell, D. R. Lide*, J. Chem. Phys. *41*, 1413 (1964); b) *L. E. Sutton:* Tables of Interatomic Distances and Configuration in Molecules and Ions, Spec. Publ. No. 11, The Chemical Society, London 1958.
[5] Cf. *B. K. Teo, M. B. Hall, R. F. Fenske, L. F. Dahl*, Inorg. Chem. *14*, 3103 (1975).
[6] *C. H. Wei, L. F. Dahl*, Inorg. Chem. *4*, 493 (1965).
[7] *S. A. Khattab, L. Markó, G. Bor, B. Markó*, J. Organomet. Chem. *1*, 373 (1964).
[8] *F. Richter, H. Vahrenkamp*, Angew. Chem. *90*, 474 (1978); Angew. Chem. Int. Ed. Engl. *17*, 444 (1978).

Direct Photolysis of Uranium Hexafluoride as a Preparatively Utilizable Endothermic Reaction[**]

By *Frank S. Becker* and *Eberhard Jacob*[*]

For the laser isotope separation of uranium the photodissociation of UF_6 by an infrared multiphoton process or by a combination of infrared and ultraviolet irradiation is considered to be one of the most promising approaches. In connection with such experiments it is important to know to what extent the photodissociation is possible without the use of a scavenger and what part the fluorine can play in the following reactions.

It is well known that the photodissociation of UF_6 is feasible in the presence of scavengers (H_2, CO, SO_2)[1]. Photodissociation of pure UF_6 by UV light in an argon matrix at 10 K is small[2a] and at 27 K impossible[2b]. Experiments with α rays[3a] electron-beams[3b] and UV light[1c,3c] at room temperature yielded only very small quantities.

On use of a suitable experimental set-up, we were able to dissociate by UV light about 50 g of UF_6 in the gas phase at room temperature according to

$$2\,UF_6 \xrightarrow[39\,h]{h\nu} 2[UF_5]_s + F_2 \qquad (1)$$

nearly quantitatively (98.8%) into β-UF_5 and ultrapure F_2. This endothermic photoreaction ($+132 \pm 19$ kJ/mol[4]) is accompanied by a transformation of photon energy into chemical energy. The energy balance of usual photoreactions is exothermic, because the always endothermic photoexcitation is more than compensated by the exothermic character of the following reactions[5].

A series of photolysis experiments showed a strong influence of the reaction cell geometry on the final attainable dissociation yield of the UF_6. Special care has to be taken to avoid deposition of UF_5 on the irradiation window. In addition to a vertical window position the presence of F_2 proves to be useful, because the photofluorination of UF_5[5a] hinders the formation of a deposit on the window. At constant UF_6 pressure (solid state UF_6) the increasing F_2 pressure brings the reaction to equilibrium. Nevertheless, a nearly complete UF_6 dissociation according to eq. (1) can be attained by creating suitable UV-shaded regions where the produced UF_5 can be irreversibly deposited. From time to time, the F_2 formed should be partially withdrawn (cf. Fig. 1). A fast production of UF_5 is indicated by a dense white fog, which should be convected into the shaded regions to obtain high yields.

A simplified kinetic consideration shows that the polymerization of the UF_5 molecules should be the rate determining step of reaction (1)[3c,6]. These kinetic conditions make possible the thermodynamically unexpected endothermic reaction.

The direct photodissociation of UF_6 is a more effective way of preparing β-UF_5 than the photoinduced UF_6 reduction with CO[1b] which was described only a short time ago (optimum amount of UF_5: 5 g per experiment). The attained yields of the direct dissociation are higher, compared with the photoreduction[1], because only in the presence of fluo-

[*] Dr. E. Jacob
Abteilung Physikalische Chemie, M.A.N. – Neue Technologie
Postfach 500620, D-8000 München 50 (Germany)

Dipl.-Phys. F. S. Becker
Projektgruppe für Laserforschung der Max-Planck-Gesellschaft
D-8046 Garching (Germany)

[**] Chemistry of Uranium Fluorides and Oxide Fluorides, Part 3. We wish to thank Prof. *K. L. Kompa*, Garching, and Prof. *F. Seel*, Saarbrücken, for helpful comments. Part 2: *E. Jacob*, Z. Anorg. All. Chem. *400*, 45 (1973).

rine is free entrance of the UV light into the reaction cell effected. In addition, the direct dissociation of UF_6 is a method for the preparation of small amounts (1–2 bar l per experiment) of ultrapure fluorine[7, 8].

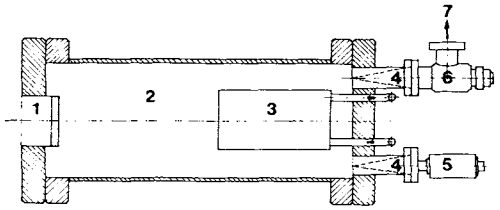


Fig. 1. Photoreactor: 1, sapphire window of I. D. 44 mm in NW 100 CF flange (Odelga-Physik D-7441 Aich); 2, nipple NW 100 CF (Balzers Hochvakuum, D-6200 Wiesbaden); 3, cold finger (∅ 55 × 100 mm) in NW 100 CF flange; 4, dust filter (porous stainless steel cone); 5, pressure transducer (0–1000 mbar, Bell and Howell); 6, NW 16 CF valve (Balzers);, 7, to vacuum line. — All components consisted of stainless steel and the flanges were copper sealed and He leak controlled. UV-light source: 1000 W mercury super high pressure lamp (Osram HBO 1000 or Philips CS 1000) with quartz condensor for parallell light beam, 100 mm water filter for IR elimination. The irradiation was performed in horizontal position.

In principle, the direct photodissociation of UF_6 hints at the possibility of performing the laser isotope separation without a scavenger. On the other hand, it is of fundamental interest to learn to what extent the unspecific reaction

$$UF_6 + F \rightarrow UF_5 + F_2$$

would compensate the isotopically selective dissociation of UF_6 already accomplished.

Procedure

The photodissociation is performed in the reactor depicted in Figure 1. After evacuation down to 10^{-5} mbar, the cold finger is filled with liquid N_2 and UF_6 (47.668 g, 135.4 mmol) is frozen into the reactor. Afterwards the cold finger is warmed up to 1–2 degrees below room temperature by means of a thermostat. The UF_6 pressure during the irradiation lies between 120 and 180 mbar. The progress of the photolysis can be monitored by the pressure rise caused by F_2 production. After 17 h the F_2 production comes to a standstill. The cold finger is filled with liquid N_2 again and the nondissociated UF_6 is frozen out. The F_2 is collected in a 63 K cold trap[8b], leaving about 30–40 mbar. After warming up the cold finger the photolysis is continued, and the fluorine withdrawal is repeated after 6 and 16 h respectively. After a total irradiation time of 39 h at 25 °C, 98.8% of the UF_6 has decomposed. After pumping off the remaining F_2, the reactor is opened in a glovebox. It is possible to remove 43.6 g (130.9 mmol) of a powdery light-green deposit from the walls. X-ray analysis shows the existence of β-UF_5[9a]. Chemical analysis of the UF_5 is accomplished by fluorination to UF_6 with IF_7 while monitoring the weight[9b]. A PVT measurement of the gas collected with the 15 K cryopump ("cryo-Töplerpump")[2b] gave 1641 mbar l of mass-spectroscopically pure fluorine. According to (1) 0.5 mole F_2 is produced per mole of dissociated UF_6.

Received: August 21, 1979;
revised: November 12, 1979 [Z 417 IE]
German version: Angew. Chem. *92*, 226 (1980)

[1] a) *J. J. Katz, E. Rabinowitch:* The Chemistry of Uranium. Dover Publ., New York 1961, p. 441; *K. L. Kompa, G. C. Pimentel,* J. Chem. Phys. *47*, 857 (1967); *L. B. Asprey, R. T. Paine,* J. Chem. Soc., Chem. Comm. 920 (1973), U. S. Pat. 3929601 (1974/75); *G. W. Halstead, P. G. Eller, L. B. Asprey, K. V. Salazar,* Inorg. Chem. *17*, 2967 (1978); b) *R. T. Paine, L. B. Asprey,* Inorg. Synth. *19*, 137 (1979); c) *O. Hartmannshenn, J. C. Barral,* C. R. Acad. Sci. *C 272*, 2139 (1971); *L. B. Asprey, R. T. Paine,* 7th Int. Symp. Fluorine Chem., Santa Cruz, Calif. (1973), Abstr. I-47.

[2] a) *R. T. Paine, R. S. McDowell, L. B. Asprey, L. M. Jones,* J. Chem. Phys. *64*, 3081 (1976); b) *E. Jacob,* unpublished results.

[3] a) *H. A. Bernhardt, W. Davies, Jr., C. H. Shiflett,* Proc. 2nd Int. Conf. Peaceful Uses At. Energy, Geneva, P/522, 62 (1958); b) *A. I. Migachev, A. P. Senchenkov,* At. Energy *16*, 510, 631 (1964); c) *K. C. Kim, R. Fleming, D. Seitz, M. Reisfeld,* Chem. Phys. Letters *62*, 61 (1979).

[4] ΔH_{298}, calculated according to data in *D. L. Hildenbrand,* J. Chem. Physics. *66*, 4788 (1979).

[5] For example: a) $2\,[UF_5]_6 + F_2 \xrightarrow{h\nu} 2UF_6$; *J. Slivnik, K. Lutar, A. Smalc,* J. Fluorine Chem. *11*, 643 (1978); b) all strongly exothermic photoreductions of UF_6: compare ref. [1].

[6] a) The detailed reaction mechanism is determined probably by the actual partial pressures of UF_6 and F_2; b) we have observed an extensively quantitative photodissociation of UF_6 according to eq. (1) in the pressure range between 0.1 and 100 mbar too.

[7] Care must be taken regarding the UF_6 purity. We used 99.99+% UF_6.

[8] a) Depleted UF_6 is available in large amounts, cf. *G. A. Olah, J. Welch, Tse-Lok Ho,* J. Am. Chem. Soc. *98*, 6717 (1976); b) for the purification of F_2, see *E. J. Jacob, K. O. Christie,* J. Fluorine Chem. *10*, 169 (1977).

[9] a) *W. H. Zachariasen,* Acta Crystallogr. *2*, 296 (1949); b) *E. Jacob,* DAS 2504840 (1978).

BOOK REVIEWS

Kirk-Othmer: Encyclopedia of Chemical Technology. Editorial board: *H. F. Mark, D. F. Othmer, C. G. Overberger,* and *G. T. Seaborg.* John Wiley & Sons, New York 1979, 3rd Edition. Vol. 5: Castor Oil to Chlorosulfuric Acid. xxv, bound, £ 60; Vol. 6: Chocolate and Cocoa to Copper. xxiii, 869 pp., bound, £ 60.

The fifth and sixth volume of the new edition of Kirk-Othmer[*] are now available. The principal contributions to Volume 5 are: Catalysis (55 pp.); Cellulose and cellulose derivatives (90 pp.); Ceramics (80 pp.); Chemotherapeutics (100 pp.); and Chlorocarbons (180 pp.). In volume 6 the greatest space is devoted to: Coal and coal conversion processes (90 pp.); Coatings (95 pp.); Cobalt and cobalt compounds (40 pp.); Colors (80 pp.), and Complex compounds (40 pp.).

As in the previous volumes, the individual chapters are scientifically impeccable and lucidly written. Production and work-up processes are almost always accompanied by clear flowcharts and important technical details are backed up by drawings or photographs. The properties of the products, specifications, and analytical methods are given adequate treatment, as are environmental and safety aspects. Econom-

[*] Angew. Chem. Int. Ed. Engl. *18*, 704 (1979)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0303-0228 $ 02.50/0

ic data pertaining to the processes are also invariably instructive.

The balance between the various chapters does not always seem to be maintained. Pharmaceutical and medical topics occupy more space than would be expected from the title of the work. For example, it could be asked whether the section on chemotherapeutics deserves more space than that on coal and coal conversion processes. Articles on computers or even contact lenses (each 20 pp.) do not strictly belong in a handbook of chemical technology.

It is also noticeable that recent European process developments are frequently missing. For instance, there is no mention of the process for manufacturing carbon tetrachloride from chlorinated residues (high pressure chlorolysis) in the article about chlorocarbons. No account is given on recent advances in the coking and fluidized bed combustion of coal. In this respect, the American authors could perhaps do a little more to present an international picture.

R. Steiner [NB 490 IE]

Synthetische Arzneimittel (Synthetic Drugs). *S. Ebel.* Verlag Chemie, Weinheim 1979. x, 631 pages, bound, DM 98.00.

In this textbook and handbook the chapters are arranged according to pharmacological indications. Within each chapter there is a brief introduction, followed by sections on synthesis, stability, biotransformation, and finally examples of analyses.

The concise introductions omit details and concentrate on essentials, taking into account the more recent developments and modern views on the action mechanism. Throughout, they are so useful and pleasant to read that it is easy to overlook the few instances of over-informal phrasing (*e.g.* "chlordiazepoxide and diazepam hold an almost scary proportion of the market", p. 225).

The lucid presentation of basic chemical structures and variable groups has been achieved excellently by means of the two-tone printing; the same is true of the use of color to emphasize the metabolically newly formed groups.

It is also gratifying that in the case of drugs with several designations the page number is given in the index after every name, thus saving one the trouble of searching for the "right" name. The errors—including printing errors—are limited in number and should be easy to correct later. Thus, the hypoglycemic action of sulfonamides had already been discovered in 1942 (p. 466); some cardiac agents with a calcium antagonistic action (Nifedipine, Segontin, Verapamil) are more than just coronary dilators (p 444/5); azole antimycotics do not act as histidine synthesis inhibitors, but affect steroid synthesis (p. 572).

Although the book is striking in its wealth of material on drug metabolism, it lacks a chapter that would actually appear indispensable for such a textbook, namely one dealing with the principles of the biotransformations (hydrolysis, oxidation, *etc.*); such a section would make it easier for the student to recognize the salient points amidst the plethora of data. In addition, "the feel for the success of a chemical synthesis" (see cover notes) would definitely be better demonstrated if the formula section were curtailed in favor of a few explanations.

It may well be that the aims of a textbook (clear presentation of the basics, critical delimitation of outdated and modern preparations) and a handbook (comprehensive collection of data) are difficult to combine in a single work of this size. The reviewer read this very consistent and fluent book with pleasure, and is of the opinion that it tends rather toward being a handbook; however, it deserves to be given greater recognition as a textbook too.

Hans Joachim Kabbe [NB 495 IE]

Molecular and Crystal Structure Models. *A. Walton.* Ellis Horwood Ltd., Chichester/John Wiley and Sons, London 1978. 201 pages, bound, £ 9.00.

Anne Walton has written the first book of consumer information for professional model users. It is *the* reference work for the teacher wishing to illustrate his lectures with molecular models.

The book rightly foregoes a comprehensive philosophical and didactic discussion of the subject, which can be found elsewhere, and instead describes a good 80 (!) commercially available molecular and crystal structure model systems with a high degree of accuracy often with the aid of photographs. It gives the scale, the available parts, the technical characteristics, the preferred fields of application and more besides. No prices are quoted, only the phrases "cheap", "fairly cheap", "rather expensive", and "expensive". The reader will find space-filling models for molecules (12 systems) and crystals (26), ball-and-stick models (25), skeleton models (10), orbital models (5), such for macromolecules and dynamic models. Further chapters provide a guide for making these models oneself and introduce molecular pictures ("planar models"). The appendix lists manufacturers and suppliers.

One could wish for a separate classified bibliography. Because of its encyclopedic nature, only regular supplements and revisions will preserve the undisputed value of this book in the future. A critical comparative evaluation of similar models would be a worthwhile feature. And to extend the train of thought logically, when will a competent team get together to recommend one or two model systems most suitable for the private user? The germs for the crystallization of this idea are already there (*e.g. K. Beyermann:* Molekülmodelle. Verlag Chemie, Weinheim 1979).

Werner Offermann, Fritz Vögtle [NB 498 IE]

Radicals. *D. C. Nonhebel, J. M. Tedder,* and *J. C. Walton.* Cambridge University Press, Cambridge 1979. 200 pages, bound, £ 5.50.

Since in most textbooks the chemistry of radicals is only touched upon, the present pocket-size book clearly fills a gap. In 17 chapters the authors discuss the theme in an introductory qualitative way, but with up-to-date information that covers the full scope of the field. There are subsections on physicochemical methods (ESR, CIDNP) and chemical-engineering aspects (combustion, oxidation, polymerization), on organic reaction mechanisms, on modern preparative methods, and even on the significance of radicals in biological systems. The only addition that the reviewer would like to have seen is a chapter on bond dissociation energies.

Particular praise is due for the highly appropriate way in which the authors have selected their material from the wide range of possibilities, the careful restriction to qualitative application of theory, the sensible selection of modern examples, and the clear style and careful classification. No book can be more highly recommended as an introduction to the field. The most important recent reviews and monographs are cited and point the way to a deeper understanding of radical chemistry. Original references are not given.

Christoph Rüchardt [NB 493 IE]

Organofluorine Chemicals and Their Industrial Applications. Edited by *R. E. Banks*. John Wiley & Sons, London 1979. 255 pages, bound, £ 17.50.

Since its discovery in 1886, fluorine, that most aggressive and reactive element, has made slow but persistent penetration into industry. Fluorine products are nowadays encountered daily in all spheres of life, *e.g.* as the active principles in pharmaceutical preparations, as heat-resistant and chemically resistant materials, as blood, artery, and bone substitute materials, inhalation anesthetics, aerosol propellants, surfactants, *etc.*

The present book contains twelve chapters written by experts active in the study of organofluorine chemistry and its industrial significance.

The subject matter is presented lucidly, and the many references make it possible to go deeper into the field. The book should be within the reach of all chemists concerned with fluorine chemistry in industry, research, or teaching, and can be recommended without any reservations.

Alois Haas [NB 496 IE]

The Chemistry of Silica. Solubility, Polymerization, Colloid and Surface Properties, and Biochemistry. *R. K. Iler*. John Wiley and Sons, Chichester 1979. xxiv. 886 pages, bound, £ 39.50.

Iler's monograph on "The Colloid Chemistry of Silica and Silicates", published in 1955 was in its time extremely useful and informative. It is now the author's aim, at the end of his professional career in industry, to bring out a second edition of this book, giving a picture of the latest situation. However, so much that is new in this field has since been published that a limitation became necessary; the chapters on insoluble silicates, clay minerals and silicic esters had to be left out. Even so, the scope of the work has increased severalfold.

The author concentrates first of all on the occurrence of silica, the dissolution and precipitation equilibria of silicic acids, and on the water-soluble silicates. Much space is given to the treatment of condensation equilibria and to the formation of the industrially important silica sols and gels. Colloid-chemical processes, especially coagulation and flocculation, are discussed in detail. Control of the pore structure of silica gel is described, as is the manufacture and application of finely divided, precipitated or pyrogenically prepared SiO_2. In the description of surface chemistry special reference is made to the OH groups on the SiO_2 surface, their esterification, and other methods of hydrophobization, and also the adsorption behavior with respect to inorganic ions and polymer molecules. The last chapter is on silica in biochemistry, in which context the toxicology of SiO_2, silicic acid derivatives, and Si compounds is considered. The present state of knowledge about the causes and chemotherapy of silicosis is given in detail.

This is a book by a practical man for practical men. It contains a wealth of information. The number of literature sources quoted runs to more than 3200, though some of them are obviously cited in several chapters and are then numbered again. The citations include many references to patents. On the other hand, it is remarkable that in a monograph on silica there is no discussion of the nature and the peculiarities of the siloxane bond; accordingly its hydrophobic character, for example, is introduced without comment.

The work will undoubtedly become an indispensable aid to all those involved with silica and silicic acids. The contents justify the high price. The reader might often wish that the results from the quoted papers had been presented in greater detail, but this could not have been done in a single volume. Even as things are, it was only possible to compress the test into one volume because a relatively fine print was used. This unfortunately means that the reader is soon fatigued—at least this was the effect on the reviewer.

Hanns-Peter Boehm [NB 499 IE]

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form - by photoprint, microfilm, or any other means - nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar*, **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 4
April 1980
Pages 231–332

Viroids: A Class of Subviral Pathogens

By Hans J. Gross and Detlev Riesner[*]

Infectious RNA molecules lacking a protein coat have recently been shown to be the cause of several diseases in higher plants. These molecules, termed viroids, have been characterized as circular chains composed of about 360 nucleotide residues. They therefore comprise a class of infectious pathogens even smaller than viruses or bacteriophages. As a result of work on viroids it is now possible for the first time to give a complete description of the structure of a eukaryotic pathogen. Viroids possess structural and dynamic properties which have not as yet been observed with other nucleic acids. This article summarizes and discusses the results of predominantly biochemical and physicochemical studies on viroids.

1. Introduction

Viroids are a new and independent class of pathogens which are distinguished from viruses and bacteriophages by the absence of a protein coat and by their unusually small size (Fig. 1). They are of considerable practical importance since they are the cause of disease in several economically important crops. In addition, the infectious and pathogenic properties of this group of RNA molecules of hitherto unknown structure make them interesting objects for molecular biological research.

Viroids occur in particular in tropical and subtropical climatic zones, and are also found in greenhouse plants in temperate and cold zones. They can attack potato[1,2], citrus fruit[3,4], chrysanthemum[5–7], cucumber plants[8], coconut palms[9,10], hops[11], the ornamental plant *Columnea erythropae*[12] and the avocado tree[13]. In 1971—72 groups of researchers in America[1,4], Canada[2] and Germany[3], looking for the causes of these plant diseases found that the infectious agents were unencapsidated (lacking a protein coat) ribonucleic acids of an unexpectedly small size.

It had been known since the early 1960's that free nucleic acids could be infectious and cause plant diseases. The existence of a new type of pathogen termed viroid (=virus-like)[1], was first established in 1971—72 when it became clear that the agents producing the diseases mentioned above were extremely small. The name viroid was based on the observation that the symptons of an infection, which occurred

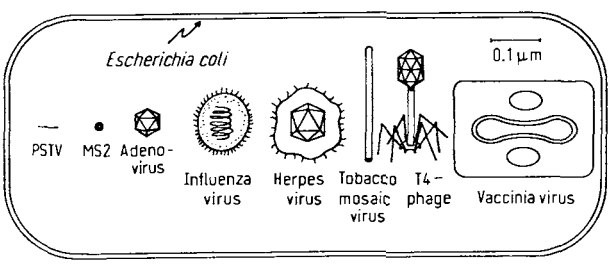


Fig. 1. Comparison of the size of "potato spindle tuber viroid" (PSTV) with viruses and the bacterium *Escherichia coli*.

[*] Priv.-Doz. Dr. H. J. Gross
Max-Planck-Institut für Biochemie
D-8033 Martinsried bei München
Prof. Dr. D. Riesner
Institut für Organische Chemie und Biochemie
der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt

 © Verlag Chemie, GmbH, 694 Weinheim, 1979 0570-0833/80/0404-0231 $ 02.50/0

after an incubation period of weeks or months (or in some cases even years) closely resembled those produced by well known plant viruses. These include inhibition of growth and warping or yellowing of the leaves; the fruit of the infected plant can also be affected, *e. g.* yellow cucumbers or spindle-like potatoes.

The propagation of viroids seems to occur chiefly *via* tools used by man in pruning, cultivation and harvesting, but it also seems quite likely that the infection can be transmitted without human intervention, for example *via* pollen at fertilization.

Certain plants in developing countries are particularly prone to viroid infection. In the Philippines, whole groves of coconut palms have been eradicated by the Cadang-Cadang viroid. It is at present not possible to treat diseased plants, and therefore the only remedy is to limit the propagation of the viroid by appropriate measures and to obtain fresh seed from viroid-free plants.

So far, viroids have only been found in plants, but the fact that other pathogens such as viruses, bacteria and mycoplasma are widely distributed suggests that viroids or viroid-like agents may also occur in man and other animals.

As a result of work on viroids, it is now possible for the first time to collect detailed information about the chemical and physical structure of a pathogenic agent of eukaryotic origin. This should provide an important basis for investigating the replication and pathogenic action of these agents.

This article is concerned chiefly with structural studies which are now to a large extent concluded. Ideas about replication and pathogenesis are very much in their infancy and these are discussed briefly at the end of the article. Readers who are interested in biological or microbiological aspects are referred to specialized reviews[1-14].

2. Biochemical Characterization

Four groups of researchers, namely *T. O. Diener,* Beltsville, USA[1], *R. P. Singh,* Fredericton, Canada[2], *H. L. Sänger,* Giessen[3] and *J. S. Semancik,* Riverside, USA[4], independently discovered that viroids were small, infectious unencapsidated ribonucleic acids.

Certain unusual features which distinguished viroids from other pathogens suggested that a different type of agent was involved; in contrast to many viruses and bacteriophages they were highly sensitive to RNA degrading enzymes (RNases), but were unusually resistant to the effects of organic solvents. These observations suggested that they were composed of RNA with a very simple structure. Animals injected with viroid preparations did not develop antibodies to viroid specific proteins which may have been presumed to be present. It was also noted that viroids were very mobile in an electric field but not in a centrifugal field, from which it was concluded that they have an exceptionally low molecular weight.

The development of a successful procedure for isolating viroids from diseased plants found in the potato field or groves of citrus fruit or coco palms was a long and tedious process. A necessary initial step was to find appropriate test plants which could be cultivated in large numbers in greenhouses, and which would also show clear symptoms of viroid infection as rapidly as possible. Early attempts to isolate for example the citrus exocortis viroid were dependent on young citrus shoots which only showed symptoms several months after infection. It soon became clear that the young tomato plant was a more amenable host, developing symptoms after only a few weeks under optimum conditions. The tomato had another very helpful characteristic which was that most viroids known at the time replicated on it and produced symptoms similar to those shown in Figure 2a.



Fig. 2. a) Symptoms of viroid-infection. Healthy tomato plant (left), diseased (right). b) Test of infectivity on tomato plants. The characteristic smaller size of the plants in the middle shows that the fractions used for infection contained viroid. From back to front increasing concentrations were used for infection. (We are indebted to Prof. *Sänger,* Giessen, for the figure.)

The same general scheme is employed for isolating all viroids[14,15]. Leaf material is homogenized, extracted with phenol, and the nucleic acids remaining in the aqueous phase are precipitated with ethanol. Repeated precipitation and extraction steps are used to free the precipitate (which contains the infectious material) from large nucleic acids and also from polysaccharides whose presence complicates the purification a great deal. Repeated preparative polyacrylamide gel electrophoresis finally yields a nucleic acid which is infectious, and which is absent from similar preparations derived from healthy plants.

In developing a purification procedure, the biological infectivity of the fractions containing viroid must be established at each stage; this means that the analysis of each fractionation step involves infecting whole series of plants and examining them after several weeks for symptoms of disease.

Such a test series is shown in Figure 2b, which illustrates a variation in infectivity resembling a chromatographic elution profile. In the standard preparations which have now been developed, the occurrence of a specific band in polyacrylamide gel electrophoresis can be used to diagnose the presence of a viroid. However, despite these developments, the purification is still very tedious, and the yield is extremely small. As a rough guide, about 0.1 mg of pure viroid can be obtained from 5000 diseased plants. Thus, biochemical and physicochemical investigations of the structure have to be carried out with the smallest possible quantity of substance.

Many investigations, especially sequencing, require radioactively labeled viroids or viroid fragments. Several fundamental difficulties had to be overcome in order to obtain these. It is of course in principle possible to label viroids *in vivo* with radioactive ^{32}P[16], but because of their slow replication, and time consuming isolation, one obtains material whose specific activity is far too low for detailed structural investigations.

Radioactively labeled 5-iodocytosine can be produced *in vitro* by chemical labeling. This method has occasionally been used with viroids[17-19], but is of limited applicability since only fragments containing cytosine are labeled. The only generally applicable method at present available for viroids is to label them enzymatically with ^{32}P *in vitro*[21-23]. The method involves transferring the γ-[^{32}P] phosphate group from γ-[^{32}P]-ATP to the free 5′-hydroxy group of nucleic acids or fragments derived from them by 5′-polynucleotide kinase from phage T_4 infected *E-coli* cells. However, the procedure is not without its own practical difficulties: *(i)* γ-[^{32}P]-ATP of high purity and specific activity has to be regularly synthesized in the laboratory, *(ii)* 5′-polynucleotide kinase from phage T_4 infected bacteria must be isolated absolutely free from ribonucleases, *(iii)* the short half-life of ^{32}P imposes a continual pressure for rapid work, and *(iv)* viroid preparations have to be as pure as possible, since there is a risk that contaminating nucleic acids would be preferentially labeled *in vitro*.

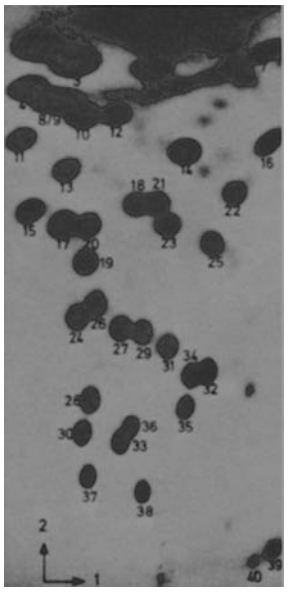


Fig. 3. Fingerprint of the oligonucleotides of PSTV after cleavage with RNase T_1. PSTV was hydrolyzed by RNase T_1, and the 3′-terminal phosphate residues of the oligonucleotides produced were removed with phosphatase. After inactivation of the phosphatase the oligonucleotides were radioactively labeled *in vitro* with [γ-^{32}P]-ATP and 5′-polynucleotide-kinase and separated in two dimensions; 1st dimension: electrophoresis at pH = 3.5/5000 V on cellulose acetate [67]; 2nd dimension: homochromatography on thin layers of DEAE-cellulose [68]. The labeled oligonucleotides were made visible by autoradiography (cf. also Section 4.1). B indicates the position of the blue dye xylene cyanol after an optimum running time.

A sample of viroid can be characterized very precisely by cleavage with specific ribonucleases and labeling the oligonucleotides produced at the 5′ end with [^{32}P]-phosphate. When the oligonucleotide mixture produced is subjected to two dimensional chromatography and analyzed by autoradiography, a characteristic "fingerprint" of the viroid is produced (Fig. 3) which can provide the clearest evidence for the purity of the viroid preparation[21]; only a few percent of RNA impurity from the host produces many other oligonucleotides which can readily be detected from the occurrence of additional dark spots in the autoradiogram. Fingerprints can be used to identify different viroids unambiguously, and were important in initially establishing that viroids associated with different plant diseases had different nucleotide sequences[17,21].

3. Physical Properties

3.1. Molecular Weight

Estimates had been made on the size of viroids long before methods for isolating them had been fully established. These estimates were obtained by comparing the rates of sedimentation in sucrose gradients and R_f-values in gel electrophoresis with the behavior of ribonucleic acids of known molecular weight[1,3,4,24]. The position of the viroid band was found using the rather time-consuming and inconvenient infectivity tests described earlier. These estimates depended chiefly on comparing the mobilities of viroids with those of other nucleic acids, and a condition for obtaining reliable estimates of molecular weight is that comparisons should be made between species whose structures are similar; false values would be obtained if for example the behavior of a spherical and a rod-like molecule were compared. The shape of the viroid molecule was not known, and in an attempt to overcome this problem to some extent, comparisons were made between nucleic acids which had all been converted into the random coil configuration in the hope that they would also have similar structures[25]. However, it later became apparent that even the random coil form of the viroid had a structure different from that of other nucleic acids. It is not surprising therefore that estimates of the molecular weight in the literature ranged from 25000 to 130000. But despite this variation, these values did establish quite clearly that these pathogens were about an order of magnitude smaller than the nucleic acid components of the smallest phages, and that based on their size they constituted a new group of molecular pathogenic agents. Inactivation of viroids by UV light or ionizing radiation gave a target size which indicated a molecular weight of about 100000[26].

When pure viroids became available, the molecular weight could be determined, using the analytical ultracentrifuge, from the concentration distribution measured by the optical absorption[15]. The sedimentation-diffusion equilibrium

method yields estimates of molecular weight which are independent of any assumptions about the shape of the molecule. These studies gave values for the molecular weight of between 110000 and 127000 for different viroids; the viroid responsible for the potato spindle tuber disease (PSTV), which is discussed in detail below, was shown to have a molecular weight of 127000 ± 5000.

3.2. Molecular Shape

The shape of nucleic acids of the size of viroids can be studied by high resolution electron microscopy. In such pictures, viroids appear uniformly as rod-like molecules[15,27]; in the preparative procedure used for the sample shown in Figure 4a the average length was about 370 Å and the width 20 Å.

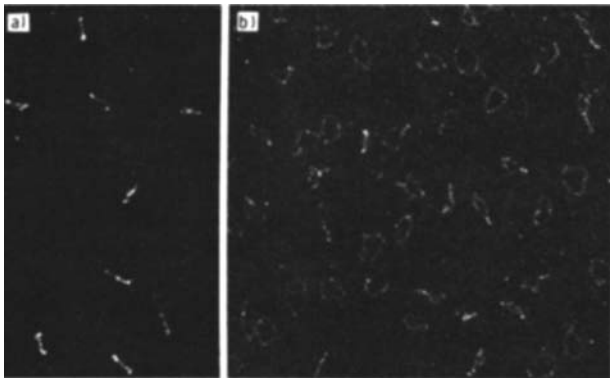


Fig. 4. Electron micrographs of viroids. a) In the native state: viroids were spread at room temperature with benzyldimethylalkylammonium chloride, stained with uranyl acetate, and observed in dark-field illumination ("alkyl", $C_{12}/C_{16} = 60/40$); b) in the denatured or partially denatured state: viroids were spread at 70 °C in the presence of urea. Enlargement 92500 times.

Since under certain circumstances the results obtained from electron microscopy can be influenced by artefacts arising in the preparation of the sample, the shape was also examined by investigating the hydrodynamic properties of viroids under physiological conditions[15]. By determining the molecular weight and sedimentation coefficient independently, an axial ratio of 20:1 was estimated—a value in good agreement with the electron microscope results.

3.3. Ring Structure of the Nucleotide Chain

Section 5 describes in detail how the formation of Watson-Crick base pairs leads to a well defined structure for viroids. Anticipating this discussion somewhat, we note here that the characteristic double helical structure produced by strands running in opposite senses can be formed either between two separate chains or by folding a single chain back on itself. In order to investigate the structure of a nucleotide chain in the denatured state, the base pairs are disrupted by urea, by formamide or by elevated temperatures, and the resulting structure is sometimes fixed with formaldehyde. The molecular weights of viroids in the native and denatured states were the same, indicating that they are composed of a single nucleotide chain.

When highly purified samples of viroid were denatured and examined by electron microscopy, the pictures showed the nucleotide chains to be almost exclusively circular[15] (Fig. 4b); since under the conditions used to prepare the samples all base pairs should have been dissociated, this suggests that the structure was a covalently closed ring. This conclusion was clearly confirmed by chemical methods[15]. It was not possible to transfer ^{32}P to the native viroid using the 5′-transphosphorylation reaction discussed in Section 2, showing that the viroid lacked a 5′ terminus. Similarly, treatment with periodate followed by reduction with $B^3H_4^-$ did not lead to the incorporation of radioactivity into the viroid, showing that it lacked a 3′ terminus with associated vicinal 2′- and 3′-OH groups which would have been susceptible to oxidation. The finding that viroids have a covalently closed ring structure, meanwhile amply confirmed by electron microscope studies in other laboratories and with other species of viroid[20,28], was a surprising development, since they are the first example of a naturally occurring covalently closed RNA ring. Ring structures had previously only been found in DNA, and these were of much higher molecular weight. Circular RNA molecules of various sizes have recently also been found in the cytoplasm of eukaryotic cells[29], but conclusions about their structures presently depend solely on electron microscope pictures.

Samples of viroid also contain, in addition to circular molecules, some linear chains in a proportion which depends on the method used in the preparation[15,28]. However, it was shown that linear chains can arise very readily from Mg^{2+}-catalyzed cleavage of the rings, and that the linear viroids produced show little or no infectivity[30]. It is not yet known to what extent linear viroids occur natively in the infected plant cells, possibly as an intermediate stage in the production of the mature viroid[30,31].

4. Nucleotide Sequence of PSTV

The first complete primary structure of a viroid, the cause of the potato tuber spindle disease, was established in 1978[23]. This achievement may appear relatively straightforward compared with the work which elucidated the sequence of the bacteriophage MS 2[32] which has about 3600 ribonucleotide residues. But, as has already been pointed out, it is not possible to label the viroid *in vivo* with ^{32}P, unlike the situation for phage MS 2; in addition, the quantities of viroid RNA available were exceedingly small. The chemical methods of DNA sequencing which have recently been developed into routine procedures[33] could not be used, since in the case of viroids it is not yet possible to enzymatically generate complete copies of complementary DNA with defined starting points. A relatively new and untried procedure had to be used to obtain the sequence based only on ^{32}P labeling *in vitro* (see Section 2).

4.1. Total Hydrolysis with Specific Ribonucleases

Figure 3 illustrates a fingerprint of PSTV obtained after complete hydrolysis with ribonuclease T_1, which cleaves on the 3′ side of guanosine. A different characteristic fingerprint is obtained if pancreatic ribonuclease is used for cleavage[21]. The 40 oligonucleotides from the RNase T_1-digest, each labeled at the 5′ terminus with ^{32}P (Fig. 3), and the corresponding 32 oligonucleotides from the pancreatic digest,

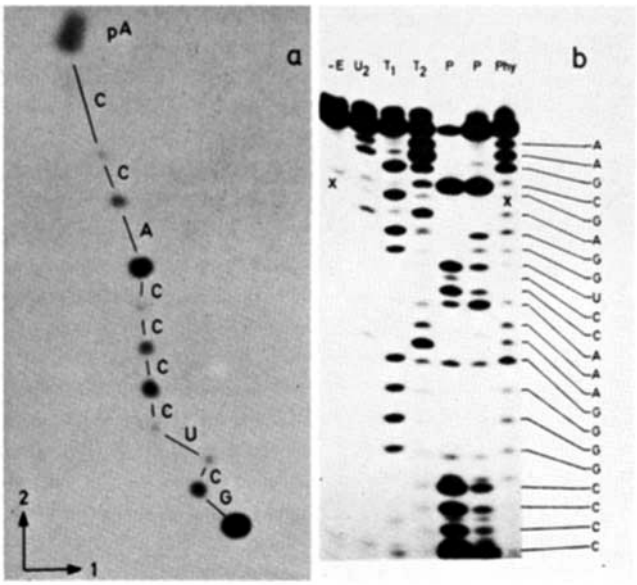


Fig. 5. Sequence analysis of 5′-^{32}P-labeled RNA-fragments. a) The fragment No. 37 from the RNase-T_1-fingerprint of PSTV (Fig. 3) was cleaved with nuclease P_1 [34] under limiting conditions, so as to obtain a mixture of fragments, all of which are labeled at the 5′-terminal and differ in chain length. After two-dimensional separation (electrophoresis/homochromatography) and autoradiography the sequence of the nucleotides may be directly read off from the differences in mobility of neighbored oligonucleotides (in 5′-3′-direction top to bottom) [35]. b) The PSTV-fragment No. 69 (cf. Fig. 7) was distributed in eight aliquots. These were digested under limiting conditions with the RNases U_2, T_1, T_2, pancreatic RNase (P), and Phy I in order to localize subsequently the adenosines, guanosines, pyrimidines, and cytidines by polyacrylamide-electrophoresis and autoradiography [36, 37]. The nucleotide sequence may be directly read off (in 5′-3′-direction bottom to top) from the autoradiogram. X indicates the position of the blue dye xylene cyanol after optimal running time. The hydrolysis with P was carried out twice in order to meet optimum conditions.

were all eluted separately from the fingerprint chromatograms. The 5′ terminal nucleotide residue of each was identified by total hydrolysis with nuclease P_1[34]; this produces 5′-mononucleotides, but only that from the 5′ terminus is labeled with ^{32}P. The terminal residues were identified by autoradiography of thin layer chromatograms run together with authentic samples of the nucleotide. The nucleotide sequence of a 5′-[^{32}P]-labeled oligonucleotide was determined by partial cleavage with nuclease P_1. Ideally, the conditions for this partial hydrolysis should be so arranged that only a single phosphodiester bond is cleaved at a random position for most of the oligonucleotides present, and a small proportion should not be attacked at all. The mixture of products is separated by two dimensional electrophoresis and chromatography, and the chromatogram examined autoradiographically. The electrophoretic mobility in the first dimension depends on the base composition, whereas the chromatographic mobility in the second dimension is approximately inversely proportional to the chain length of the oligonucleotide, so that the largest oligonucleotide has the lowest mobility. The resulting autoradiogram shows a specific pattern of partial hydrolysis resulting from the loss of one or more nucleotides from the 3′ end (Fig. 5a); the nucleotide sequence can simply be read from this pattern from the angle and separation between the successive spots.

4.2. Partial Hydrolysis

The oligonucleotides obtained from the pancreatic and RNase T_1 cleavages now have to be ordered into the complete sequence. For a normal linear RNA, this could involve enzymatically labeling the 5′ or 3′ ends with ^{32}P and using various procedures to establish the structure progressively from the two termini. A different method had to be adopted with circular viroid RNA. Samples of a few micrograms of PSTV were partially cleaved under various conditions with different enzymes so as to produce as many long PSTV fragments as possible. The conditions used were essentially: low temperature and/or low concentrations of RNase, or high salt concentrations which stabilize the secondary structure of the viroid. The mixture containing such long fragments was subjected to two-dimensional polyacrylamide gel electrophoresis after labeling the 5′ ends with [^{32}P]-phosphate; Fig-



Fig. 6. Separation of long 5′-^{32}P-labeled PSTV oligonucleotides. After partial hydrolysis of PSTV with nuclease from *S. aureus* the oligonucleotides produced were labeled enzymatically and separated by two-dimensional polyacrylamide gel electrophoresis. 1st dimension: 10% polyacrylamide, pH = 3.5; 2nd dimension: 20% polyacrylamide, pH = 8.3 [69, 70]. The oligonucleotides were made visible by autoradiography, cut out, and isolated by electrophoretic elution.

ure 6 shows a typical autoradiogram. The appropriate small portions of the gel were cut out, and after electrophoretic elution about 50—70 long 5′-labeled fragments could be obtained in a pure state. The nucleotide sequence of these fragments, which contained between 20 and 100 residues, was determined using recently developed electrophoretic procedures[36, 37]. An aliquot of each fragment was treated with the guanosine specific RNase T_1 under limiting conditions. Visible spots in the autoradiogram are only produced by those decomposition products from the original RNA fragment which have a [^{32}P]-labeled 5′ end and a guanosine at the 3′ end. The number of such sub-fragments produced corresponds to the number of guanosine residues present in the original RNA fragment, and the length of these sub-fragments depends on the distance of the guanosine from the 5′-[^{32}P]-phosphate. The electrophoretic separation of this hydrolyzate in 0.35 mm polyacrylamide layers yields a pattern of bands from which the ordering of guanosines in a sequence can be read off (Fig. 5b). Other aliquots of the RNA fragment were treated similarly with RNase U_2 or pancreatic RNase, in order to locate the adenosine and pyrimidine residues in the sequence. Uridine and cytidine were distinguished by using RNase Phy I from *Physarum polycepha-*

lum[38] or the endonucleases from *Staphylococcus aureus* and from *Neurospora crassa*[39]. The position of the nucleotide reference frame was obtained using RNase T_2, which can cleave any phosphodiester band.

4.3. Overlapping Fragments and the Complete Sequence

Since the fragments which had been sequenced were obtained by partial cleavage using enzymes of different base specifities, they often overlapped the same section of the viroid sequence. The segments shown in Figure 7 comprise a large proportion of the fragments sequenced. The partial sequences can be combined using these overlapping regions to yield the complete sequence of the PST viroid (outside circle in Fig. 7). Since these overlaps cover the entire circular viroid chain, this analysis of the sequence firmly establishes the ring structure of the PST viroid.

5. Structure in Solution

5.1. Structural Hierarchy of Nucleic Acids

The nucleotide sequence, or primary structure, is the lowest step of a hierarchy which includes secondary and tertiary structures as higher levels of structural organization. The type of structural hierarchy involved depends on the nature of the macromolecule, since structures are stabilized by various kinds of interactions and are subject to different steric restrictions (for protein structure cf. [40]). The important element in the secondary structure of nucleic acids is the Watson-Crick double helix, in which the bases adenine and uracil (or thymine in DNA) are linked by two hydrogen bonds, and guanine and cytosine by three hydrogen bonds. Base pairing between guanosine and uracil can also occur in double helices formed between strands whose sequences are not fully complementary. The secondary structure of a nucleic acid denotes the complete two dimensional scheme of all possible base pairs formed either between two separated strands, or by simple folding back of a single strand. Base pairs formed between single stranded regions which are remote from one another and whose immediate neighborhood is already highly structured, do not form part of the secondary structure. For example, Figure 8a illustrates a typical secondary structure; the additional base pairs shown in Figure 8b (assuming that sterically they could be formed at all) would not comprise part of the secondary structure.

The secondary structure is therefore a theoretical model which describes the state of lowest free energy, and which

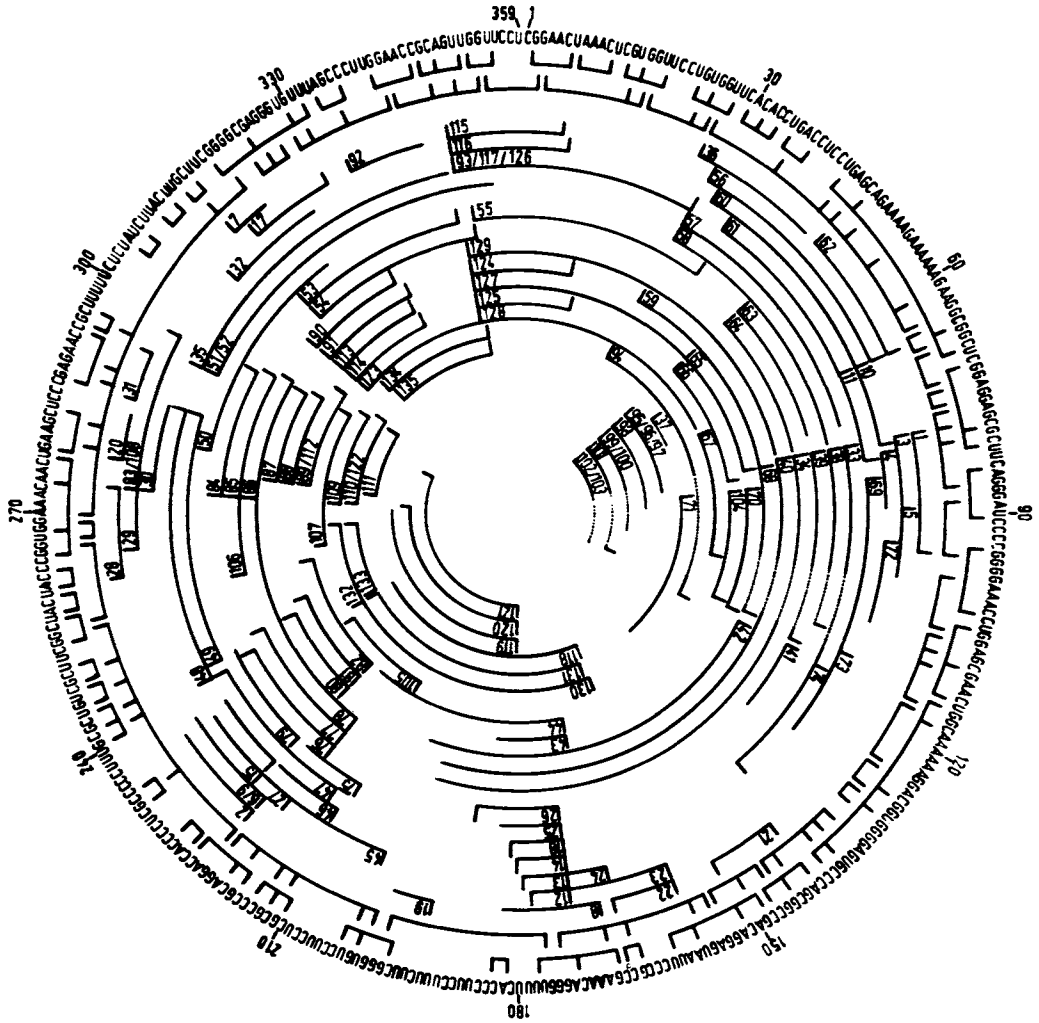


Fig. 7. Primary structure of PSTV. The nucleotides were numbered clockwise from 1 to 359. The brackets in the two outer circles indicate the products of total hydrolysis with RNase A and RNase T_1, respectively. The numbered segments in the inner rings indicate long PSTV-fragments, the nucleotide sequence of which was worked out. From a combination of this information the complete circular primary structure of PSTV was obtained.

only takes normal AU, GC and GU base pairs into account.

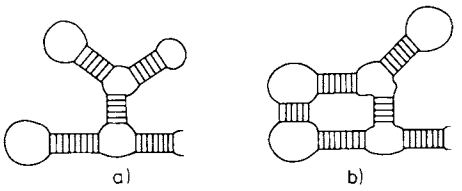


Fig. 8. Examples of the secondary structure of nucleic acids. a) nucleic acid with secondary structure only, b) nucleic acid with secondary and tertiary structure.

In general, the tertiary structure is considered to be the three dimensional configuration of a macromolecule, and thus every nucleic acid necessarily possesses a tertiary structure. However, we would like to use a more restricted definition of tertiary structure, and consider it to be those structural features resulting from interactions which are not a part of the secondary structure. The folding of the clover leaf structural model of transfer RNA into the compact tertiary structure revealed by X-ray crystallography is a familiar example[41, 42]. Chemical or physical investigations simultaneously probe the combined secondary and tertiary aspects of structure.

5.2. Secondary Structure of PSTV

Two stages are involved in finding the secondary structure which is most stable energetically: firstly, models with a higher degree of base pairing are constructed, and then the differences in free energy between each of these models and the fully unpaired state is calculated. The first step can be approached systematically using a computerized graphical procedure[43] with minor modifications for dealing with circular structures[44]. This involves representing all possible intramolecular helices in the form of a matrix, and designing complete structures based on these helices. The highest number of base pairs is the criterion for favorable structures in the first approximate stage, but studies with 10—20% fewer base pairs are also brought into consideration in the second quantitative stage in which free energies are calculated.

In order to calculate the free energy difference between the desired secondary structure model and the fully unpaired state, the former is considered to arise from the latter as the product of a multistage process of known elementary steps whose contributions to the overall free energy are then summed. The elementary steps with their associated thermodynamic parameters are known from many studies on oligonucleotides; they are depicted in Table 1.

Table 1. Stability parameters of ribonucleic acids. The values for the equilibrium constants, reaction enthalpies, and reaction entropies can be found in the literature [45]. The growth parameters of base pairing (see 1) not only depend upon the type of base pair to be formed but also upon the type of the preceding base pair. Loop formation (see 2) depends upon the factor γ, which describes the probability of pairing of bases which are within a favorable distance, and upon the loop weighting function $\rho(p+1)$ which describes the probability of approaching the favorable distance and includes the geometry of the loop. I_{tot} = total number of nucleotides of the molecule

1) Base pairing

s_{GG}, s_{GA}, s_{AA} (CC, CU, UU) experimental

2) Loop formation

a) hairpin loop

$p<13$: experimental, Monte-Carlo-calculations

$p \geq 13$: $\rho(p+1) = 0.319 \cdot p^{-3/2}$

b) internal loops

$r \leq 8$: experimental

$r > 8$: $\rho_i = \rho(r+1)$

c) bulge loops

$t \leq 8$: experimental

$t > 8$: $\rho_b = \rho(t+1)$

3) Base pairing in circles

$$K = \gamma \frac{\rho(p+1) \cdot \rho(q+1)}{\rho(I_{tot})} \cdot s^{n-1}$$

The secondary structure shown in Figure 9 is by far the most favored structure energetically for the PST viroid[23, 44]; trivial shifts in the regions of small helices and large loops are possible but thermodynamically unlikely[44]. Branched structures such as those shown in Figure 8 lead to at least 30 fewer base pairs, and about a 50% less favorable free energy. At low temperatures, the structure most favored thermodynamically is that with the largest possible number of base pairs. At the conclusion of the sequencing work, a model was described[23], based on maximizing the number of base pairs and taking into account the accessibility of single stranded regions to enzymes and chemical reagents (cf. Fig. 10); this model is almost identical to the thermodynamically optimized model.

5.3. Experiments on the Secondary and Tertiary Structures of PSTV

A variety of chemical, physical and enzymatic methods which have been used successfully to investigate the structures of other nucleic acids were adapted with minor modifi-

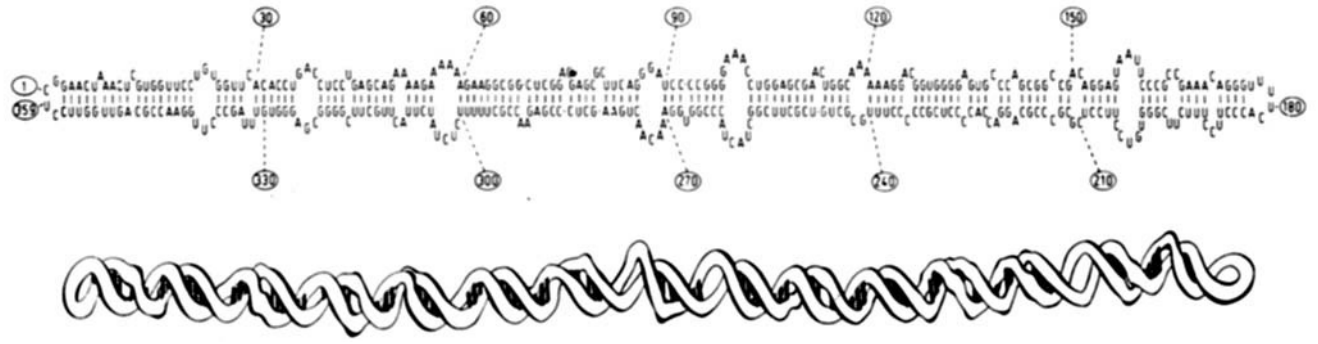


Fig. 9. Structure of PSTV. Base pairing scheme (top), three dimensional representation (bottom).

cations for studying viroids. They are not described in detail here, but the salient points are shown schematically in Figure 10. Further information about the structure is provided by thermodynamic and kinetic methods which are described in Section 6. NMR measurements have also been carried out, but, owing to the low resolution of the spectra, these were merely able to establish that there was a high degree of base pairing, and could not provide more detailed information[49].

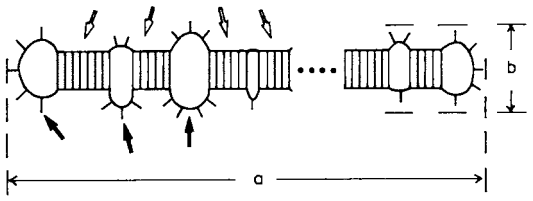


Fig. 10. Structural probes for viroids. ⇦⇨: accessibility of double helices for dye binding [44, 46] and double-strand specific nucleases [47]; in PSTV, however, the double helices are not cleaved by the double-strand specific RNase III because of their low number of base pairs [47]. ←: accessibility of unpaired regions for enzymatic digestion [23], chemical modification of cytidine to uridine with bisulfite [22, 23], and oligonucleotide binding [48]. *a*: length in the electron micrograph [15, 25]; *a/b*: axial ratio from the independent determination of the molecular weight and the sedimentation coefficient [15].

Of the methods outlined in Figure 10, those concerned with oligonucleotide binding ought to be described more fully, since a modification of commonly used methods was developed especially for studying viroids[48]. It was found that specific transfer RNAs were a particularly suitable form of oligonucleotide for such studies; these form base pairs between the anticodon triplet and a complementary triplet of another transfer RNA[50], or a corresponding sequence in a single stranded region of another nucleic acid. The principal advantage of using transfer RNAs is that the binding constant for this interaction lies between 10^5 and 10^6 M^{-1}, about two to three orders of magnitude stronger than simple tri- or tetra-nucleotides. In some cases the binding was followed spectroscopically, otherwise hydrodynamic methods were used. This approach was used to probe the accessibility of various single stranded regions in the viroid to binding of specific tRNAs. The results, which are shown schematically in Figure 10a, indicated that binding was found experimentally in those cases when it would have been expected from the model of the secondary structure.

The results of the structural experiments on the geometry of the molecule (revealed by electron microscopy and hydrodynamic studies), and on the accessibility of double stranded regions to dye binding, and of single stranded regions to chemical modification, enzymatic cleavage and oligonucleotide binding, can all be summarized very simply: the PST viroid does not possess additional elements of tertiary structure which would modify the shape or restrict the accessibility from what would be predicted by the model of the secondary structure. Thus, this model can be used directly as the basis of a three dimensional representation of the molecule (Figure 9b). The overall impression is approximately that of a section of double helix; the internal single stranded regions are irregularities in the structure which endow the molecule with a degree of flexibility, as well as being regions which could possibly interact with other RNA-species, as the tRNA binding experiments show.

The fact that the structure of the PST-viroid is completely characterized by interactions in the secondary structure is not the rule, but very much an exception among ribonucleic acids. Transfer RNA, messenger RNA, ribosomal RNA and single stranded viral RNA all possess pronounced and partially globular tertiary structures, which are not at all characterized by a scheme of two-dimensional base pairing. It ought also to be admitted that it is the very absence of additional elements of tertiary structure which has enabled much of the structural work on viroids to reach firm conclusions, and in particular to make an exhaustive thermodynamic and kinetic treatment of PSTV (see Section 6) at all feasible, despite its relatively high molecular weight of 120000.

The culmination of the structural description of a species is normally considered to be a crystallographic analysis, which can define the complete set of atomic coordinates. At the moment this is not feasible for viroids owing to lack of material. Detailed information about the conformations of internal single stranded regions could only come from single crystal studies; analysis of fibers would hardly be able to reveal new aspects of their structure. Since, according to our present view of viroid structure, the single-stranded regions are flexible in solution, it may well prove to be the case that they appear unsharp in the X-ray picture. It is therefore by no means certain that the enormous effort involved in attempting to obtain this information would be worthwhile.

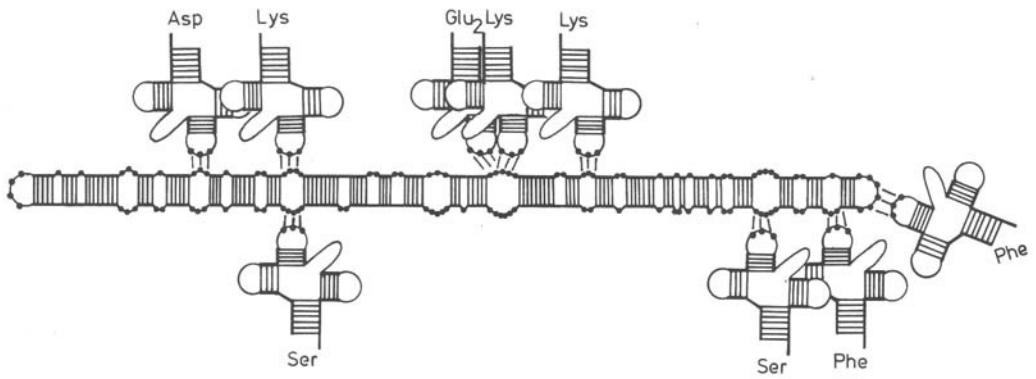


Fig. 10a. Binding of specific tRNAs to unpaired regions of PSTV. For all tRNAs depicted, binding has been demonstrated experimentally. For two other species no binding could be detected; there is also no sequence in one of the unpaired regions of PSTV, which is complementary to the anticodons of the non-binding species [48]. The anticodon-regions of $tRNA_2^{Glu}$, $tRNA^{Lys}$ and $tRNA^{Phe}$ contain odd nucleotides, the optical absorption or fluorescence of which changes characteristically due to the binding to the viroid and was used for a direct optical titration.

6. Structural Dynamics

The characteristics of the structural transitions undergone by nucleic acids are dependent on and can be inferred from the participating structures themselves. Also, it should not be thought that even *in vivo* nucleic acids have fixed, rigid structures, but rather that they can be functionally active in various conformations.

6.1. Denaturation Curves

A nucleic acid can be denatured by increasing the temperature which converts the double helical state into coiled single strands. This transition can readily be monitored from the increase in absorbance at 260 nm, and the associated curve is termed the optical denaturation curve, or less precisely but more colloquially the melting curve. Such curves have been obtained for various viroids[15,49,51-54], and Figure 11 illustrates the curve for PSTV together with those for t-RNA[55] and double stranded viral RNA[56]. Denaturation curves are characterized by two parameters: the mid-point temperature (T_m) at which half of the total hypochromic effect has been reached, and the transition width ($\Delta T_{1/2}$) which is the temperature interval between the half lengths on the denaturation curve, which resembles a Gaussian distribution. The close connection between structure and structural transitions is evident on comparing the three curves. Without going into the quantitative treatment of cooperative transitions in biopolymers (cf. [55,57,58]), the following general conclusions can be drawn from the theory as regards transitions in nucleic acids. In single stranded nucleic acids such as, *inter alia*, t-RNA and 5S-RNA, several short double helical segments of low enthalpy (cf. Fig. 8) denature independently, leading to an overlapping of several broad transition curves. In contrast to this behavior, in homogeneous double stranded nucleic acids, a large number of neighboring base pairs denature in a highly cooperative process; the enthalpies of many base pairs are assimilated into a single step, and, in accord with the van't Hoff relationship, this produces a sharp transition over a very narrow range of temperature.

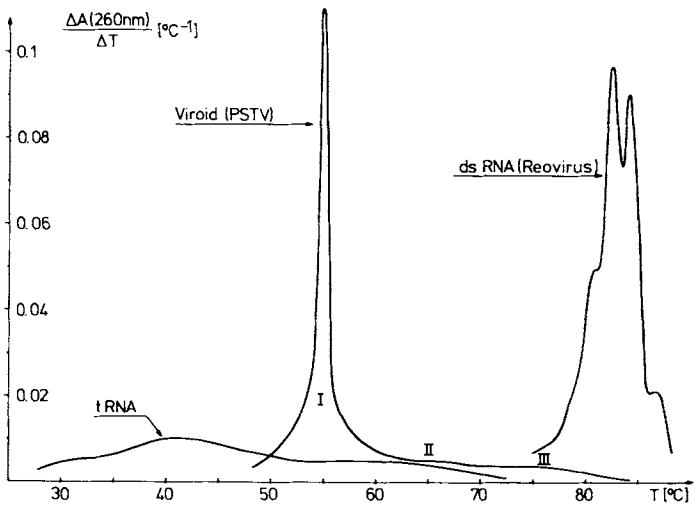


Fig. 11. Optical denaturation curves of PSTV [54], tRNA [55] and double-stranded (ds) RNA from Reovirus [56]. The curves are presented in the differentiated form as commonly used today. Multistep transitions are easily recognizable because of the appearance of several peaks. The interpretation of part II and III in the curve of PSTV as well-resolved transitions follows from detailed kinetic experiments [54]. Buffer conditions: pH = 7 and 0.02 M Na^+.

Viroids unite two thermodynamic properties which appear to be at variance according to the ideas described above: the transition occurs at low temperature in a region characteristic of single stranded nucleic acids, but the cooperativity of the transition is as high as that of homogeneous double strands. Similar denaturation curves are obtained from calorimetric measurements, in which the additional heat capacity ΔC_p is measured[59]. The time-dependence of the denaturation, obtained from relaxation measurements after a temperature jump, shows that 80–90% of the process occurs in a single-step reaction, emphasizing the high degree of cooperativity of the transition[52,54]. The denaturation curves of all other viroids investigated show the same behavior qualitatively, although the actual values of T_m and $\Delta T_{1/2}$ for each viroid do deviate from one another by respectively a few degrees and a few tenths of a degree[53].

Initial calculations, made at a time when the sequence of the PST viroid was not known, were able to explain these properties from a general model of the secondary structure[53]. This model was not based on a particular viroid sequence, but incorporated much of the known experimental data such as: T_m, $\Delta T_{1/2}$, the size and circularity of the molecule, as well as its G:C content and the calorimetrically determined reaction enthalpy *etc.* Optical denaturation curves for various models were calculated using the known stability parameters for ribonucleic acids (Table 1) and compared with those obtained experimentally. Good agreement was obtained for one model in which short double helices (four to seven base pairs) alternating with small unpaired regions (two to six bases) were arranged in a linear unbranched structure. Such a general model is in complete agreement with the specific model for PSTV.

6.2. Mechanism of Denaturation

The properties of the structural transition were subsequently interpreted in terms of both the general model and the specific structure of PSTV[44,54]. Further analysis of the results showed that two additional transitions (designated II and III in Fig. 11) could be observed after the principal highly cooperative transition had occurred. This indicates that small regions of the viroid are still base paired after dissociation of the major part of its structure. Despite the small hypochromic effect associated with these transitions, kinetic measurements were able to reveal the number of base pairs in the double helical arms, the size of the unpaired loops and the G:C content.

These stable regions have a feature which is unusual in nucleic acids. Thermodynamic[54], enzymatic[44] and electron microscopic studies[44] indicate that they are not a part of the native structure, but are formed during the highly cooperative major transition. The structures of these newly formed looped regions in the viroid are collected in Table 2; there is good agreement between the expected and observed parameters characterizing these base paired regions, and furthermore there are no other areas within the native structure which would have led to comparable agreement.

The mechanism of denaturation of PSTV modified to incorporate these newly formed stable regions is shown in Figure 12. The overall structure dissociates in a highly coopera-

tive process in which three new stable loops are formed (see also Table 2). The structures shown in the dashed box are kinetic intermediates which are not present in significant concentrations at equilibrium. The sequence of steps which produces these intermediate states must therefore be a theoretical model which is in agreement with the experimental results, especially with those obtained from kinetic studies. All of the stable areas are formed according to the same general principle (see arrows in Fig. 12). A section which is already

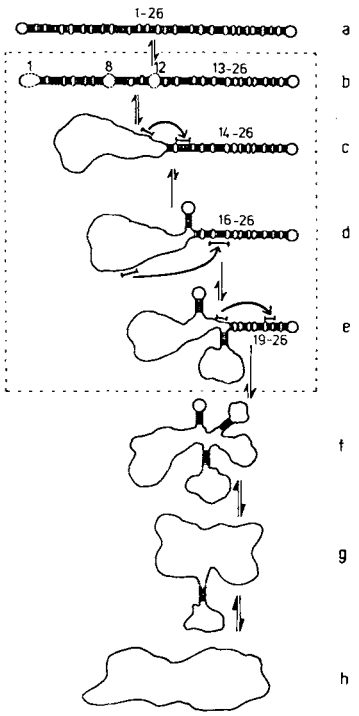


Fig. 12. Denaturation of PSTV. The numbers 1—26 indicate the 26 double helices of the native structure. The states in the dashed box (b—e) are kinetic intermediates. The transitions a→f, f→g, and g→h correlate with part I, II, and III of the denaturation curve in Figure 11.

denatured can form one of the stable structures by pairing with a section which is itself only in a partially base-paired state. The left half of the molecule has a strongly destabilizing influence on the right half, and induces a kind of long distance cooperativity; thus, a high degree of cooperativity in the transition can be examined by this special mechanism without having to postulate any other kind of interaction than the familiar one between nearest neighbors (Table 1). The mechanism can also be depicted in a simple $\Delta G^0(T)$ diagram (Fig. 13). Neglecting the stable arms, the transition temperatures would be calculated to be T_1 and T_2 for a two step dissociation of the native structure. However, from a temperature of T_I ($< T_1$), the branched structure is most stable, and this then dissociates stepwise at the experimentally determined temperatures of T_{II} and T_{III}. The half-opened linear structure does not occur in measurable concentrations at any temperature.

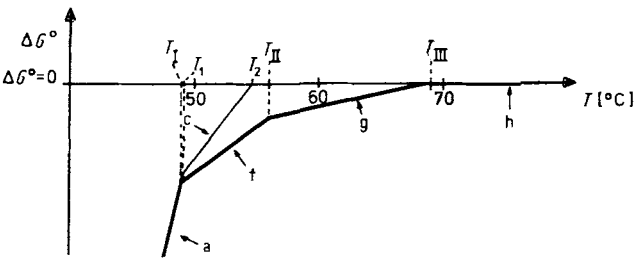


Fig. 13. $\Delta G^0(T)$-diagram of the conformations of PSTV. The difference from the totally denaturated state was calculated. The bold line belongs to the thermodynamically most stable states. T_I, T_{II}, and T_{III} are the mid-point temperatures of the three transitions (cf. Fig. 11 and 12). The thin line between T_1 and T_2 belongs to a hypothetical state which would exist if mere dissociation without new formation of stable hairpins were possible.

The dynamics of the structural transitions of viroids are characterized by two mechanistic features which have not previously been observed in any other nucleic acid. The unusually high cooperativity is attributable to the formation of stable loops, and the principal structural transition is not a simple process of denaturing base pairs, but the result of competition between a linear and a branched structure.

7. Structure and Function

Viroids are distinguished from other ribonucleic acids by a combination of three mutually dependent features: circularity, an unusual secondary structure, and the dynamics of a highly cooperative structural transition.

Table 2. Comparison of calculated (calc.) and observed (obs.) properties of the stable hairpins of PSTV [54]. The calculations were carried out for 1 M NaCl. Under these conditions complications which arise from the polyelectrolyte properties of nucleic acids may be avoided. The observed values were extrapolated to 1 M NaCl [54].

	T_m [°C]		G:C content [%]		Loop size		Base pairs	
	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.
79 87 CGCUUCAGG 14 GCGAGGUCC 110 102	91	89–94	67	77±5	14	20±10	9	2×7–11
127 135 CGGUGGGGA 24 GCGCCCCUU 168 160	95		75		24		9	
227 236 CCCUCGCCCC 82 GGGAGCGGGG 328 319	105	102	90	90±5	82	>40	10	10

The question arises to what extent the structure determined for PSTV is applicable to other viroids. In the case of tRNA it was necessary to establish several structures before the clover leaf model was widely accepted. However, with viroids we are in a completely different situation. By comparing the thermodynamic properties of different viroids[53,54], it can be concluded that they are all constructed according to the same general principle (Figures 9a and 9b). Calculations on circular RNA molecules of the same size and base composition as viroids but with random sequences showed that such viroid analogs formed 20—30 fewer base pairs than PSTV, and exhibited a lower thermal stability and markedly reduced cooperativity[44]. Figure 14 illustrates the simulated denaturation curve of such a random sequence; the reduced cooperativity is particularly noteworthy. Comparative mechanistic studies on viroids[44,54] have shown that the principle of the denaturation scheme in Figure 12, which incorporates the formation of branched structures as an essential element, is common to all other viroids investigated. The chance of this mode of denaturation being realized in a random sequence is very small. These specific properties must therefore be encoded in the particular nucleotide sequence of each viroid, and there are only a limited number of sequences which would produce molecules with such properties. Unlike tRNA, it is possible even when the structure of only a single viroid is known (Figure 9) to draw firm and definite conclusions about the structures of other viroids.

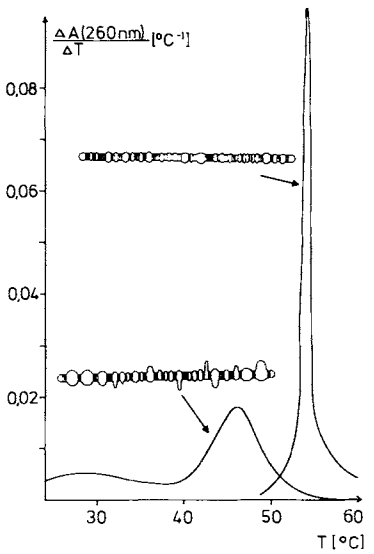


Fig. 14. Thermodynamic comparison of PSTV with a viroid-analogous random sequence. The curve of the viroid-analogous sequence (bottom) was calculated first for 1 M ionic strength and then extrapolated to the conditions of the experimental curve of PSTV (top).

It has not yet proved possible to ascribe specific biological roles to the very unusual structure and dynamic properties which viroids exhibit; at present we can only conjecture about the relationship between structure and function. In the rest of this section we discuss a few selected aspects of the functional consequences of the structure of viroids, but do not attempt to give a comprehensive account of the many, and to some extent contradictory hypotheses which have been proposed.

The significance of the ring structure is clear from the finding that viroids in a circular conformation are several orders of magnitude more infectious than the linear molecules (see Section 3); the circular structure would certainly offer a high degree of protection from exonucleases which degrade nucleic acid chains from the ends.

The linear or stretched out structure of the native viroid, composed of alternating sections of short helices and single stranded regions, can most reasonably be interpreted as a fine compromise between maximal structural stability and functional flexibility. It follows from this that the native structure is still completely intact just below the transition temperature, and that the complete transition is achieved much more readily than in a completely homogeneous double-stranded RNA. Similar alternations between double helices and unpaired regions have also been found in the initiation regions for the replication of phage DNA[60], although they are appreciably shorter than in viroids. It is altogether unclear whether the unusual dynamics of the structural transition are important in the replication of the viroid; the identity of the host enzymes which participate in the replication is not yet known, nor has it proved possible to replicate viroids specifically in a cell free system. However, it seems certain that host RNA- or DNA-polymerases are involved, since the viroid RNA is too small to contain sufficient information for the synthesis of its own specific polymerase. Inhibition experiments have provided evidence that the DNA dependent RNA polymerase II is involved either directly or indirectly in viroid replication[61]. This enzyme is responsible for the synthesis of messenger-RNA in uninfected plants; the fact that it is localized in the cell nucleus can be linked to the early finding that viroids are found in fractions enriched in nuclei[3,62]. It is by no means clear whether the complementary strand to the viroid is present in the form of DNA or RNA, nor indeed whether viroid sequences are a part of the genome of healthy plants or are introduced into the cell *de novo* on infection. The literature contains evidence claiming to support each of the incompatible proposals[63]; some of these results are unconvincing either because impure material was used or because they neglected to take the unusual structure of viroids into account. The finding that sequences complementary to viroids occur in the form of RNA only in infected plants has now been established by several recent studies, but the complementary RNA has not been further characterized as regards size or function.

Various intensive searches have also been instigated for proteins which could be coded for by the viroid. It could be supposed theoretically that the PST viroid could code for peptide chains up to a total length of 283 amino acids[23] but such peptides have not yet been identified experimentally. The idea that viroids do code for proteins or peptides must certainly be considered as a possibility, but there is a good deal of support for the view that they do not carry the information for proteins but merely code for their own structures.

8. Outlook

Studies on viroids have revealed a novel structural principle which produces a natural nucleic acid with unusual features. For the first time, the structure of a eukaryotic pathogenic agent has been elucidated, which appears to code only for its own molecular structure and not for its own proteins.

Since the principles underlying the structure of viroids now appear to be established, this should provide a firm basis for other kinds of investigations into these extraordinary species.

The replication and pathogenic action of viroids do not readily accord with conventional ideas, and it is therefore to be expected that much of the work in the immediate future will be devoted to these problems. It might reasonably be hoped that such work would not only illuminate the mode of action of viroids, but also lead to a better understanding of some more fundamental aspects of molecular biology.

More emphasis will also be laid on applied aspects of the subject, which are of major importance in agriculture and horticulture; other plant diseases may also be recognized as being of viroid origin. At present it is not possible to protect plants against viroids, but knowledge of the structure and progress in understanding the function and mode of action of these agents should enable specific inhibitors to be developed.

Viroids are also of considerable interest in medicine, since it has often been suggested that viroid-like pathogens are also active in man and other animals. The best investigated examples of the many suggestions put forward are scrapie in sheep, and the Kuru disease and the Jacob-Creutzfeldt syndrome in man. These three conditions are degenerative disorders of the central nervous system, which have been attributed to "slow-virus" infections, but the agents responsible for them have never been identified. From the many and partly contradictory results, it can at least be concluded that entities of sub-viral size are responsible[64–66]. The possibility that viroids are involved will increasingly have to be considered, but only the future will show whether the action of viroids is restricted to plants or whether similar agents also exist in man and other animals.

Our own results which are discussed in this article arose from close cooperation with Prof. H. L. Sänger (Giessen). Also involved in this were our co-workers H. Alberty, Dr. H. Domdey, Dr. K. Henco, Dr. P. Jank, J. Langowski, Dr. Ch. Lossow, Dr. M. Raba, U. Rokohl, and U. Wild. This work was generously supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Received: January 9, 1980 [A 312 IE]
German version: Angew. Chem. *92*, 233 (1980)
Translated by Dr. *James Hoggett*, York, UK.

[1] *T. O. Diener*, Virology *45*, 411 (1971).
[2] *R. P. Singh, M. C. Clark*, Biochem. Biophys. Res. Commun. *44*, 1077 (1971).
[3] *H. L. Sänger*, Adv. Biosci. *8*, 103 (1972).
[4] *J. S. Semancik, L. G. Weathers*, Nature New Biol. *237*, 242 (1972).
[5] *M. Hollings, O. M. Stone*, Ann. Appl. Biol. *74*, 333 (1973).
[6] *T. O. Diener, R. H. Lawson*, Virology *51*, 94 (1973).
[7] *C. P. Romaine, R. K. Horst*, Virology *64*, 86 (1975).
[8] *H. J. M. van Dorst, D. Peters*, Neth. J. Plant Pathol. *80*, 85 (1974).
[9] *J. W. Randles*, Phytopathology *65*, 163 (1975).
[10] *J. W. Randles, E. P. Rillo, T. O. Diener*, Virology *74*, 128 (1976).
[11] *M. Sasaki, E. Shikata*, Proc. Jpn. Acad. *B 53*, 109 (1977).
[12] *R. A. Owens, D. R. Smith, T. O. Diener*, Virology *89*, 388 (1978).
[13] *W. Thomas, N. A. Mohamed*, Aust. Plant Pathol. Newslett., March *1979*, 1; *J. L. Dale, R. N. Allen, ibid.*, March *1979*, 3; *P. Palukaitis, T. Hatta, D. M. Alexander, R. H. Symons*, Virology *99*, 145 (1979).
[14] *T. O. Diener, A. Hadidi, R. A. Owens* in *K. Maramorosch, H. Koprowski:* Methods in Virology. Academic Press, New York 1977, Vol. 6, p. 185 ff.; *E. Dickson* in *T. C. Hall, J. W. Davies:* Nucleic Acid in Plants. Vol. V-A., CRC Press, Cleveland, in press; *T. O. Diener:* Viroids and Viroid Diseases. Wiley, New York 1979; *H. L. Sänger*, Robert-Koch-Mitt. *1*, 71 (1979).
[15] *H. L. Sänger, G. Klotz, D. Riesner, H. J. Gross, A. K. Kleinschmidt*, Proc. Nat. Acad. Sci. USA *73*, 3852 (1976).
[16] *H. L. Sänger, K. Ramm* in *R. Markham, D. R. Davies, D. A. Hopwood, R. W. Horne:* Modifications of the Information Content of Plant Cells. North Holland, Amsterdam 1975, p. 229 ff.
[17] *E. Dickson, W. Prensky, H. D. Robertson*, Virology *68*, 309 (1975).
[18] *E. Dickson, T. O. Diener, H. D. Robertson*, Proc. Nat. Acad. Sci. USA *75*, 951 (1978).
[19] *E. Dickson, H. D. Robertson, C. L. Niblett, R. K. Horst, M. Zaitlin*, Nature *277*, 60 (1979).
[20] *J. Randles, T. Hatta*, Virology *96*, 47 (1979).
[21] *H. J. Gross, H. Domdey, H. L. Sänger*, Nucleic Acids Res. *4*, 2021 (1977).
[22] *H. Domdey, P. Jank, H. L. Sänger, H. J. Gross*, Nucleic Acids Res. *5*, 1221 (1978).
[23] *H. J. Gross, H. Domdey, Ch. Lossow, P. Jank, M. Raba, H. Alberty, H. L. Sänger*, Nature *273*, 203 (1978).
[24] *R. P. Singh, J. J. Michniewicz, S. A. Narang*, Can. J. Biochem. *52*, 809 (1974).
[25] *T. O. Diener, D. R. Smith*, Virology *53*, 359 (1973).
[26] *T. S. Semancik, T. J. Morris, L. G. Weathers*, Virology *53*, 448 (1973).
[27] *J. M. Sogo, Th. Koller, T. O. Diener*, Virology *55*, 70 (1973).
[28] *W. McClements, P. Kaesberg*, Virology *76*, 477 (1977).
[29] *Hsu Ming-Ta, M. Coca-Prados*, Nature *280*, 339 (1979).
[30] *H. L. Sänger, K. Ramm, H. Domdey, H. J. Gross, K. Henco, D. Riesner*, FEBS Lett. *99*, 117 (1979).
[31] *R. A. Owens, F. Erbe, A. Hadidi, R. L. Steere, T. O. Diener*, Proc. Nat. Acad. Sci. USA *74*, 117 (1977).
[32] *W. Fiers, R. Contreras, F. Duerinck, G. Haegmean, J. Merregaert, W. Min Jou, A. Raeymakers, G. Vokkaert, M. Ysebaert, J. van de Kerckhove, F. Nolf, M. van Montagu*, Nature *256*, 273 (1975).
[33] *A. M. Maxam, W. Gilbert*, Proc. Nat. Acad. Sci. USA *74*, 560 (1977).
[34] *M. Fujimoto, A. Kuninaka, H. Yoshino*, Agric. Biol. Chem. *9*, 1555 (1974).
[35] *M. Silberklang, A. Prochiantz, A.-L. Haenni, U. L. RajBhandary*, Eur. J. Biochem. *72*, 465 (1977).
[36] *H. Donis-Keller, A. M. Maxam, W. Gilbert*, Nucleic Acids Res. *4*, 2527 (1977).
[37] *A. Simoncsits, G. G. Brownlee, R. S. Brown, J. R. Rubin, H. Guilley*, Nature *269*, 833 (1977).
[38] *D. Pilly, A. Niemeyer, M. Schmidt, J. P. Bargetzi*, J. Biol. Chem. *253*, 437 (1978).
[39] *G. Krupp, H. J. Gross*, Nucleic Acids Res. *6*, 3481 (1979).
[40] *G. Schulz*, Angew. Chem. *89*, 24 (1977); Angew. Chem. Int. Ed. Engl. *16*, 23 (1977).
[41] *A. Rich, U. L. RajBhandary*, Annu. Rev. Biochem. *45*, 805 (1976).
[42] *S.-H. Kim*, Prog. Nucl. Acid. Res. Mol. Biol. *17*, 181 (1976).
[43] *I. Tinoco, Jr., O. C. Uhlenbeck, M. D. Levine*, Nature *230*, 362 (1971).
[44] *D. Riesner, K. Henco, U. Rokohl, G. Klotz, A. K. Kleinschmidt, H. Domdey, P. Jank, H. J. Gross, H. L. Sänger*, J. Mol. Biol. *133*, 85 (1979).
[45] Stability parameters of ribonucleic acids are given in *e.g.: P. N. Borer, B. Dengler, I. Tinoco, Jr., O. C. Uhlenbeck*, J. Mol. Biol. *86*, 843 (1974); *J. Gralla, D. M. Crothers, ibid. 73*, 497 (1973); *D. Pörschke, O. C. Uhlenbeck, F. H. Martin*, Biopolymers *12*, 1313 (1973); *J. Gralla, D. M. Crothers*, J. Mol. Biol. *78*, 301 (1973); *H. Rubin, N. R. Kallenbach*, J. Chem. Phys. *62*, 2766 (1975); *J. E. Scheffler, E. L. Elson, R. L. Baldwin*, J. Mol. Biol. *48*, 145 (1970). The utility of various different parameters for the calculation of the stability of viroids is discussed in [44, 53, 54].
[46] *R. P. Singh, R. E. Williams*, Can. J. Biochem. *56*, 934 (1978).
[47] *E. Dickson*, Thesis, Rockefeller University, New York 1976.
[48] *U. Wild, K. Ramm, H. L. Sänger, D. Riesner*, Eur. J. Biochem. *103*, 227 (1980).
[49] *J. S. Semancik, T. J. Morris, L. G. Weathers, B. F. Rodorf, D. R. Kearns*, Virology *63*, 160 (1975).
[50] *H. Grosjean, D. G. Söll, D. M. Crothers*, J. Mol. Biol. *103*, 499 (1976).
[51] *T. O. Diener*, Virology *50*, 606 (1972).
[52] *K. Henco, D. Riesner, H. L. Sänger*, Nucleic Acids Res. *4*, 177 (1977).
[53] *J. Langowski, K. Henco, D. Riesner, H. L. Sänger*, Nucl. Acids Res. *5*, 1589 (1978).
[54] *K. Henco, H. L. Sänger, D. Riesner*, Nucleic Acids Res. *6*, 3041 (1979).
[55] *D. Riesner, R. Römer* in *J. Duchesne:* Physico-chemical Properties of Nucleic Acids. Academic Press, London 1973, Vol. II, p. 237 ff.
[56] *G. Steger, H. Müller, D. Riesner*, Biochim. Biophys. Acta *606*, 274 (1980).
[57] *J. Engel, G. Schwarz*, Angew. Chem. *82*, 468 (1970); Angew. Chem. Int. Ed. Engl. *9*, 389 (1970).
[58] *D. Poland:* Cooperative Equilibria in Physical Biochemistry. Clarendon Press, Oxford 1978.
[59] *H. Klump, D. Riesner, H. L. Sänger*, Nucleic Acids Res. *5*, 1581 (1978).
[60] A comprehensive amount is given in: "DNA: Replication and Recombination", Cold Spring Harbor Symp. Quant. Biol. *43* (1979).
[61] *H.-P. Mühlbach, H. L. Sänger*, Nature *278*, 185 (1979).
[62] *T. O. Diener*, Virology *43*, 75 (1971).
[63] For a discussion of the experimental details see: *T. O. Diener*, Science *205*, 859 (1979).

[64] St. Prusiner, W. J. Hadlow, D. E. Garfin, S. P. Cochran, J. R. Baringer, R. E. Race, C. M. Eklund, Biochemistry 17, 4993 (1978).
[65] T. G. Malone, R. F. Marsh, R. P. Hanson, J. S. Semancik, Nature 278, 575 (1979).
[66] C. Gibbs, D. C. Gajdusek, R. Latarjet, Proc. Nat. Acad. Sci. USA 75, 6268 (1978).
[67] F. Sanger, G. G. Brownlee, B. G. Barrell, J. Mol. Biol. 13, 373 (1965).
[68] G. G. Brownlee, F. Sanger, Eur. J. Biochem. 11, 395 (1969).
[69] R. E. Lockard, B. Alzner-DeWeerd, J. E. Heckman, J. MacGree, M. W. Tabor, U. L. RajBhandary, Nucleic Acids Res. 5, 37 (1978).
[70] R. T. Walker, U. L. RajBhandary, Nucleic Acids Res. 5, 57 (1978).

Photochemical Rearrangements and Fragmentations of Benzene Derivatives and Annelated Arenes

By Gerd Kaupp[*]

In this article the numerous intramolecular reactions of electronically excited benzene derivatives, which in many instances are only mentioned in original papers, are systematically analyzed and arranged according to reaction types. All known reaction types can be classified, and subdivided into reactions of the benzene ring (ionization, ring opening, ring alteration), reactions with participation of side chains (α-, β-, γ-cleavage, homolysis, heterolysis), reactions of substituents with side chains (cyclization, dealkylation, cleavage of protective groups), and reactions of side chains with the aromatic ring (substitution, addition, dearomatization, cyclization). The selectivity of the energetically feasible competing reactions is primarily determined by geometric factors. Applications of the empirical effects are numerous and varied in preparative organic chemistry. Many of the reactions under discussion are already utilized industrially (*e.g.* in photochromism, UV stabilization, photography, information storage, printing, coating and polymer technology, and pharmacy).

1. Introduction

The field of aromatic photochemistry has been unusually widely investigated. All benzene derivatives absorb light in readily accessible wavelength regions. A large portion of the many reaction types can as yet only be extracted from original publications. That excited molecules must choose between these reaction types as well as luminescence and chemically unproductive deactivations, is in most cases a consequence of high energy excesses after the absorption of light. The plethora of available reference material calls for a classification. Present theoretical concepts are obviously able to systematize only a part of the intramolecular photochemistry of aromatic compounds[1], and even then there is the risk that a sub-group of so called "forbidden reactions"[1] will not be adequately represented by examples. Therefore, another didactic approach would seem to be indicated: Arrangement of the entire material according to reaction types enables a comprehensive treatise of all practically important aspects. As this will immediately reveal the common features of or differences between the various types, which may be used for extrapolative purposes, consideration is given at the same time to the interest in advanced theoretical concepts and questions related to practical applications in syntheses (*e.g.* planning, improvement in yields, more complete product distribution, choice of protective groups, asymmetric syntheses and reactive intermediates), in chemical technology (*e.g.* photochromes, absorbers, initiators, polymer and phototechnology, printing, photoconductors), in ecology (*e.g.* degradation of insecticides and herbicides, energy storage), and in biology and pharmacy (*e.g.* vitamin B_2 and B_c, alkaloids, tumor inhibitors).

Photochemical syntheses are particularly valuable, if one can achieve high selectivities for the desired reactions. A directed synthesis is possible by suitable choice of reaction conditions (*e.g.* reaction medium, concentration, temperature, pressure, light intensity, wavelength, sensitization) and by structural variations of the substrates. Steric factors and cage effects are more important here than in thermochemistry, where energetic effects usually dominate. This treatise considers only as many typical examples of any single reaction type as appears necessary for the characterization of the specific requirements (best possible yield) and variability (indication of synthetic scope). Some further examples are accessible from the literature. The photoreactions of styrenes and stilbenes[2] are not dealt with here, unless their aromatic rings undergo direct chemical change.

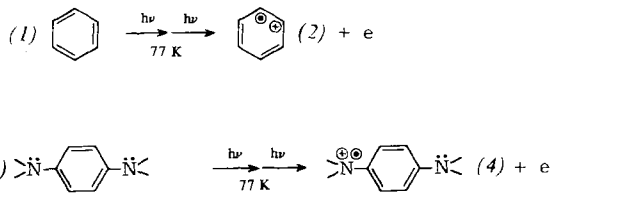
2. Reactions of the Benzene Ring

2.1. Ionization

Perhaps the most simple photoreaction of arenes is the splitting off of an electron to produce radical cations. Benzene *(1)* [first ionization potential (IP) in the gas phase: 9.25

[*] Prof. Dr. G. Kaupp
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

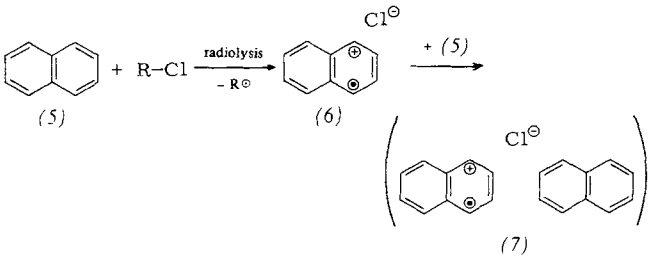
eV] is ionized upon absorption of vacuum UV-, x-, γ-rays, electrons (cf. photoelectron and mass spectroscopy) or of two photons (*via* its triplet; $\lambda = 253.7$ nm) at 77 K. If adsorbed on SiO_2 at 77 K *(1)* may form *(2)*, as detected by its ESR spectrum (7 lines, $a_H = 4.5$ gauss)[3]. Even easier is the biphotonic ionization of *(3)* to give the cation *(4)* (*Wurster*'s Blue) and electrons, which are trapped in holes of 3-methylpentane at 77 K within 1 ns. The VIS/NIR spectra of *(4)* and the immobile electron are measurable for several minutes, *i.e.* the system constitutes a storage system for light energy. The luminescent recombination of *(4)* and e may be stimulated photochemically, thermally, or electrically. Furthermore, the system also constitutes an electric conductor with high dark resistance[4].



In boric acid glasses the IPs of annelated arenes are about 2.3 eV lower than in the gas phase. The electrons are captured by protons (formation of H_2). Even at room temperature one obtains the colored radical cations after absorption of two photons using normal light intensities or the IP may be already surpassed by the absorption of one photon (*e.g.* $\lambda = 235$—245 nm in the case of anthracene). Thus, the radical cations of naphthalene, pyrene, anthracene, 3,4-benzopyrene, perylene, and tetracene could be measured[5].

With laser sources, biphotonic ionizations are possible in solutions at room temperature. In this case the ionization mechanisms of *e.g. (3)*, pyrene, and perylene are different in polar and non-polar solvents[6].

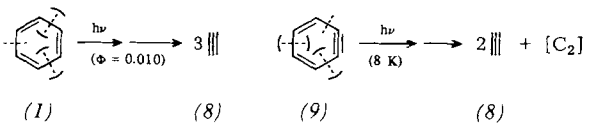
The ionization of arenes and annelated arenes [*e.g. (5)*] may also be sensitized at 77 K by alkyl chlorides (*e.g. n*-BuCl/2-methylbutane = 1:1)[7], when γ- (^{60}Co)[7,8] or x-rays ($Cu_{K\alpha}$)[9] are employed. γ-Radiolysis at 77 K served for the measurement of UV/VIS/NIR spectra of numerous radical cations, which combine with the neutral arenes to give dimer radical cations *(7)*, even on raising the temperature only very slightly[7,8,10].



2.2. Ring Opening Reactions

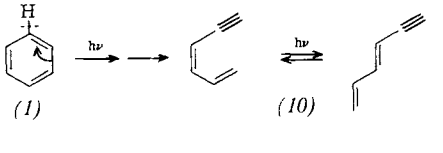
2.2.1. [2+2+2]-Cycloreversion

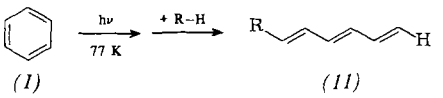
The tendency of the benzene ring to cleave into three acetylene fragments, which is the reverse of a known photochemical benzene synthesis[11], appears to be less pronounced than in some six-membered heterocycles[12]. Nevertheless, it could be shown that *(8)* is formed as a primary product on photolysis of gaseous *(1)* with unfiltered light from a low pressure mercury arc[13]. However, this reaction proceeds with little specificity, for there is competition from several primary and secondary photolyses. Already at 8 K, dehydrobenzene *(9)* photolyses slowly to *(8)* and C_2[14].



2.2.2. Ring-Chain Isomerization

The ring opening of benzene with 1,3-H-shift in the gas phase leads to the stereoisomeric 1,3-hexadien-5-ynes *(10)*[15]. This may be compared with the preparatively useful photolyses of furans (oxazoles) to give oxoketenes (oxoketeneimines)[16]. However, it is not yet clear, whether *(10)* is formed in part *via* fulvene [*(35)* in Section 2.3.3]. The photolysis of benzene *(1)* in glasses at 77 K is striking. One obtains rather sharply structured UV-spectra ($\lambda_{max} = 255$, 264, 275 nm), which point to the formation of substituted 1,3,5-hexatrienes *(11)* *via* ring opening and solvent addition[17]. Thus, low temperature photolyses in glassy media may be severely disturbed by traces of benzene.



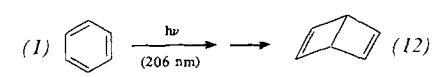


2.3. Ring Alterations

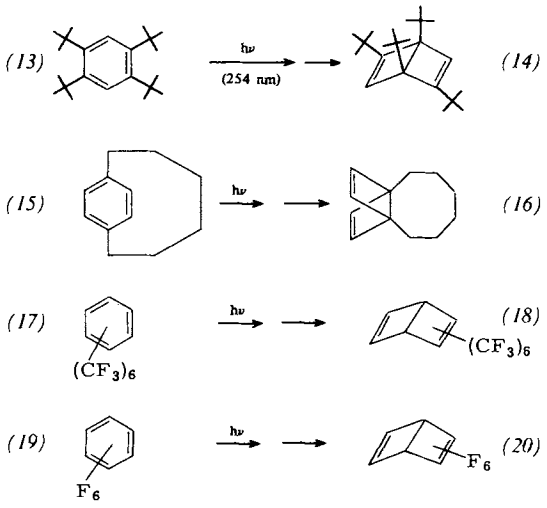
Photochemical ring isomerizations transform benzene (or its derivatives) into Dewar benzenes, benzvalenes, fulvenes, and rearranged benzene derivatives. The product ratios are strongly dependent on the experimental conditions[18]. Owing to photochemical and thermal lability it is not always possible to isolate all of these products.

2.3.1. Dewar Benzenes

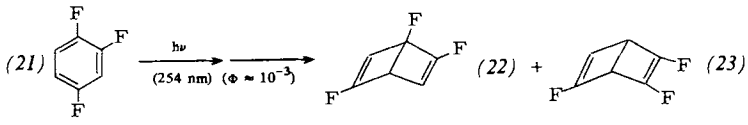
Benzene *(1)* is converted into Dewar benzene *(12)* apparently only upon short wavelength irradiation in solution[15a,19].



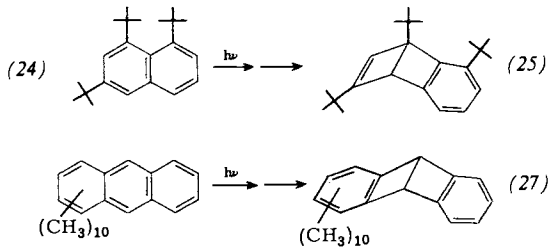
Fewer difficulties are encountered with the alkyl-derivatives [*(13)*→*(14)*[20]; *(15)*→*(16)*[21]], trifluoromethyl-derivatives [*(17)*→*(18)*[22]], and fluoro-derivatives [*(19)*→*(20)*[23]]. In some cases remarkable selectivities are observed [*(21)*→*(22)* + *(23)*, but not 1,2,4-trifluorobicyclo[2.2.0]hexa-



2,5-diene][24], and the corresponding reactions can be achieved with substituted naphthalenes [*(24)*[25]] and anthracenes [*(26)*[26]]. The same reaction type has also been well investigated in the case of pyridine and pyridine derivatives[27].

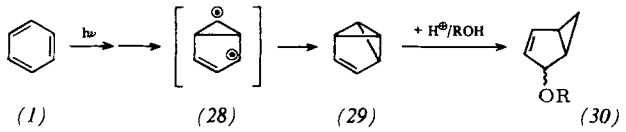


The highly energetic Dewar benzenes have been used for thermal and photochemical transformations.

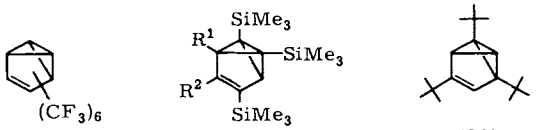


2.3.2. Benzvalenes

Even long wavelength excitation of liquid or dissolved benzene *(1)* leads to formation of benzvalene *(29)*[28], which may be isolated by vapor phase chromatography. A diradical "prebenzvalene" or "prefulvene" *(28)* is assumed to be an intermediate in this reaction[18]. The addition of water, alco-



hols, and acetic acid to *(29)* to give the bicycles *(30)*[29] can be catalyzed with acids. The substituted benzvalenes *(31)*[30], *(32)*[31], *(33)*[31], and *(34)*[32] are also obtainable from the corresponding benzene derivatives.

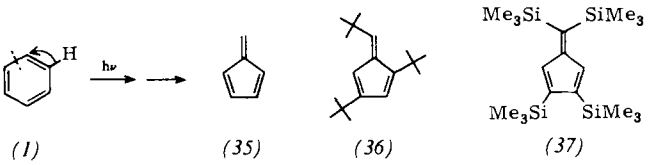


(31) *(32)*, R^1 = H, R^2 = $SiMe_3$
(33), R^1 = $SiMe_3$, R^2 = H

(34)

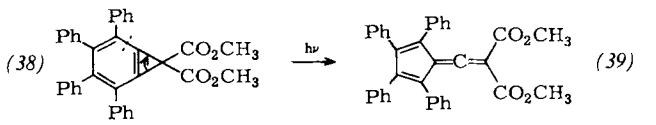
2.3.3. Fulvenes

The photolysis of benzene in solution or in the gas phase leads *via* ring contraction and H-migration to fulvene *(35)*, which can be isolated by vapor phase chromatography[15a].



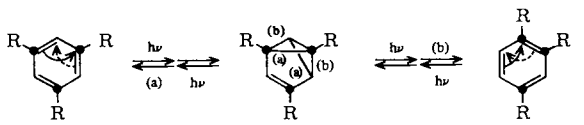
(1) *(35)* *(36)* *(37)*

However, it is still not possible to definitely decide whether *(35)* is a primary product of benzene photolysis [*e.g.* formation *via* prefulvene *(28)*[18]], as benzvalene *(29)* gives benzene and fulvene with rather high quantum yields upon photolysis. The isolation of the fulvenes is often rendered difficult by their tendency to polymerize. *(36)*[32] and *(37)*[31] have been characterized. A productive synthesis of highly substituted, stable fulveneallenes such as *(39)* (66%) has been reported[33].



2.3.4. Shifts of Ring Carbons

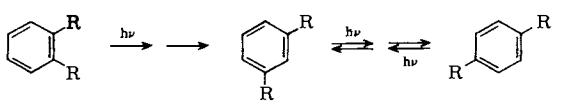
Suitably substituted benzvalenes (Section 2.3.2) and prismanes, which are photochemically formed from Dewar benzenes[2] (Section 2.3.1), may react further to either of two different benzene derivatives. These reactions lead to a rearrangement of the ring carbons, which stay linked to their substituents (apparent 1,2- and duplicated 1,2-substituent migration). Thus, 1,3,5-trideuterio-[34], 1,3,5-trimethyl-[35], and 1,3,5-tri-*tert*-butylbenzene[36] form almost uncontaminated photoequilibria with their 1,2,4-isomers *via* benzvalenes [Eq. (a)].



(a)

R = D, CH_3, $C(CH_3)_3$

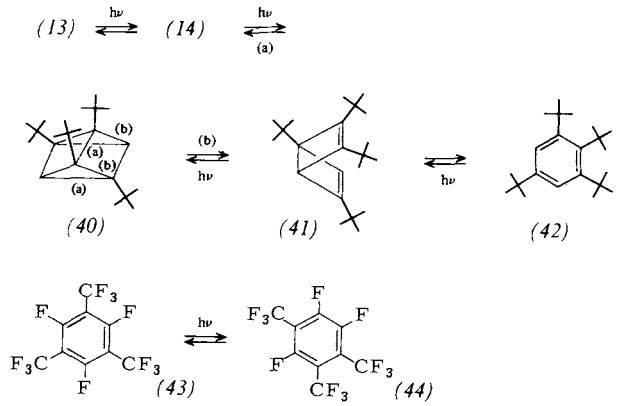
Correspondingly, *o*-xylene[37] and *o*-di-*tert*-butylbenzene[38] form at first the *meta*- and then the *para*-isomers, presumably again *via* benzvalenes [Eq. (b)]:



(b)

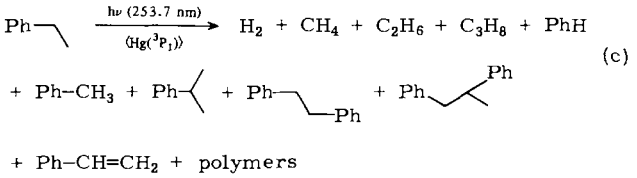
R = CH_3, $C(CH_3)_3$

In the case of benzene derivatives, which photochemically form Dewar benzenes but not benzvalenes, such isomerizations should proceed *via* prismanes. Examples are *(13)*[20] and *(43)*[39].



3. Reactions with Participation of Side Chains

Upon photolysis, the side chains of substituted arenes may be cleaved or rearranged or may react with the benzene ring. Homolyses, heterolyses, and cyclization reactions may occur. As a rule these primary photoprocesses are followed by consecutive thermal reactions as in the case of ethylbenzene [Eq. (c)][40] or in the photodegradation and photo-crosslinking of



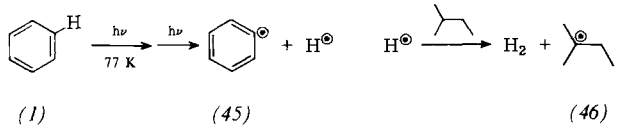
(c)

polystyrene[41] *via* radicals, which can be detected by ESR spectroscopy at 77 K[42]. Nevertheless, it is still possible to present a lucid classification according to reaction types.

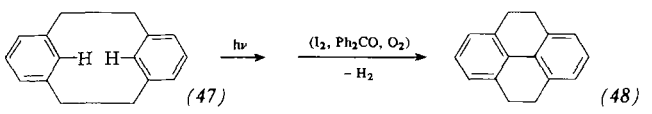
3.1. α-Cleavage

3.1.1. Homolysis into Aryl Radicals

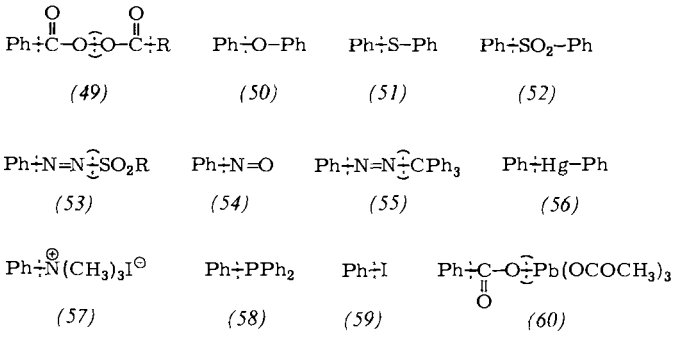
The biphotonic irradiation of (hexadeuterio-) benzene *(1)* at 77 K (λ = 230—260 nm) leads to the (pentadeuterio-) phenyl radical *(45)*, which has been detected by ESR spectroscopy[43]. The hydrogen atom generated simultaneously reacts with isopentane to give H_2 and the radical *(46)*[43]. The formation of biphenyl, which has been observed several times



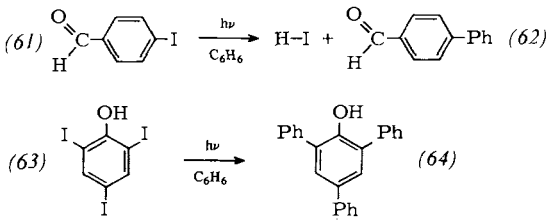
upon irradiation of gaseous and dissolved benzene[44], would also suggest the formation of *(45)*, which either dimerizes or else combines with benzene with the intervention of an oxidizing agent to form biphenyl. This is similar to the transannular dehydrogenation of *(47)* to give *(48)*, a reaction which proceeds with or without oxidizing agents[45].



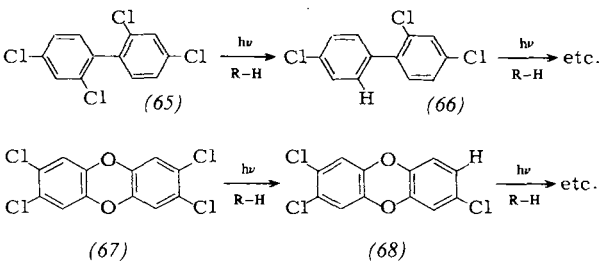
Phenyl radicals *(45)* are formed in small amounts on photolysis of ethylbenzene[40]. They occur in larger amounts upon photolysis of *e.g.* benzoyl peroxides *(49)*[46], diphenyl ether *(50)* (photo-Fries rearrangement, see Section 4.1.2)[47], diphenyl sulfide *(51)*[48], diphenyl sulfone *(52)*[49], phenyldiazosulfones *(53)*[50], nitrosobenzene *(54)*[51], alkylazobenzenes [*e.g.* *(55)*[52]], numerous phenyl-metal compounds [*e.g.* *(56)*[53]], phenylammonium salts *(57)*[54], triphenylphosphane *(58)*[55], halobenzenes [*e.g.* *(59)*[56]], and lead(IV) benzoates *(60)*[57].



These photocleavages into radicals are of considerable importance in view of the increasing demands for initiators[58] for photografting and photo-crosslinking (coatings, printing plates, microelectronics, photoengraving, *etc.*)[59]. In all cases phenylation takes place following photocleavage (*e.g.* formation of biphenyl with benzene). The major application of this reaction is in the directed synthesis of more complicated compounds such as *(62)* (90%)[60] or *(64)*[56]. The phenyl radicals are able to react with solvents by accepting chlorine (*e.g.* CCl_4), bromine (*e.g.* $CHBr_3$) or hydrogen atoms (*e.g.* cyclohexane) or they may react with trivalent boron, phosphorus,

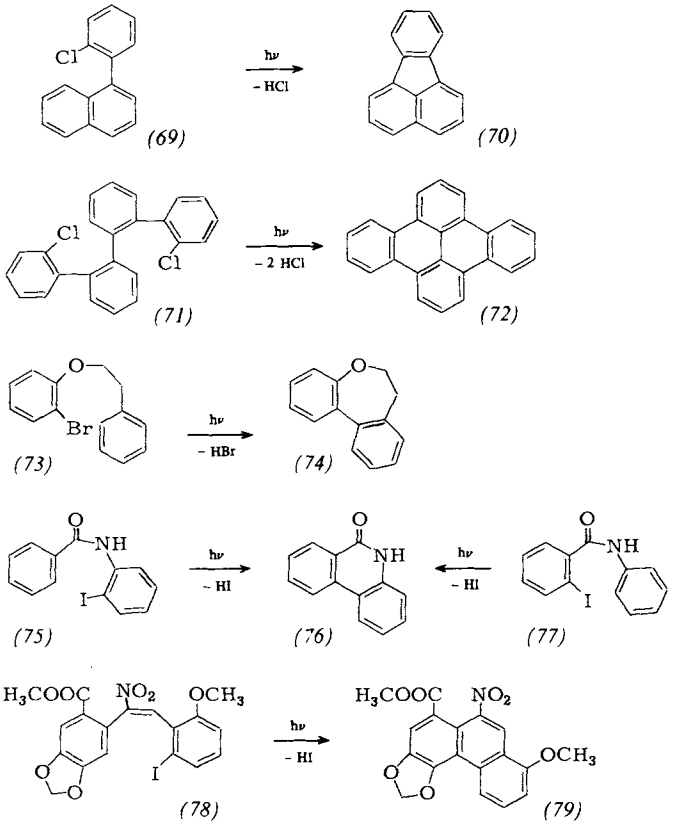


and arsenic compounds to give phenyl-element compounds[56]. The photochemical homolysis of the aryl-chlorine bonds of bioactive compounds such as polychlorobiphenyls [*e.g.* *(65)*[61]] or TCDD *(67)*[62] is of considerable importance in environmental chemistry. Usually one obtains an increasing detoxification *via* consecutive dechlorination. In nature, the aryl radicals formed may also be trapped by oxygen to give oxygen-containing decomposition products.

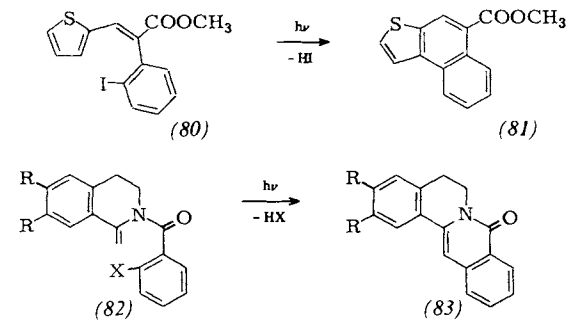


3.1.2. Substituting Cyclizations

As in the case of intermolecular phenylations [see *(62), (64)*] it can be assumed that the variable intramolecular syntheses (substituting photocyclizations of aryl halides) of *(70)* (72%)[63], *(72)* (87%)[64], *(74)* (35%)[65], *(76)* [48% from *(75)*, 18% from *(77)*][66] and of the tumor inhibitor aristolochioic acid (methyl ester) *(79)* (54%)[67] are initiated by a homolysis of the Ar—X bonds[56].

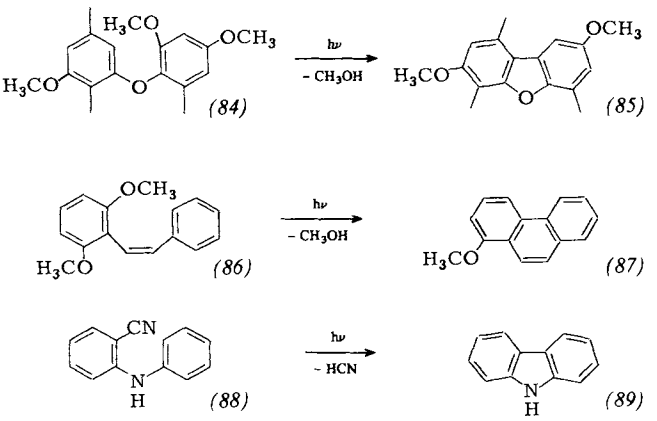


Numerous applications for alkaloid syntheses have already been reported[68]. The aryl radicals first formed can also be trapped by the C—H bonds of heterocycles [see *(80)*][69] or C=C double bonds [see *(82)*][70].

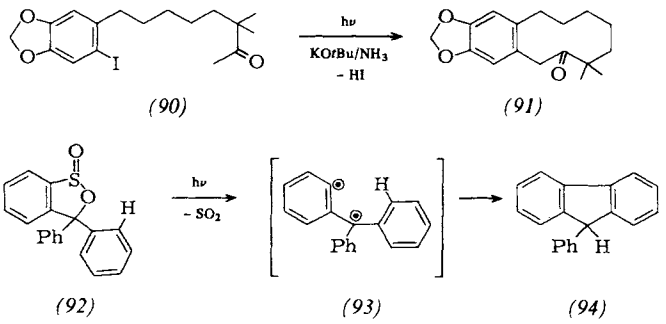


R = OCH_3; X = F, Cl, Br, OCH_3, $OCOCH_3$, SCH_3, NO_2

It is not certain whether the homolysis mechanism applies here and in the substituting cyclizations with loss of methanol [*(84)* (35%)[71], *(86)* (90%)[72]] or hydrogen cyanide [*(88)*[73]], or whether there is first cyclization followed by elimination.

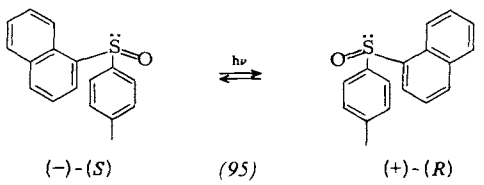


Intramolecular nucleophilic photosubstitutions [*e.g.* to give 35% *(91)*[74]] and the complicated elimination followed by cyclization of *(92)* to give *(94)* (42%)[75] also belong to this section.

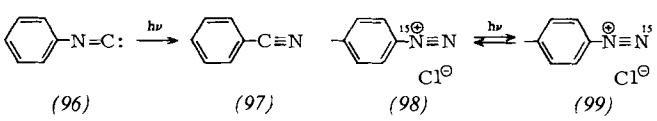


3.1.3. Reversal of Substituents

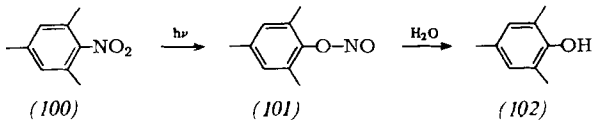
The original α-bonds have to be cleaved when the linking sites of substituents are interchanged. However, the photoracemization of diaryl sulfoxides such as *(95)* could also be explained by assuming inverting vibrations of the pyramidal sulfur[76].



More clear cut are the isomerizations of phenyl isocyanide *(96)* (gas phase)[77], (labeled) diazonium salts *(98)* / *(99)*[78],

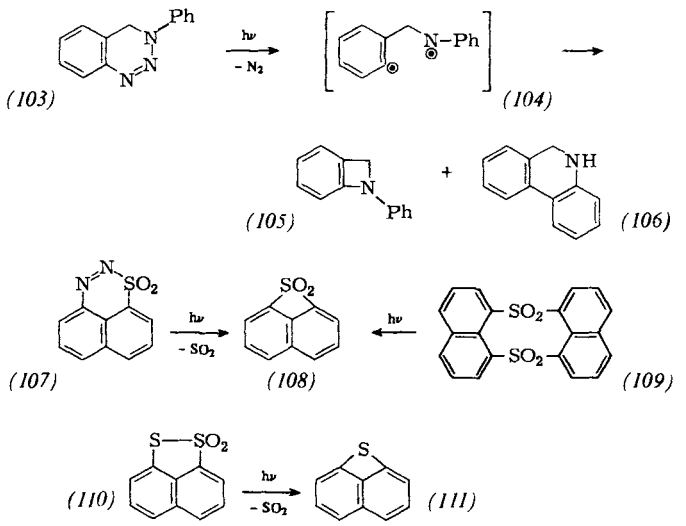


and nitroarenes such as *(100)*[79] [cf. Smiles rearrangement, *e.g. (530)* in Section 4.1.2].



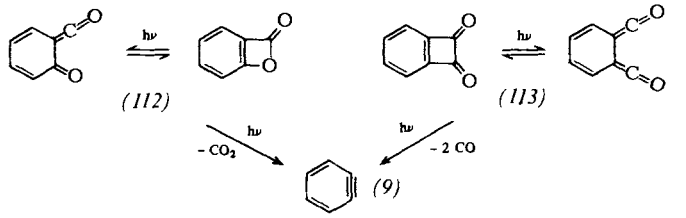
3.1.4. Ring Contraction

Homolytic α-cleavages with ring contraction by elimination deserve interest. Thus, the reactions of *(103)*[80], *(107)*[81], *(109)*[81], and *(110)*[82] yield the unusual *o*- or *peri*-coupled heterocyclic four-membered rings *(105)* (50%), *(108)* (25%; 20%) and *(111)* (97%).

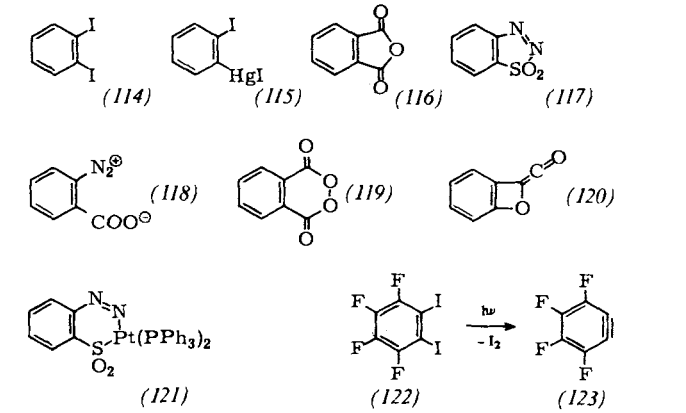


3.1.5. Formation of Dehydrobenzenes

On cleavage of two *ortho* bonds on a benzene ring, one obtains dehydrobenzene *(9)*, which dimerizes or trimerizes to give bi- or triphenylene and which may also be trapped by 1,3-dienes to give Diels-Alder adducts. The reactions of *(112)*

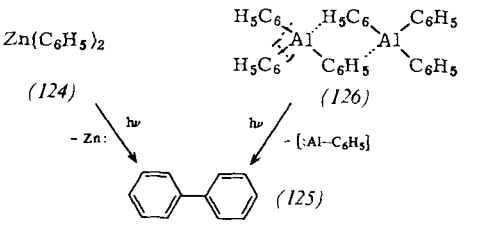


and *(113)* proceed at temperatures as low as 8 K[14]. Further starting materials for *(9)* are *(114)*[83], *(115)*[84], *(116)* (also in the plasma of glow discharges)[85], *(117)*[86], *(118)*[87], *(119)*[14,84], *(120)*[88], and *(121)*[89]. Substituted dehydrobenzenes such as *(123)*[90] are also obtainable.

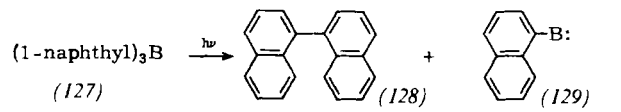


3.1.6. Formation of Biphenyls

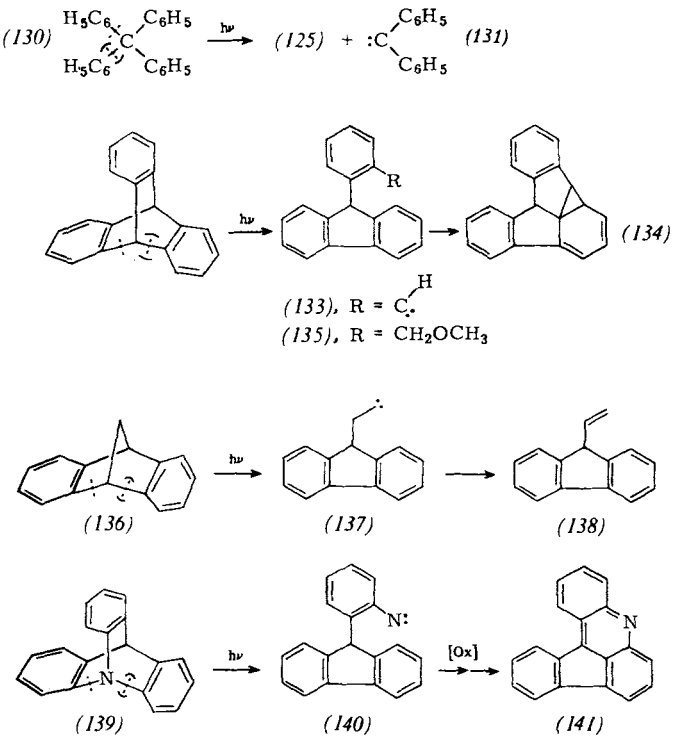
If two or more phenyl groups are linked to one atom, two α-cleavages can lead to the elimination of biphenyl *(125)* and reduction of the central atom without liberation of phenyl



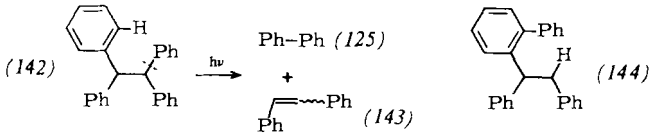
radicals (cf. Section 3.1.1). This reaction path is preferred by diphenylzinc *(124)*[91], dimeric triphenylaluminum *(126)*[92], and tri-1-naphthylborane *(127)*[93].



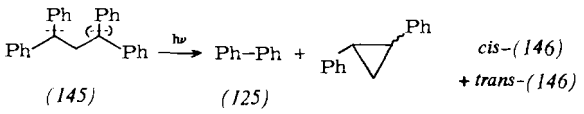
Tetraphenylmethane *(130)*[94], triptycene *(132)*[95], dibenzonorbornadiene *(136)*[96], and azatriptycene *(139)*[97] react completely analogously. Two benzene rings combine, producing carbenes [*(131), (133), (137)*] and presumably the nitrene *(140)*, which can be transformed or trapped in different ways[98]. Thus, the methyl ether *(135)* is formed from *(132)* in methanol.



Even two phenyl groups, which are linked to different carbon atoms, may be eliminated intramolecularly. From *(142)* one obtains *(125)* and *(143)* together with *(144)*[99] (this biphenyl derivative is formed by intramolecular substitution).

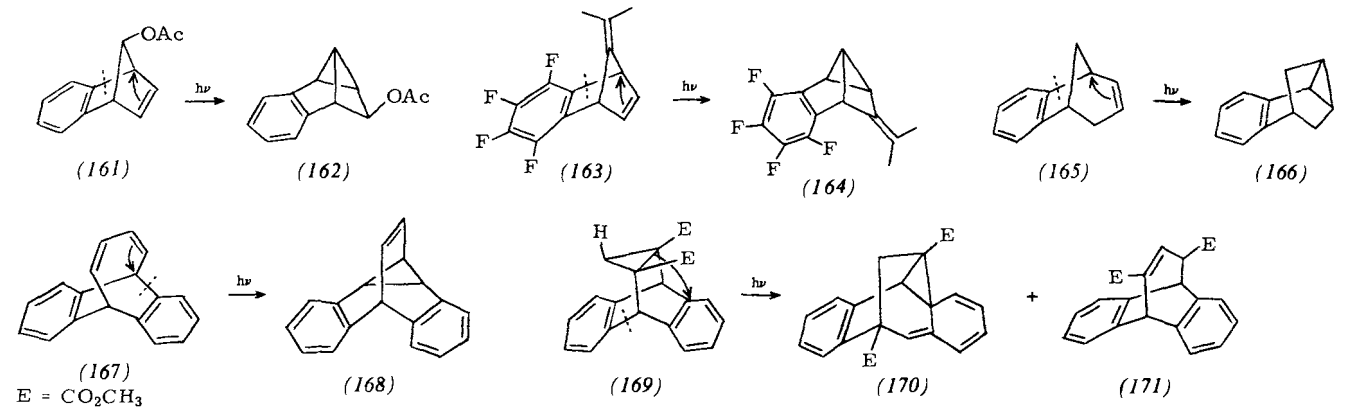


Correspondingly, the homologous compound *(145)* decomposes into biphenyl *(125)* and *(146)*[100].

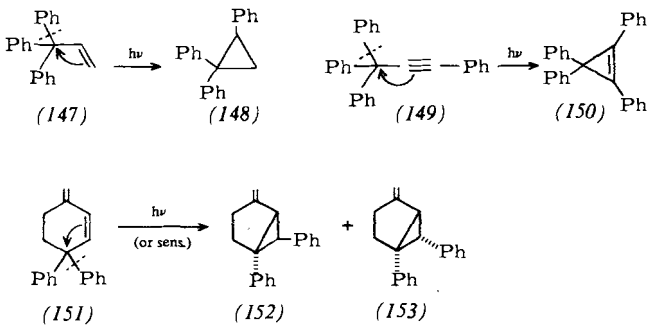


3.1.7. Di-π-methane Rearrangement

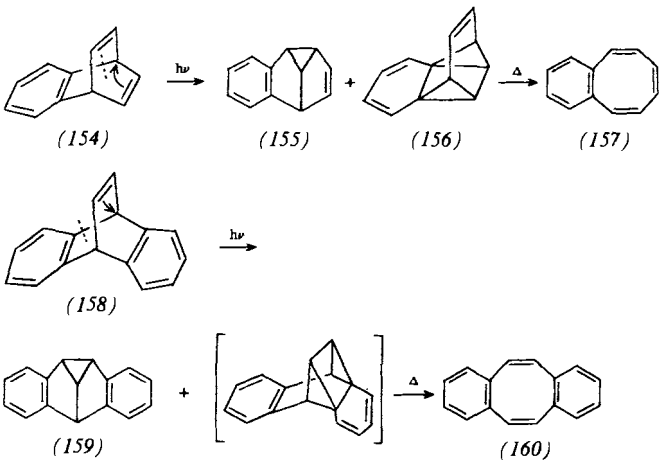
α-Cleavages of aryl-C-bonds with 1,2-shift to an adjacent double bond have been termed "di-π-methane rearrangements"[101]. Numerous rearrangements of acyclic [*e.g.* *(147)*[102], *(149)*[103]], monocyclic [*e.g.* *(151)*][104], and bicyclic compounds are known (for further 1,2- and 1,4-phenyl shifts see [2]).



In the case of benzo- *(154)*[101] and dibenzobarrelene *(158)*[101] the ratio of di-π-methane rearrangement and intramolecular [2+2]-cycloaddition upon direct and sensitized excitation[105] (cf. Section 4.3.4) has been carefully studied.

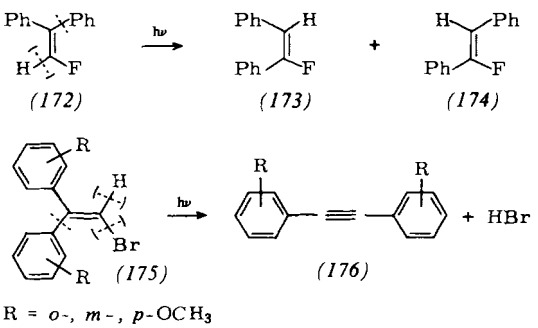


Numerous variations in ring size have been realized. Thus, *(162)* (stereospecific, 85%)[106], *(164)* (94%)[107], *(166)* (94%)[108], *(168)* (84%)[109], and *(170)*[110] have been obtained. In competition with the di-π-methane rearrangement in *(169)*, a 1,2-shift produces *(171)*[110] (for further side reactions see [98a,b]).



3.1.8. 1,2-Shifts along Double Bonds

After absorption of light a phenyl group and the hydrogen atom in 2-monosubstituted 1,1-diphenyl-1-alkenes may migrate in opposite directions. Thus, *(172)* gives the isomers *(173)* (28%) and *(174)* (23%)[111]. Also in the photoelimination of HBr from *(175)*[112] [see *(36)* in [2]] at least one aryl group has to migrate along the double bond.

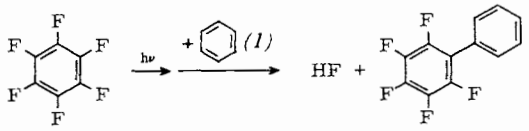


3.1.9. Heterolysis

It is not possible to draw a sharp borderline between homolytic and heterolytic α-cleavages; some of the reactions discussed in Sections 3.1.1 through 3.1.8 might proceed heterolytically or *via* zwitterionic intermediates.

In the photolysis of hexafluorobenzene *(19)* there exist striking peculiarities, even though the products correspond

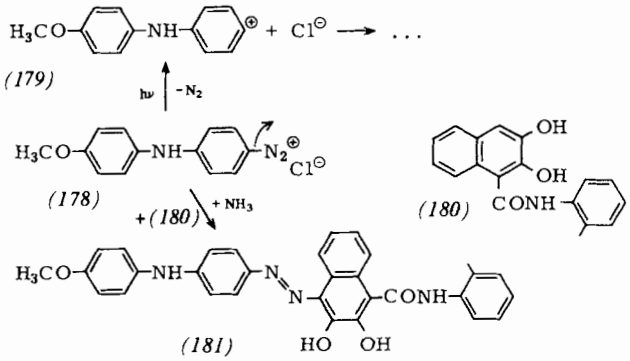
to those of formally related radical reactions [*e.g.* the synthesis of *(177)*][113]. However, a homolysis of the aryl-F bond is excluded for energetic reasons. The reaction is considerably



(19) *(177)*

enhanced by addition of minor quantities of acetonitrile, methanol, or trifluoroacetic acid[113]. Whether or not this might indicate a photoheterolysis (to give aryl cation and $F^{\ominus}$) has not yet been investigated.

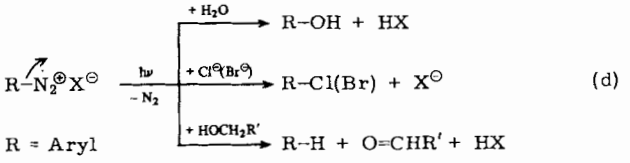
Nitrogen eliminations from aryldiazonium salts are by necessity heterolytic. The photochemical version of this process has practical impact in diazotype-copying (*e.g.* Ozalid® process)[59, 114]. Thus, *p*-aminobenzenediazonium salts [*e.g.* Variamine Blue B salt *(178)*] are mixed with phenols [*e.g. (180)*] in acidic foils. They are irradiated through the pattern to be copied with high-pressure mercury arcs and thus selectively decomposed. Exposure to ammonia then causes azo-coupling in the unirradiated regions, forming the blue dye *(181)* and thus producing a positive image.



(179) *(178)* *(180)* *(181)*

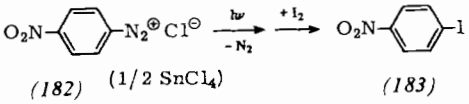
Copying rates of 30 patterns per second and developing times of 90 seconds have been achieved[114a].

In solution the photodecomposition of diazonium salts may be used for the formation of phenols[115, 116], aryl halides[116], or other benzene derivatives (in alcohols perhaps *via* free radicals, following electron transfer from $X^{\ominus}$)[117, 118]. The yields are frequently higher than in the corresponding thermal processes.

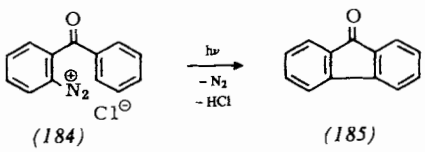


(d)

The preparative possibilities are well represented by the syntheses of *(183)* (92%)[118] and *(185)* (40%)[119].



(182) *(183)*



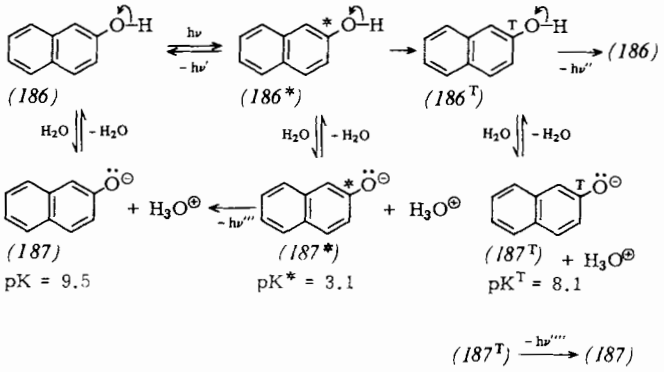
(184) *(185)*

3.2. β-Cleavage

The photolysis of substituted benzene derivatives may lead to cleavage not only of α- but also of β-bonds. Again this occurs either hetero- or homolytically. It is not always clearly distinguishable which of the mechanisms occurs, and it is to be expected that solvent effects will influence the polarity of β-cleavages.

3.2.1. Heterolyses

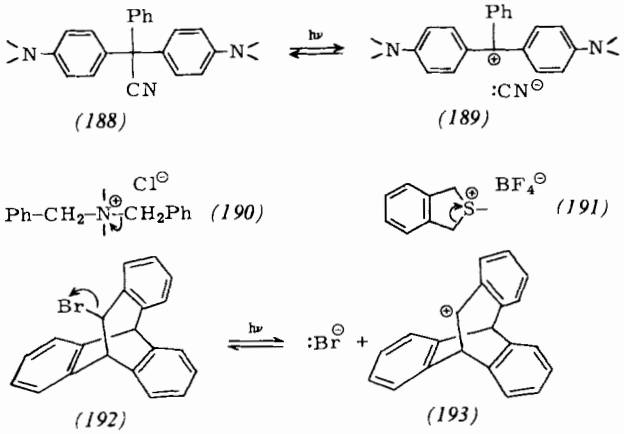
The acid/base reactions of electronically excited phenols [*e.g. (186)*][120] undoubtedly proceed heterolytically. These de- and re-protonations are adiabatic reactions (as in the analogous acid/base reactions of anilines, acridines, *etc.*). Thus, one obtains the fluorescing or phosphorescing anions, respectively, from the strong acids *(186*)* (singlet) or *(186^T)* (triplet)[120].



(186) *(186*)* *(186^T)* *(187)* *(187*)* *(187^T)*

pK = 9.5 pK* = 3.1 pK^T = 8.1

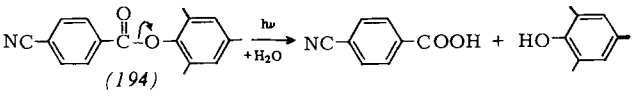
In polar solvents, leucomalachite green cyanide *(188)*[121] and further leuco cyanides may reversibly photolyze into ions. The photoreaction of *(188)* has been used in actinometry [quantum yield for the formation of *(189)*: $\Phi = 1.0$][121b]. In polar solvents benzylammonium- *(190)*[122] and benzylsulfonium salts [*e.g. (191)*][123] and the bromohomotriptycene *(192)*[124] undergo photoheterolysis. There is also little doubt,



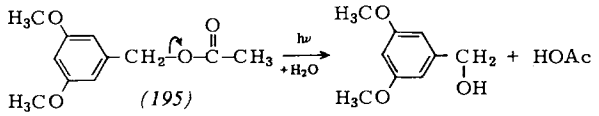
(188) *(189)* *(190)* *(191)* *(192)* *(193)*

that the photohydrolyses (-solvolyses) of aryl benzoates [*e.g. (194)*][125], benzylic esters [*e.g. (195)*][126], and the isomerization of labeled *(196)* to the isotopomers *(197)* in the ratio 1:1[127] have to be included here (see also Section 3.2.14).

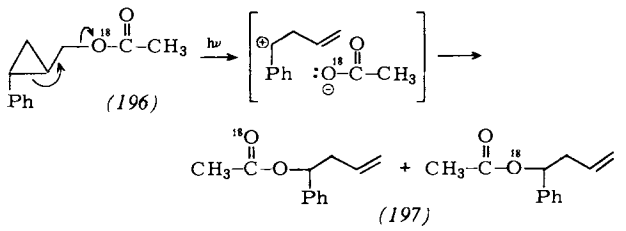
It is possible that even some photo-Fries rearrangements (see Section 4.1.2) proceed *via* ionic intermediates. Benzyl anions *(199)* are obtained on photodecarboxylation of aryl-



(194)



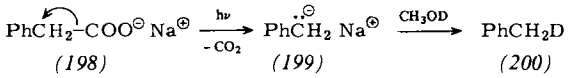
(195)



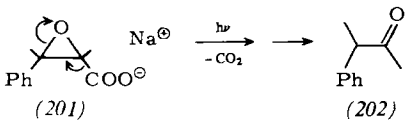
(196)

(197)

acetic acid salts *(198)*[128]. The yields of alkylbenzenes [*e.g. (200)*] are almost quantitative[128]. Finally the corresponding reaction of *(201)* proceeds with heterolysis of the oxirane ring[129].



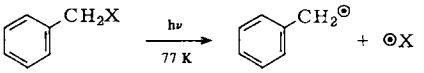
(198) (199) (200)



(201) (202)

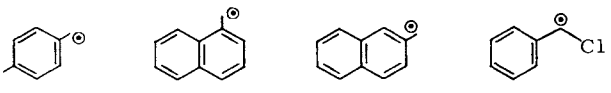
3.2.2. Homolysis into Radicals

Homolytic β-cleavages are apparently very widespread in the photochemistry of substituted arenes. Toluene and toluene derivatives [*e.g. (203)*] form benzyl radicals [*e.g. (204)*], which can be spectroscopically detected at low temperatures[130]. From the large number of examples studied,

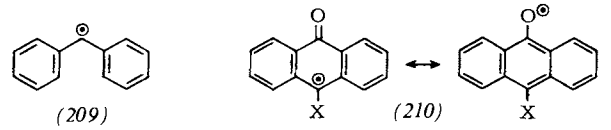


(203) (204)

X = H, Cl, OH, NH_2, CN, COOH, CH_2NH_2, CH_2OH, CH_2CH_2OH



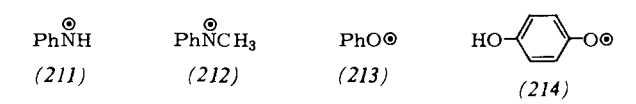
(205) (206) (207) (208)



(209) (210)

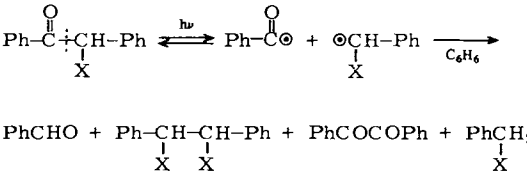
X = H, Cl, Br

(205), (206), (207), (208), (209)[130], and *(210)*[131] [cf. *(611), (612)* in Section 4.2.2] are included here. The hydrogen abstractions in these reactions require the absorption of two photons (electronically excited triplets)[132]. The corresponding photolysis of anilines and phenols generates the radicals *(211), (212)* (from methyl- or dimethylaniline), *(213)*, and *(214)*[130].



(211) (212) (213) (214)

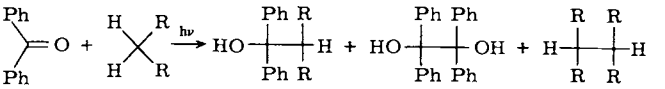
The generation of free radicals by photochemical β-cleavage is of major industrial importance (cf. radicals by α-cleavage in Section 3.1.1). Useful initiators for polymerization and crosslinking[58,59] are found especially among benzoin derivatives. These react in benzene [primarily according to Eq. (e)] to yield the usual, radical-derived products[133].



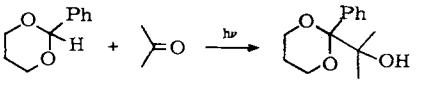
(e)

With these radical initiators (X = H, CH_3, Ph, OR) it is possible to crosslink, for instance, fumaric acid polyesters with styrene. On using 1—3% of initiator, hardening or drying of say 0.1 mm thick films, primings, coatings, and printing inks is achieved within seconds through illumination with high pressure mercury arcs, which provide outputs of 10 kW/m^2. This method is utilized commercially for finishing and coating furniture and automobiles, printing plates, microcircuits, and precision instruments.

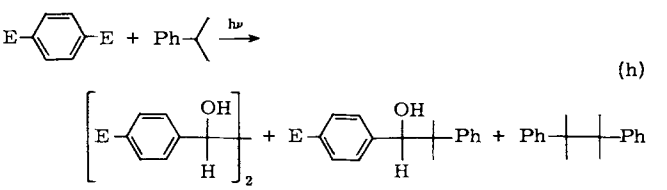
The β-cleavages of toluene (-derivatives) upon direct excitation may be compared with ketone or benzoic ester sensitized reactions. As shown in Eqs (f)[134], (g)[135], and (h)[136], H-abstraction affords benzyl radicals, which dimerize or combine with further radicals.



R = *p*-CH_3O-C_6H_4 (f)



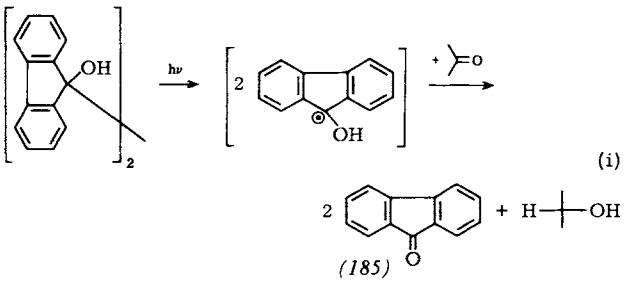
(g)



(h)

E = CO_2CH_3

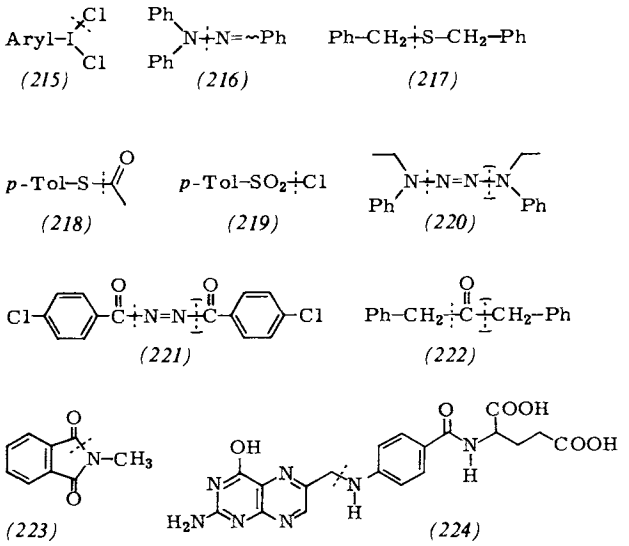
Aryl pinacols cleave at the central bond upon photolysis. The radicals formed can be oxidized by acetone [Eq. (i)][137]. Numerous other β-cleavages are known, the versatility of which can be demonstrated by some selected examples, such as *(215)*[138], *(216)*[139], *(217)*[140], *(218)*[141], *(219)*[142], *(220)*[143], *(221)*[144], *(222)*[145], *(223)*[146]. *(224)* (pteroylglutamic acid,



(i)

(185)

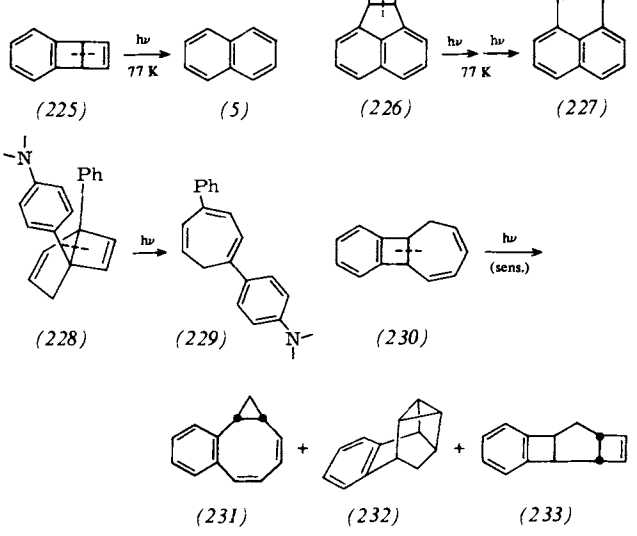
folic acid, vitamin B_c) also undergoes the corresponding photocleavage[147]. The resulting radicals undergo the usual reactions (*e.g.* addition to double bonds or oxidation with O_2, *etc.*).



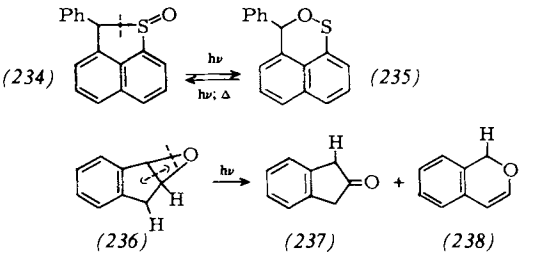
(215) (216) (217) (218) (219) (220) (221) (222) (223) (224)

3.2.3. Ring Enlargement

Arenes, which are condensed to carbo- or heterocyclic rings, may undergo β-cleavage followed by ring enlargement *via* widely differing mechanisms. The reaction of *(225)* proceeds at 77 K to give initially electronically excited *(5)* (apparently adiabatic reaction), because product fluorescence [more intense than that of *(225)*] and product phosphorescence were measured[148]. For the formation of *(227)* at 77 K the triplet of *(226)* has to absorb a second photon[149]. *(228)* with *cis*-chromophores[150] undergoes cyclobutene opening without complications[151]. *(230)* rearranges to the ring-enlarged products *(231)* (17%) and *(232)* (17%) [there is also formation of *(233)* (60%)]. *(231)* (80%) predominates upon sensitized excitation[152]. Ring enlargement of *(234)* proceeds

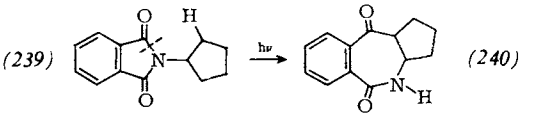


(225) (5) (226) (227) (228) (229) (230) (231) (232) (233)



(234) (235) (236) (237) (238)

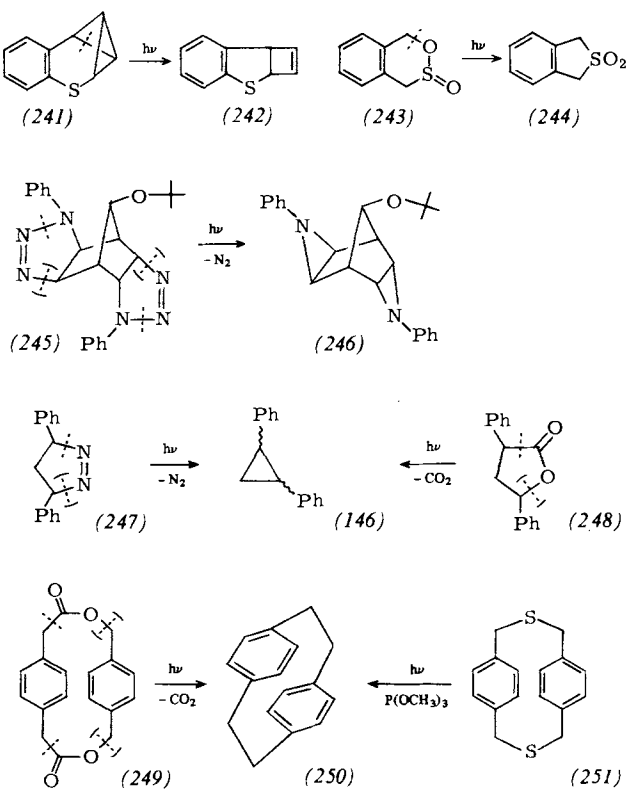
more slowly than photoracemization[153]. The syntheses of *(237)* (42%) and *(238)* (30%)[154] require H-shifts following the β-cleavages. In the reaction of *(239)* to give *(240)* (48%)[155] a C—H-bond adds to the original β-bond.



(239) (240)

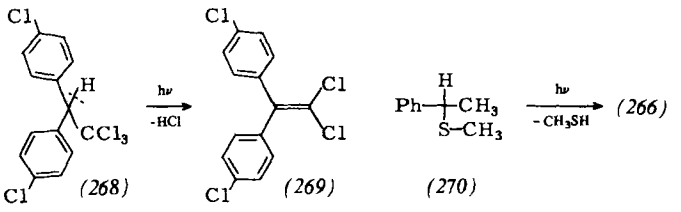
3.2.4. Ring Contraction

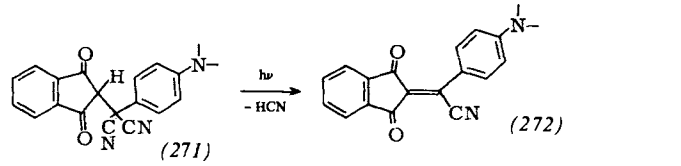
The ring contraction reactions of arenes, which are annelated to carbo- or heterocycles, may lead to isomerizations as in the case of *(241)*[156] and *(243)*[157] or more frequently to

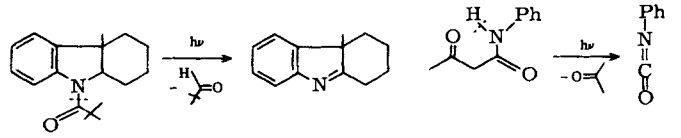


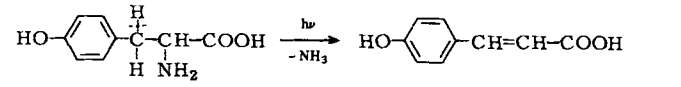
(241) (242) (243) (244) (245) (246) (247) (146) (248) (249) (250) (251)

fragmentations. Cleavable fragments are N_2 [synthesis of aziridines: *e.g. (245)→(246)*[158]; synthesis of cyclopropanes: *e.g. (247)→(146)*[159]], CO_2 [*(248)→(146)* (51%)[133b]; *(249)→(250)* (70%)[160]], sulfur (reductively) [*(251)→(250)* (80%)[161]; metacyclophanes[162]], SO_2 from sulfones and sultones [*(252)→(253)* (95%); *(254)→(253)* (95%)[157]; *(255)→(256)* (75%)[163]], CO [*(257)→(258)* (*trans* 89%, *cis* 11%)[164]; *(259)→(260)* in addition to racemization of *(259)*[165]], ethylene [*(261)→(262)* (91%)[166]], and benzaldehyde [*(263)→(264)*, which forms a dimer above 233 K][167]. Such syntheses are versatile and promise numerous further applications.



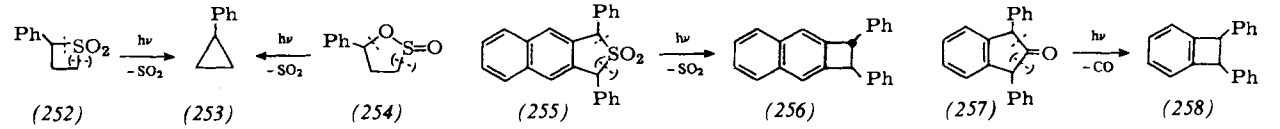


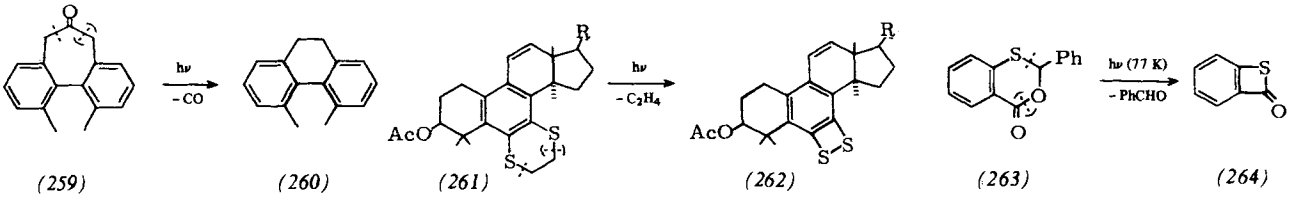


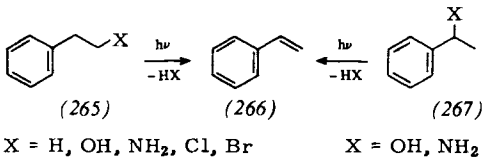


3.2.5. 1,2-Elimination

Photochemical β- and γ-cleavages of benzene derivatives can lead to 1,2-eliminations. Thus, ethylbenzenes with 2- *(265)* or 1-substituted side chains *(267)* form styrene *(266)* upon elimination of HX at 77 K[130]. This reaction type is of ecological importance in the photodegradation of DDT *(268)* (direct and sensitized excitation) to give DDE *(269)*[168]; it is observed with thioethers such as *(270)*[140a, 169], and it is used for the synthesis of merocyanine dyes *(272)*[170] or 3*H*-indoles





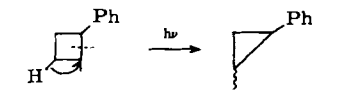


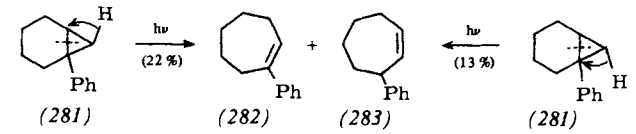
[*e.g. (274)*, 57%] from *N*-acylindolines *(273)*[171]. The elimination of acetone from *(275)*[172] has been termed a "Norrish type II-cleavage" (cf. p. 891 ff. in [101]). The photochemical elimination of NH_3 from tyrosine *(277)*[173] is of biological interest.

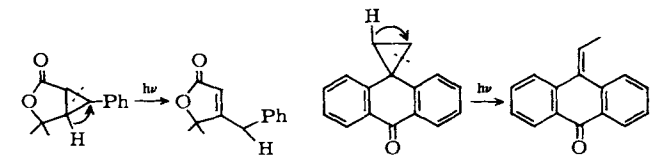
3.2.6. H-(Alkyl-)Migration

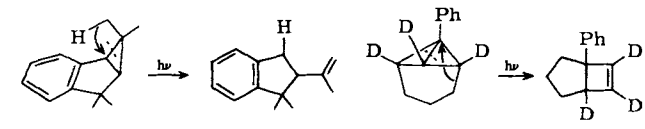
Subsequent to photochemical β-cleavages remote hydrogens may migrate to the centers of the cleavage. Phenylcyclobutane *(279)* undergoes ring contraction to give *(280)* (*cis* and *trans*)[174]. Phenylcyclopropanes such as *(281)*[175] and *(284)*[176] or spirocyclopropanes such as *(286)*[177] undergo ring opening and form a new double bond.

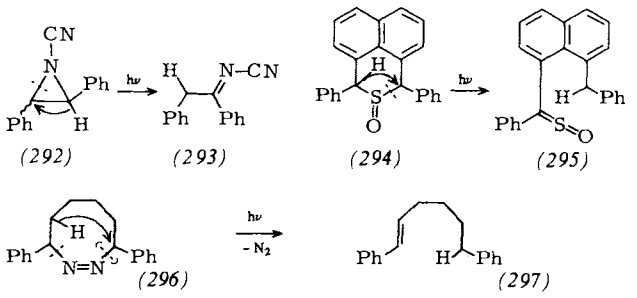
In the case of the homoindene *(288)* a hydrogen atom of the methyl substituent migrates[178], whereas the polycycle *(290)* undergoes an alkyl shift to give *(291)* (50%)[179]. Hydrogen migrations may be observed with aziridines *(292)*[180], sulfoxides *(294)* (>80%)[181], and even in the case of N_2-eliminations from cyclic azo compounds such as *(296)* [65% *(297)*][182].







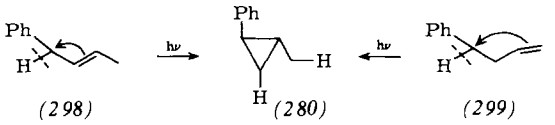




(292) (293) (294) (295) (296) (297)

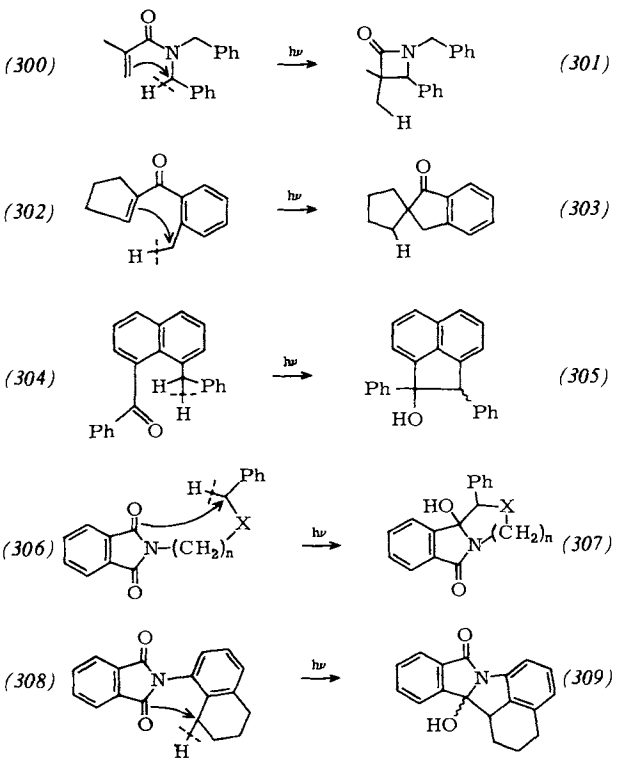
3.2.7. Addition to Double Bonds

The reversal of the olefin-forming reactions which require hydrogen migration to the benzylic site [Section 3.2.6, *e.g. (281)→(283)*], leads to additions of benzylic C—H-bonds to double bonds. Thus, upon photolysis of *(298)*[183] and *(299)*[184] one obtains the cyclopropane *(280)*. This reaction



(298) (280) (299)

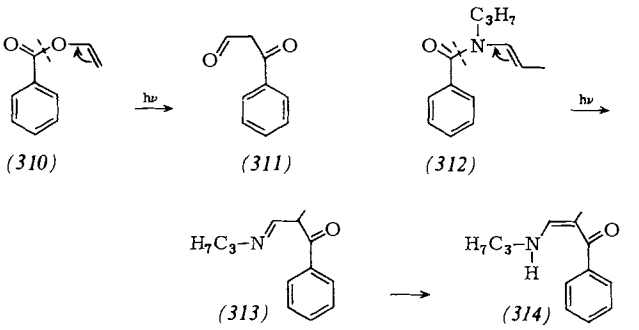
type may also be used for the synthesis of four- [*e.g.* β-lactam *(301)* (84%)][185] and five-membered rings [*(303)* (94%)][186]. From a synthetical point of view the extension of this process to C=O-double bonds of ketones and imides is particularly productive (cf. "Norrish type II cyclizations": p. 798ff. in [101]). Thus, one obtains the alcohols *(305)* (*E*-: 53%; *Z*-: 38%)[187] and the heterocycles *(307)* [X=S: 27%[188]; X=NCH$_2$Ph, $n=1$; 2; 3[189]] and *(309)* (77%)[190].



(300) (301) (302) (303) (304) (305) (306) (307) (308) (309)

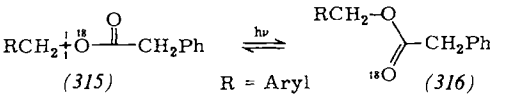
3.2.8. 1,3-Shifts

In β-cleavages with a 1,3-shift a benzoyl (or benzyl) group migrates to the opposite end of an allyl system. This happens in the case of photochemical Claisen rearrangements of benzoic acid vinyl esters [*e.g. (310)*][191] and amides [*(312)*][192].

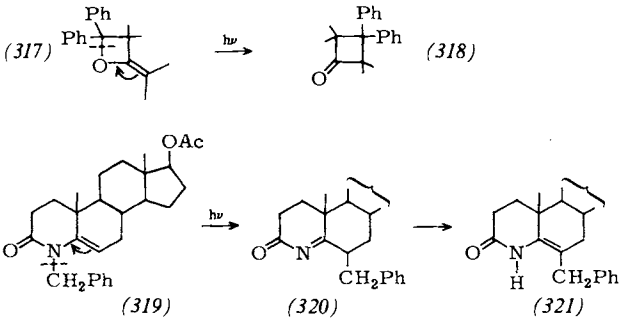


(310) (311) (312) (313) (314)

Benzyl (or 1-, 2-naphthylmethyl) groups in esters may also migrate from the ether-oxygen to the carbonyl-oxygen [*(315)→(316)*][128]. Similar rearrangements take place in benzyl enol ethers [*e.g. (317)*][193] and cyclic enamides such as *(319)* [to give 43% *(321)*][194].



(315) R = Aryl (316)

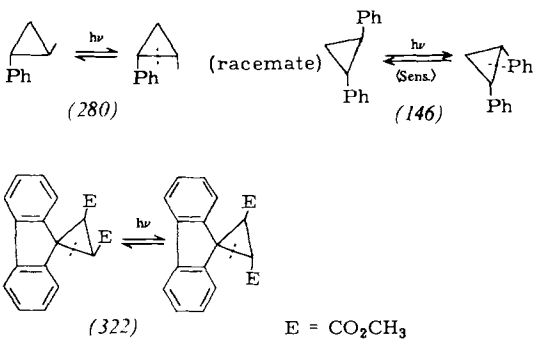


(317) (318) (319) (320) (321)

Phenyl allyl ethers rearrange only partially with 1,3-shift of the phenoxy group when irradiated[195]. Photo-Fries rearrangement to allylphenols predominates (see Section 4.1.2).

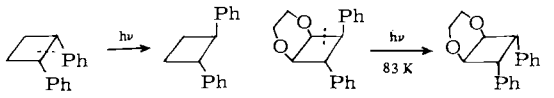
3.2.9. Stereoisomerizations

Stereoisomerizations of aryl-substituted small ring cycloalkanes require cleavage and, after (partial) internal rotation, reformation of β-bonds. Thus, *trans- (280)* reacts to give *cis-(280)* in the gas phase (quantum yield $\Phi=0.12$)[196]. The photoequilibrium *cis/trans-(322)* can be established in solution



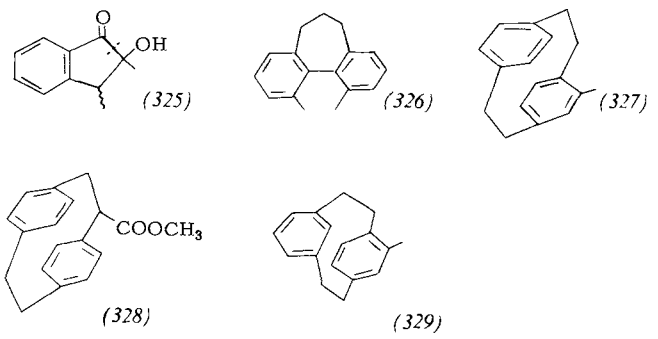
(280) (racemate) (146) (322) E = CO$_2$CH$_3$

(97–98% *trans*)[197]. In the case of *(146)* the *trans/cis*-isomerization was studied with the chiral sensitizer *N*-[1-(1-naphthyl)ethyl]acetamide. In the photoequilibrium (*cis/trans* = 1.03) the antipode of the *trans*-form (spec. rotation: +28°), whose sensitization is geometrically more difficult[198], prevails. [2+2]-Cycloreversions (Section 3.2.11) compete with the geometric isomerizations of the cyclobutanes *(323)*[199] and *(324)*[150b]. The formation of *cis-(324)* succeeds upon photolysis of the *trans*-isomer even at 83 K, *i. e.* without thermal activation[150b].



(323) *(324)*

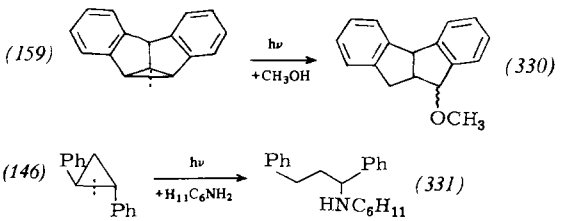
While the *trans/cis*-photoisomerization of *(325)*[200] necessarily requires ring opening, in the case of larger rings this could also proceed *via* conformational change without transient bond breaking. One may mention here the photoracemizations of *(326)*[165] as well as of the cyclophanes *(327)*, *(328)*, and *(329)*[201].



(325) *(326)* *(327)* *(328)* *(329)*

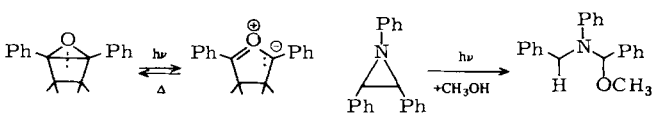
3.2.10. 1,3-Diradicals; Ylides

The photolysis of aryl-substituted cyclopropanes leads to β-cleavage. This produces 1,3-diradicals, which may add alcohols, amines, or dienophiles. Thus, dibenzosemibullvalene *(159)* gives *(330)* (*syn*-: 48%; *anti*-: 19%) in methanol[202] and *(146)* reacts in cyclohexylamine to give *(331)* (30%)[203].



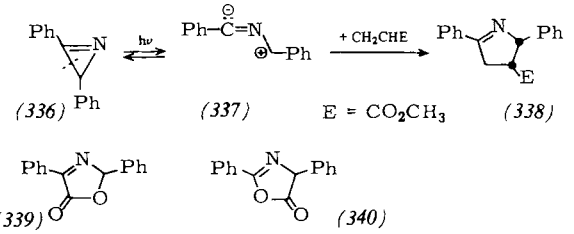
(159) *(330)* *(146)* *(331)*

Upon photolysis (λ = 253.7 nm) in benzene or diglyme, *(332)* forms violet solutions, in which the presence of so-called "carbonyl-ylides" *(333)*[204] is surmised. From *(334)* one obtains the solvolyzing product *(335)* (>33%), in competition



(332) *(333)* *(334)* *(335)*

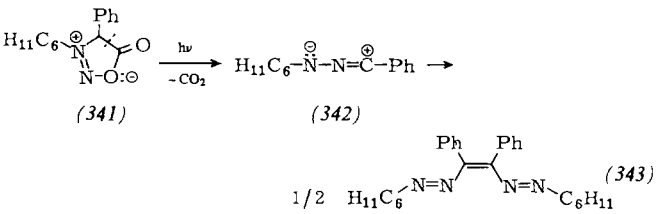
with fragmentation to phenylcarbene and benzylidene aniline (24%)[205] (cf. Section 3.2.12). The reactive intermediates in the photolysis of phenyl-substituted azirines are conventionally formulated as nitrile ylides [*e.g. (337)*; 77 K: λ_{max} = 344, 244 nm]. From *(336)* and methyl acrylate one obtains *(338)*[206]. *(337)* may add CO_2 to give *(339)* and *(340)* (1:1)[207].



(336) *(337)* E = CO_2CH_3 *(338)*

(339) *(340)*

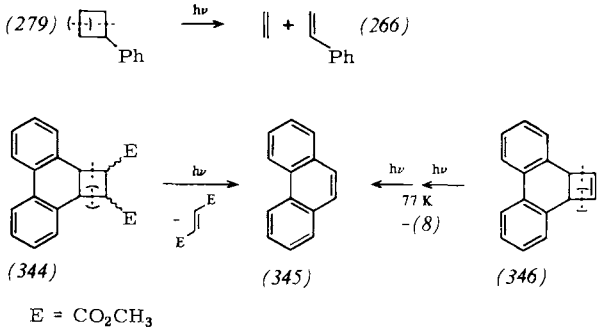
The photodecarboxylation of the phenylsydnone *(341)* yields the nitrile imine *(342)*, which dimerizes to *(343)*[208].



(341) *(342)* *(343)*

3.2.11. Cycloreversions (Without Carbene Formation)

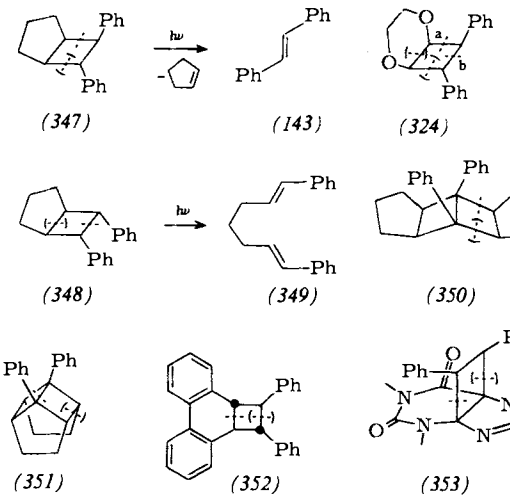
Numerous examples for photocycloreversions are known in the series of aryl-substituted cyclobutanes, cyclohexenes, *etc.*[150,199,209]. Thus, *(279)* decomposes at 298 K and at 83 K to give ethylene and styrene *(266)*, and *(344)* reacts with high quantum yields (*trans*: Φ = 0.8; *cis*: Φ = 0.4)[210] to give *(345)*.

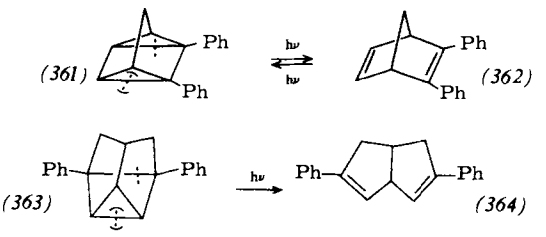


(279) *(266)* *(344)* *(345)* *(346)* *(8)*

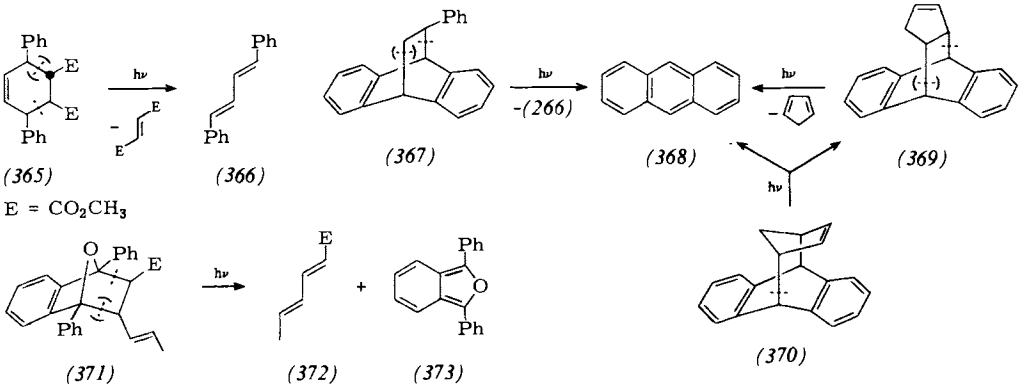
E = CO_2CH_3

In the case of *(346)* the elimination of acetylene proceeds at 77 K biphotonically *via* the triplet[211]. Orientation selectivities are understandable and predictable on the basis of the *cis*-effect[212], which is inherent in the kinetically[98a] and stereochemically[150b] derived diradical mechanism. The best possible release of steric hindrance in the primary step is decisive, and not the stability of the diradical formed[150]. Thus, *(347)* reacts at 289 K and at 83 K to give *(143)* [in addition to *(348)*][150b], whereas *(348)* forms *(349)*[199]. *(324)* prefers the cleavage *a* [31% *cis-(324)* and 45% *(143)*], but because of the inevitable light absorption by the *anti*-phenyl group 24% of stereoisomeric 1,8-diphenyl-3,6-dioxa-1,7-octadienes (cleavage *b*) are also formed[150b]. *(350)*, *(351)*[199], *(352)*[213a], and *(353)*[213b] photocleave, as expected, only in the indicated





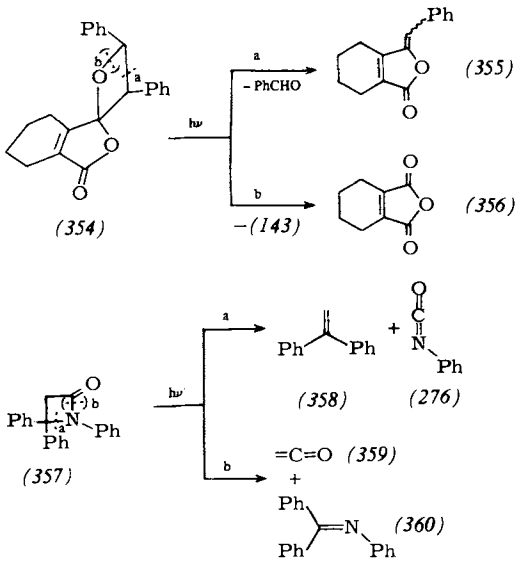
deactivation *via* unproductive ring motions. Photochemical retro-Diels-Alder reactions ([4+2]-type) then succeed at 298 K and 83 K, as do [2+2]-, [4+4]-, [4+6]-, *etc.* reactions. They show no peculiarities, as may be exemplified with *(365)*[199], *(367)*[209b], *(369)*[209b], and *(371)*[209a] (cf. also 40% O_2-abstraction upon short wavelength excitation of 9,10-diphenylanthracene endoperoxide[217]).

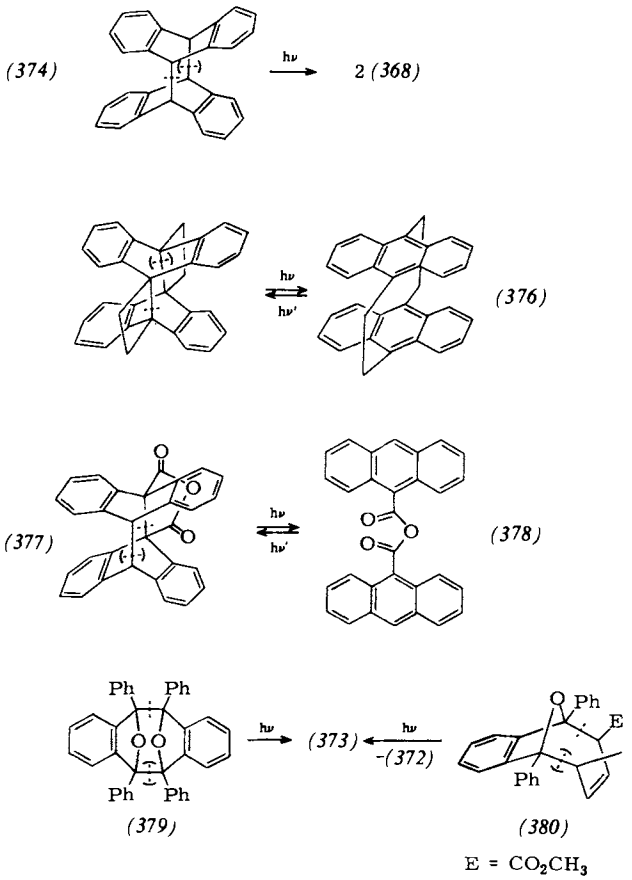


sense. Even spirooxetanes [*e.g. (354)*[214]; *a/b* = 17/83 (λ = 253.7 nm)][215] and β-lactams [*e.g. (357)*; *a/b* = 64/19][216] exhibit pronounced orientation selectivities in their [2+2]-photocycloreversions.

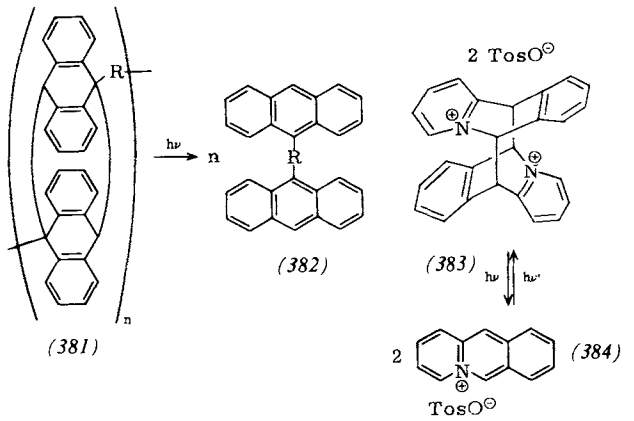
[2+2]-Photocycloreversions can be observed with the polycyclic compounds *(361)* and *(363)*, even at 83 K[98a].

Cyclovinylogous photocycloreversions must be promoted with steric or conformational effects, in order to avoid rapid



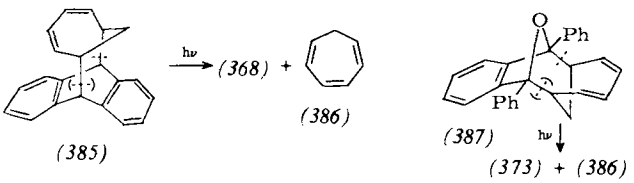


(370) undergoes [4 + 4]-photocycloreversion to *(368)* in addition to the 1,3-shift (allylic rearrangement) to yield *(369)*[209b]. Numerous further [4 + 4]-cleavages are known (reviews:[98a], [218]). Thus, anthracene dimers such as *(374)*[98a, 219], *(375)*[98a], and *(377)*[98a, 218] or rigid (di-)benzocyclooctadienes such as *(379)* and *(380)*[209a] photocleave at 298 K and 83 K, as indicated. These reactions promise practical applications. Thus, photolabile polymers such as *(381)* can be pro-



duced[220] and the system *(383)*⇌*(384)* is possibly suitable for holographic storage of information[221]: Starting with single crystals of the dimer *(383)* one may photoreversibly generate thermostable images or diffraction gratings (over several thousand cycles), which may be read outside their regions of UV-absorption, because of the considerable change in refractive index.

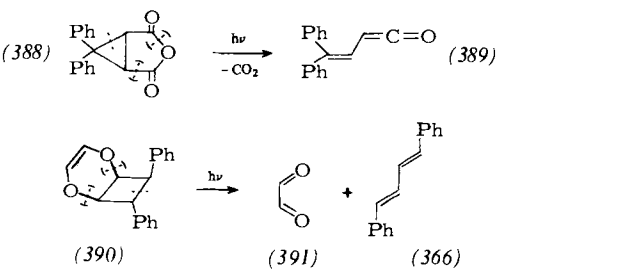
The reactions of *(385)* and *(387)* (298 K or 83 K)[222] are significant examples of [6 + 4]-photocycloreversions.



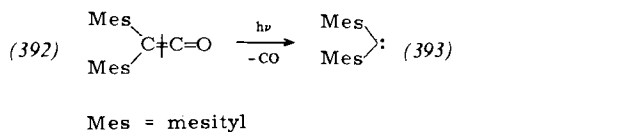
Altogether three bonds are cleaved in the [2 + 2 + 2]- and [4 + 2 + 2]-photocycloreversions of *(388)*[223] and *(390)*[150b], respectively. Further cycloreversions are mentioned in Sections 3.1.5, 3.2.12, 4.2.1, 4.2.3 ([6 + 6]-type), 4.3.4, and 4.3.5 (cycloadditions).

3.2.12. Carbenes, Nitrenes, and Other Low Valent Fragments

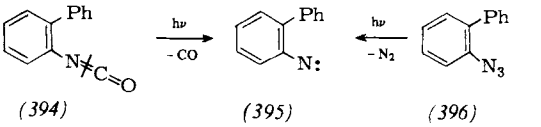
Upon cleavage of double bonds or cycloreversions of usually odd-numbered rings one obtains carbenes, nitrenes, or other low valent fragments such as CO, S, SO, SO_2, N_2, SiR_2. These reactions may be classified either with respect to the number of π-electrons (*i.e.* index 0 for carbenes *etc.*) or with respect to the number of atoms (*i.e.* index 1 for carbenes *etc.*).

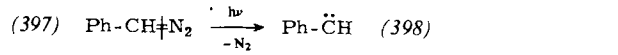


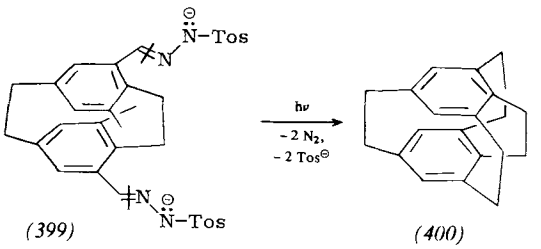
The type [0 + 0] ([1 + 1]) is represented by the cleavages of arylketenes [*(392)*[224]], -isocyanates [*(394)*[225]], -azides [*(396)*[226]], -diazoalkanes [*(397)*[227]], and -tosylhydrazone anions [*(399)*[228]]. The carbenes and nitrenes, thus formed, may undergo the usual dimerizations [*e.g. (393)*[224]], insertions [*e.g. (359)*→carbazole *(89)*[225, 226], *o*-biphenylcarbene → fluorene[229], *(399)*→*(400)*[228]], and additions to double bonds (yielding three-membered rings) or amines (*e.g.* phenylnitrene + NEt_3 → 2-(diethylamino)-3*H*-azepine[230]); upon matrix isolation at 10 K, 1-aza-1,2,4,6-cycloheptatetraene could be detected as an intermediate[230a] (review on the numerous synthetic applications: p. 1158—1282 in [101]).



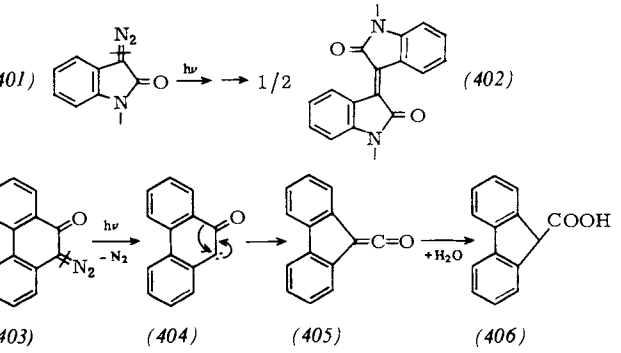
Mes = mesityl

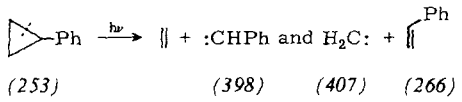




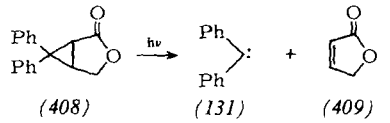


Arylacylcarbenes of suitable constitution may dimerize [*e.g.* dimethylisoindigo *(402)* (11%) from *(401)*][231] or undergo the Wolff rearrangement. From *(403)* one obtains *(406)* *via* the hydrolizable ketene *(405)*[232]. Owing to the solubility of carboxylic acids such as *(406)* in alkaline media, *o*-quinonediazides having long side chains find widespread application for offset printing plates in rotary press printing (Süs reaction)[59, 114c].

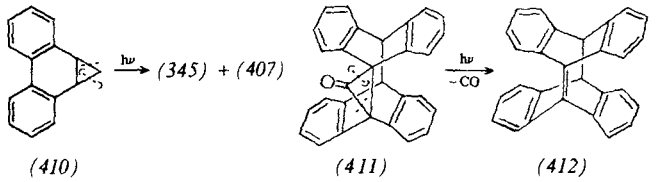




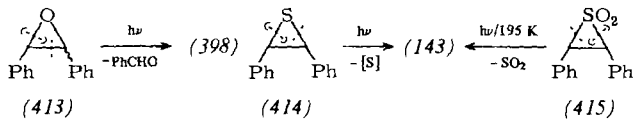
(253) (398) (407) (266)



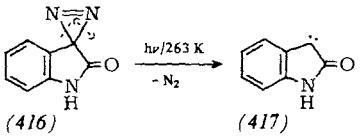
(408) (131) (409)



(410) (411) (412)

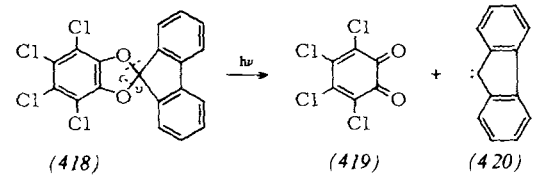


(413) (414) (415)

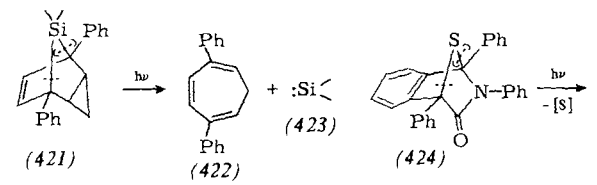


(416) (417)

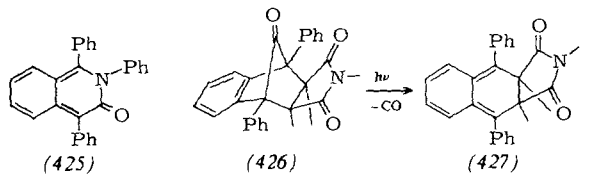
The type [2+0]- ([2+1]-) cycloreversions may be represented by the photolyses of *(253)*[233], *(408)*[223], *(410)*[234], *(411)*[235], *(413)*[236], *(414)*[237], *(415)*[238], and *(416)*[239], which demonstrate the variability and synthetic utility of such cleavages. The [4+0]- ([4+1]-) reactions of *(418)* (30%)[233], *(421)*[240], *(424)* (55%)[241], and *(426)* (80%)[242] are preparatively useful (related examples in Section 4.2.1). The [2+2+0]- ([2+2+1]-) cycloreversions of *(428)*[233], *(430)*[243],



(418) (419) (420)



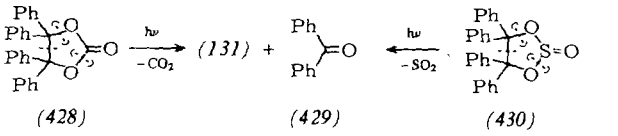
(421) (422) (423) (424)



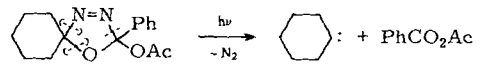
(425) (426) (427)

and *(431)*[159c] are significant in that they provide a new method for the generation of the carbenes *(131)* and *(432)*.

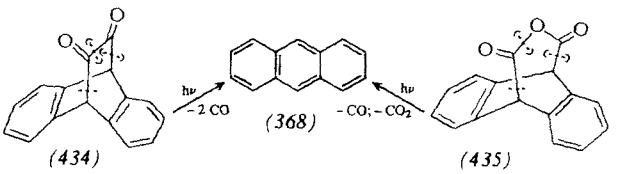
Even higher cyclovinylogous types are realized in the photolyses of *(434)*[244] ([4+0+0] or [4+1+1]) and *(435)*[245] ([4+2+0] or [4+2+1]).



(428) (429) (430)

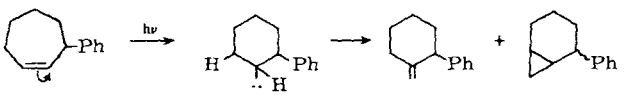


(431) (432) (433)



(434) (368) (435)

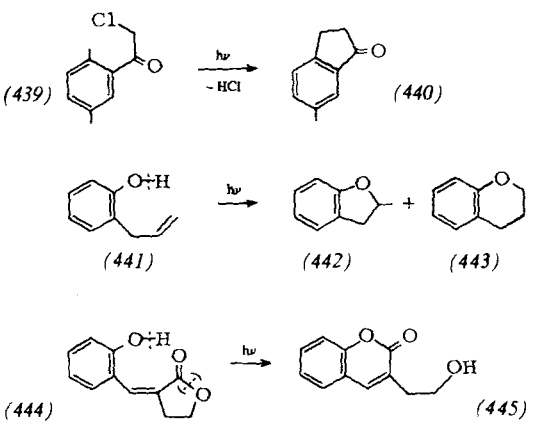
Further modes of formation of carbenes and nitrenes were described in Section 3.1.6 as α-cleavages. An interesting variant is the β-cleavage of *(283)* (α-cleavage w.r.t. the double bond). C—H-insertion affords the products *(437)* and *(438)*[175].



(283) (436) (437) (438)

3.2.13. Reactions of Substituents with Side Chains

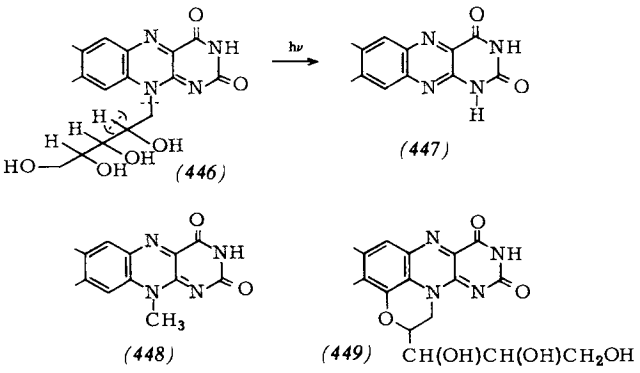
The cyclization with elimination of HCl from *(439)* presumably proceeds *via* an *o*-quinodimethane intermediate[246] (cf. Section 4.2.1). Phenolic OH-groups may add to double bonds of *o*-side chains. *(441)* gives *(442)* (24%) and *(443)* (2%)[247]. The photolysis of *(444)* leads to an intramolecular



(439) (440) (441) (442) (443) (444) (445)

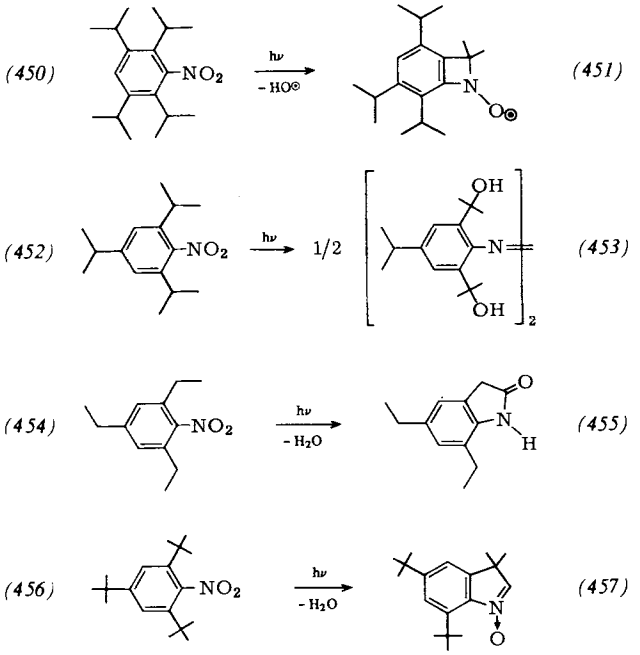
transesterification[248]. Photochemical dealkylations of aminoarenes such as riboflavine (vitamin B_2, previously called lactoflavine) *(446)* to give lumichrome *(447)* (45%)[249] are of considerable importance. In alkaline solution, also lumiflavine *(448)*[249] and presumably *(449)*[250] (cf. Section 4.1.3) are formed. Several further (iso-)alloxazines can undergo corresponding dealkylations[250].

The modes of reaction of nitroarenes with *o*-alkyl substituents depends on the extent of steric hindrance[251]. In the



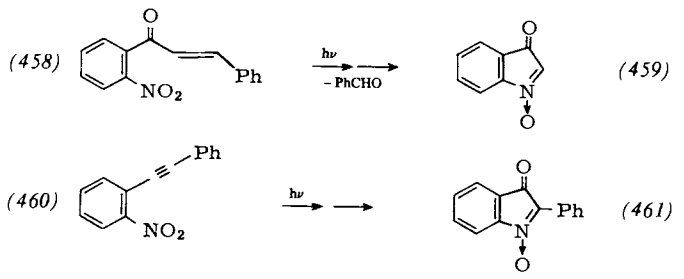
(446) (447) (448) (449) $CH(OH)CH(OH)CH_2OH$

reactions of *(450)* and *(452)* benzylic H-atoms (β-cleavage) participate. However, it is also possible to transfer H-atoms, which are more remote from the benzene ring, to the nitro group, as is shown with the reactions of *(454)* and *(456)*. Un-



(450) (451) (452) (453) (454) (455) (456) (457)

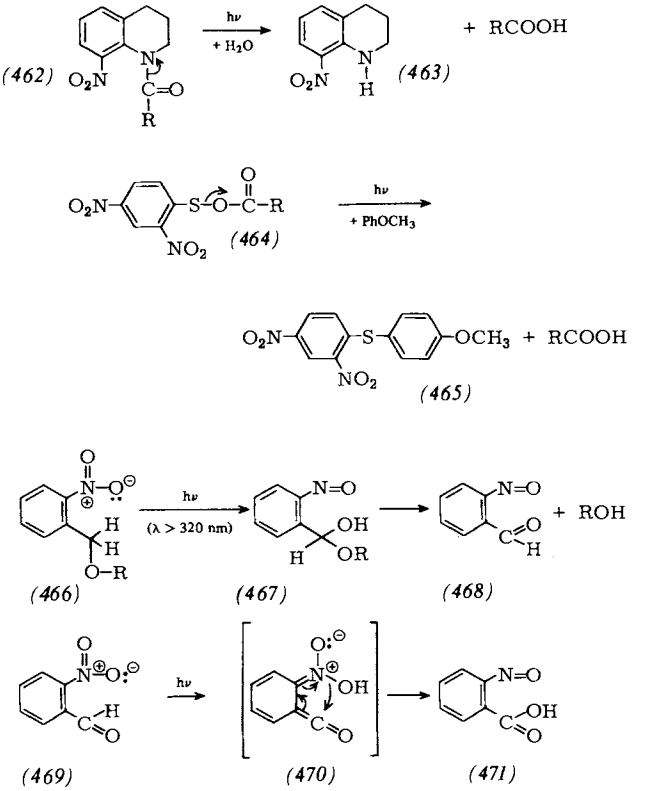
doubtedly, in all these cases complicated multistep reactions are involved, in which *o*-quinoid *aci*-nitrocompounds and or diradicals presumably occur as intermediates (also an *o*-quinomethide oxime intermediate in the case of *(452)*→*(453)*; cf. Section 4.2.1). The synthesis of indoxyl *N*-oxide (indigo synthesis) from *(458)*[252] and of phenylisatogen *(461)* from *(460)*[253] have been long known. These need be mentioned here, even though there are several mechanistic alternatives.



(458) (459) (460) (461)

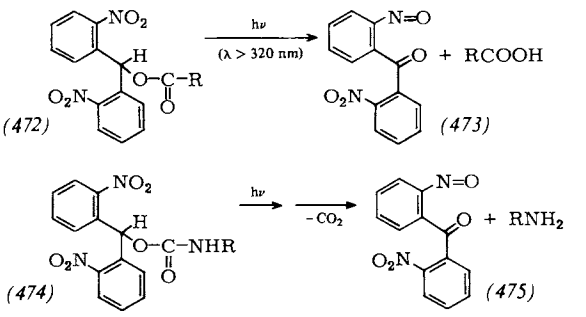
3.2.14. Light-Sensitive Protecting Groups

The principle of β-cleavage of substituted benzenes allows the protection of carboxylic acids, alcohols, and primary or secondary amines followed by mild and almost quantitative regeneration under neutral conditions, which is particularly suited to the requirements of peptide, carbohydrate, and nucleic acid syntheses. Thus, photohydrolyses of amides such as *(462)* (100%)[254] and heterolytic cleavages of the dinitrobenzenesulfenyl esters *(464)* (83–92%)[255] are possible. From the ether *(466)*, the alcohol (*e.g.* D-glucose, 100%) may be liberated photochemically[256]. The semiacetal *(467)* is presum-



(462) (463) (464) (465) (466) (467) (468) (469) (470) (471)

ably formed, in analogy to the transformation of *o*-nitrobenzaldehyde *(469)* into *o*-nitrosobenzoic acid *(471) via (470)*[257], after initial H-transfer to the nitro group (cf. Section 4.2.1) by OH-transfer with rearomatization. *(472)* and *(474)* correspondingly regenerate the carboxylic acids (100%) and amines (70—95%), respectively[258].

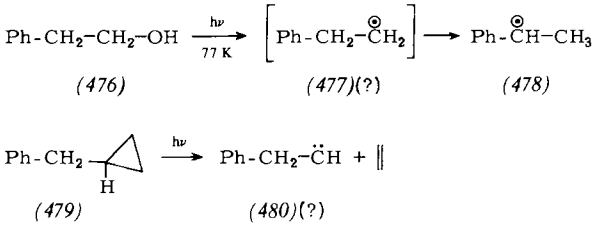


(472) (473) (474) (475)

3.3. γ-Cleavage

It is not certain whether the electronic energy which is absorbed by benzene chromophores may cause dissociative vi-

brational excitations in γ-bonds separated by two insulating centers. The spectroscopic detection of *(478)* [in addition to β-cleavages of *(476)* (also formation of styrene) at 77 K][130] still does not prove an intermediate *(477)*. A more complicated mechanism [*e.g. via* styrene *(266)*] could operate, particularly as H-atoms are able to diffuse in ether/isopentane/ethanol-glass (EPA) at 77 K . Ethylene [and perhaps benzylcarbene *(480)*?] is formed from *(479)* besides the products of α- and β-cleavage[259]. Again this, by itself, does not constitute proof of a direct cleavage of two γ-bonds. Rather, ethyl-

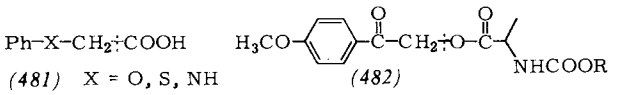


(476) *(477)*(?) *(478)*

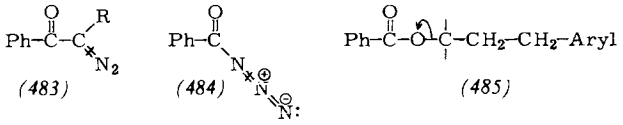
(479) *(480)*(?)

ene could well be generated by reactions of alkyl or phenyl radicals (which form simultaneously) with the cyclopropane ring in *(479)*.

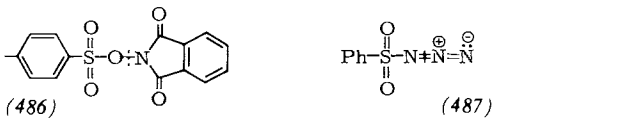
When the benzene chromophore is extended with O-, S-, NH-, C=O-, SO_2-groups, the γ-bonds (w.r.t. the benzene ring) may be cleaved photolytically. However, it is probably more correct to classify these reactions as β-cleavages of ethers (thioethers, amines) [*e.g.* phenoxyacetic acid *(481)*][260] and ketones [*e.g. (482)*[261], *(483)*, *(484)*][262], as α-cleavages of



(481) X = O, S, NH *(482)*



(483) *(484)* *(485)*



(486) *(487)*

carboxylic esters [*e.g. (485)*][263] and amides [*e.g. (486)*][264], or as fragmentation of sulfonylazides [*e.g. (487)*][265], *etc.*, even though the influence of the arene ring on the absorption and on the secondary reactions (*e.g.* Wolff and Curtius rearrangement in the case of *(483)* and *(484)*, resp.) cannot be dismissed.

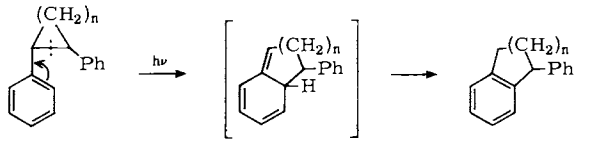
4. Reactions at the Benzene Ring

Benzene rings may be altered by participation of side chains leading to substitution, lengthening of the conjugated system, addition, cycloaddition, and cyclization. These processes provide a large number of preparatively and industrially important reactions.

4.1. Substitutions

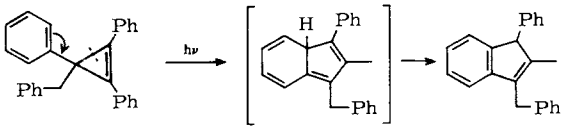
4.1.1. Alkylation with Three- and Four-Membered Rings

Phenylcyclopropanes and phenylcyclobutanes like *(146)* and *(323)* may, *inter alia*, rearrange to cyclic alkylation products such as *(489)*[266] and *(491)*[267] by parallel addition of a ring bond to the benzene ring (also describable as 1,3-alkyl shift) followed by H-shift (cross-addition in Section 4.3.2).

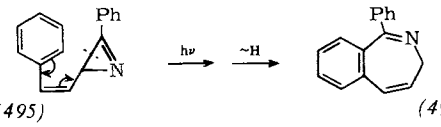


(146), n = 1 *(488)*, n = 1 *(489)*, n = 1
(323), n = 2 *(490)*, n = 2 *(491)*, n = 2

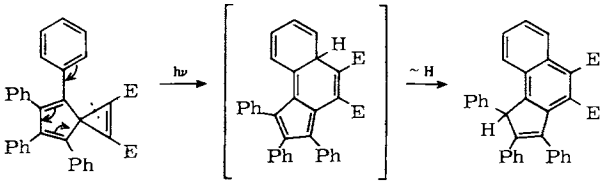
Arylcyclopropenes and -azirines like *(492)*[268], *(495)* [80% *(496)*][269], and *(497)* [40% *(499)*][270] react analogously.



(492) *(493)* *(494)*



(495) *(496)*

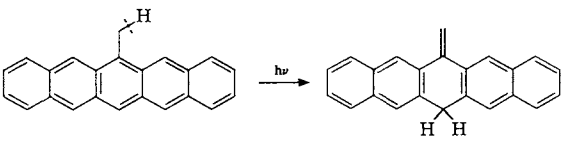


(497) *(498)* *(499)*

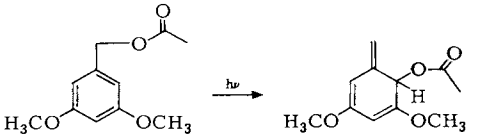
E = CO_2CH_3

4.1.2. Photo-Fries Rearrangement

On photolysis, 6-methylpentacene *(500)* forms the more stable isomer *(501)*[271], while the triene *(503)* (17%)[272] may be formed from *(502)*. These reactions are models for the primary reactions of photo-Fries rearrangements, which usually

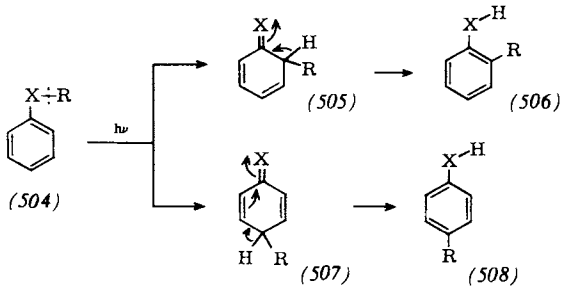


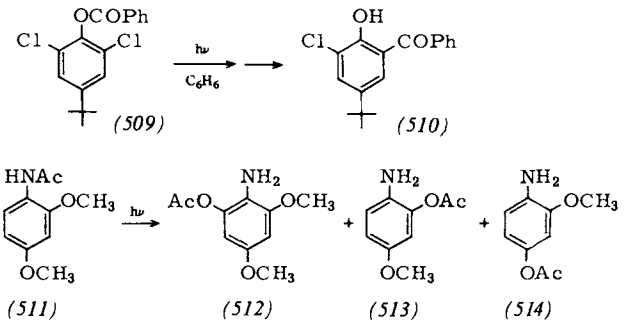
(500) *(501)*



(502) *(503)*

proceed further to give the substituted arenes by rapid H-shift. One obtains *o*- and *p*-substituted products by 1,3- and 1,5-migration of R and counter migration of H. The radical migration proceeds primarily within the solvent cage[273]. However, due to cage escape, considerable amounts of inter-





the presence of oxygen[302b]. Also of practical interest are the corresponding rearrangements in polymeric phenyl esters, which are accompanied by chain destruction and yellowing[305].

Table 1. Photo-Fries rearrangements of phenyl esters, *N*-phenylamides and other aryl derivatives *(504)*. Yields referred to converted educt.

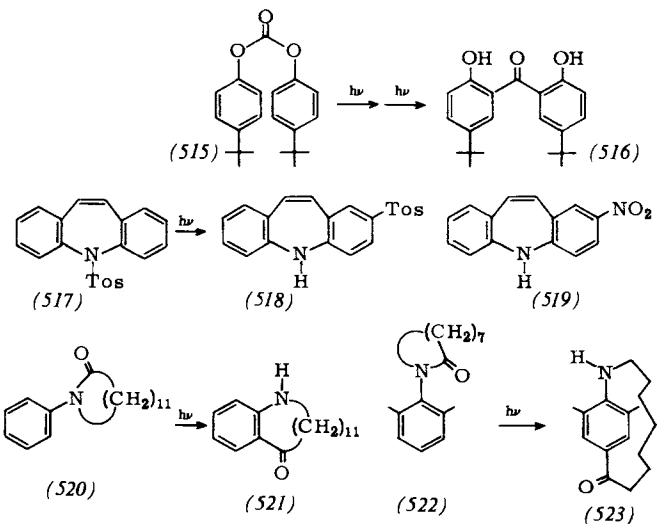
X	R	Conversion [%]	Yield [%] *(506)*	Yield [%] *(508)*	Solvent	Ref.
O	$COCH_3$	100	19	15	EtOH	[278]
O	COPh	100	20	28	EtOH	[279]
O	Ph	20	27	22	*i*-PrOH	[47a]
O	$COOC_2H_5$		+ [a]	+ [a]	*i*-PrOH	[280]
O	$CONHCH_3$	25	57	[b]	*t*-BuOH	[281]
O	CH_2COOH		18 [c]	10 [c]	95% EtOH	[282]
O	CH_2COOCH_3	100	58	25	CH_3OH	[283]
O	$CSC_6H_4p\text{-}CH_3$		15	—	C_6H_{12}	[284]
O	$C(CH_3)_3$		7	10	CH_3OH	[285]
O	CH_2CHCH_2	98	30	29	CH_3OH	[286]
O	CH_2Ph		18 [c]	14 [c]	95% EtOH	[282, 287]
O [d]	4,6-dimethoxytriazinyl		48	27	EtOH	[288]
O	$SO_2C_6H_5$	49	24	16	C_6H_6	[289]
NH	$SO_2C_6H_4p\text{-}CH_3$	29	—	26	EtOH	[290]
NH	COPh	27	14	14	EtOH	[291]
NCH_3	$COCH_3$	10	28	18.5	Et_2O	[292]
NH	COOEt	14	37	8	EtOH	[293]
NCH_3	$N(CH_3)C_6H_4p\text{-}OCH_3$	83	65 [c]	[e]	*c*-C_6H_{12}	[294]
NCH_3 [d]	NO_2		2 :	1	CH_3CN	[295]
NAc	$COCH_3$		3 :	2.5	CH_3CN	[296]
Se	COC_6H_5		33 [c]	[b]	C_6H_6	[297]
S	$COC_6H_4o\text{-}Cl$	85	31 [c, f]	—	C_6H_6	[297]
Se	$COC_6H_4o\text{-}Cl$		19 [c, f]	—	C_6H_6	[297]
$Si(CH_3)_2$	$Si(CH_3)_3$	53	+ [g]	—	C_6H_6	[298]
CH_2	$COCH_3$	100	0.9	0.3	*t*-BuOH	[299]

[a] Yield not quoted. [b] *p*-Methyl-*(504)*. [c] Yield referred to total educt. [d] 1-Naphthyl-X-R instead of phenyl-X-R. [e] *p*-Methoxy-*(504)*. [f] Final product is thioxanthone (selenoxanthone), the cyclization product of *(505)* with HCl-elimination. [g] *(505)* has been trapped with 2.2 M 2,3-dimethylbutadiene (37%).

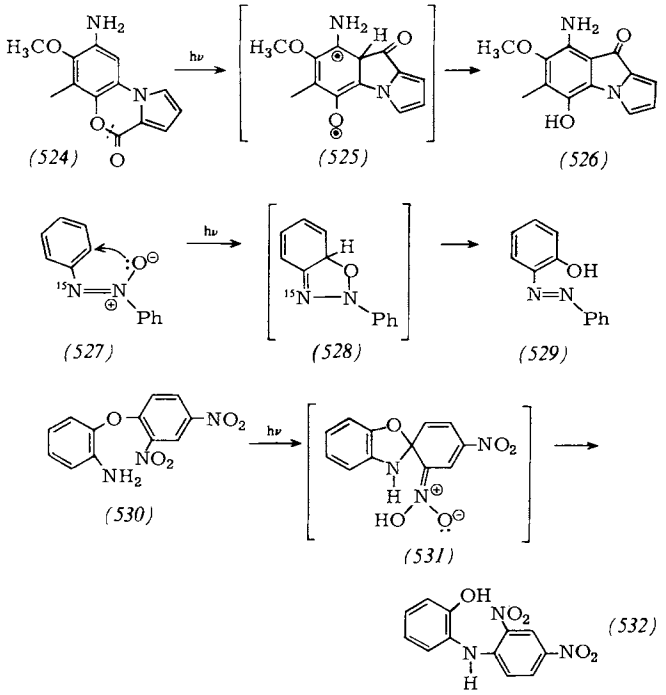
molecular products (Aryl—XH) are found in most cases. Improvements in the yields of rearranged products could be achieved by two-phase photochemistry with phenolic esters on silica gel[274]. In the gas phase one does not always obtain the same products[275] (cf. [195]). Table 1 summarizes the numerous possible variants[276, 277].

In place of hydrogen *o*-Cl, *o*-Br, *o*-I, and *o*-,*p*-methoxy substituents may also be displaced (presumably in the form of $X^{\oplus}$ and HCHO). Thus reactions of *(509)* to give *(510)*[279] and of *(511)* to give *(513)* and *(514)* in addition to *(512)*[300] have been observed.

Photo-Fries rearrangements have also been performed with various substituted arenes (and heterocycles). The synthetic utility may be demonstrated by the selected examples *(515)* [36% *(516)*, two-fold rearrangement][301], *(517)*[302a], *(520)* [$\Phi = 0.082$; 80% *(521)*][303], and *(522)* [32% *(523)*][304]. *(519)* is formed on irradiation of *N*-nitrosodibenzoazepine in

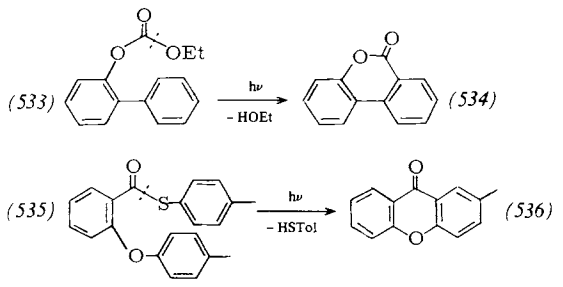


The *meta*-photo-Fries rearrangement of *(524)*[306] is sterically enforced. A close relationship exists between the Fries-, Wallach- (of azoxybenzenes to give *o*-hydroxyazobenzenes) and Smiles-rearrangements (of activated aminophenoxyethers to give arene amino alcohols). Thus, *(527)* rearranges *via (528)* to *(529)*[307] and *(530)* reacts correspondingly *via (531)* to yield *(532*[308].

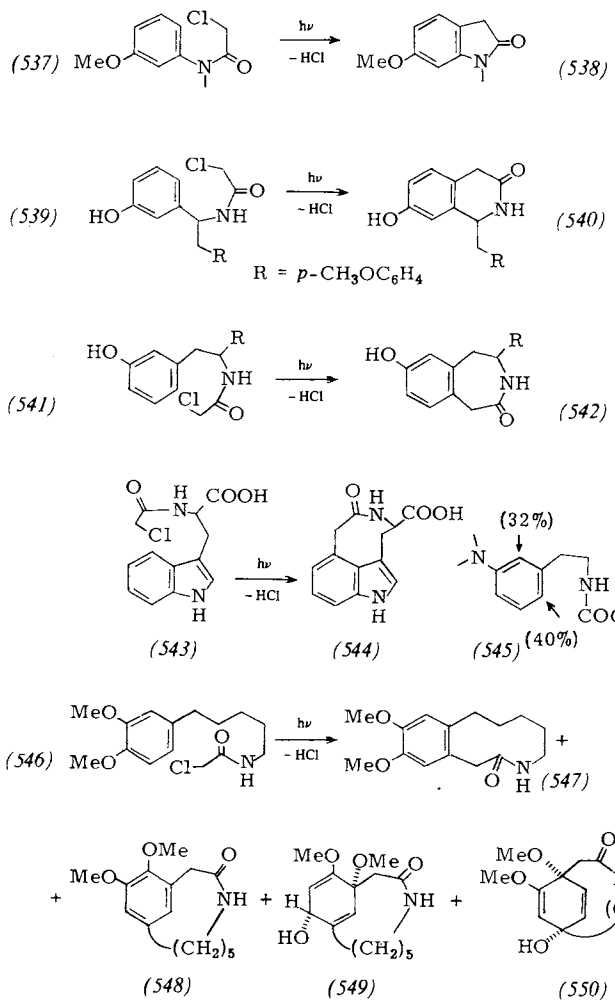


4.1.3. Cyclizing Substitutions

Together with numerous special cases of cyclizing substitutions[309], Friedel-Crafts acylations (cf. the reactions in Section 4.1.2) and alkylations are synthetically useful. Thus, the carbonic ester group in *(533)*[310] and the thiocarbonic ester moiety in *(535)* exhibit acylating action (86%)[311]. Particularly well studied are the productive cyclizing alkylations of



benzene rings possessing chloroacetylamide side chains which frequently lead to pharmacologically interesting lactams. Five-, six-, seven-, eight-membered, and even larger rings may be constructed. The benzene ring should, if possible, contain an activating *m*-hydroxy (*m*-methoxy; *m*-amino) substituent. In the presence of *p*-hydroxy groups, side reactions such as [4+2]-cyclodimerization of the intermediate predominate[312]. Characteristic examples are the syntheses of *(538)* (74%)[313], *(540)* (49%)[314], *(542)* (R=H: 71%, R=COOH: 25%)[315], and *(544)* (40%)[316]. *(545)* cyclosubstitutes in the *o*- (32%) and *p*-positions (40%) w.r.t. the dimethylamino substituent[317]. *(546)* in acetonitrile/water afforded 10% *(547)*, 16% *(548)*, and—by hydroxylation of the intermediary cations—23% *(549)* and 20% *(550)*[318].

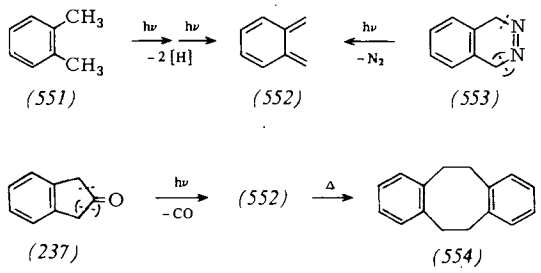


Formally related to these photochemical Friedel-Crafts alkylations are the cyclizations of phenyl enamines, enol ethers, and vinyl ketones in Section 4.4.2. H-migration leads to formation of five-membered rings.

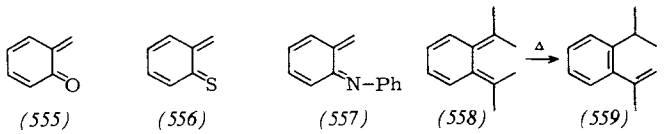
4.2. Formation of Quinodimethanes

4.2.1. *o*-Quinodimethanes (Photochromes, UV-Stabilizers)

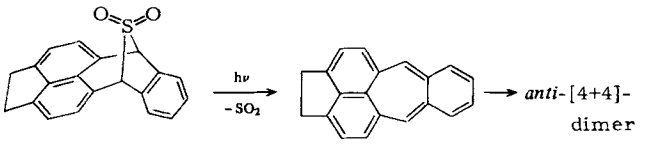
On absorption of light, 1,2-disubstituted benzene derivatives may undergo β-cleavage and produce usually very labile *o*-quinodimethanes. Thus, at 77 K two hydrogen atoms are split off from *(551)*[319] or one nitrogen molecule from *(553)*[320]. *(552)*, which dimerizes to give *(554)*, may also be generated by photodecarbonylation of *(237)*[321]. According-



ly, the intermediates *(555)*[322], *(556)*[323], and *(557)*[324], which are potent addition partners (for dienophiles and nucleophiles), or *(558)*, which apparently immediately rearranges[325], may be generated by photodecarbonylation.

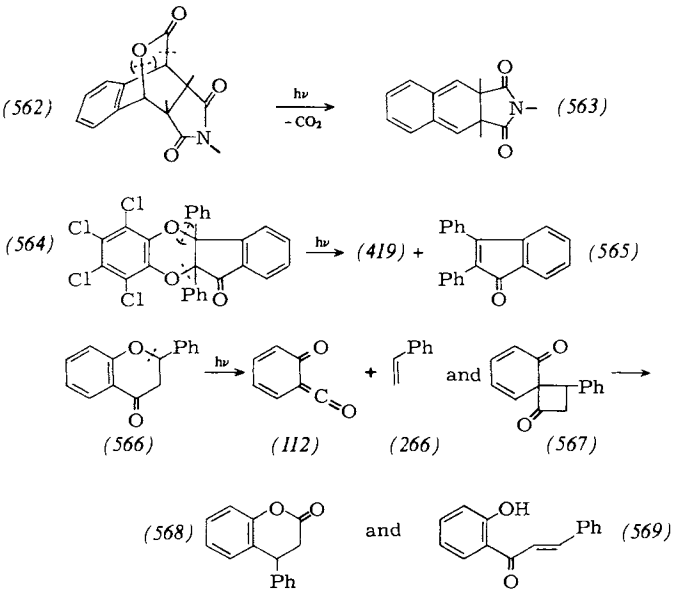


(555) *(556)* *(557)* *(558)* *(559)*



(560) *(561)* *anti*-[4+4]-dimer

(561) has been formed by photochemical SO_2-elimination[326]. Suitably substituted tetrahydronaphthalenes such as *(562)*[327] or *(564)*[328] undergo photochemical retro-Diels-Alder reactions (cf. Section 3.2.11). The corresponding reaction of *(566)* to give *(112)* proceeds less selectively (4%). There is competing formation of the spirocyclobutane *(567)*, which rearranges to give *(568)* (15%) and *(569)* (20%)[329].



(562) *(563)*

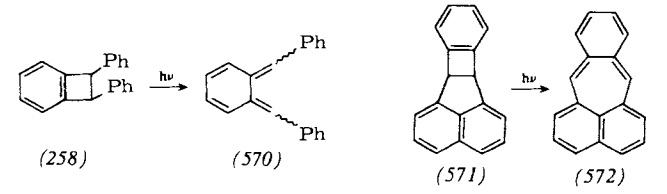
(564) *(419)* + *(565)*

(566) *(112)* *(266)* *(567)*

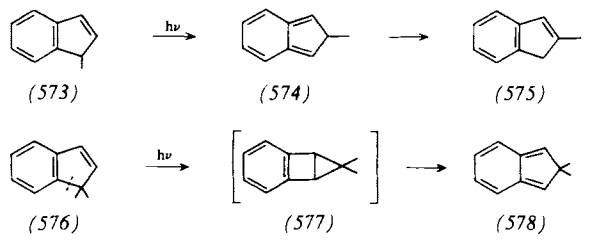
(568) and *(569)*

At 77 K numerous benzocyclobutenes undergo (frequently biphotonic) photolytic ring openings to form *o*-quinodimethane derivatives. Typical examples are the reactions of *(258)*[330] and *(571)*[331].

The photoisomerization of substituted indenes like *(573)* proceeds *via* isoindenes *(574)*[332]. It is not clear whether these involve β-cleavages. Thus, 1,1,3-triphenylindene undergoes 1,2-phenyl-migration to yield 1,2,3-triphenylindene[332b],



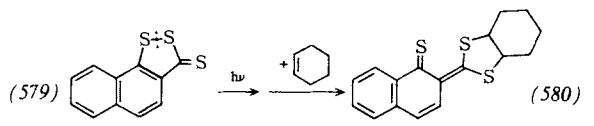
(258) *(570)* *(571)* *(572)*



(573) *(574)* *(575)*

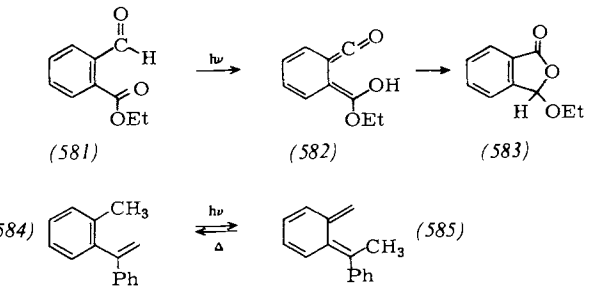
(576) *(577)* *(578)*

whereas *(576)* forms *(578)*[332] (*via* α-cleavage), which can be trapped with cyclohexene (cf. Section 3.1.7). Photolysis of *(579)* in cyclohexene gives *(580)*, which does not dimerize[333].



(579) *(580)*

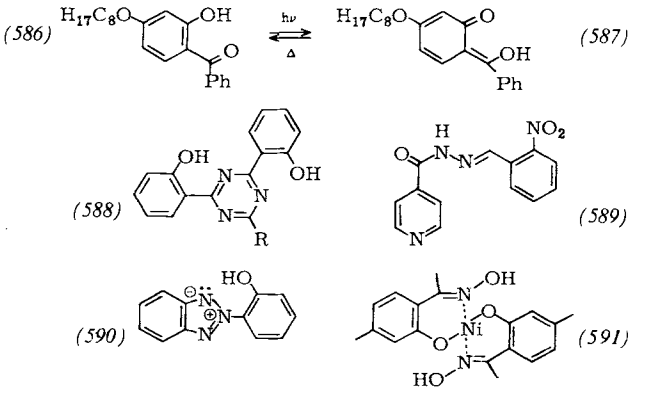
Hydrogen migrations between *o*-substituents are particularly versatile and productive for the generation of *o*-quinoid compounds. If secondary cyclizations, such as in the photolysis of *(581)*[334] are avoided, (see also benzocyclobutenols from *o*-alkylarylketones: p. 799 in [101]) one obtains photochromic systems (deuterium-labeled *(584)* undergoes H/D-exchange)[335].



(581) *(582)* *(583)*

(584) *(585)*

Useful hydrogen donors are methyl, formyl, hydroxyl, amino, and mercapto substituents. Hydrogen acceptors are C—C-double and triple bonds, carbonyl, imino, azo, cyano, nitro, nitroso (cf. Sections 3.2.13 and 3.2.14), sulfoxyl, and sulfonyl groups. The reactions can be used for light protection in the textile and cosmetics industries, because the photoproducts revert to the starting material with release of heat[336]. Among the technically applicable UV-stabilizers are *o*-hydroxybenzophenones such as *(586)*[336,337], *o*-hydroxyphenyltriazines *(588)*[336,338], and compounds such as



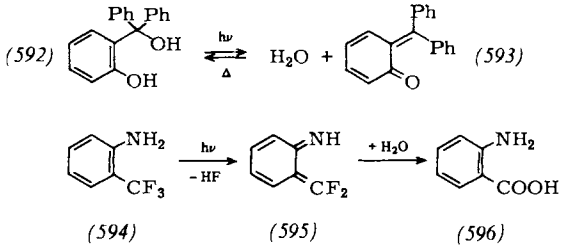
(586) *(587)*

(588) *(589)*

(590) *(591)*

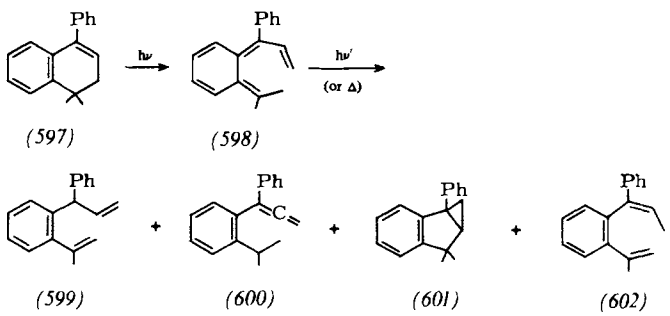
(589)[339], *(590)*[336,340], and *(591)*[336]. Trapping reactions of *o*-quinodimethanes generated by this technique (*e.g.* from *o*-benzylbenzophenone)[341] with dienophiles to produce tetrahydronaphthalenes are of preparative interest.

The reactions of *(592)*[342] and *(594)*[343] are useful 1,4-eliminations.

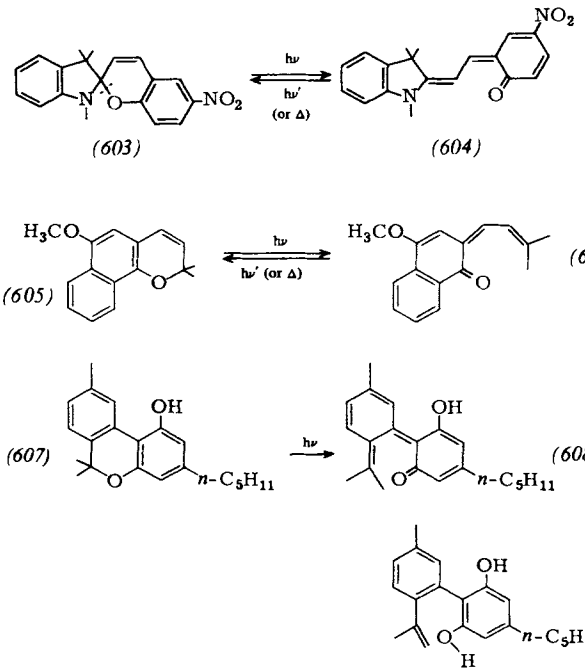


(592) *(593)* *(594)* *(595)* *(596)*

1,2-Dihydronaphthalene derivatives are an important source of conjugated *o*-quinodimethanes. At 92 K *(597)* photolyzes to give *(598)* (λ_{max} = 402 nm), which photochemically or thermally (above 143 K) forms *(599)*, *(600)*, *(601)*, and *(602)*[344]. This ring opening reaction occurs with 2*H*-1-benzopyrans[345], 2*H*-1-benzothiopyrans[346], 2*H*-1-benzothiopyran 1,1-dioxides[347], and 1,2-dihydroquinolines[348]. The photochromic spiropyrans [*e.g. (603)*][349] and spirothiopyrans[346] are particularly important. The photochemically formed merocyanine dyes [*e.g. (604)*] may be bleached with light of longer wavelength. This may be utilized for reusable photochromic films[350]. The ring opening of the plant constituent lapachenol *(605)* leads to the yellow *(606)*, which is quite stable at ambient temperature[345]. Whether or not this is used by plants for regulation purposes, has apparently not been widely investigated. Cannabinol *(607)* reacts photochemically to give cannabinodiol *(609)*[351]. Presumably an intermediate *(608)* occurs.



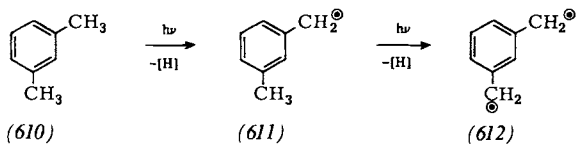
(597) *(598)* *(599)* *(600)* *(601)* *(602)*



(603) *(604)* *(605)* *(606)* *(607)* *(608)* *(609)*

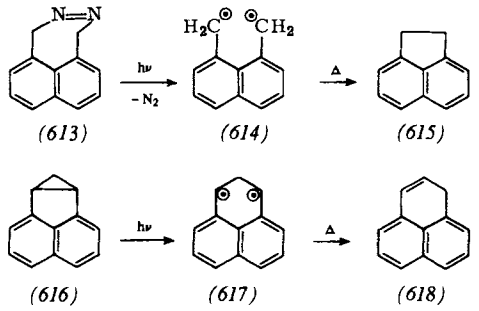
4.2.2. *m*-Quinodimethanes

β-cleavage upon irradiation of *m*-xylene *(610)* at 77 K yields the *m*-xylyl radical *(611)* and *m*-quinodimethane *(612)*, which absorbs and fluoresces at shorter wavelengths[319]. Similarly 1,8-naphthoquinodimethanes like *(614)*[352] and *(617)*[353] have to be generated by photochemical β-cleavage at 77 K (N_2-elimination or cyclopropane opening), because of facile thermal rearrangements. Accord-



(610) *(611)* *(612)*

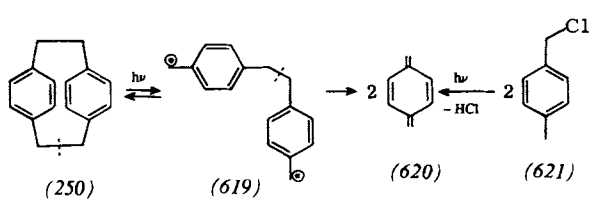
ing to latest ESR measurements *m*- and *peri*-quinodimethanes do not occur in the singlet[353] but in the triplet configuration[354].



(613) *(614)* *(615)* *(616)* *(617)* *(618)*

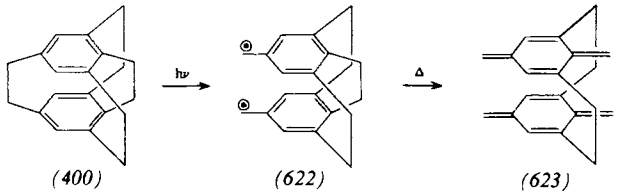
4.2.3. *p*-Quinodimethanes

[2.2]Paracyclophanes can undergo [6 + 6]-photocycloreversions if energy consuming ring motions are mechanically hindered by using highly viscous media[355]. Thus, on short wavelength irradiation (253.7 nm) of *(250)* at 77 K one obtains the UV and fluorescence spectra of the 1,4-diradical *(619)*, which upon thawing to about 90 K forms *(620)*[356]. Irradiation at 83 K immediately produces *(620)*[355], which is

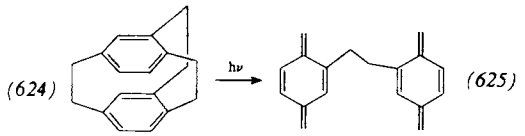


(250) *(619)* *(620)* *(621)*

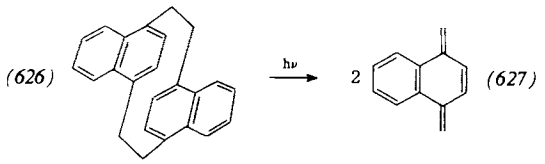
also obtained by HCl-elimination from *(621)*[222]. It is important for the diradical theory, that even *cisoid* representatives like *(622)*, which experience considerable interaction be-



(400) (622) (623)

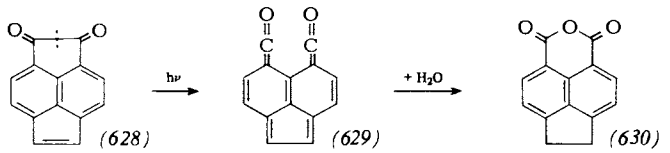


(624) (625)



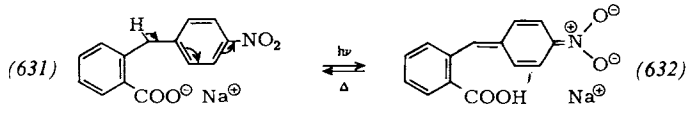
(626) (627)

tween the radical centers, are stable at 77 K or 83 K and form bis-*p*-quinodimethanes such as *(623)* at considerably higher temperatures[356]. Further representatives for [6 + 6]-photocycloreversions are found with *(624)*[222] and *(626)*[355] (at 83 K).

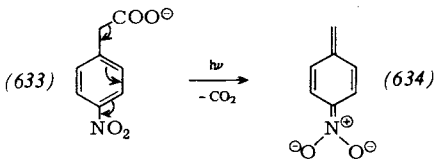


(628) (629) (630)

Only one β-cleavage is required for the formation of *(629)*[357].

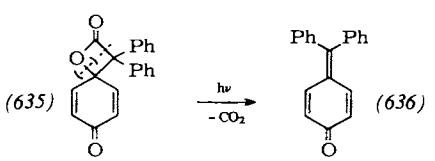


(631) (632)

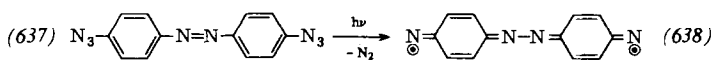


(633) (634)

The same is true for the (presumably heterolytic) reaction of *(631)* to give the yellow dye *(632)*[358] and for the decarboxylation of *(633)*[359]. The decarboxylation of *(635)*[360] and the photolysis of the diazide *(637)* to generate the triplet *(638)*[361] also belong here.



(635) (636)



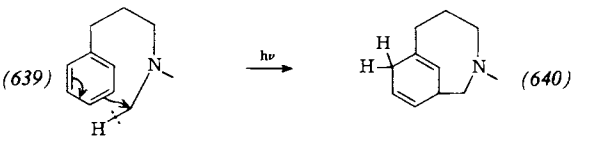
(637) (638)

4.3. Additions to the Benzene Ring

Electronically excited benzene rings are readily susceptible to additions. Particularly favorable conditions exist, if R—H or C—C bonds, carbenes, or double bonds in side chains or other benzene rings are geometrically well placed w.r.t. the absorbing chromophore.

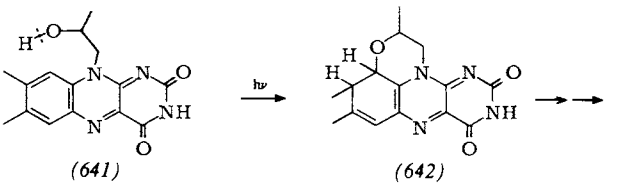
4.3.1. Addition of C—H and O—H Bonds

(639) photocyclizes by 1,4-C—H-addition at the positions 2 and 5 to yield *(640)*[362]. *(641)* undergoes O—H-addition

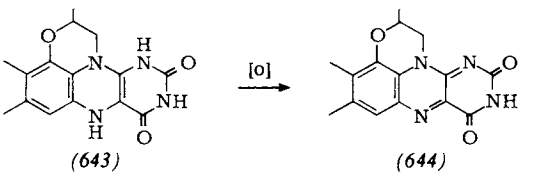


(639) (640)

(especially in presence of high concentrations of divalent anions: *e.g.* 2 M $SO_4^{2\ominus}$ presumably first giving *(642)*, which is stabilized by H-migration to form *(643)*. Subsequent oxidation (O_2) affords *(644)* (cf. the side product *(449)* from vitamin B_2)[363]. These reaction modes deserve a systematic study, as do also conceivable intramolecular additions of S—H and N—H bonds (the photocyclization of 3-[ω-(anilino)alkoxy]nitrobenzenes[364] involves the nitro group in the addition step; cf. also [309b]).



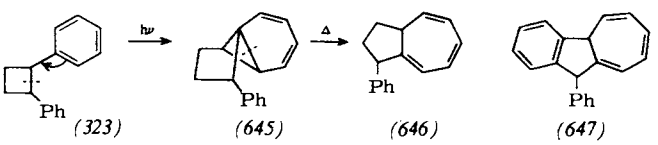
(641) (642)



(643) (644)

4.3.2. Addition of C—C Bonds

Absorption of light by 1,2-diphenylcyclobutanes leads to cross-addition of the β-bond to a phenyl group (also describable as a 1,2-shift). Thus, *(323)* reacts to give the norcaradiene derivative *(645)*, which in turn isomerizes to *(646)*[267] [basically a 1,2-H-shift in *(645)* might also produce *(491)*].

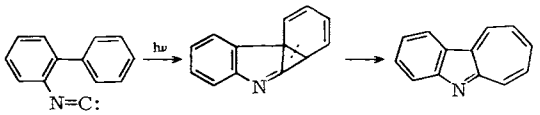


(323) (645) (646) (647)

The same reaction type applies to 1,2,3,4-tetraphenylcyclobutanes[365] and 2,3-diphenylcyclobutenes[366], as shown *e.g.* by the synthesis of *(647)*.

4.3.3. Addition of Carbenes

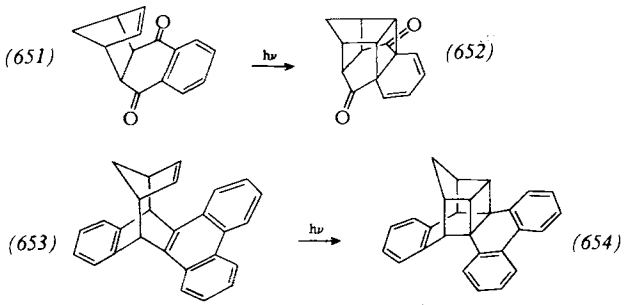
If carbene or nitrene fragments are generated (*e. g.* photochemically) at a favorable distance from the aromatic ring, thermal [2+0]- ([2+1]-) cycloadditions or C—H-insertions follow (cf. Sections 3.1.6 and 3.2.12). *o*-Biphenyl isocyanide *(648)* only undergoes a [2+0]-addition to the adjacent benzene ring upon irradiation. One finally obtains *(650)*[367].



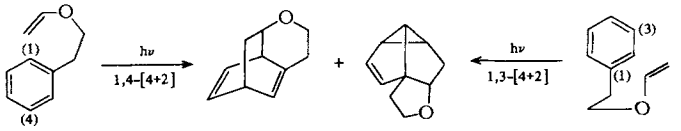
(648) *(649)* *(650)*

4.3.4. Addition of Double Bonds

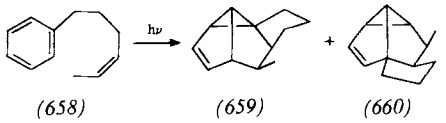
Suitably oriented double bonds in side chains may be added to electronically excited benzene rings. The reactions of *(651)* [80% *(652)*][368a], *(158)* [with subsequent rearrangement to give 75% *(160)*][101] (cf. corresponding syntheses of benzoazepines, benzoxepins[98a,b], and formation of 1-phenylindane from 1,3-diphenylpropene[101]), and *(653)* to *(654)*[368b] have to be classified as [2+2]-additions.



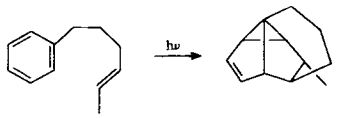
[4+2]-additions may proceed according to the 1,4-, and also to the 1,3-mode, as is the case with *(655)*. One obtains the polycycles *(656)* and *(657)* in the ratio 15:1[369]. *(658)* forms the isomers *(659)* and *(660)*, while *(661)* forms *(662)*[370]. *(663)* cyclizes (cross-addition of the [4+2]-type) to give *(664)* [and thence *(665)*][371], while in *(666)* the double bond adds to the diene system of the biphenyl moiety[372]. A [4+4]-addition has been observed with *(669)*. The highly



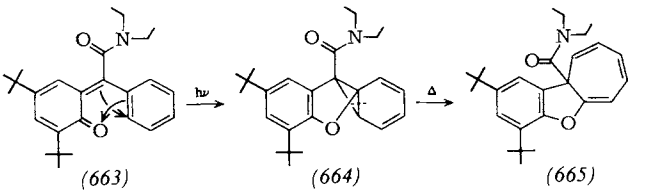
(655) *(656)* *(657)* *(655)*



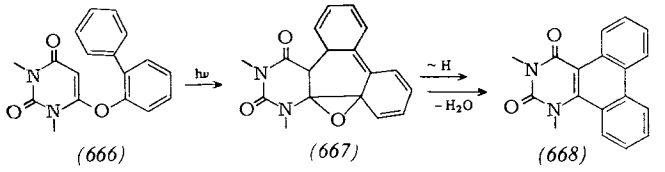
(658) *(659)* *(660)*



(661) *(662)*

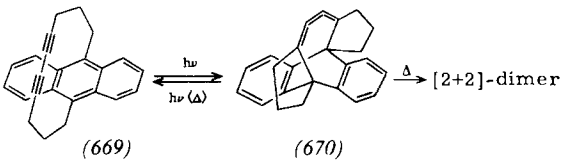


(663) *(664)* *(665)*



(666) *(667)* *(668)*

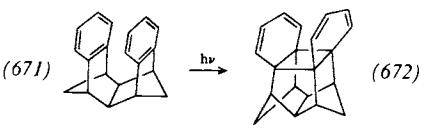
strained *(670)* could be spectroscopically detected at 77 K. It dimerizes at 293 K to a [4]radialene derivative[373].

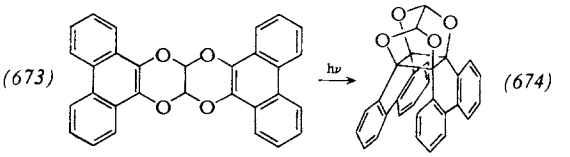


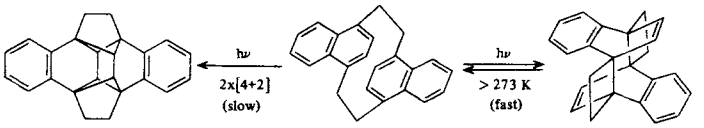
(669) *(670)*

4.3.5. Addition of Benzene Rings

Intramolecular cyclodimerizations of arenes, which are linked together through side chains, are numerous. Thus, [2+2]- [*(672)*[374], *(674)*[375]], [4+2]- [*(675)*[376]], and [4+4]-additions [*(676)*[377]] can be readily accomplished.

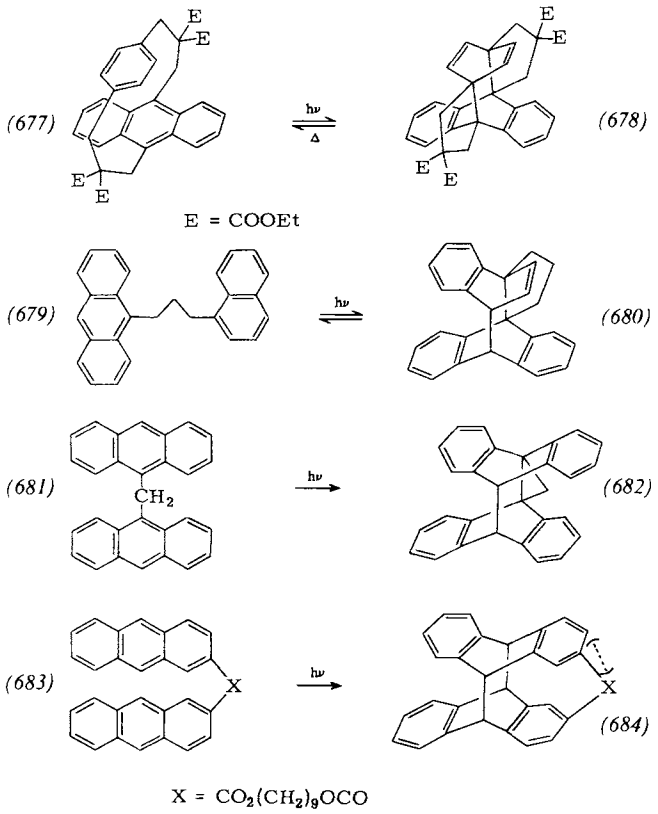






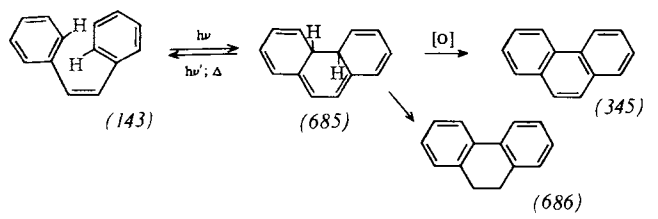
(675) *(626)* *(676)*

Intramolecular [4+4]-photocycloadditions involving anthracene moieties are particularly productive [*e. g.* *(376)*→*(375)*; *(378)*→*(377)*][98a]. *(376)*, which after light absorption must be designated as an excimer, does not react in one step but, according to kinetic analysis, *via* a (diradical) intermediate *(375)* ($\Phi_{forw.}=0.30$; $\Phi_{back}=0.6$; no fluorescence)[98a]. Hence, it is to be assumed, that (diradical) intermediates will be involved also in the further, less favorable examples. The suitability of such [4+4]-cycloadditions with exothermal reformation of the starting material for energy storage purposes has been investigated[218,378]. As typical representatives, the reactions of *(677)*[379], *(679)*[380], *(681)*[218], and *(683)* [to give both isomers *(684)*][381] may be mentioned.



4.4. Cyclizations of Conjugated Systems

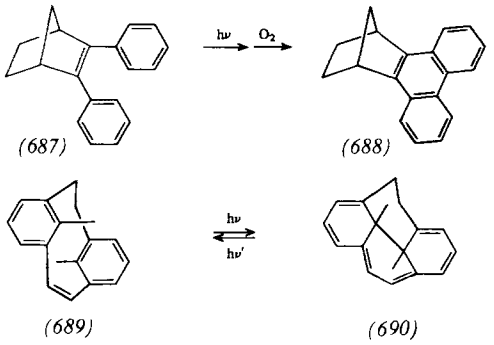
Cyclizations of the type hexatriene ⇌ cyclohexadiene[2] may be performed with *cis*-stilbene *(143)* (in photoequilibrium with *trans*-stilbene) and related conjugated aromatic compounds. Initially, polyenes of the *trans*-4a,4b-dihydrophenanthrene type *(685)* are formed, which usually are thermo- and photolabile[382] and which are irreversibly oxidized by *e.g.* I_2 or O_2 to give phenanthrene (derivatives) *(345)*[383].



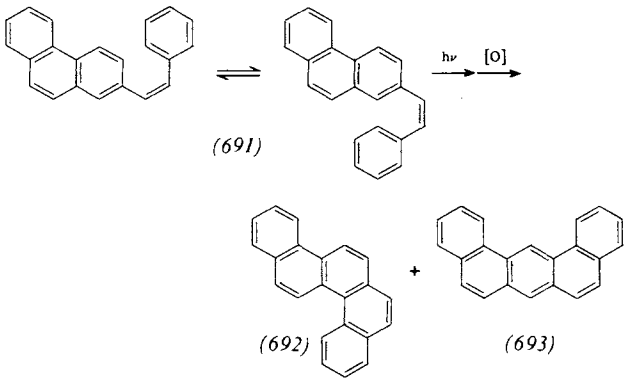
This phenanthrene synthesis fails only occasionally due to isomerization of the intermediate. 9,10-Dihydrophenanthrenes *(686)* are formed primarily under the influence of electron-withdrawing substituents X[150a,384]. Even analogously generated 4b-methyl-4a,4b-dihydrophenanthrenes are readily oxidized by oxygen to give phenanthrene derivatives[385]. The current number of applications also in pharmaceutical and natural product chemistry is impressive[386]. Only a few typical representatives shall be mentioned here. A compilation of the possibilities for structural variation would appear more important.

4.4.1. Six-Membered Ring Formation

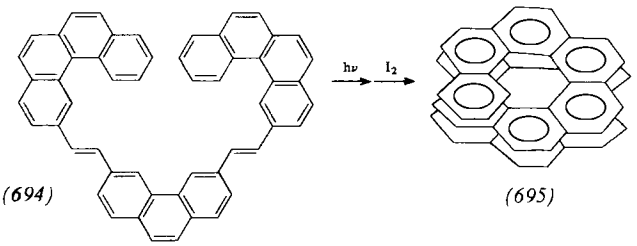
Oxidative cyclizations of fixed *cis*-stilbenes such as *(687)* ($\Phi = 0.43$)[98a] occur with particularly high quantum yields (cf. 1,2-bis(β-naphthyl)cyclopentene[387]). The same is true for the cyclization of *(689)* ($\Phi = 1.0$) to the photolabile ($\Phi' = 0.02$) dihydrophenanthrene derivative *(690)*[388].



Stilbenes whose central double bond is not part of a ring form homogeneous phenanthrenes, if substituted in the 2,2'-, 4,4'- or α,α'-position. Otherwise mixtures of isomers are obtained. Steric effects govern the preferred orientation for the ring closure[389]. Thus, 2-styrylphenanthrene *(691)* affords *(692)* and *(693)* in the ratio 99:1[390].

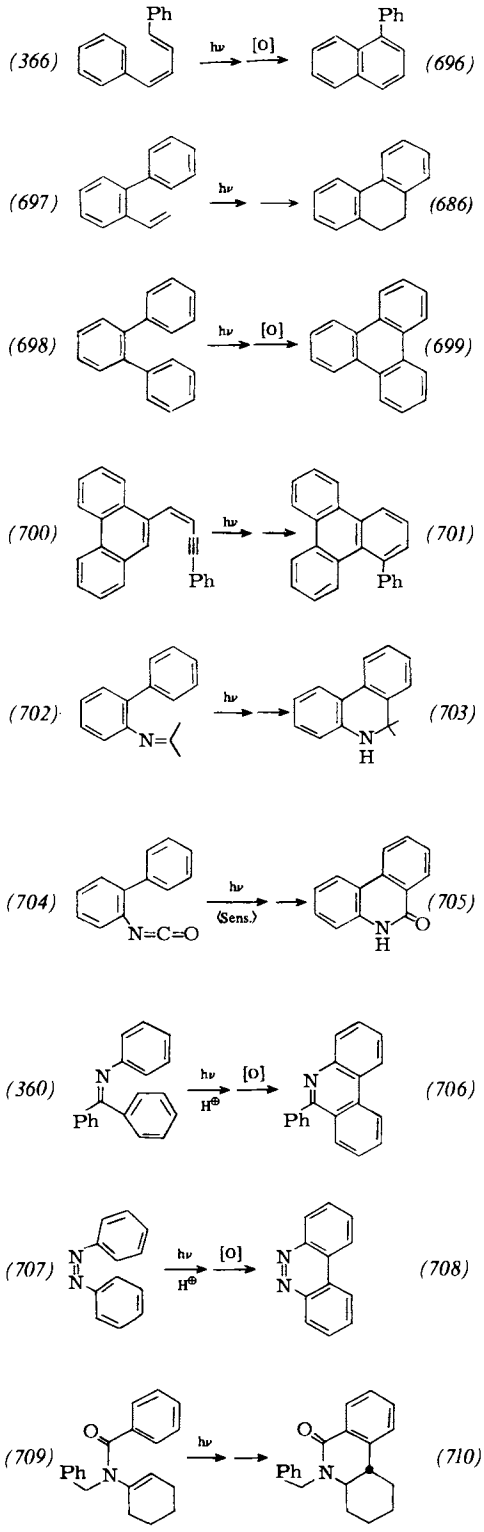


Numerous helicenes, which occur with right- and left-handed helices, have been synthesized, *e.g.* tridecahelicene *(695)* (52%)[391].



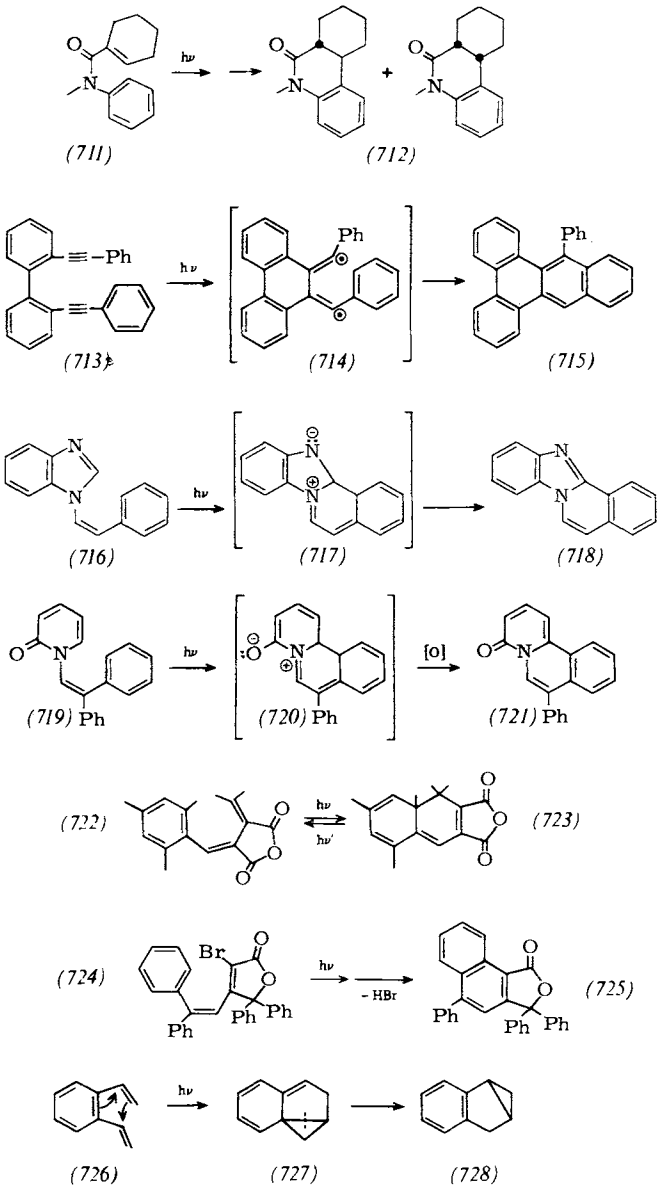
The stilbene unit may be widely varied by removal, addition, or displacement of aryl rings and by modification of the double bond without losing its ability for cyclization. This is shown by the syntheses of *(696)* (50%)[392], *(686)* (100%)[393], *(699)* (88%)[394], *(701)* (6%)[395], *(703)* (66%)[225], *(705)* (70%)[225], *(706)* (46%)[396], *(708)* (45%)[397], *(710)* (35%)[398], and *(712)* (59%)[399].

The special cases with *(i)* a more extended conjugated system *(713)*[400], *(716)*[401] and *(ii)* participation of conjugated acceptor double bonds [*e.g. (719)* (60%)][402], also illustrate the wide variability of this type of reaction.



The photochromic system *(722)/(723)*, which is thermally stable up to 160 °C, contains methyl groups which prevent interfering oxidation of the red *(723)*[403]. On cyclization of *(724)* the naphthalene derivative *(725)* (84%) is formed by HBr-elimination[404] (cf. Section 3.1.2).

As with aliphatic hexatrienes[2] there is the possibility for *o*-divinylbenzenes to undergo the bicyclo[3.1.0]hexene formation. *(726)* reacts to give *(727)*, which then rearranges to give *(728)*[405].



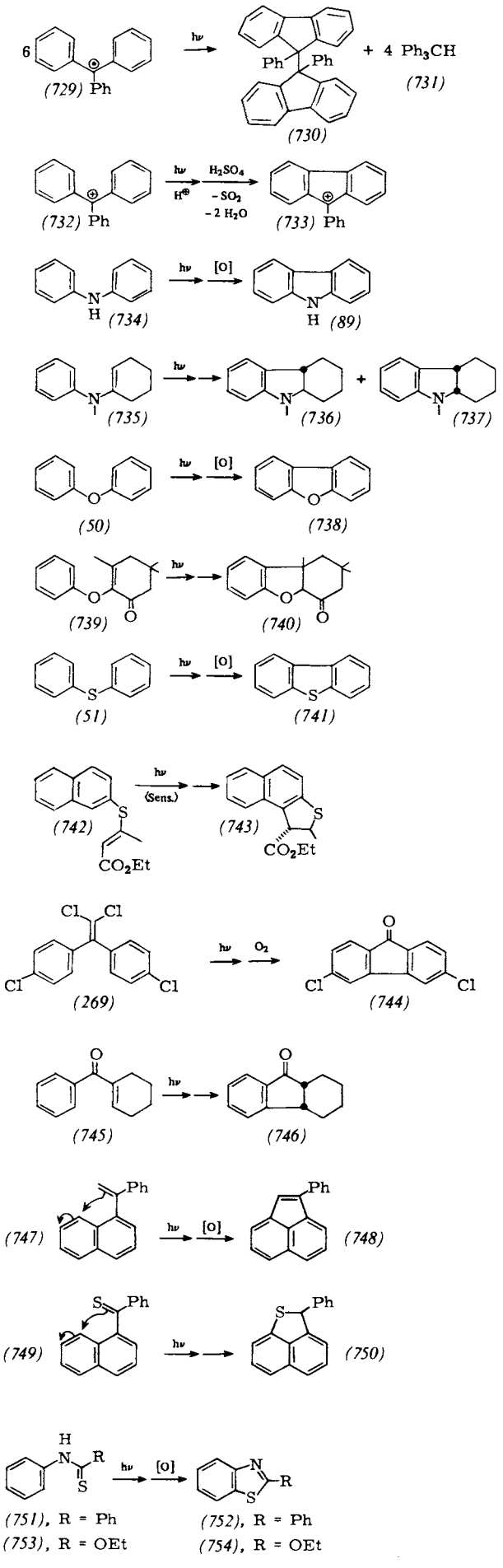
4.4.2. Formation of Five-Membered Rings

When the central double bond in stilbene *(143)* or 1-phenyl-1,3-butadiene is replaced by three-valent carbon [*(729)*[406]; *(732)*[407]], nitrogen [*(734)*[408]; *(735)*[409]], oxygen [*(50)*[410]; *(739)*[411]], sulfur [*(51)*[410]; *(742)*[412]] or by a cross-conjugated double bond [*(269)*][413] or a carbonyl group [*(745)*][186], one obtains photocyclization followed by oxidation or H-migration to give five-membered ring compounds. The yields are usually high and the synthetic possibilities have been widely exploited.

The photodegradation of the DDT-metabolite DDE *(269)*[413] is of considerable ecological importance.

Further cyclizations giving five-membered rings succeed by bridging the *peri*-positions of naphthalene in *(747)*[414] and *(749)*[415], even though this requires the intermediacy of a zwitterion or diradical. It is to be assumed, that these orientations are enforced by conformational effects, as the larger substituent (Ph) avoids proximity to the *peri*-position.

Further variations are possible. For example, *(751)*[416] and *(753)*[417] can be oxidatively cyclized.



5. Outlook

The long and lively development of arene photochemistry has produced a large variety of reaction types. Many of them are of preparative, industrial, biological, pharmaceutical, and ecological importance. No doubt other useful reaction types, which compete with those described in the present report, will be discovered. The classification of the available material chosen here may assist in locating still existing gaps, for it purposely does not concentrate on mechanistic aspects (*e.g.* singlet/triplet, high/low temperature, gas/condensed phase, adiabatic/diabatic) nor on the mere number of presently known examples but, by selection of characteristic examples, contributes to an understanding of the requirements for the most selective (high yield) course of specified reaction types. In conjunction with the exploitation of frequently clearly predictable orientation- and regio-selectivities in the available reaction types, further development in this sector promises new examples of the combined application of several reaction types for the realization of more sophisticated rearrangements [*e.g. (154)→(157); (158)→(160)*; cf. the combination of alkene photochemistry[2] ([2+2]-cycloaddition) and arene photochemistry (β-cleavage) in ref. [418]].

Not only the preparative aspects but also the kinetic/mechanistic aspects of aromatic photochemistry warrant further extensive investigation in order to disclose as many reactivity effects as possible and thereby enable useful extrapolations.

I am indebted to my colleagues who participated in the above studies performed by our research group: R. Dyllick-Brenzinger, H.-W. Grüter, E. Jostkleigrewe, K. Krieger, C. Küchel, K. Rösch, M. Stark, E. Teufel, and I. Zimmermann. Support for this work from the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: March 28, 1979 [A 300 IE]
supplemented: June 25, 1979
German version: Angew. Chem. *92*, 245 (1980)

[1] *D. Bryce-Smith, A. Gilbert*, Tetrahedron *32*, 1309—1326 (1976); *ibid. 33*, 2459—2490 (1977).
[2] Review of alkene photochemistry: *G. Kaupp*, Angew. Chem. *90*, 161 (1978); Angew. Chem. Int. Ed. Engl. *17*, 150 (1978).
[3] *T. Tanei*, Bull. Chem. Soc. Japan *41*, 833 (1968).
[4] Review: *A. C. Albrecht*, Acc. Chem. Res. *3*, 238 (1970).
[5] *R. Lesclaux, J. Joussot-Dubien*, C. R. Acad. Sci. *263*, 1177 (1966).
[6] *M. Ottolenghi*, Chem. Phys. Lett. *12*, 339 (1971); one-photon ionization of 3-aminoperylene in NaLS-micelles with green light (λ = 530 nm): *J. K. Thomas, P. L. Piciulo*, J. Am. Chem. Soc. *101*, 2502 (1979); *100*, 3239 (1978).
[7] *B. Badger, B. Brocklehurst*, Trans. Faraday Soc. *65*, 2576, 2583, 2588 (1969).
[8] *T. Shida, S. Iwata*, J. Am. Chem. Soc. *95*, 3473 (1973); *T. Shida, Y. Nosaka, T. Kato*, J. Phys. Chem. *82*, 695 (1978); in 2-methyltetrahydrofuran one also obtains anion radicals of arenes.
[9] *G. Kaupp, H. Littke*, unpublished results.
[10] For the structure of dimer radical cations see *F. Gerson, G. Kaupp, H. O. Nishiguchi*, Angew. Chem. *89*, 666 (1977); Angew. Chem. Int. Ed. Engl. *16*, 657 (1977).
[11] *D. F. Howarth, A. G. Sherwood*, Can. J. Chem. *51*, 1655 (1973).
[12] *E. A. Chandross, G. Smolinsky*, Tetrahedron Lett. *1960*, No. 13, 19; *E. Mathias, H. Heicklen*, Mol. Photochem. *4*, 483 (1972); *I. R. Fraser, L. H. Low, N. A. Weir*, Can. J. Chem. *53*, 1456 (1975).
[13] *I. K. Foote, M. H. Mallon, J. N. Pitts*, J. Am. Chem. Soc. *88*, 3698 (1966).

[14] *O. L. Chapman, K. Mattes, C. L. McIntosh, J. Pakansky, G. V. Calder, G. Orr*, J. Am. Chem. Soc. *95*, 6134 (1973).

[15] a) *H. R. Ward, J. S. Wishnok*, J. Am. Chem. Soc. *90*, 5353 (1968); b) *L. Kaplan, S. P. Walch, K. E. Wilzbach, ibid. 90*, 5646 (1968); c) different polyene spectra resulting from photolysis of benzene in degassed hexane have been reported: *K. H. Grellmann, W. Kühnle*, Tetrahedron Lett. *1969*, 1537.

[16] *E. E. van Tamelen, T. H. Whitesides*, J. Am. Chem. Soc. *93*, 6129 (1971); *D. W. Kurtz, H. Shechter*, Chem. Commun. *1966*, 689; *I. P. Ferris, R. W. Trimmer*, J. Org. Chem. *41*, 13 (1976).

[17] *E. J. Anderton, H. T. J. Chilton, G. Porter*, Proc. Chem. Soc. London *1960*, 352; toluene behaves in the same fashion at 83 K in ether/ethanol (1:1) (λ_{max} = 240 sh, 249 sh, 260 sh, 267, 271 sh, 277, 282 sh nm) and under these conditions no benzyl radical spectrum is obtained: *G. Kaupp, E. Jostkleigrewe*, unpublished.

[18] *D. Bryce-Smith, A. Gilbert*, Tetrahedron *32*, 1309 (1976).

[19] *D. Bryce-Smith, A. Gilbert, D. A. Robinson*, Angew. Chem. *83*, 803 (1971); Angew. Chem. Int. Ed. Engl. *10*, 745 (1971).

[20] *E. A. Arnett, J. M. Bollinger*, Tetrahedron Lett. *1964*, 3803.

[21] *S. L. Kammula, L. D. Iroff, M. Jones, J. W. van Straten, W. H. de Wolf, F. Bickelhaupt*, J. Am. Chem. Soc. *99*, 5815 (1977).

[22] *M. G. Barlow, R. N. Haszeldine, M. J. Kershaw*, Tetrahedron *31*, 1649 (1975); and references cited therein.

[23] *I. Haller*, J. Am. Chem. Soc. *88*, 2070 (1966); J. Chem. Phys. *47*, 1117 (1967); *G. Gamaggi, F. Gozzo, G. Cevidalli*, Chem. Commun. *1966*, 313.

[24] *G. P. Semeluk, R. D. S. Stevens*, Chem. Commun. *1970*, 1720.

[25] *W. L. Mandella, R. W. Franck*, J. Am. Chem. Soc. *95*, 971 (1973).

[26] *H. Hart, B. Ruge*, Tetrahedron Lett. *1977*, 3143.

[27] See *e.g. K. E. Wilzbach, D. J. Rausch*, J. Am. Chem. Soc. *92*, 2178 (1970); *R. D. Chambers, R. Middleton*, J. Chem. Soc. Chem. Commun. *1977*, 154; *Y. Ogata, K. Takagi*, J. Org. Chem. *43*, 944 (1978).

[28] *K. E. Wilzbach, J. S. Ritscher, L. Kaplan*, J. Am. Chem. Soc. *89*, 1031 (1967); *L. Kaplan, K. E. Wilzbach, ibid. 90*, 3291 (1968).

[29] *J. A. Berson, N. M. Hasty*, J. Am. Chem. Soc. *93*, 1549 (1971); *L. Kaplan, D. J. Rausch, K. E. Wilzbach, ibid. 94*, 8638 (1972).

[30] *M. G. Barlow, R. N. Haszeldine, R. Hubbard*, J. Chem. Soc. *C 1970*, 1232; related examples: *M. G. Barlow, R. N. Haszeldine, M. J. Kershaw*, Tetrahedron *31*, 1694 (1975).

[31] *R. West, M. Furue, V. N. M. Rao*, Tetrahedron Lett. *1973*, 911.

[32] *I. E. DenBesten, L. Kaplan, K. E. Wilzbach*, J. Am. Chem. Soc. *90*, 5868 (1968).

[33] *H. Dürr, H.-J. Ahr*, Tetrahedron Lett. *1977*, 1991.

[34] *K. E. Wilzbach, A. L. Harkness, L. Kaplan*, J. Am. Chem. Soc. *90*, 1116 (1968).

[35] *L. Kaplan, K. E. Wilzbach, W. G. Brown, S. S. Yang*, J. Am. Chem. Soc. *87*, 675 (1965).

[36] *K. E. Wilzbach, L. Kaplan*, J. Am. Chem. Soc. *87*, 4004 (1965).

[37] *K. E. Wilzbach, L. Kaplan*, J. Am. Chem. Soc. *86*, 2307 (1964).

[38] *E. E. van Tamelen, S. P. Pappas, K. L. Kirk*, J. Am. Chem. Soc. *93*, 6092 (1971).

[39] *M. G. Barlow, R. N. Haszeldine, M. J. Kershaw*, J. Chem. Soc. Perkin Trans. I *1974*, 1736.

[40] *R. R. Hentz, M. Burton*, J. Am. Chem. Soc. *73*, 532 (1951); *Y. Yamamoto, S. Takamuku, H. Sakurai*, Bull. Chem. Soc. Jpn. *44*, 574 (1971); *H. Mikuni, A. Takase, M. Murano, M. Takahashi, ibid. 46*, 1048 (1973).

[41] *J. F. Rabek, B. Ranby*, J. Polym. Sci. Polym. Chem. Ed. *12*, 273; 295 (1974); for promotion of photodegradation, sensitizers such as 1,4-naphthoquinone are added: *K. Nakamura, T. Yamada, K. Honda*, Chem. Lett. *1973*, 35.

[42] *R. F. Cozzens, W. B. Moniz, R. B. Fox*, J. Chem. Phys. *48*, 581 (1968).

[43] *T. Tanei*, Bull. Chem. Soc. Jpn. *40*, 2456 (1967); *T. Tanei, H. Hatano, ibid. 42*, 3369 (1969).

[44] *H. R. Ward, J. S. Wishnok*, J. Am. Chem. Soc. *90*, 5353 (1968); *90*, 1085 (1968), footnote 5a.

[45] *T. Sato, K. Nishiyama, S. Skimada, K. Hata*, Bull. Chem. Soc. Jpn. *44*, 2858 (1971); *K. Sorimachi, T. Morita, H. Shizuka, ibid. 47*, 987 (1974); it is also possible that C C-bonding precedes the dehydration.

[46] a) *J. Pacansky, G. P. Gardini, J. Bargon*, J. Am. Chem. Soc. *98*, 2665 (1976); b) decarboxylation of phenyl esters: *H. J. Hageman*, Tetrahedron *25*, 6015 (1969); c) decarboxylation of quinolinecarboxylic acids: *G. A. Epling, N. K. N. Ayengar, A. Lopes, U. C. Yoon*, J. Org. Chem. *43*, 2928 (1978).

[47] a) *H. J. Hageman, H. L. Louwerse, W. J. Mijs*, Tetrahedron *26*, 2045 (1970); b) in polymers (flash photolysis): *N. S. Allen, J. F. McKellar*, J. Appl. Polym. Sci. *21*, 1129 (1977).

[48] *W. Carruthers*, Nature *209*, 908 (1966).

[49] *N. Kharasch, A. I. A. Khodair*, Chem. Commun. *1967*, 98.

[50] Applications in copying procedures: *J. A. Sprung, W. A. Schmidt*, US-Pat. 2465760 (1949), General Aniline & Film Corp.; Chem. Abstr. *43*, 7846d (1949); *M. Kobayashi, S. Fujii, H. Minato*, Bull. Chem. Soc. Jpn. *45*, 2039 (1972); diazosulfides: *J. B. Zijp*, Mol. Photochem. *7*, 399 (1976).

[51] *L. R. C. Barclay, D. L. Carson, J. A. Gray, M. Prossman, P. B. Khazanie, J. R. Milton, C. E. Scott*, Can. J. Chem. *56*, 2665 (1978), and references cited therein; cf. dissociations and rearrangements of nitrobenzenes in [79].

[52] *L. Horner, W. Naumann*, Justus Liebigs Ann. Chem. *587*, 93 (1954); *N. A. Porter, M. O. Funk*, J. Chem. Soc. Chem. Commun. *1973*, 263.

[53] *K. C. Bass*, Organomet. Chem. Rev. *1*, 391 (1966); phenyl-Hg and -Pb compounds: *J. M. Blair, D. Bryce-Smith, B. W. Pengilly*, J. Chem. Soc. *1959*, 3174; phenyl-Pb, -Sn, -As compounds: *D. B. Peterson, D. A. G. Walmsley, R. J. Povinelli, M. Burton*, J. Phys. Chem. *71*, 4506 (1967); $SbPh_5$: *K.-w. Shen, W. E. McEwen, A. P. Wolf*, J. Am. Chem. Soc. *91*, 1283 (1969); aryl-Tl compounds: *E. C. Taylor, F. Kienzle, A. McKillop, ibid. 92*, 6088 (1970); $CdPh_2$: *G. A. Razuvaev, V. N. Pankratova*, J. Gen. Chem. USSR *36*, 1698 (Engl.); $BiPh_3$: *G. A. Razuvaev, G. G. Petukhov, V. A. Titov, O. N. Druzhkov, ibid. 35*, 479 (1965); *D. H. Hey, D. A. Shingleton, G. H. Williams*, J. Chem. Soc. *1963*, 5612; ESR from phenyl-Pb, -Sn, -Hg compounds: *E. G. Janzen, B. J. Blackburn*, J. Am. Chem. Soc. *91*, 4481 (1969); LiPh: *H. J. S. Winkler, H. Winkler*, J. Org. Chem. *32*, 1695 (1967); naphthyl-Sn compounds: *J. Nasielski, E. Hannecart*, J. Organomet. Chem. *63*, 233 (1973).

[54] *T. D. Walsh, R. C. Long*, J. Am. Chem. Soc. *89*, 3943 (1967); triphenylsulfonium salts: *J. W. Knapczyk, W. E. McEwen, ibid. 91*, 145 (1969).

[55] *L. Horner, J. Dörges*, Tetrahedron Lett. *1965*, 763, *M. L. Kaufman, C. E. Griffin, ibid. 1965*, 769; 773; *W. T. Cook, J. S. Vincent, I. Bernal, F. Ramirez*, J. Chem. Phys. *61*, 3479 (1974).

[56] *R. K. Sharma, N. Kharasch*, Angew. Chem. *80*, 69 (1968); Angew. Chem. Int. Ed. Engl. *7*, 36 (1968).

[57] *E.g.* photochemical iododecarboxylation: *P. A. Sheldon, J. K. Kochi*, Org. React. *19*, 279 (1972).

[58] *G. Oster, N.-L. Yang*, Chem. Rev. *68*, 125 (1968).

[59] Review on industrial applications: *M. Pape*, Pure Appl. Chem. *41*, 535 (1975).

[60] *N. Kharasch, L. Göthlich*, Angew. Chem. *74*, 651 (1962); Angew. Chem. Int. Ed. Engl. *1*, 459 (1962); examples from the pyridine series see *e.g. E. Ager, G. E. Chivers, H. Suschitzky*, J. Chem. Soc. Perkin Trans. I *1973*, 1125.

[61] *L. O. Ruzo, M. J. Zabik, R. D. Schnetz*, J. Am. Chem. Soc. *96*, 3809 (1974); recent study: *N. J. Bunce, Y. Kumar, L. Ravanal, S. Safe*, J. Chem. Soc. Perkin Trans. II *1978*, 880.

[62] *D. G. Crosby, A. S. Wong, J. R. Plimmer, E. A. Woolson*, Science *173*, 748 (1971).

[63] *W. A. Henderson, R. Lopresti, A. Zweig*, J. Am. Chem. Soc. *91*, 6049 (1969).

[64] *T. Sato, S. Shimada, K. Hata*, Bull. Chem. Soc. Jpn. *44*, 2484 (1971).

[65] *N. E. Brightwell, G. W. Griffin*, J. Chem. Soc. Chem. Commun. *1973*, 37.

[66] *D. H. Hey, G. H. Jones, M. J. Perkins*, J. Chem. Soc. Perkin Trans. I *1972*, 1150; recent examples: *S. Lalitha, S. Rajeswari, B. R. Pai, H. Suguna*, Indian J. Chem. *15B*, 180 (1977); correspondingly 2-iodoazobenzenes: *L. Bunati, P. Spagnolo, A. Tundo, G. Zanardi*, J. Chem. Soc. Chem. Commun. *1979*, 141.

[67] *S. M. Kupchan, H. C. Wormser*, J. Org. Chem. *30*, 3792 (1965); cephalotaxine: *S. M. Weinreb, M. F. Semmelhack*, Acc. Chem. Res. *8*, 158 (1975).

[68] *E.g. S. M. Kupchan, J. L. Moniot, R. M. Kanojia, J. B. O'Brien*, J. Org. Chem. *36*, 2413 (1971); *T. Iwakuma, H. Nakai, O. Yonemitsu, B. Witkop*, J. Am. Chem. Soc. *96*, 2564 (1974); *N. Yoneda, M. Tomie*, Jap. Kokai 7686, 486 (1976), Tanabe Seiyaku Co.; Chem. Abstr. *86*, 106413c (1977).

[69] *G. DeLuca, G. Martelli, P. Spaguolo, M. Tiecco*, J. Chem. Soc. *C 1970*, 2504.

[70] *G. R. Lenz*, J. Org. Chem. *39*, 2839 (1974); recent example: *H. Ida, S. Aoyagi, C. Kibayashi*, J. Chem. Soc. Perkin Trans. I *1977*, 120.

[71] *J. A. Elix, D. P. H. Murphy, M. V. Sargent*, Synth. Commun. *2*, 427 (1972).

[72] *R. G. F. Giles, M. V. Sargent*, J. Chem. Soc. Chem. Commun. *1974*, 215.

[73] *J. P. Ferris, R. F. Antonucci*, J. Am. Chem. Soc. *96*, 2010 (1974).

[74] *M. F. Semmelhack, T. M. Bargar*, J. Org. Chem. *42*, 1481 (1977).

[75] *T. Durst, J. C. Huang, N. K. Sharma, D. J. H. Smith*, Can. J. Chem. *56*, 512 (1978).

[76] *K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Coyne, G. S. Hammond*, J. Am. Chem. Soc. *87*, 4958 (1965).

[77] *B. K. Dunning, D. H. Shaw, H. O. Pritchard*, J. Phys. Chem. *75*, 580 (1971) this reaction resembles the mechanistically uninvestigated "photo-Curtius rearrangement" (of benzoylnitrene to give phenyl isocyanate): *Y. Hayashi, D. Swern*, J. Am. Chem. Soc. *95*, 5205 (1973).

[78] *E. S. Lewis, R. E. Holliday, L. D. Hartung*, J. Am. Chem. Soc. *91*, 430 (1969).

[79] *Y. Kitaura, T. Matsuura*, Tetrahedron *27*, 1583 (1971), and references cited therein; recent examples: *E. Lippert, J. Kelm*, Helv. Chim. Acta *61*, 279 (1978).

[80] *E. M. Burgess, L. McCullagh*, J. Am. Chem. Soc. *88*, 1580 (1966); correspondingly 2-*tert*-butylbenzazete (dimer): *C. W. Rees, R. C. Storr, P. J. Whittle*, Tetrahedron Lett. *1976*, 4647; review on N_2-eliminations: *N. Meier, K.-P. Zeller*, Angew. Chem. *89*, 876 (1977); Angew. Chem. Int. Ed. Engl. *16*, 835 (1977); benzothiirene intermediates: *R. C. White, J. Scoby, T. D. Roberts*, Tetrahedron Lett. *1979*, 2785.

[81] *R. W. Hoffmann, W. Sieber*, Justus Liebigs Ann. Chem. *703*, 96 (1967).

[82] *J. Meinwald, S. Knapp, S. K. Obendorf, R. E. Hughes*, J. Am. Chem. Soc. *98*, 6643 (1976).

[83] *N. Kharasch, R. K. Sharma,* Chem. Commun. *1967*, 492, and references cited therein.

[84] *G. Wittig, H. F. Ebel,* Justus Liebigs Ann. Chem. *650*, 20 (1961); cf. the photolysis of *o*-anisyllithium: *W. H. Glaze, A. C. Ranade,* J. Org. Chem. *36*, 3331 (1971).

[85] *G. Porter, J. I. Steinfeld,* J. Chem. Soc. *A 1968*, 877; *H. Suhr, A. Szabo,* Justus Liebigs Ann. Chem. *752*, 37 (1971).

[86] *R. W. Hoffmann, W. Sieber, G. Guhn,* Chem. Ber. *98*, 3470 (1965).

[87] *M. E. Schafer, R. S. Berry,* J. Am. Chem. Soc. *87*, 4497 (1965), and references cited therein.

[88] *O. L. Chapman, C.-C. Chang, J. Kolc, N. R. Rosenquist, H. Tomioka,* J. Am. Chem. Soc. *97*, 6586 (1975).

[89] *T. L. Gilchrist, F. J. Graveling, C. W. Rees,* Chem. Commun. *1968*, 821.

[90] *J. P. N. Brewer, I. F. Eckhard, H. Heaney, M. G. Johnson, B. A. Marples, T. J. Ward,* J. Chem. Soc. *C 1970*, 2569.

[91] *G. A. Razuvaev, G. G. Petukhov, R. F. Galiulina, N. N. Shabanova,* J. Gen. Chem. USSR (Engl.) *34*, 3863 (1964).

[92] *J. J. Eisch, J. L. Considine,* J. Am. Chem. Soc. *90*, 6257 (1968); cf. the formation of *(125)*, which proceeds primarily within the solvent cage, upon irradiation of phenyllithium in ether: *E. E. van Tamelen, J. I. Brauman, L. E. Ellis,* J. Am. Chem. Soc. *93*, 6141 (1971).

[93] *B. G. Ramsay, D. M. Anjo,* J. Am. Chem. Soc. *99*, 3182 (1977); *(125)* from lithium tetraphenylborate: *J. C. Doty, P. J. Grisdale, T. R. Evans, J. L. R. Williams,* J. Organomet. Chem. *32*, C 35 (1971), and references cited therein.

[94] *T. D. Walsh, D. R. Powers,* Tetrahedron Lett. *1970*, 3855; cf. the ecologically important formation of polychlorobiphenyls (PCBs) from DDT: *T. H. Maugh,* Science *180*, 578 (1974).

[95] *H. Iwamura, K. Yoshimura,* J. Am. Chem. Soc. *96*, 2652 (1974).

[96] *J. Ipaktschi,* Chem. Ber. *105*, 1989 (1972).

[97] *G. Wittig, G. Steinkoff,* Justus Liebigs Ann. Chem. *676*, 21 (1964).

[98] With benzo-7-azanorbornadienes the formation of aminofulvenes apparently does not proceed *via* the corresponding carbene- but instead *via* 1-indenealdehydeimine intermediates: a) *G. Kaupp,* Justus Liebigs Ann. Chem. *1973*, 844; b) *G. Kaupp, J. Perreten, R. Leute, H. Prinzbach,* Chem. Ber. *103*, 2288 (1970).

[99] *W. C. Schumann, D. B. Vashi, J. A. Ross, R. W. Binkley,* J. Org. Chem. *37*, 21 (1972).

[100] *R. W. Binkley, W. C. Schumann,* J. Am. Chem. Soc. *94*, 8743 (1972).

[101] Houben-Weyl-Müller: Methoden der Organischen Chemie, Thieme, Stuttgart, Vol. 4/5a, b; p. 413ff., 1975.

[102] *G. W. Griffin, A. F. Marcantonio, H. Kristinsson, R. C. Petterson, C. S. Irving,* Tetrahedron Lett. *1965*, 2951; recent examples: *A. B. B. Ferreira, K. Salisbury,* J. Chem. Soc. Perkin Trans. II *1978*, 995.

[103] *B. Halton, M. Kulig, M. A. Battiste, J. Perreten, D. M. Gibson, G. W. Griffin,* J. Am. Chem. Soc. *93*, 2327 (1971).

[104] *H. E. Zimmerman, G. E. Samuelson,* J. Am. Chem. Soc. *91*, 5307 (1969); 1-nitro-3,3-diphenylcyclohexene: *H. E. Zimmerman, L. C. Roberts, R. Arnold,* J. Org. Chem. *42*, 621 (1977); cf. the isomerization of 1,1,3- into 1,2,3-triphenylindene in Section 4.2.1.

[105] Substituent effects and diradical mechanism: [98a, b]; *L. A. Paquette, D. M. Cottrell, R. A. Snow,* J. Am. Chem. Soc. *99*, 3723 (1977); *R. G. Paddick, K. E. Richards, G. J. Wright,* Aust. J. Chem. *29*, 1005 (1976); *C. O. Bender, J. Wilson,* Helv. Chim. Acta, *59*, 1469 (1976); *M. Demuth, C. O. Bender, S. E. Braslavsky, H. Görner, U. Burger, W. Amrein, K. Schaffner, ibid. 62*, 847 (1979).

[106] *J. J. Tufariello, D. W. Rowe,* J. Org. Chem. *36*, 2057 (1971); recent examples: *R. C. Hahn, R. P. Johnson,* J. Am. Chem. Soc. *99*, 1508 (1977).

[107] *B. Hankinson, H. Heaney, A. P. Price, R. P. Sharma,* J. Chem. Soc. Perkin Trans. I *1973*, 2569.

[108] *R. C. Hahn, L. J. Rothman,* J. Am. Chem. Soc. *91*, 2409 (1969).

[109] *M. Elian, M. Banciu, L. Stănescu, E. Ciorănescu,* Rev. Roum. Chim. *21*, 89 (1976).

[110] *H. Hemetsberger, W. Holstein,* J. Chem. Soc. Chem. Commun. *1977*, 93.

[111] *B. Šket, M. Zupan,* J. Chem. Soc. Perkin Trans. I *1979*, 752.

[112] *T. Suzuki, T. Sonoda, S. Kabayashi, H. Taniguchi,* J. Chem. Soc. Chem. Commun. *1976*, 180; corresponding thermal rearrangements after metalation: *G. Köbrich,* Angew. Chem. *84*, 557 (1972); Angew. Chem. Int. Ed. Engl. *11*, 473 (1972).

[113] *D. Bryce-Smith, A. Gilbert, P. J. Twitchett,* J. Chem. Soc. Perkin Trans. I *1979*, 558; 2,3-dimethyl-2-butene reacts with *(177*)* predominantly in the sense of the substituting addition: *ibid. 1978*, 232.

[114] a) *R. Suter, T. Haefeli,* Chimia *13*, 230 (1959); b) *N. Baumann,* Chem. Rundsch. *26*, 1 (1973); c) to be distinguished from the photolysis of *o*-diazoquinones (derivatives of 6-diazo-2,4-cyclohexadien-1-ones) to give ketocarbenes → ketenes → carboxylic acids, which are soluble in alkaline media (Süs-process in offset-printing): [59]; *J. F. Willems, E. Brinckman, G. Delzenne, A. Poot,* Ber. Bunsenges. Phys. Chem. *80*, 1196 (1976); *O. Süs, J. Munder, H. Steppen,* Angew. Chem. *74*, 985 (1962).

[115] *T. Matsuura, K. Omura,* Synthesis *1974*, 173.

[116] *O. Süs,* Justus Liebigs Ann. Chem. *557*, 237 (1947); crystalline diazonium tetrafluoroborates may be converted to aryl fluorides in good yields: *R. C. Petterson, A. DiMaggio, A. L. Hebert, T. J. Haley, J. P. Mykytka, I. M. Sarkar,* J. Org. Chem. *36*, 631 (1971).

[117] *L. Horner, H. Stöhr,* Chem. Ber. *85*, 993 (1952); for the occurrence of radicals cf. *P. J. Zandstra, E. M. Evleth,* J. Am. Chem. Soc. *86*, 2664 (1964).

[118] *W. E. Lee, J. G. Calvert, E. W. Malmberg,* J. Am. Chem. Soc. *83*, 1928 (1961).

[119] *R. Huisgen, W. D. Zahler,* Chem. Ber. *96*, 736 (1963); utilization for natural product syntheses: *T. Kametani, M. Koizumi, K. Fukumoto,* J. Chem. Soc. *C 1971*, 1792.

[120] *G. Jackson, G. Porter,* Proc. R. Soc. *A 260*, 13 (1961); *C. O. Leiber, D. Rehm, A. Weller,* Ber. Bunsenges. Phys. Chem. *70*, 1086 (1966); Chem.-Ing.-Technik *39*, 563 (1967).

[121] a) *G. H. Brown, S. R. Adisesh, J. E. Taylor,* J. Phys. Chem. *66*, 2426 (1962); b) *J. G. Calvert, H. J. L. Rechen,* J. Am. Chem. Soc. *74*, 2101 (1952); c) formation of crystal violet: *C. I. Lin, P. Singh, E. F. Ullman, ibid. 98*, 6711 (1976); cyclic di- and triphenylcarbinols: *M. R. Feldman, N. G. Thame,* J. Org. Chem. *44*, 1863 (1979).

[122] *M. A. Ratcliff, J. K. Kochi,* J. Org. Chem. *36*, 3112 (1971).

[123] *A. L. Maycock, G. A. Berchtold,* J. Org. Chem. *35*, 2532 (1970).

[124] *S. J. Cristol, G. C. Schloemer,* J. Am. Chem. Soc. *94*, 5916 (1972).

[125] Review: *M. Pfau, M. Julliard,* Bull. Soc. Chim. Fr. *1977*, 785; correspondingly sulfates and phosphates: *R. O. DeJongh, E. Havinga,* Rec. Trav. Chim. Pays Bas *87*, 1327 (1968).

[126] *D. A. Jaeger,* J. Am. Chem. Soc. *97*, 902 (1975).

[127] *S. S. Hixson, R. E. Factor,* Tetrahedron Lett. *1975*, 3111; complicated substituent effects: *S. S. Hixson, J. A. Gere, L. A. Franke,* J. Am. Chem. Soc. *101*, 3677 (1979).

[128] *G. A. Epling, A. Lopes,* J. Am. Chem. Soc. *99*, 2700 (1977).

[129] *S. P. Singh, J. Kagan,* J. Org. Chem. *35*, 3839 (1970).

[130] *G. Porter, E. Strachan,* Trans. Faraday Soc. *54*, 1595 (1958).

[131] *W. Koch, T. Saido, Z. Yoshida,* Tetrahedron *28*, 3191 (1972).

[132] *P. M. Johnson, A. C. Albrecht,* The Chemistry of Ionization & Excitation, Conference on Radiation Chemistry Photochemistry, Newcastle-upon-Tyne, 1966/67, p. 91.

[133] a) *H.-G. Heine, W. Hartmann, D. R. Kory, J. G. Magyar, C. E. Hoyle, J. K. McVey, F. D. Lewis,* J. Org. Chem. *39*, 691 (1974), references cited therein. CIDNP-experiments with phenyl benzyl ketone: *G. L. Closs, R. J. Miller,* J. Am. Chem. Soc. *101*, 1639 (1979); b) benzylphenyl acetates: *R. S. Givens, B. Matuszewski, N. Levi, D. Leung,* J. Am. Chem. Soc. *99*, 1896 (1977); c) phenylacetic acid anhydride: *A. A. M. Roof, H. F. van Woerden, H. Cerfontain,* Tetrahedron *32*, 2967 (1976); d) phenylacetic acid: see [128]; e) 2-hydroxyindanones: *N. K. Hamer,* J. Chem. Soc. Perkin Trans. I *1979*, 1285.

[134] *E. Bergmann, S. Fujise,* Justus Liebigs Ann. Chem. *483*, 65 (1930); cf. *K. Maruyama, A. Osuka, Y. Naruta,* Bull. Chem. Soc. Japan *51*, 3047 (1978); the combinations of diphenylamine and benzophenone are more complicated: *C. Pac, K. Mizuno, T. Tosa, H. Sakurai,* J. Chem. Soc. Perkin Trans. I *1974*, 561.

[135] *E. P. Serebryakov, D. L. Rakhmankulov, V. N. Uzikova, S. S. Zlot-skii,* J. Org. Chem. USSR (Engl.) *10*, 668 (1974).

[136] *K. Fukui, K.-I. Senda, Y. Shigemitsu, Y. Odaira,* J. Org. Chem. *37*, 3176 (1972); corresponding reactions with phthalimides: *Y. Kanaoka, K. Sakai, R. Murata, Y. Hatanaka,* Heterocycles *3*, 719 (1975).

[137] *A. Schönberg, A. Mustafa,* J. Chem. Soc. *1944*, 67; cf. benzhydrylamines: *M. Fischer,* Chem. Ber. *101*, 731 (1968); cf. the rearrangement with decarbonylation of truxones: *R. A. E. Ceustermans, H. J. Martens, G. J. Hoornaert,* J. Org. Chem. *44*, 1388 (1979).

[138] *R. Breslow, J. Rothbard, F. Herman, M. L. Rodriguez,* J. Am. Chem. Soc. *100*, 1213 (1978).

[139] *R. W. Binkley,* J. Org. Chem. *35*, 2796 (1970); hydrazides: *R. S. Davidson, A. Lewis,* Tetrahedron Lett. *1973*, 4679.

[140] a) *W. H. Laarhoven, T. J. H. M. Cuppen, R. J. F. Nivard,* Rec. Trav. Chim. Pays-Bas *87*, 1415 (1968); b) dibenzylsulfone: footnote 7 in [133b]; cf. *R. F. Langler, Z. A. Marini, J. A. Pincock,* Can. J. Chem. *56*, 903 (1978); benzylsulfonamides as photolabile protecting groups for primary and secondary amines: *J. A. Pincock, A. Jurgens,* Tetrahedron Lett. *1979*, 1029.

[141] *J. R. Grunwell, N. A. Marron, S. I. Hanhan,* J. Org. Chem. *38*, 1559 (1973); benzoic acid thioanhydrides: *K. Beelitz, K. Praefcke,* Chem.-Ztg. *102*, 67 (1978); tellurol esters: *W. Lohner, J. Martens, K. Praefcke, H. Simon,* J. Organomet. Chem. *154*, 263 (1978).

[142] *M. M. da Silva Correa, W. A. Waters,* J. Chem. Soc. *C 1968*, 1874; diaryldisulfones: *M. Kobayashi, K. Tanaka, H. Minato,* Bull. Chem. Soc. Jpn. *45*, 2906 (1972); arylsulfenyl chlorides: *e.g. N. Kharasch, Z. S. Ariyan,* Chem. & Ind. (London) *1965*, 302.

[143] *J.-D. Cheng, H. J. Shine,* J. Org. Chem. *39*, 336 (1974); phenylazotriphenylsilane: *H. Watanabe, Y. Cho, Y. Ide, M. Matsumoto, Y. Nagai,* J. Organomet. Chem. *78*, C4 (1974); bisaryltriazenes: *M. Julliard, M. Scelles, A. Guillemonat, G. Vernin, J. Metzger,* Tetrahedron Lett. *1977*, 375.

[144] *L. Horner, W. Naumann,* Justus Liebigs Ann. Chem. *587*, 93 (1954); benzylazoalkanes (CIDNP): *J. G. Green, G. R. Dubay, N. A. Porter,* J. Am. Chem. Soc. *99*, 1264 (1977).

[145] *P. S. Engel,* J. Am. Chem. Soc. *92*, 6074 (1970); *W. K. Robbins, R. H. Eastman, ibid.* 6076; influence of detergents: *N. J. Turro, W. R. Cherry, ibid. 100*, 7431 (1978).

[146] Addition mechanisms: *P. H. Mazzochi, S. Minamikawa, P. Welson,* Tetrahedron Lett. *1978*, 4361.

[147] *H. M. Rauen, H. Waldmann,* Hoppe-Seylers Z. Physiol. Chem. *286*, 180 (1951); *S. Scheindlin, A. Lee, I. Griffith,* J. Am. Pharm. Assoc. Sci. Ed. *41*, 420 (1952).

[148] *R. V. Carr, B. Kim, J. K. McVey, N. C. Yang, W. Gerhartz, J. Michl,* Chem. Phys. Lett. *39*, 57 (1976).

[149] *J. Meinwald, G. E. Samuelson, M. Ikeda,* J. Am. Chem. Soc. *92*, 7604 (1970); cf. *A. Castellan, J. Kolc, J. Michl, ibid. 100*, 6687 (1978).

[150] a) *G. Kaupp, M. Stark,* Chem. Ber. *111*, 3608 (1978); b) review on *cis*-effect: *G. Kaupp, M. Stark, H. Fritz, ibid. 111*, 3624o(1978).

[151] *W. Abraham, K. Buck, D. Kreysig,* Tetrahedron Lett. *1978*, 4109.

[152] *R. C. Hahn, R. P. Johnson,* J. Am. Chem. Soc. *98*, 2600 (1976).

[153] *A. G. Schultz, R. H. Schlessinger,* Chem. Commun. *1970*, 1294; the photochemical ring enlargements of 3-oxo-2-phenyl-3*H*-indole 1-oxide to give 4-oxo-2-phenyl-4*H*-1,3-benzoxazine (93%) [*D. R. Eckroth, R. H. Squire,* Chem. Commun. *1969*, 312], of quinoline *N*-oxides to give 1,3-benzoxazepines, and related reactions [*G. G. Spence, E. C. Taylor, O. Buchardt,* Chem. Rev. *70*, 231 (1970)] proceed *via* oxiranes, which subsequently rearrange with β-cleavage.

[154] *H. Kristinsson, R. A. Mateer, G. W. Griffin,* Chem. Commun. *1966*, 415.

[155] *Y. Kanaoka, K. Koyama, J. L. Flippen, I. L. Karle, B. Witkop,* J. Am. Chem. Soc. *96*, 4719 (1974).

[156] *W. L. Dilling, N. B. Tefertiller, A. B. Mitchell,* Mol. Photochem. *5*, 371 (1973).

[157] *T. Durst, J. C. Huang, N. K. Sharma, D. J. H. Smith,* Can. J. Chem. *56*, 512 (1978).

[158] *G. W. Klumpp, A. V. Veefkind, W. L. deGraaf, F. Bickelhaupt,* Justus Liebigs Ann. Chem. *706*, 47 (1967); numerous further examples: *P. Scheiner,* Tetrahedron *24*, 2757 (1968); benzazete synthesis: *C. W. Rees, R. C. Storr, P. J. Whittle,* J. Chem. Soc. Chem. Commun. *1976*, 411.

[159] a) *C. G. Overberger, R. E. Zangaro, J.-P. Anselme,* J. Org. Chem. *31*, 2046 (1966); b) cyclopropenes from aryl-3*H*-pyrazoles: *H. Dürr, S. Fröhlich, B. Schley, H. Weisgerber,* J. Chem. Soc. Chem. Commun. *1977*, 843, and references cited therein; c) oxiranes from aryl-2,5-dihydro-1,3,4-oxadiazoles: *R. W. Hoffmann, H. J. Luthardt,* Chem. Ber. *101*, 3861 (1968).

[160] *M. L. Kaplan, E. A. Truesdale,* Tetrahedron Lett. *1976*, 3665.

[161] *K. D. Gundermann, K.-D. Röker,* Justus Liebigs Ann. Chem. *1976*, 140, numerous examples; references cited therein.

[162] *V. Boekelheide, I. D. Reingold, M. Tuttle,* J. Chem. Soc. Chem. Commun. *1973*, 406.

[163] *M. P. Cava, R. H. Schlessinger, J. P. van Meter,* J. Am. Chem. Soc. *86*, 3173 (1964).

[164] As well as formation of *trans-(257): G. Quinkert, J. Palmowski, H. P. Lorenz, W.-W. Wiersdorff, M. Finke,* Angew. Chem. *83*, 210 (1971); Angew. Chem. Int. Ed. Engl. *10*, 198 (1971); cf. *o*-phenylene oxalate: *S. P. Schmidt, G. B. Schuster,* J. Org. Chem. *43*, 1823 (1978).

[165] *K. Mislow, A. J. Gordon,* J. Am. Chem. Soc. *85*, 3521 (1963).

[166] *R. B. Boar, D. W. Hawkins, J. F. McGhie, D. H. R. Barton,* J. Chem. Soc. Perkin Trans. I *1977*, 515.

[167] *O. L. Chapman, C. L. McIntosh,* J. Am. Chem. Soc. *92*, 7001 (1970).

[168] *R. Göthe, C. A. Wachtmeister, B. Akermark, P. Baeckström, B. Jansson, S. Jensen,* Tetrahedron Lett. *1976*, 4501, and references cited therein; *L. L. Miller, R. S. Narang, G. D. Nordblom,* J. Org. Chem. *38*, 340 (1973).

[169] Cf. diphenyl disulfide eliminations: *A. Schönberg, T. Stolpp,* Justus Liebigs Ann. Chem. *483*, 90 (1930).

[170] *H. Junek, A. Hermetter, H. F. Colbrie, H. Aigner,* Tetrahedron Lett. *1973*, 2993.

[171] *B. W. Lardelli, H. J. Rosenkranz, H.-J. Hansen, H. Schmid, B. Blank, H. Fischer,* Helv. Chim. Acta *56*, 2628 (1973); indolines may be photooxidized to give 3*H*-indoles.

[172] *J. Reisch, D. Niemeyer,* Tetrahedron Lett. *1968*, 3247.

[173] *B. Monties,* C. R. Acad. Sci. *C 269*, 1069 (1969).

[174] *S. Y. Ho, R. A. Gorse, W. A. Noyes,* J. Phys. Chem. *77*, 2609 (1973).

[175] *S. J. Cristol, C. S. Ilenda,* J. Am. Chem. Soc. *97*, 5862 (1975); further examples: *D. R. Arnold, R. W. R. Humphreys, ibid. 101*, 2743; *A. Padwa, T. J. Blacklock, R. Loza,* Tetrahedron Lett. *1979*, 1671.

[176] *P. C. M. van Noort, H. Cerfontain,* Tetrahedron Lett. *1977*, 3899.

[177] *J. C. Moutet, G. Reverdy,* Bull. Soc. Chim. Fr. *1978*, II—442.

[178] *L. Ulrich, H.-J. Hansen, H. Schmid,* Helv. Chim. Acta *53*, 1323 (1970); cf. 1,4-H-shifts in 3,3-dimethyl-1,2-diarylcyclopropenes: *R. M. Morchat, D. R. Arnold,* J. Chem. Soc. Chem. Commun. *1978*, 743 and benzoate migrations in phenylhydroxymethylazirine derivatives: *A. Padwa, P. H. J. Carbsen, A. J. Tremper,* J. Am. Chem. Soc. *100*, 4481 (1978).

[179] *K. Fujita, T. Nakamura, K. Matsui, T. Shono,* Tetrahedron Lett. *1975*, 2441.

[180] *A. G. Anastassiou, R. B. Hammer,* J. Am. Chem. Soc. *94*, 303 (1972).

[181] *A. G. Schultz, R. H. Schlessinger,* Tetrahedron Lett. *1973*, 3605; cf. the analogous reaction of dihydrocoumarin to produce a ketene intermediate: *O. L. Chapman, C. L. McIntosh,* J. Am. Chem. Soc. *91*, 4309 (1969).

[182] *C. G. Overberger, J. W. Stoddard,* J. Am. Chem. Soc. *92*, 4922 (1970).

[183] *M. Comtet,* J. Am. Chem. Soc. *92*, 5308 (1970).

[184] *K. Salisbury,* J. Chem. Soc. *B 1971*, 931.

[185] *T. Hasegawa, M. Watabe, H. Aoyama, Y. Omote,* Tetrahedron *33*, 485 (1977); mechanism: *H. Aoyama, T. Hasegawa, M. Okazaki, Y. Omote,* J. Chem. Soc. Perkin Trans. I *1979*, 263.

[186] *A. B. Smith, W. C. Agosta,* J. Am. Chem. Soc. *95*, 1961 (1973); example from enone photochemistry: *M. Tada, T. Maeda, H. Saiki,* Bull. Chem. Soc. Jpn. *51*, 1516 (1978).

[187] *A. G. Schultz, C. D. DeBoer, W. G. Herkstroeter, R. H. Schlessinger,* J. Am. Chem. Soc. *92*, 6086 (1970).

[188] *Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, Y. Migita, Y. Kanaoka,* Tetrahedron Lett. *1973*, 4565; therein also six- and seven-membered ring analogues.

[189] *J. D. Coyle, G. L. Newport,* Synthesis *1979*, 381.

[190] *M. Terashima, K. Koyama, Y. Kanaoka,* Chem. Pharm. Bull. *26*, 630 (1978).

[191] *R. A. Finnegan, A. W. Hagen,* Tetrahedron Lett. *1963*, 365.

[192] Recent examples: *I. Ninomiya, T. Naito, T. Mori,* J. Chem. Soc. Perkin Trans. I *1973*, 505; references cited therein.

[193] *H. Gotthardt, R. Steinmetz, G. S. Hammond,* Chem. Commun. *1967*, 480; acyclic cases: *Y. Izawa, Y. Ogata,* J. Org. Chem. *35*, 3192 (1970); examples from steroid chemistry: *J. T. Pinkey, K. Schaffner,* Austr. J. Chem. *21*, 2265 (1968); therein also 1,5-migrations.

[194] *R. P. Gandhi, M. Singh, Y. P. Sachdeva, S. M. Mukherji,* Chem. & Ind. (London) *1973*, 382; cf. also the conversions of polyalkylbenzyl thiocyanates into -isothiocyanates: *H. Suzuki, M. Usuki, T. Hanafura,* Bull. Chem. Soc. Jpn. *52*, 836 (1979).

[195] *F. A. Carroll, G. S. Hammond,* Isr. J. Chem. *10*, 613 (1972).

[196] *K. Salisbury,* J. Am. Chem. Soc. *94*, 3707 (1972); recent examples: *H. E. Zimmerman, T. P. Cutler,* J. Org. Chem. *43*, 3283 (1978).

[197] *G. Ravier, C. Decker, A. M. Braun, J. Faure,* Tetrahedron Lett. *1977*, 1919.

[198] *G. S. Hammond, R. S. Cole,* J. Am. Chem. Soc. *87*, 3256 (1965).

[199] *G. Kaupp, M. Stark,* Chem. Ber. *110*, 3084 (1977).

[200] *N. K. Hamer,* J. Chem. Soc. Chem. Commun. *1977*, 239.

[201] *M. H. Delton, R. E. Gilman, D. J. Cram,* J. Am. Chem. Soc. *93*, 2329 (1971); *M. H. Delton, D. J. Cram, ibid. 92*, 7623 (1970).

[202] *S. S. Hixson, D. W. Garrett,* J. Am. Chem. Soc. *93*, 5294 (1971).

[203] *S. S. Hixson,* J. Chem. Soc. Chem. Commun. *1972*, 1170; further examples: *P. C. M. van Noort, H. Cerfontain,* J. Chem. Soc. Perkin Trans. II *1979*, 822; 1,2-diphenylcyclopropyl anions: *M. A. Fox,* J. Am. Chem. Soc. *101*, 4008 (1979).

[204] *D. R. Arnold, L. A. Karnischky,* J. Am. Chem. Soc. *92*, 1404 (1970); *A. M. Trozzolo, T. M. Leslie, A. S. Sarpotdar, R. D. Small, G. J. Ferrandi, T. DoMinh, R. L. Hartless,* Pure Appl. Chem. *51*, 261 (1979); unsymmetrically substituted representatives: *V. Markowski, R. Huisgen,* Tetrahedron Lett. *1976*, 4643.

[205] *H. Nozaki, S. Fujita, R. Noyori,* Tetrahedron *24*, 2193 (1968).

[206] *E.g. A. Padwa, M. Dharan, J. Smolanoff, S. I. Wetmore,* Pure Appl. Chem. *33*, 269 (1973); *A. Orahovats, H. Heimgartner, H. Schmid, W. Heinzelmann,* Helv. Chim. Acta *58*, 2662 (1975); therein reactions of *(337)* with *(336)* and dimerization of *(337)*; recent examples: *A. Padwa, P. H. J. Carlsen,* J. Org. Chem. *43*, 3757 (1978).

[207] *A. Padwa, S. I. Wetmore,* J. Am. Chem. Soc. *96*, 2414 (1974).

[208] *Y. Huseya, A. Chinone, M. Ohta,* Bull. Chem. Soc. Jpn. *45*, 3202 (1972) recent examples and trapping reactions: *H. Gotthardt, F. Reiter,* Chem. Ber. *112*, 1206, 1635 (1979); correspondingly benzonitrile sulfides: *A. Holm, J. J. Christiansen, C. Lohse,* J. Chem. Soc. Perkin Trans. I *1979*, 960.

[209] a) *G. Kaupp, E. Teufel,* J. Chem. Res. *1978* (M), 1301; *1978* (S), 100; b) *G. Kaupp,* Justus Liebigs Ann. Chem. *1977*, 254.

[210] *G. Kaupp,* Angew. Chem. *85*, 766 (1973); Angew. Chem. Int. Ed. Engl. *12*, 765 (1973); therein also *trans-(344)* → *cis-(344)* and reaction at 83 K.

[211] *M. A. Souto, J. Kolc, J. Michl,* J. Am. Chem. Soc. *100*, 6692 (1978).

[212] *G. Kaupp,* Angew. Chem. *86*, 741 (1974); Angew. Chem. Int. Ed. Engl. *13*, 817 (1974).

[213] a) *G. Kaupp, W. H. Laarhoven,* Tetrahedron Lett. *1976*, 941; b) *G. Kaupp, H.-W. Grüter,* unpublished.

[214] *G. Kaupp, M. Stark,* Angew. Chem. *90*, 803 (1978); Angew. Chem. Int. Ed. Engl. *17*, 758 (1978).

[215] *G. Kaupp, M. Stark,* unpublished.

[216] *M. Fischer,* Chem. Ber. *101*, 2669 (1968).

[217] *J. Rigaudy, C. Breliere, P. Seribe,* Tetrahedron Lett. *1978*, 687.

[218] *W. R. Bergmark, G. Jones, I. E. Reinhardt, A. M. Halpern,* J. Am. Chem. Soc. *100*, 6665 (1978); further examples: *A. Castellan, J.-M. Lacoste, H. Bouas-Laurent,* J. Chem. Soc. Perkin Trans. II *1979*, 411.

[219] "Sandwich-dimers" from *(374): E. A. Chandross,* J. Chem. Phys. *43*, 4175 (1965); cleavage of dianthracene anion at 77 K with red light: *T. Shida, S. Iwata,* J. Chem. Phys. *56*, 2858 (1972).

[220] *F. C. DeSchryver, L. Anand, G. Smets, J. Switten,* J. Polym. Sci. Polym. Lett. Ed. *9*, 777 (1971).

[221] *W. J. Tomlinson, E. A. Chandross, R. L. Fork, C. A. Pryde, A. A. Lamola,* Appl. Opt. *11*, 533 (1972).

[222] *G. Kaupp, E. Teufel,* unpublished.

[223] *T. W. Flechtner, L. J. Szabo, L. J. Koenig,* J. Org. Chem. *41*, 2038 (1976); recent example: *P. C. M. van Noort, H. Cerfontain,* J. Chem. Soc. Perkin Trans. II *1978*, 757.

[224] *H. E. Zimmerman, D. H. Pashovich,* J. Am. Chem. Soc. *86*, 2149 (1964); therein correspondingly *(393)* from dimesityldiazomethane; comparable

cleavages of *S,S*-diphenyl-*N*-acylsulfilimines: *N. Furukawa, M. Fukumura, T. Nishio, S. Oae,* Phosphorus and Sulfur *5*, 231 (1978).
[225] *J. S. Swenton, T. J. Ikeler, G. L. Smyser,* J. Org. Chem. *38*, 1157 (1973).
[226] *P. A. Lehman, R. S. Berry,* J. Am. Chem. Soc. *95*, 8614 (1973); further examples: *H. Wamhoff, C. von Waldow,* Chem. Ber. *110*, 1730 (1977).
[227] *H. Tomioka,* J. Am. Chem. Soc. *101*, 256 (1979), and references cited therein.
[228] *W. Gilb, K. Menke, H. Hopf,* Angew. Chem. *89*, 177 (1977); Angew. Chem. Int. Ed. Engl. *16*, 191 (1977); cf. the formation of *(614)* from 8-methyl-1-naphthylcarbene in [352b].
[229] *D. B. Denney, P. K. Klemchuk,* J. Am. Chem. Soc. *80*, 3289 (1958).
[230] *B. Nay, E. F. V. Scriven, H. Suschitzky, D. R. Thomas, S. E. Carroll,* Tetrahedron Lett. *1977*, 1811, references cited therein; with $KOCH_3 \rightarrow$ 3*H*-azepin-2-one: *E. F. V. Scriven, D. R. Thomas,* Chem. Ind. (London) *1978*, 385; anthracene derivatives: *J. Rigaudy, C. Igier, J. Barcelo,* Tetrahedron Lett. *1979*, 1837.
[230a] *O. L. Chapman, R. S. Sheridan, J.-P. Le Roux,* Rec. Trav. Chim. Pays-Bas *98*, 334 (1979); cf. *O. L. Chapman, R. S. Sheridan,* J. Am. Chem. Soc. *101*, 3690 (1979).
[231] *E. J. Moriconi, J. J. Murray,* J. Org. Chem. *29*, 3577 (1964).
[232] *O. Süs, H. Steppan, R. Dietrich,* Justus Liebigs Ann. Chem. *617*, 20 (1958); matrix-isolation of such ketenes at 8 K: *O. L. Chapman,* Pure Appl. Chem. *51*, 331 (1979).
[233] *G. W. Griffin,* Angew. Chem. *83*, 604 (1971); Angew. Chem. Int. Ed. Engl. *10*, 537 (1971).
[234] *D. B. Richardson,* J. Am. Chem. Soc. *87*, 2763 (1965).
[235] *N. M. Weinshenker, F. D. Greene,* J. Am. Chem. Soc. *90*, 506 (1968).
[236] *H. Kristinsson, G. W. Griffin,* J. Am. Chem. Soc. *88*, 1579 (1966); recent example: *C. E. Griffin, E. Kraas, H. Terasawa, G. W. Griffin, D. Lankin,* J. Heterocycl. Chem. *15*, 523 (1978); phenylnitrene from cyclohexane-spirophenyloxazirane: *E. Meyer, G. W. Griffin,* Angew. Chem. *79*, 648 (1967); Angew. Chem. Int. Ed. Engl. *6*, 634 (1967).
[237] *T. Sato, Y. Goto, T. Tohyama, S. Hayashi, K. Hata,* Bull. Chem. Soc. Jpn. *40*, 2975 (1967); *(345)* was isolated.
[238] *F. G. Bordwell, J. M. Williams, E. B. Hoyt, B. B. Jarvis,* J. Am. Chem. Soc. *90*, 429 (1968).
[239] *E. Voigt, H. Meier,* Chem. Ber. *108*, 3326 (1975).
[240] *H. Sakurai, Y. Kobayashi, Y. Nakadaira,* J. Organomet. Chem. *120*, C-1 (1976).
[241] *S. Nakazawa, T. Kiyosawa, K. Hirakawa, H. Kato,* J. Chem. Soc. Chem. Commun. *1974*, 621.
[242] *D. W. Jones, G. Kneen,* Chem. Commun. *1971*, 1356.
[243] *G. W. Griffin, A. Manmade,* J. Org. Chem. *37*, 2589 (1972).
[244] *J. Strating, B. Zwanenburg, A. Wagenaar, A. C. Udding,* Tetrahedron Lett. *1969*, 125; cf. isoindene from benzonorbornene-5,6-dione: *R. A. Russell, T. S. Lee, ibid. 1977*, 49.
[245] *A. Zweig, K. R. Huffman, J. B. Gallivan, M. K. Orloff, F. Halverson,* J. Am. Chem. Soc. *96*, 1449 (1974).
[246] *W. R. Bergmark,* J. Chem. Soc. Chem. Commun. *1978*, 61.
[247] *T. Kitamura, T. Imagawa, M. Kawanisi,* Tetrahedron *34*, 3451 (1978); therein alkali influence and 1,2-aryl migration; cf. cannabidiol: *A. Shani, R. Mechoulam,* Tetrahedron *27*, 601 (1971), and literature cited therein.
[248] *I. R. Bellobono, L. Zanderighi, S. Omarini, B. Marcandalli, C. Parini,* J. Chem. Soc. Perkin Trans. II *1975*, 1529.
[249] *P. Karrer, T. Köbner, H. Salomon, F. Zehender,* Helv. Chim. Acta *18*, 266 (1935).
[250] Recent review: *M. Gladys, W.-R. Knappe,* Chem. Ber. *107*, 3658 (1974); and references cited therein.
[251] *D. Döpp,* Top. Curr. Chem. *55*, 49 (1975); therein further examples and references; recent examples: *D. Döpp, E. Brugger,* Liebigs Ann. Chem. *1979*, 554; *o*-nitrosoanilines from *o*-nitromethylanilines: *R. E. McMahon,* Tetrahedron Lett. *1966*, 2307.
[252] *C. Engler, K. Dorant,* Ber. Dtsch. Chem. Ges. *28*, 2497 (1895).
[253] *K. Pfeiffer,* Justus Liebigs Ann. Chem. *411*, 72 (1916).
[254] *B. Amit, D. A. Ben-Efraim, A. Patchornik,* J. Chem. Soc. Perkin Trans. I *1976*, 57.
[255] *D. H. R. Barton, Y. L. Chow, A. Cox, G. W. Kirby,* J. Chem. Soc. *1965*, 3571.
[256] *U. Zehavi, B. Amit, A. Patchornik,* J. Org. Chem. *37*, 2281; 2285 (1972).
[257] Section 7a in *P. de Mayo, S. T. Reid,* Quart. Rev. *15*, 393 (1961); corresponding hydrazones: *Y. Maki, T. Furuta, M. Suzuki,* J. Chem. Soc. Perkin Trans. I *1979*, 553.
[258] *A. Patchornik, B. Amit, R. B. Woodward,* J. Am. Chem. Soc. *92*, 6333 (1970); 3-nitro-4-bromomethylbenzoylpolyethyleneglycol as a support for peptide syntheses in the liquid phase: *F. S. Tjoeng, W. Staines, S. St. Pierre, R. S. Hodges,* Biochim. Biophys. Acta *490*, 489 (1977).
[259] *P. A. Leermakers, G. F. Vesley,* J. Org. Chem. *30*, 539 (1965).
[260] *P. R. Bowers, K. A. McLauchlan, R. C. Sealy,* J. Chem. Soc. Perkin Trans. II *1976*, 915, and references cited therein; cf. the related photodissociation of the dianion of 2,5-diphenylhexane: *H. C. Wang, G. Levin, M. Szwarc,* J. Phys. Chem. *83*, 785 (1979).
[261] Protecting group: *J. C. Sheehan, K. Umezawa,* J. Org. Chem. *38*, 3771 (1973).
[262] p. 893 ff., 1173 ff. and 1271 ff. in [101].
[263] *C. I. Lin, P. Singh, E. F. Ullman,* J. Am. Chem. Soc. *98*, 7848 (1976).
[264] *J. I. G. Cadogan, A. G. Rowley,* J. Chem. Soc. Perkin Trans. I *1975*, 1069.
[265] p. 1281 ff. in [101]; polymer crosslinking: *G. A. Delzenne,* Encyclopedia of Polymer Science and Technology, Suppl. Vol. 1. Wiley, New York 1976, p. 401 ff.
[266] *E. W. Valyocsik, P. Sigal,* J. Org. Chem. *36*, 66 (1971); correspondingly triphenyl-α-lactam: *J. Sheehan, I. Lengyel, ibid. 28*, 3252 (1963).
[267] *M. Sauerbier,* Chem.-Ztg. *96*, 530 (1972); tetrahydronaphthalene derivatives are also formed upon sensitized dimerization of styrenes [*T. Asanuma, T. Gotoh, A. Tsuchida, M. Yamamoto, Y. Nishijima,* J. Chem. Soc. Chem. Commun. *1977*, 485] or upon γ-radiolysis of stilbene [*H. Güsten, D. Schulte-Frohlinde,* Justus Liebigs Ann. Chem. *1976*, 22].
[268] *A. Padwa, R. Loza, D. Getman,* Tetrahedron Lett. *1977*, 2847, and references cited therein; recent examples: *J. O. Stoffer, J. T. Bohanon,* J. Chem. Soc. Perkin Trans. II *1978*, 692.
[269] *A. Padwa, J. Smolanoff,* Tetrahedron Lett. *1974*, 33.
[270] *H. Dürr, L. Schrader, H. Seidl,* Chem. Ber. *104*, 391 (1971).
[271] *E. Clar,* Chem. Ber. *82*, 495 (1949).
[272] *D. A. Jaeger,* J. Am. Chem. Soc. *96*, 6216 (1974).
[273] *C. E. Kalmus, D. M. Hercules,* J. Am. Chem. Soc. *96*, 449 (1974).
[274] *D. Avnir, P. de Mayo, I. Ono,* J. Chem. Soc. Chem. Commun. *1978*, 1109.
[275] *E.g. J. W. Meyer, G. S. Hammond,* J. Am. Chem. Soc. *94*, 2219 (1972).
[276] Benzyl benzoate [*M. Afzat,* Chem. & Ind. (London) *1974*, 37] does not undergo a photo-Fries rearrangement: *C. Bak, K. Praefke,* Z. Naturforsch. *B 33*, 420 (1978).
[277] Review: *D. Bellüs,* Adv. Photochem. *8*, 109 (1971).
[278] *J. C. Anderson, C. B. Reese,* J. Chem. Soc. *1963*, 1781.
[279] *H. Kobsa,* J. Org. Chem. *27*, 2293 (1962).
[280] *E. A. Caress, I. E. Rosenberg,* J. Org. Chem. *36*, 769 (1971), and references cited therein.
[281] *D. J. Trecker, C. S. Foote, C. L. Osbom,* Chem. Commun. *1968*, 1034.
[282] *D. P. Kelly, J. T. Pinhey, R. D. G. Rigby,* Aust. J. Chem. *22*, 977 (1969).
[283] *R. W. Binkley, T. R. Oakes,* J. Org. Chem. *39*, 83 (1974).
[284] *D. Rungwerth, K. Schwetlick,* Z. Chem. *14*, 17 (1974).
[285] *J. J. Houser, M.-C. Chen,* Chem. Commun. *1970*, 1447; therein 1% *m*-product.
[286] *H.-R. Waespe, H. Heimgartner, H. Schmidt, H.-J. Hansen, H. Paul, H. Fischer,* Helv. Chim. Acta *61*, 401 (1978); therein solvent influence and by-products; dimethyl derivative in [195].
[287] *H.-J. Timpe, H.-J. Friedrich, R. Dietrich, J. Böckelmann, I. Friedel,* Z. Chem. *18*, 25 (1978), and references cited therein.
[288] *Y. Ohta, H. Shizuka, S. Sekiguchi, K. Matsui,* Bull. Chem. Soc. Jpn. *47*, 1209 (1974); therein also 41% *o*- and 27% *p*-rearrangement of 1-naphthyl acetate.
[289] *Y. Ogata, K. Takagi, S. Yamada,* J. Chem. Soc. Perkin Trans. II *1977*, 1629; *J. L. Stratenus, E. Havinga,* Rec. Trav. Chim. Pays-Bas *85*, 434 (1966).
[290] *H. Nozaki, T. Okada, R. Noyori, M. Kawanisi,* Tetrahedron *22*, 2177 (1966).
[291] *D. J. Carlsson, L. H. Gan, D. M. Wiles,* Can. J. Chem. *53*, 2337 (1975); displacement of *p*-Br and *p*-I: *H. Shizuka,* Bull. Chem. Soc. Jpn. *42*, 57 (1969).
[292] *H. J. Hageman,* Rec. Trav. Chim. Pays-Bas *91*, 1447 (1972).
[293] *D. Bellüs, K. Schaffner,* Helv. Chim. Acta *51*, 221 (1968).
[294] *H. J. Shine, J. D. Cheng,* J. Org. Chem. *36*, 2787 (1971).
[295] *D. V. Banthorpe, J. A. Thomas,* J. Chem. Soc. *1965*, 7158.
[296] *Y. Katsuhara, H. Maruyama, Y. Shigemitsu, Y. Odaira,* Tetrahedron Lett. *1973*, 1323; *N*-acylbenzoxazol-2(3*H*)-ones: *S. Ishida, Y. Hashida, H. Shizuka, K. Matsui,* Bull. Chem. Soc. Jpn. *52*, 1135 (1979).
[297] Review: *C. Bak, K. Praefcke,* Z. Naturforsch. *B 33*, 106 (1978), and references cited therein; correspondingly bis(2-acetylaminophenyl) disulfide [X = S, R = SAr]: *Y. Maki, M. Sako,* J. Chem. Soc. Perkin Trans. I *1979*, 1478.
[298] *M. Ishikawa, T. Fuchikami, M. Kumada,* J. Organomet. Chem. *118*, 139 (1976).
[299] *Y. Ogata, K. Takagi, Y. Izawa,* Tetrahedron *24*, 1617 (1968).
[300] *J. S. Bradshaw, R. D. Knudsen, E. L. Loveridge,* J. Org. Chem. *35*, 1219 (1970); cf. [46b].
[301] *W. M. Horspool, P. L. Pauson,* J. Chem. Soc. *1965*, 5162; cf. *A. Davis, J. H. Golden, ibid. B 1968*, 425.
[302] *L. J. Kricka, M. C. Lambert, A. Ledwith,* J. Chem. Soc. Chem. Commun. *1973*, 244; *M. R. Bendall, J. B. Bremner, J. F. W. Fay,* Aust. J. Chem. *25*, 2451 (1972).
[303] *M. Fischer,* Chem. Ber. *102*, 342 (1969); recent examples: *R. P. Gandhi, M. Singh, Y. P. Sachdeva, S. M. Mukherji,* Tetrahedron Lett. *1973*, 661.
[304] *M. Fischer,* Tetrahedron Lett. *1969*, 2281.
[305] *D. Bellüs, Z. Maňásek, P. Hrdlovič, P. Sláma,* J. Polym. Sci. *C 16*, 267 (1967).
[306] *D. R. Crump, R. W. Franck, R. Gruska, A. A. Ozorio, M. Pagnotta, G. J. Siuta, J. G. White,* J. Org. Chem. *42*, 105 (1977).
[307] *L. A. Neiman, V. S. Smolyakov, T. A. Saluvere,* J. Org. Chem. *USSR 9*, 2395 (1973) (Engl.); see also *R. H. Squire, H. H. Jaffé,* J. Am. Chem. Soc.

95, 8188 (1973); *N. J. Bunce, J.-P. Schoch, M. C. Zerner, ibid. 99*, 7986 (1977); thereby diazonium ions, which may be trapped: *D. Döpp, D. Müller*, Tetrahedron Lett. *1978*, 3863.

[308] *K. Matsui, M. Maeno, S. Suzuki*, Tetrahedron Lett. *1970*, 1467; further examples: *K. Mutai, S.-i. Kanno, K. Kobayashi, ibid. 1978*, 1273.

[309] a) *Y. Mukai, M. Suzuki, T. Hosokami, T. Furuta*, J. Chem. Soc. Perkin Trans. I *1974*, 1354; b) *H. D. Locksley, I. G. Murray*, J. Chem. Soc. *C 1970*, 392; c) *N. Yoneda, M. Tomie*, Jap. Kokai 7686486; Chem. Abstr. *86*, 106413 (1977). *H. J. Hageman, W. G. B. Hysmans*, Chem. Commun. *1969*, 837; *M. Ogata, H. Kano*, Tetrahedron *24*, 3725 (1968); *J. Reisch*, Dtsch. Apoth.-Ztg. *114*, 2028 (1974); *H. Sakuragi, S. Ishikawa, T. Nishimura, M. Yoshida, N. Inamoto, K. Tokumaru*, Bull. Chem. Soc. Jpn. *49*, 1949 (1976).

[310] *N. C. Yang, A. Shani, G. R. Lenz*, J. Am. Chem. Soc. *88*, 5369 (1966).

[311] *J. Martens, K. Praefcke, V. Schulze*, Synthesis *1976*, 532.

[312] *T. Iwakuma, H. Nakai, O. Yonemitsu, D. S. Jones, I. L. Karle, B. Witkop*, J. Am. Chem. Soc. *94*, 5136 (1972); *96*, 2570 (1974).

[313] *T. Hamada, Y. Okuno, M. Ohmori, T. Nishi, O. Yonemitsu*, Heterocycles *8*, Spec. Issue, 251 (1977).

[314] *M. Ikeda, K.-I. Hirao, Y. Okuno, N. Numao, O. Yonemitsu*, Tetrahedron *33*, 489 (1977); therein numerous further examples.

[315] *O. Yonemitsu, T. Tokuyama, M. Chaykovsky, B. Witkop*, J. Am. Chem. Soc. *90*, 776 (1968); *N*-chloroacetylnormescalin cyclosubstitutes correspondingly in the *o*-position w.r.t. the OH-group; *N*-chloroacetylmescalin cyclization: *O. Yonemitsu, H. Nakai, Y. Kanaoka, I. L. Karle, B. Witkop, ibid. 92*, 5691 (1970).

[316] *O. Yonemitsu, P. Cerutti, B. Witkop*, J. Am. Chem. Soc. *88*, 3941 (1966); vinylogous system: *N. G. Anderson, R. G. Lawton*, Tetrahedron Lett. *1977*, 1843; correspondingly *N*-chloroacetyl-2-(α-naphthyl)ethylamine: *C. M. Foltz*, J. Org. Chem. *36*, 24 (1971).

[317] *N. Numao, O. Yonemitsu*, Heterocycles *4*, 1095 (1976).

[318] *T. Hamada, M. Ohmori, O. Yonemitsu*, Tetrahedron Lett. *1977*, 1519.

[319] *E. Migirdicyan, J. Baudet*, J. Am. Chem. Soc. *97*, 7400 (1975), and references cited therein; formally related is the sensitized 1,4-elimination of methylamine from 9-aminomethylacridine to give acridine: *G. A. Digenis, V. H. Mikranian*, Tetrahedron Lett. *1972*, 2049.

[320] *C. R. Flynn, J. Michl*, J. Am. Chem. Soc. *96*, 3280 (1974); therein corresponding photolysis of sodium 2,3-dihydro-1*H*-isoindolyl-2-*p*-toluenesulfonimidate; corresponding photolysis of azoxy compounds: *W. R. Dolbier, K. Matsui, J. Michl, D. V. Horák, ibid. 99*, 3876 (1977); 2,3-naphthoquinodimethane: *M. Gisin, J. Wirz*, Helv. Chim. Acta *59*, 2273 (1976).

[321] *G. Quinkert, K. Opitz, W. W. Wiersdorff, J. Weinlich*, Tetrahedron Lett. *1963*, 1863; crystalline derivatives of *(552)*: [242]; recent examples: *K. K. de Fonseka, J. J. McCullough, A. J. Yarwood*, J. Am. Chem. Soc. *101*, 3277 (1979).

[322] *O. L. Chapman, C. L. McIntosh*, Chem. Commun. *1971*, 383; therein also photodesulfonation of 3*H*-1,2-benzoxathiol 2,2-dioxide to give *(555)*.

[323] *C. Jacqmin, J. Nasielski, G. Billy, M. Remy*, Tetrahedron Lett. *1973*, 3655; cf. monothio-*o*-benzoquinone ⇌ benzoxathiete: *P. de Mayo, A. C. Weedon, G. S. K. Wong*, J. Org. Chem. *44*, 1977 (1979).

[324] *M. Fischer*, Chem. Ber. *102*, 3495 (1969).

[325] *J. E. Starr, R. H. Eastman*, J. Org. Chem. *31*, 1393 (1966).

[326] *M. P. Cava, R. H. Schlessinger*, Tetrahedron *21*, 3065 (1965).

[327] *D. W. Jones, G. Kneen*, J. Chem. Soc. Perkin Trans. 1 *1975*, 175; cf. the formation of *(373)* from *(371)*, *(379)*, *(380)*, *(387)* in [209a] and the reaction of *(434)* in [244]; formation of *(373)* from 1,4-diphenylphthalazine *N*-oxide *via* diazoketone: *K. B. Tomer, N. Harrit, I. Rosenthal, O. Buchardt, P. L. Kumler, D. Creed*, J. Am. Chem. Soc. *95*, 7402 (1973).

[328] *W. M. Horspool*, J. Chem. Soc. *C 1971*, 400.

[329] *P. O. L. Mack, J. T. Pinkey*, J. Chem. Soc. Chem. Commun. *1972*, 451; corresponding rearrangements of 3-chromanones and isothiochroman-4-ones: *A. Padwa, A. Au, W. Owens*, J. Org. Chem. *43*, 303 (1978), and references cited therein; cf. the rearrangement of 1,2-benzisoxazolinones to give benzoxazolinones: *L. J. Darlage, T. H. Kinstle, C. L. McIntosh*, J. Org. Chem. *36*, 1088 (1971); cf. the decarboxylation of *(119)* to give *(112)* at 8 K: [14].

[330] *K. H. Grellmann, J. Palmowski, G. Quinkert*, Angew. Chem. *83*, 209 (1971); Angew. Chem. Int. Ed. Engl. *10*, 196 (1971); cf. *(113)*: [14]; *H. A. Staab, J. Ipaktschi*, Chem. Ber. *101*, 1457 (1968); the bisketene form of *(113)* rearranges at 20 °C to produce the cyclic carbene, which can also be trapped (cf. [88]); benzo- and naphthocyclobutanols: *M.-L. V. Villaume, C. Carré, P. Caubère*, J. Chem. Soc. Perkin Trans. I *1979*, 1395; α,ω-dinitrile also from 2,3-diazidonaphthalene: *A. Yabe*, Bull. Chem. Soc. Jpn. *51*, 789 (1979).

[331] *A. Castellan, J. Kolc, J. Michl*, J. Am. Chem. Soc. *100*, 6687 (1978), and references cited therein; therein benzo derivatives; naphthoquinodimethanes: *R. P. Steiner, R. D. Miller, H. J. Dewey, J. Michl, ibid. 101*, 1820 (1979).

[332] a) *D. Giacherio, H. A. Morrison*, J. Am. Chem. Soc. *100*, 7109 (1978), and references cited therein; b) *K. K. de Fonseka, C. Manning, J. J. McCullough, A. J. Yarwood, ibid. 99*, 8257 (1977).

[333] *R. Okazaki, K. Sunagawa, M. Kotera, N. Inamoto*, Tetrahedron Lett. *1976*, 3815.

[334] *R. J. Spangler, J. H. Kim, M. P. Cava*, J. Org. Chem. *42*, 1693 (1977); *(582)* may be trapped to produce Diels-Alder adducts.

[335] *F. Scully, H. Morrison*, J. Chem. Soc. Chem. Commun. *1973*, 529; *J. M. Hornback*, Tetrahedron Lett. *1976*, 3389.

[336] *H. J. Heller*, Eur. Polym. J. *5*, 105 (1969, Bratislava Supplement); modes of operation of *(591)*: *R. P. R. R. Ranaweera, G. Scott*, Eur. Polym. J. *12*, 825 (1976).

[337] *I. Hechenbleikner*, DOS 2061019 (1971), Cincinnati Milacron Chemical; Chem. Abstr. *76*, 4503h (1972); cf. *H. Brunetti, H. J. Peterli, H. Mueller, H. Heller*, DOS 1959399 (1970), Geigy; Chem. Abstr. *73*, 36150v (1970); protective surface grafting: *P. J. Birchill, D. M. Pinkerton*, J. Polym. Sci. Polym. Symp. *55*, 185 (1976).

[338] See *e.g. W. B. Harda, J. P. Milionis, F. G. Pinto*, Belg. Pat. 614726 (1962), American Cyanamid; Chem. Abstr. *59*, 8765h (1963); Neth. Appl. 302946 (1965), Geigy; Chem. Abstr. *64*, 12700e (1966).

[339] *R. M. Ellam, P. B. East, A. Kelly, R. M. Khan, J. B. Lee, D. C. Lindsey*, Chem. & Ind. (London) *1974*, 74.

[340] *H. Heller, J. Rody, E. Keller*, Swiss. Pat. 412336 (1966), Geigy; Chem. Abstr. *66*, 66231v (1967); cf. *W. O. Drake*, DOS 2019140 (1970), Phillips Petroleum; Chem. Abstr. *74*, 23515p (1971).

[341] *E.g. M. Pfau, S. Combrisson, J. E. Rowe, N. D. Heindel*, Tetrahedron *34*, 3459; 3469 (1978).

[342] *S. Hamai, M. Kokulun*, Bull. Chem. Soc. Jpn. *47*, 2085 (1974).

[343] *P. Seiler, J. Wirz*, Helv. Chim. Acta *55*, 2693 (1972).

[344] *U. Widmer, H. Heimgartner, H. Schmid*, Helv. Chim. Acta *58*, 2210 (1975), and references cited therein.

[345] *J. Kolc, R. S. Becker*, Photochem. Photobiol. *12*, 383 (1970).

[346] *R. S. Becker, J. Kolc*, J. Phys. Chem. *72*, 997 (1968).

[347] *C. R. Hall, D. J. H. Smith*, Tetrahedron Lett. *1974*, 3633.

[348] *M. Ikeda, S. Matsugashita, Y. Tamura*, J. Chem. Soc. Perkin Trans. I *1976*, 2587; *J. Kolc, R. S. Becker*, J. Chem. Soc. Perkin Trans. II *1972*, 17.

[349] *R. Exelby, G. Grinter*, Chem. Rev. *65*, 247 (1965); *C. Balny, R. Guglielmetti, M. Mossé, J. Metzger*, Photochem. Photobiol. *16*, 69 (1972); *I. Y. Kasparova, A. V. Zubkov, Y. E. Gerasimenko*, Kinet. Katal. *19*, 1435 (1978) (Russ.); Cheminform 7913-148 (1979); model chromophore: *P. Apprioce, J. Brelivet, C. Trebaul, R. Guglielmetti*, J. Photochem. *6*, 47 (1977).

[350] See [114b]; further technological applications: *A. Weissberger, E. C. Taylor:* The Chemistry of Heterocyclic Compounds Vol. 31, p. 81, Interscience, Wiley, New York, 1977.

[351] *A. Bowd, D. A. Swann, J. H. Turnbull*, J. Chem. Soc. Chem. Commun. *1975*, 797.

[352] a) *R. M. Pagni, M. N. Burnett, J. R. Dodd*, J. Am. Chem. Soc. *99*, 1972 (1977). b) *(614)* from (8-methyl-1-naphthyl)diazomethane: *M. S. Platz, ibid. 101*, 3398 (1979); cf. *ibid. 101*, 4425 (1979).

[353] *J. F. Muller, D. Muller, H. J. Dewey, J. Michl*, J. Am. Chem. Soc. *100*, 1629 (1978); cf. however [354].

[354] *M. Gisin, E. Rommel, J. Wirz, M. N. Burnett, R. M. Pagni*, J. Am. Chem. Soc. *101*, 2216 (1979); *J. Michl*, private communication (Feb. 6, 1979).

[355] *G. Kaupp*, Angew. Chem. *88*, 482 (1976); Angew. Chem. Int. Ed. Engl. *15*, 442 (1976).

[356] *G. Kaupp, E. Teufel, H. Hopf*, Angew. Chem. *91*, 232 (1979); Angew. Chem. Int. Ed. Engl. *18*, 215 (1979).

[357] *B. M. Trost*, J. Am. Chem. Soc. *91*, 918 (1969).

[358] *J. D. Margerum*, U. S. Pat. 3741628 (1973), Hughes Aircraft; Chem. Abstr. *80*, 9120y (1974).

[359] *J. D. Margerum, C. T. Petrusis*, J. Am. Chem. Soc. *91*, 2467 (1969).

[360] *J. L. Chitwood, P. G. Gott, J. J. Krutak, J. C. Martin*, J. Org. Chem. *36*, 2216 (1971).

[361] *B. Singh, J. S. Brinen*, J. Am. Chem. Soc. *93*, 540 (1971), and references cited therein; *p*-dialkylaminophenyl azide: *R. C. Baetzold, L. K. J. Tong, ibid. 93*, 1347, 1394 (1971).

[362] *D. Bryce-Smith, A. Gilbert, G. Klunklin*, J. Chem. Soc. Chem. Commun. *1973*, 330.

[363] *M. S. Jorns, P. Hemmerich*, Z. Naturforsch. *27b*, 1040 (1972).

[364] *K. Mutai, S.-i. Kanno, K. Kobayashi*, Chem. Lett. *1978*, 931.

[365] *M. Sauerbier*, Tetrahedron Lett. *1972*, 551.

[366] *M. Sauerbier*, Tetrahedron Lett. *1972*, 547.

[367] *J. DeJong, J. H. Boyer*, J. Org. Chem. *37*, 3571 (1972); therein also *in situ* generation of *(648)* by irradiation of *o*-biphenylisothiocyanate; recent examples (naphthalene derivatives): *J. H. Boyer, J. R. Patel*, J. Chem. Soc. Perkin Trans. I *1979*, 1070; therein also formation of benzophenanthridines.

[368] a) *A. S. Kushner*, Tetrahedron Lett. *1971*, 3275; b) *G. Kaupp, H.-W. Grüter*, Chem. Ber., in press.

[369] *A. Gilbert, G. Taylor*, J. Chem. Soc. Chem. Commun. *1978*, 129; further 1,3-photoadditions: *ibid. 1979*, 229.

[370] *W. Ferree, J. B. Grutzner, H. Morrison*, J. Am. Chem. Soc. *93*, 5502 (1971); recent example: *M. Pallmer, H. Morrison*, J. Chem. Soc. Chem. Commun. *1978*, 558.

[371] *W. Verboom, H. J. T. Bos*, Tetrahedron Lett. *1978*, 1229; cf. the photoreversible [6+2]-addition of 1,2,3,4,5-pentaphenylhepta-1,3,5-triene: *N. F. Woolsey, L. J. Radonovich, F. M. Saad, F. J. Koch*, J. Org. Chem. *44*, 2483 (1979).

[372] *R. D. Youssefyeh, M. Weisz*, J. Am. Chem. Soc. *96*, 315 (1974).

[373] *T. Hayashi, N. Mataga, T. Inoue, T. Kaneda, M. Irie, S. Misumi,* J. Am. Chem. Soc. *99*, 523 (1977).

[374] *H. Prinzbach, G. Sedelmeier, C. Krüger, R. Goddord, H.-D. Martin, R. Gleiter,* Angew. Chem. *90*, 297 (1978); Angew. Chem. Int. Ed. Engl. *17*, 271 (1978).

[375] *C. H. Krauch, S. Farid, D. Hess,* Chem. Ber. *99*, 1881 (1966).

[376] *H. Wasserman, P. M. Keehn,* J. Am. Chem. Soc. *91*, 2374 (1969).

[377] *G. Kaupp, I. Zimmermann,* Angew. Chem. *88*, 482 (1976); Angew. Chem. Int. Ed. Engl. *15*, 441 (1976).

[378] *A. W. H. Mau,* J. Chem. Soc. Perkin Trans. I *1978*, 603.

[379] *T. Shinmyozu, T. Inazu, T. Yoshino,* Chem. Lett. *1978*, 405.

[380] *E. A. Chandross, A. H. Schiebel,* J. Am. Chem. Soc. *95*, 611 (1973).

[381] *F. C. De Schryver, M. De Brackeleire, S. Toppert, M. van Schoor,* Tetrahedron Lett. *1973*, 1253.

[382] *T. Knittel, G. Fischer, E. Fischer,* J. Chem. Soc. Chem. Commun. *1972*, 84; *C. Goedicke, H. Stegemeyer,* Chem. Phys. Lett. *17*, 492 (1972).

[383] *E. g. H. H. A. Tinnemans, W. H. Laarhoven,* J. Am. Chem. Soc. *96*, 4611; 4617 (1974); from diethyl 4,4′-stilbenedicarboxylate one obtains 80% diethyl 3,6-phenanthrene and 20% diethyl 2,6-anthracenedicarboxylate; the mechanism of their formation appears to be still unknown: *S. D. Cohen, M. V. Mijovic, G. A. Newman,* Chem. Commun. *1968*, 722.

[384] *P. H. G. ophet Veld, W. H. Laarhoven,* J. Am. Chem. Soc. *99*, 7221 (1977), and references cited therein.

[385] *C. E. Ramey, V. Boekelheide,* J. Am. Chem. Soc. *92*, 3681 (1970); *E. V. Blackburn, C. E. Londer, C. J. Timmons,* J. Chem. Soc. *C 1970*, 163.

[386] Cf. p. 511ff.; 593ff.; 1116f.; 1134f. in [101]; dianthrone-(dianthrylidene-*etc.*) photochromism: *R. Korenstein, K. A. Muszkat, E. Fischer,* J. Chem. Soc. Perkin Trans. II *1977*, 564.

[387] *T. W. Knittel, M. Kaganowitch, G. Seger, E. Fischer,* Rec. Trav. Chim. Pays-Bas *98*, 114 (1979).

[388] *H. R. Blattmann, W. Schmidt,* Tetrahedron *26*, 5885 (1970).

[389] *T. Sato, T. Morita,* Bull. Chem. Soc. Jpn. *45*, 1548 (1972); theoretical approaches: *W. H. Laarhoven, T. J. H. M. Cuppen, R. J. F. Nivard,* Tetrahedron *26*, 1069 (1970).

[390] *D. D. Morgan, S. W. Horgan, M. Orchin,* Tetrahedron Lett. *1970*, 4347.

[391] *R. H. Martin, G. Morren, J. J. Schurter,* Tetrahedron Lett. *1969*, 3683; asymmetric syntheses of helicenes: *W. H. Laarhoven, T. J. H. M. Cuppen,* J. Chem. Soc. Perkin Trans. II *1978*, 315, and references cited therein; *J. M. Vanest, R. H. Martin,* Rec. Trav. Chim. Pays-Bas *98*, 113 (1979).

[392] *G. J. Fonken,* Chem. & Ind. (London) *1962*, 1327; recent example: *F. Toda, Y. Todo,* J. Chem. Soc. Chem. Commun. *1976*, 848; cf. benzophenoneazine: *J. Gorse, R. W. Binkley,* J. Org. Chem. *37*, 575 (1972); corresponding reaction of *N-tert*-butyl(arylvinyl)keteneimines: *E. Ege, K. Gilbert,* Chem. Ber. *112*, 3166 (1979).

[393] *S. W. Horgan, D. D. Morgan, M. Orchin,* J. Org. Chem. *38*, 3801 (1973); recent examples: *R. Koussini, R. Lapouyade, P. F. de Violet,* J. Am. Chem. Soc. *100*, 6679; 6683 (1978).

[394] *T. Sato, S. Shimada, K. Hata,* Bull. Chem. Soc. Jpn. *44*, 2484 (1971).

[395] *R. J. F. M. van Arendonk, W. H. Laarhoven, P. A. J. Prick,* Rec. Trav. Chim. Pays-Bas *97*, 197 (1978).

[396] *F. B. Mallory, C. S. Wood,* Tetrahedron Lett. *1965*, 2643.

[397] *G. M. Badger, C. P. Joshua, G. E. Lewis,* Aust. J. Chem. *18*, 1639 (1965); the photorearrangement of azoxybenzene to give 2-hydroxyazobenzene is mechanistically related: see Section 4.1.2.

[398] *I. Ninomiya, T. Naito, T. Kiguchi,* J. Chem. Soc. Perkin Trans. I *1973*, 2257; recent examples: *I. Ninomija, T. Kiguchi, O. Yamamoto, T. Naito, ibid. 1979*, 1723; protoberberines: *G. R. Lenz,* J. Org. Chem. *42*, 1117 (1977).

[399] *I. Ninomiya, S. Yamauchi, T. Kiguchi, A. Shinohara, T. Naito,* J. Chem. Soc. Perkin Trans. I *1974*, 1747; cf. *ibid. 1976*, 1861; oxidative phenanthridone synthesis from benzanilides: *B. S. Thyagarajan, N. Kharasch, H. B. Lewis, W. Wolf,* Chem. Commun. *1967*, 614; phenanthridone syntheses from fluorenone phenylimine *N*-oxides are completely different: *D. R. Eckroth, T. H. Kinstle, D. O. De La Cruz, J. K. Sparacino,* J. Org. Chem. *36*, 3619 (1971).

[400] *E. Müller, J. Heiss, M. Sauerbier, D. Streichfuss, R. Thomas,* Tetrahedron Lett. *1968*, 1195; in addition 12-phenylazuleno[1,2-a]acenaphthylene is formed (cf. Section 4.3.2); cf. *H. A. Staab, J. Ipaktschi,* Chem. Ber. *104*, 1170 (1971).

[401] *R. D. Youssefyeh, M. Weisz,* J. Am. Chem. Soc. *96*, 315 (1974).

[402] *P. S. Mariano, E. Krochmal, A. Leone,* J. Org. Chem. *42*, 1122 (1977), and references cited therein; further applications: *A. De Leenheer, J. E. Sinsheimer, J. H. Burckhalter,* J. Pharm. Sci. *61*, 273 (1972).

[403] *H. G. Heller, R. M. Megit,* J. Chem. Soc. Perkin Trans. I *1974*, 923; detection of an intermediate from 1,2-bis(diphenylmethylene)cyclobutane: *G. Kaupp, H.-W. Grüter,* Angew. Chem. *90*, 53 (1978); Angew. Chem. Int. Ed. Engl. *17*, 52 (1978).

[404] *F. Toda, E. Todo,* Bull. Chem. Soc. Jpn. *49*, 2503 (1976).

[405] *J. Meinwald, J. W. Young, E. J. Walsh, A. Courtin,* Pure Appl. Chem. *24*, 509 (1970); cf. *W. Sieber, R. Heimgartner, H.-J. Hansen, H. Schmid,* Helv. Chim. Acta *55*, 3005 (1972).

[406] *J. Schmidlin, A. G. Banús,* Ber. Dtsch. Chem. Ges. *45*, 1344 (1912).

[407] *E. D. Owen, D. M. Allen,* J. Chem. Soc. Perkin Trans. II *1973*, 95.

[408] *E. W. Förster, K. H. Grellmann,* J. Am. Chem. Soc. *94*, 634 (1972), and references cited therein.

[409] *O. L. Chapman, G. L. Eian, A. Bloom, J. Clardy,* J. Am. Chem. Soc. *93*, 2918 (1971); further examples: *A. G. Schultz, W. K. Hagmann,* J. Chem. Soc. Chem. Commun. *1976*, 726; flash photolysis: *K. H. Grellmann, W. Kuehnle, T. Wolff,* Z. Phys. Chem. (Frankfurt) *101*, 295 (1976).

[410] *K. P. Zeller, H. Petersen,* Synthesis *1975*, 532; *K. P. Zeller, S. Berger,* J. Chem. Soc. Perkin Trans. II *1977*, 54.

[411] *A. G. Schultz, R. D. Lucci, W. Y. Fu, M. H. Berger, J. Erhardt, W. K. Hagmann,* J. Am. Chem. Soc. *100*, 2150 (1978); therein also morphine, codeine.

[412] *A. G. Schultz, W. Y. Fu, R. D. Lucci, B. G. Kurr, K. M. Lo, M. Boxer,* J. Am. Chem. Soc. *100*, 2140 (1978); cf. *T. Wolff, ibid. 100*, 6157 (1978).

[413] *J. R. Plimmer, V. I. Klingebiel,* Chem. Commun. *1969*, 648.

[414] *R. Lapouyade, R. Koussini, H. Bouas-Laurent,* J. Am. Chem. Soc. *99*, 7374 (1977); cf. the related photoreaction of 3-benzyl-10-phenylisoalloxazine: *W. R. Knappe,* Chem. Ber. *107*, 1614 (1974).

[415] *R. Lapouyade, P. DeMayo,* Can. J. Chem. *50*, 4068 (1972).

[416] *K. H. Grellmann, E. Tauer,* Tetrahedron Lett. *1967*, 1909.

[417] *D. Bellüs, K. Schaffner,* Helv. Chim. Acta *51*, 221 (1968).

[418] *L. A. Paquette, T. G. Wallis, K. Hirotsu, J. Clardy,* J. Am. Chem. Soc. 2815 (1977).

Heterocyclic Analogues of Methylenecyclopropanes

By Gerrit L'abbé[*]

Heterocyclic three-membered rings with an exocyclic double bond merit special interest in view of their ring strain and their fascinating chemistry. Their synthesis, thermal decomposition, ring opening, and cycloaddition reactions will be discussed in this review. α-Lactams, alkylideneaziridines, diaziridinones, and diaziridinimines belong to the best known classes, but the chemistry of alkylideneoxiranes and -thiiranes, α-lactones, α-thiolactones, thiiranimines, and aziridinimines has also been studied to some extent. Two elusive three-membered rings are oxiranimines and thiaziridinimines; the former were postulated as reactive intermediates in the thermal decomposition of α-lactams, whereas the latter were trapped efficiently with double and triple bonds during thermolysis of *N*-sulfonyliminothiatriazolines. In spite of many attempts to prepare thione derivatives of the title compounds, they are still unknown. Included in this review are also some open-chain dipolar species which are isomeric with the heterocyclic three-membered rings.

1. Introduction

Oxiranes, thiiranes, and aziridines are strained three-membered heterocycles which are discussed in many textbooks. The introduction of an exocyclic double bond on the ring leads to compounds of type *(1)* which are characterized by even greater ring strain. Hence, special methods for their preparation and isolation have been devised. The best results



(1)

X, Y, Z: carbon or heteroatoms with or without substituents

were obtained by the use of bulky substituents (such as *tert*-butyl and adamantyl) whose van der Waals repulsion interactions are opposed to ring-strain forces. Furthermore, bulky groups shield the ring from nucleophilic attack, thus contributing to its kinetic stability and isolation under appropriate basic conditions.

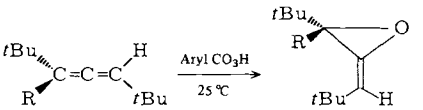
In this review, the synthetic methods leading to the title compounds are surveyed and their interesting chemistry (thermal decomposition, ring opening, cycloadditions) is discussed. Many cycloaddition reactions where the three-membered heterocycles have been postulated as reactive intermediates are also included for comparison. A characteristic feature of *(1)* is the IR stretching vibration of the exocyclic double bond at high wave number. In many cases this will be given with the structure.

2. Alkylidene Derivatives

The alkylidene derivatives of oxiranes, thiiranes, and aziridines have all been prepared and were previously generally referred to as allene derivatives in the literature: *i.e.* allene oxides, allene episulfides, and allenimines.

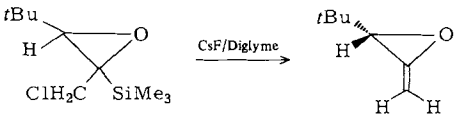
2.1. Alkylideneoxiranes

Two methods have led to the isolation of stable allene oxides: (i) epoxidation of *tert*-butyl-substituted allenes with *m*-chloroperbenzoic acid [eq. (a)][1] and (ii) β-elimination of a suitably substituted epoxysilane [eq. (b)][2]. Compounds *(2)*,



(a)

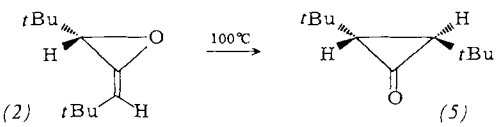
(2), R = H (IR: 1795 cm^{-1})
(3a), R = *t*Bu (IR: 1780 cm^{-1})
(3b), R = Me (IR: 1785 cm^{-1})



(4) (b)

(3), and *(4)* are the only stable alkylideneoxiranes so far known. In all the other cases studied, no allene oxides can be isolated, but products are formed which are derived therefrom[2,3]. Also, other potential routes have been explored but failed to produce stable alkylideneoxiranes[4], and a claimed synthesis of 2-isopropylidene-3,3-dimethyloxirane ("tetramethylallene oxide") was later retracted[5].

Alkylideneoxiranes are the valence isomers of the better known cyclopropanones[6], and, indeed, *(2)* is converted into *(5)* upon heating at 100 °C[1]. This isomerization, however, is

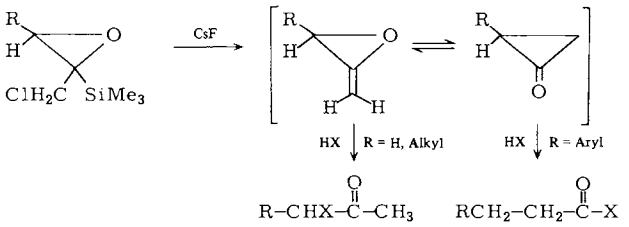


not observed for *(3)* and *(4)*[1,2]. According to *Chan, Ong, et al.*[2] the isomerization of alkylideneoxiranes into cyclopropanones proceeds *via* an oxallyl intermediate and occurs very readily with the elusive aryl substituted derivatives. This was demonstrated by generating the alkylideneoxiranes in the presence of protic nucleophiles (HX = alcohols, phenols,

[*] Prof. Dr. G. L'abbé
Department of Chemistry, University of Leuven
Celestijnenlaan 200F, B-3030 Heverlee (Belgium)

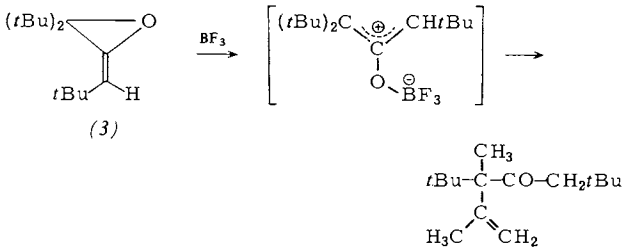
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0404-0276 $ 02.50/0

thiols, amines, *etc.*) which resulted in the formation of different products depending on whether R = alkyl or aryl (Scheme 1).



Scheme 1

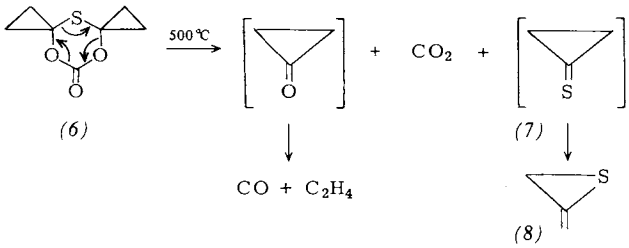
Ring-opening of the stable alkylideneoxirane *(4)* also occurs on nucleophilic attack at the formal sp^3C atom[2]. With boron trifluoride, compound *(3)* undergoes ring-opening isomerization *via* an oxyallyl cation as presumed intermediate[1].



(3)

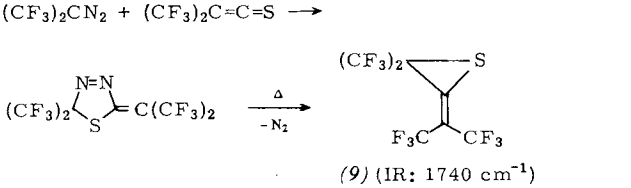
2.2. Alkylidenethiiranes

The parent compound of this series, methylenethiirane *(8)*, can be generated by flash thermolysis of the cyclic carbonate *(6)* at *ca.* 500 °C[7a]. Its formation is assumed to result from valence isomerization of the elusive cyclopropanethione *(7)*. Although *(8)* only remained stable in solution up to −30 °C, it could be reasonably well purified and characterized by spectral methods[7a]. Flash thermolysis of several other precursors also produced *(8)* which was identified by microwave spectroscopy[7b].



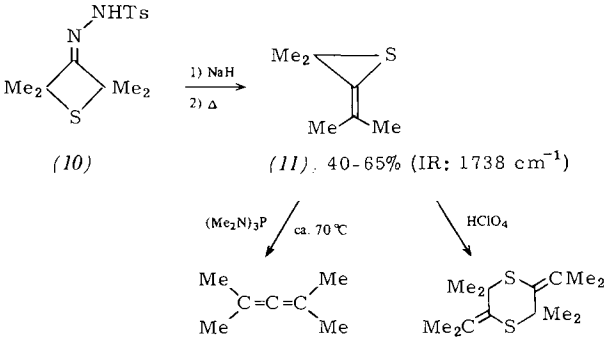
(6) *(7)* *(8)*

Only two substituted derivatives of *(8)* are known as stable substances. Thus, the fully trifluoromethylated derivative *(9)* is obtained from the reaction of the corresponding thioketene with hexafluoro-2-diazopropane, followed by thermolysis of the resulting thiadiazoline[8]. The chemistry of *(9)* is unexplored!



(9) (IR: 1740 cm^{-1})

2-Isopropylidene-1,1-dimethylthiirane ("tetramethylallene episulfide") *(11)* results from thermolysis of the sodium salt of *(10)* at 150 °C *in vacuo*[9]. It undergoes desulfurization upon heating with hexamethylphosphoramide and is dimerized to a 1,4-dithiane under acidic conditions (Scheme 2).

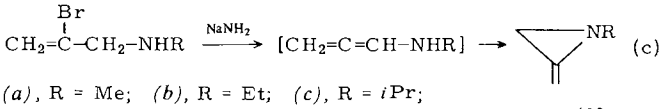


(10) *(11)*, 40-65% (IR: 1738 cm^{-1})

Scheme 2

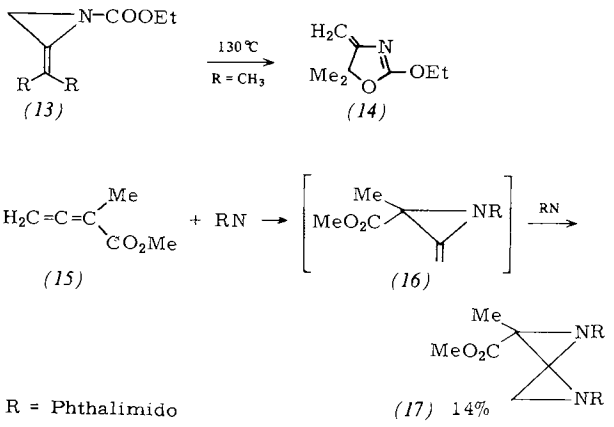
2.3. Alkylideneaziridines

N-Alkyl-substituted alkylideneaziridines *(12)* are readily prepared by dehydrohalogenation of *N*-(2-bromoallyl)alkylamines with sodium amide in liquid ammonia [eq. (c)]; *N*-alkylpropargylamines are formed as side products[10]. This reaction was carried out as long ago as 1951[11], but the correct structure of the reaction products was only established several years later[12,13]. A subsequent mechanistic study revealed the intermediacy of an allenic amine [eq. (c)][14]. Alkyl-substituted derivatives are also prepared by this method[15,16]. The IR stretching frequency of *(12)*, R = Et, lies at 1770 cm^{-1}.



(a), R = Me; *(b)*, R = Et; *(c)*, R = *i*Pr;
(d), R = *t*Bu; *(e)*, R = *c*-C_3H_5; *(f)*, R = $PhCH_2CH_2$ *(12)*

In analogy with the epoxidation reaction mentioned in eq. (a), the addition of nitrenes to allenes can be considered as another potential synthetic route to allenimines. However, the results obtained thus far are not promising. Thus, the esters *(13)*, R = H or CH_3, were only obtained in small amounts



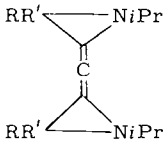
(13) *(14)*

(15) *(16)*

R = Phthalimido *(17)* 14%

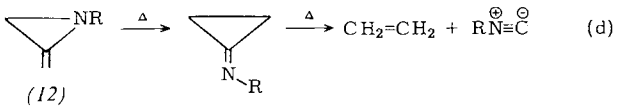
(3—8%) from ethoxycarbonylnitrene and allenes[17]. The nitrene was generated by base-catalyzed α-elimination of *N*-(*p*-nitrobenzenesulfonoxy)urethane. In another experiment, *Atkinson* and *Malpass*[18] isolated a strained diazaspiro[2.2]pentane *(17)* by reacting the allene *(15)* with phthalimidonitrene and postulated *(16)* as intermediate.

Finally, the reaction of carbon vapor (produced in a carbon arc) with imines is reported to produce a mixture of products in which *(18)* has been characterized by infrared and mass spectroscopy, but not isolated in pure form[19].



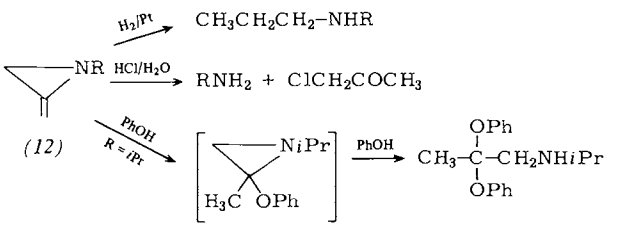
(18a), R = Ph, R' = H
(18b), R = R' = Ph

N-Alkylalkylideneaziridines undergo nitrogen inversion much easier than aziridines[20]. Their thermal decomposition proceeds *via* cyclopropanimines to give olefins and isonitriles [eq. (d)][15,21]. In contrast, *(13)* (R = CH_3) is thermolyzed at 130 °C into oxazoline *(14)*[17].



(12) (d)

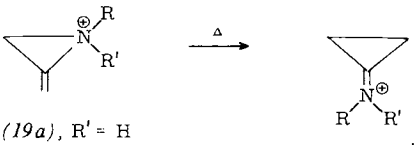
The reactions of *(12)* with hydrogen[11], dilute hydrochloric acid[13], and phenol[22] are summarized in Scheme 3.



Scheme 3

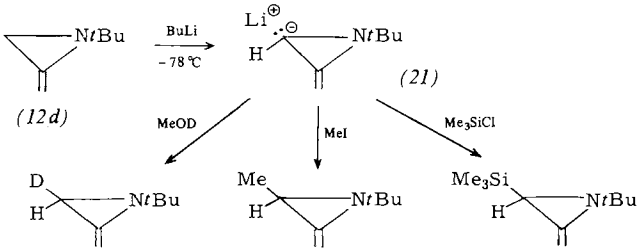
Protonation at nitrogen without ring cleavage was achieved by treatment of *(12a)*, *(12e)*, and *(12f)* with $HFSO_3/SbF_5$ in liquid sulfur dioxide at −78 °C[23a]. Similarly, methylation of *(12)* occurs cleanly with $(CH_3)_2Cl^+SbF_5Cl^-$ under the same conditions. The corresponding methyleneaziridinium ions *(19a)* and *(19b)* exhibit a remarkable thermal stability in the absence of nucleophiles, remaining unchanged, according to ^{1}H-NMR, in $HFSO_3$ solution up to +50 °C. At higher temperature, they rearrange into cyclopropaniminium ions *(20a,b)* analogous to the uncharged species [cf. eq. (d)][23b].

The carbanion *(21)* is generated when *(12d)* is treated with *n*- or *sec*-butyllithium at low temperature[16]. It can be deuterated, methylated and silylated as shown in Scheme 4. Using a silylated product in 12% optical yield, it was demonstrated that the thermal rearrangement into cyclopropanimine [cf. eq. (d)] proceeds stereospecifically, most probably with inversion at the migrating carbon atom[24].



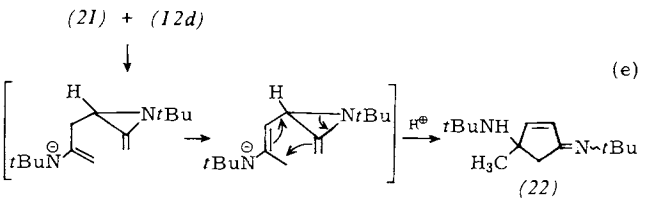
(19a), R' = H
(19b), R' = Me

(20a), R' = H; *(20b)*, R' = Me



Scheme 4

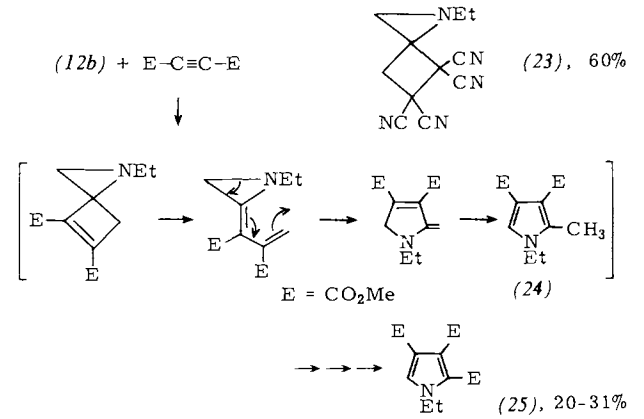
If a cooled solution of the carbanion *(21)* is allowed to warm up to −15 °C, dimerization occurs to give a *E,Z*-mixture of *(22)*. The mechanism formulated by the authors[16] is given in eq. (e).



(e)

(22)

Several cycloaddition reactions on *N*-alkylalkylideneaziridines have been carried out. Thus, *(12b)* reacts with tetracyanoethylene to give the spiro adduct *(23)*, and reaction with dimethyl acetylenedicarboxylate at room temperature is reported to yield *(25)*[25]. The course of this reaction has not been completely elucidated. The authors[25] suggest that the primary stages involve successively [2+2]-cycloaddition, ring opening of the cyclobutene, valence isomerization, and tautomerization to give *(24)*. The pathway leading from *(24)* to *(25)* is not understood.

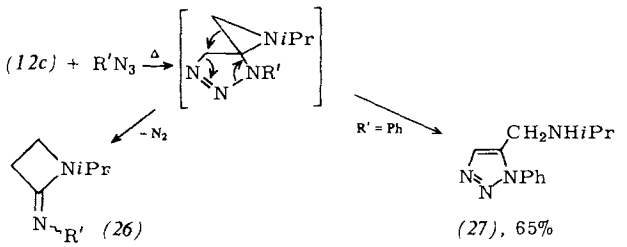


(23), 60%

(24)

(25), 20-31%

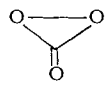
Addition onto the exocyclic C=C bond of *(12c)* also occurs when this compound is allowed to react with organic azides[22]. The spirotriazolines thus formed as intermediates are converted into four-membered ring amidines *(26)* with extrusion of molecular nitrogen. In the case of phenyl azide, the amidine *(26c)* is obtained alongside the triazoline *(27)*.



(26a), R' = Ts, 100%; (26b), R' = CO_2Et, 60%; (26c), R' = Ph, 35%; (26d), R' = CO_2tBu

3. Ketone Derivatives

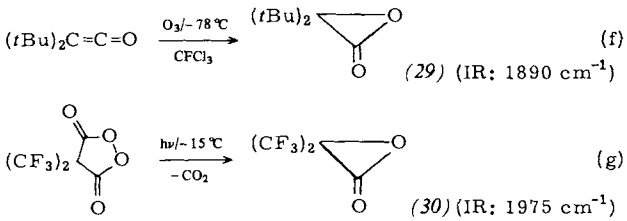
Among the heterocyclic analogues of cyclopropanones to be considered are α-lactones, α-thiolactones, α-lactams, and diaziridinones. Carbon trioxide *(28)* has been detected and analyzed by IR during the photochemical reaction of oxygen atoms with CO_2 molecules at 77 K[26], but it has not been studied chemically.



(28) (IR: 2045 cm^{-1})

3.1. α-Lactones (Oxiranones)

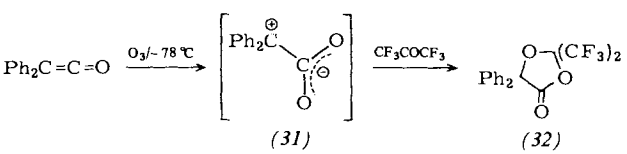
α-Lactones have been postulated as short-lived intermediates in a variety of reactions[27], but their thermal instability precluded any isolation. Only low temperature ozonolysis of di-*tert*-butylketene[28,29] and low temperature photolysis of 1,2-dioxolane-3,5-diones[30] furnished α-lactones [eq. (f), (g)] which were characterized by NMR and IR spectroscopy. The two most stable members of the class are *(29)* and *(30)*, decomposing respectively at −20 °C and at room temperature.



(29) (IR: 1890 cm^{-1}) (f)

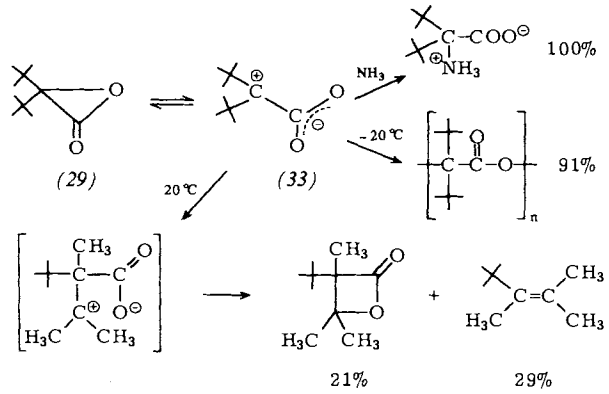
(30) (IR: 1975 cm^{-1}) (g)

In addition to the ozonolysis of di-*tert*-butylketene, *Wheland* and *Bartlett*[28] also investigated the ozonolysis of diphenylketene but could neither isolate nor detect the corresponding α-lactone. However, in the presence of hexafluoroacetone as trapping reagent, cycloadduct *(32)* was obtained in unspecified yield. The authors suggested that diphenylacetolactone is generated in its open-chain form *(31)* since the ring-closed α-lactone *(29)* is unable to undergo cycloaddition under the same conditions. Theoretical support has been gathered for this conjecture[31].



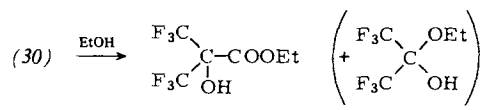
(31) *(32)*

Facile ring-opening of α-lactones to a dipolar species, *e.g. (33)*, accounts for their extreme reactivity (Scheme 5)[28]. They polymerize readily to polyesters and undergo decarbonylations, even at low temperature (hexafluoroacetone/trichlorofluoromethane solvent system).



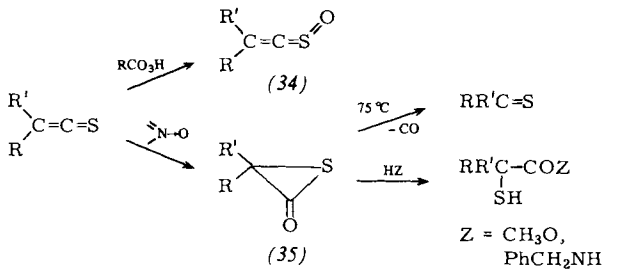
Scheme 5

Bis(trifluoromethyl)acetolactone *(30)* requires a separate comment. The formation of a zwitterion analogous to *(31)* and *(33)* is disfavored for this lactone, with the result that nucleophilic attack occurs exclusively at the carbonyl function[30].



3.2. α-Thiolactones (Thiiranones)

Whereas peroxy acids and hydrogen peroxide oxidize stable thioketenes to thioketene *S*-oxides *(34)*[32], nitrones of the 1-pyrroline 1-oxide type (>N→O) furnish α-thiolactones *(35)*[33]. These compounds are of very recent date; the only reactions reported so far are the thermal decarbonylation and the sp^2C—S bond cleavage with nucleophilic reagents such as methanol and benzylamine (Scheme 6)[33].

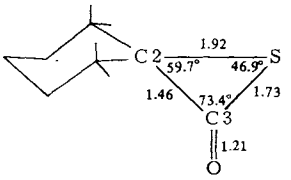


(a), R = R' = *t*Bu; *(b)*, R = *t*Bu, R' = *i*Pr; *(c)*, R + R' =

Scheme 6

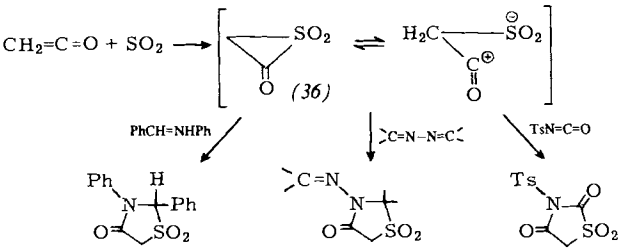
Of importance is the X-ray structure analysis of *(35c)* which shows an unusually large S—C^2 distance (1.92 Å compared with 1.81 Å for the sum of the covalent radii) and short C^2—C^3 and S—C^3 bonds[33], a situation also observed for other three-membered rings [see *(47)*, *(55)*, *(74)*, *(81)*, *(90)*].

The exocyclic C=O bond has a normal length of 1.21 Å. The small bond angle at the sulfur atom (46.9°) is also noteworthy.



(35c) (IR: 1785 cm^{-1})

To our knowledge, α-thiolactones have not been invoked as intermediates in cycloaddition reactions, but the *S,S*-dioxide *(36)* has been reported in this respect[34]. According to the authors, *(36)* is formed *in situ* when ketene is dissolved in liquid SO_2 at −78 °C, and can be trapped with imines, azines, and tosyl isocyanate (Scheme 7). Here, the supposed intermediate *(36)* undergoes sp^2C—S bond cleavage as expected, rather than sp^3C—S bond cleavage. At low temperature, *(36)* seems to have more than a transient existence.

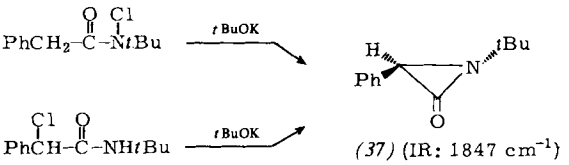


Scheme 7

3.3. α-Lactams (Aziridinones)

α-Lactams have been invoked as possible intermediates in numerous processes before the first member *(37)* was isolated by *Baumgarten* in 1962[35]. Subsequent work by many research groups established their chemistry and an excellent review exists on the subject to which the reader is referred for more details[36].

Stable α-lactams, having bulky *N*-substituents, are prepared by treatment of *N*-chloroamides or α-chloroamides with potassium *tert*-butoxide (Scheme 8)[35].

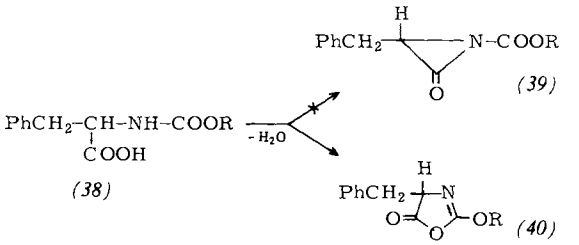


(37) (IR: 1847 cm^{-1})

Scheme 8

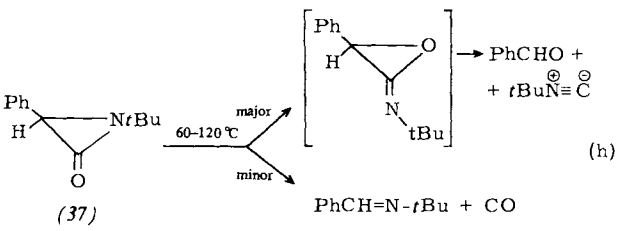
A report by *Miyoshi*[37] that *N*-functionalized α-lactams *(39)* are obtained by cyclodehydration of amino acid derivatives *(38)* proved later to be erroneous[38]; oxazolin-5-ones *(40)* are formed instead of *(39)*.

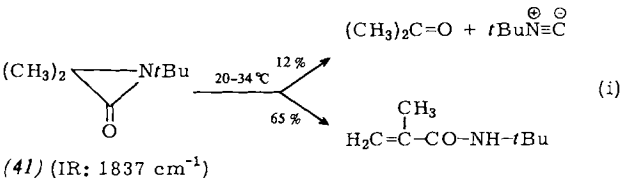
A large number of substituted α-lactams have been synthesized by the methods of Scheme 8[39], and these exhibit a considerable range of stability. For instance, the sterically hindered α-lactams 1,3-di-*tert*-butylaziridinone and 1,3-



diadamantylaziridinone are very stable (decomposition far above 100 °C), while 1-*tert*-butyl-3,3-dimethylaziridinone *(41)* undergoes slow decomposition at room temperature. No derivatives have been isolated in which an aromatic group or an *n*- or *sec*-alkyl substituent is attached to nitrogen.

Thermally, α-lactams fragment into carbonyl compounds and isocyanides, presumably *via* the elusive iminolactones as intermediates [eq. (h)][36]. (*Bott*[40] claimed to have detected an iminolactone during the synthesis of 3-adamantyl-1-*tert*-butylaziridinone, but no structure evidence was given.) If β-hydrogens are present on the α-lactam ring, thermal isomerization into α,β-unsaturated amides is an important competing reaction [eq. (i)]. In contrast, the main products of the photoinduced decomposition of α-lactams are carbon monoxide and the corresponding imines[41]. This pathway only occurs to a minor extent in some thermal degradations [cf. eq. (h)][36].

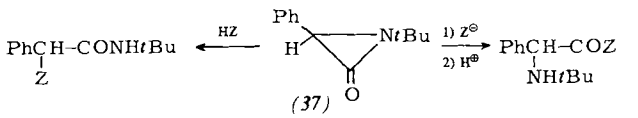




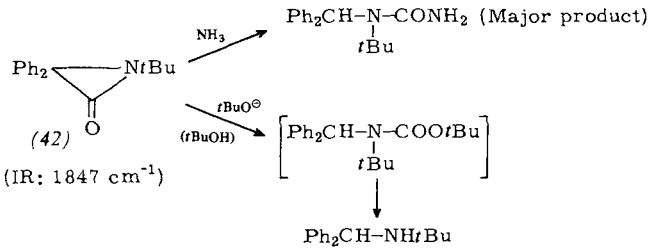
(41) (IR: 1837 cm^{-1})

In general, α-lactams undergo two types of selective ring-opening by nucleophiles (Scheme 9)[36,42]. Reaction with proton-containing nucleophiles, *e.g.* water, alcohols, thiols, amines, and mineral acids (HZ), leads exclusively to amides, corresponding to an sp^3C—N bond rupture. In contrast, reaction of α-lactams with aprotic nucleophiles, *e.g.* alkoxides, $LiAlH_4$, and sulfur ylides (Z^-), yields amino acid derivatives, resulting from sp^2C—N bond scission. The third possible way of opening the ring, namely at the C—C bond, has been observed for *(42)* (Scheme 10)[43].

The two types of ring-opening mentioned in Scheme 9 are also observed in the cycloaddition reaction of *(41)* with phenyl isocyanate[44]; adducts *(43)* and *(44)* are formed in a ratio

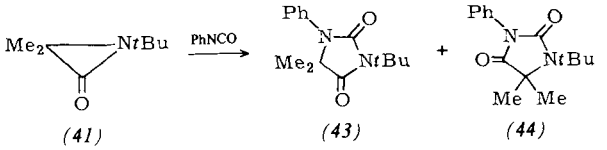


Scheme 9

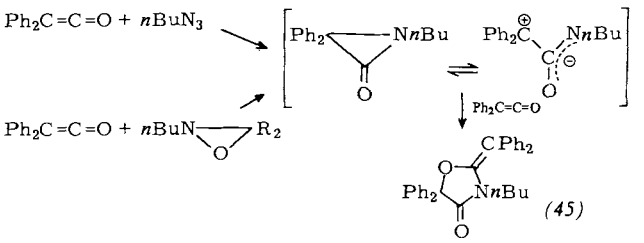


Scheme 10

of 7:3. However, when the reaction is carried out with unstable α-lactams generated *in situ* from α-bromoamides in tetrahydrofuran at −50 °C only hydantoins [cf. *(43)*] arising from sp^3C—N bond cleavage are obtained[44].

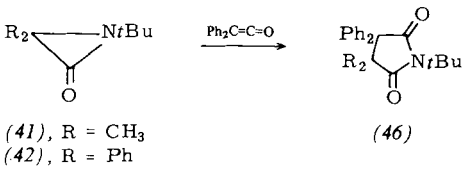


The pronounced dipolar reactivity of unstable α-lactams may also account for the formation of oxazolidinone *(45)* on reaction of diphenylketene with *n*-butyl azide[45] and oxaziridines[46] (Scheme 11). With the stable α-lactams *(41)* and

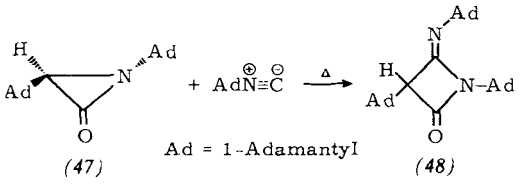


Scheme 11

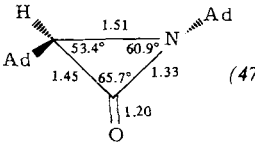
(42), addition occurs across the C=C double bond of diphenylketene to yield succinimides *(46)*[47]. This difference in selectivity between stable and unstable α-lactams may be explained by invoking steric arguments.



The sterically stabilized α-lactam *(47)* reacts with adamantyl isocyanide on warming to yield the β-lactam *(48)* in 71% yield[48]. The latter is also formed along with the corresponding aldehyde and isonitrile when *(47)* is decomposed at 115—160 °C. The weakness of the sp^3C—N bond, which is



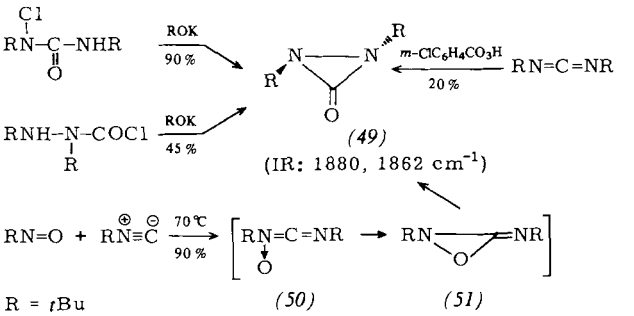
broken in this reaction, is apparent from an X-ray crystallographic study (1.51 Å compared with 1.46 Å for a normal C—N bond length)[49]. Furthermore, the substituents attached to nitrogen are not coplanar as they are in amides, inhibiting the π-resonance stabilization which is normally ascribed to amides.



(47) (IR: 1830 cm^{-1})

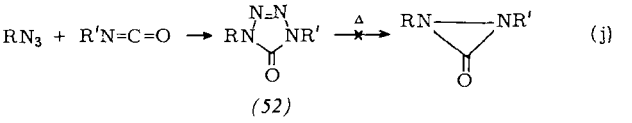
3.4. Diaziridinones

Stable diaziridinones having tertiary alkyl groups attached to both nitrogen atoms are well known. Four of the synthetic methods developed by *Greene* and co-workers are exemplified in Scheme 12 for di-*tert*-butyldiaziridinone *(49)*. They involve: (a) treatment of 1-chloro-1,3-di-*tert*-butylurea with potassium *tert*-butoxide[50]; (b) treatment of 2,3-di-*tert*-butylcarbazoyl chloride with the same reagent[50]; (c) treatment of *tert*-butyl isocyanide with a nitroso compound [a reaction which occurs *via* the intermediacy of the carbodiimide *N*-oxide *(50)* and probably also *via* the oxaziridinimine *(51)*[51]; and (d) treatment of di-*tert*-butylcarbodiimide with a peroxy acid[52].



Scheme 12

The possibility of generating diaziridinones by thermolysis of 1,4-disubstituted tetrazolinones *(52)* has also been considered. The tetrazolinones were obtained by cycloaddition reactions of organic azides with isocyanates [eq. (j)][53]. They proved, however, to be thermally stable with the exception of 1-alkyl-4-arylsulfonyl derivatives which undergo cycloreversion at 100—120 °C instead of elimination of nitrogen. Cycloreversion also occurs upon electron impact[54].



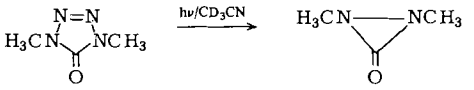
(j)

(52)

R = Alkyl, R' = Aryl, Acyl, Alkoxycarbonyl
R = Alkyl, Aryl, R' = Arylsulfonyl

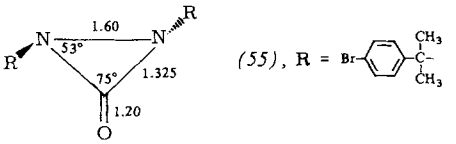
In contrast, photolysis of 1,4-dimethyltetrazolinone *(53)* produces the corresponding diaziridinone *(54)*[55].

An X-ray analysis of *(55)* has been carried out and confirmed the expected *trans* arrangement of the *N*-substit-



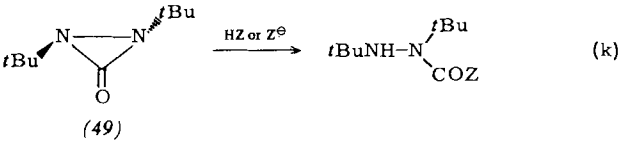
(53) (54) (IR: 1882 cm^{-1})

uents[56]. They are situated 56° above and below the plane defined by the ring atoms. Further characteristics of the ring are the unusually long N—N bond (1.60 Å compared with 1.39 Å for the N—N bond in OCH—NH—NH—CHO), the short C—N bonds, and the normal ketone C=O length.



(55), R = Br-C(CH3)2-CH3

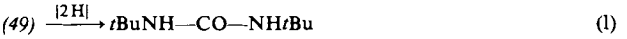
Diaziridinones undergo facile sp^2C—N ring opening with acids, but they are rather sluggish towards nucleophilic reagents [eq. (k)][50]. Thus, methanolysis of *(49)* into methyl carbazate occurs much faster under acidic conditions than in the presence of methoxide.



(49) (k)

HZ = HCl (dry), $CH_3OH/H^{\oplus}$, C_6H_5COOH, HCOOH, picric acid, $(CH_3)_2CHNH_2$
$Z^{\ominus} = CH_3O^{\ominus}$ (refluxing CH_3OH), $tBuO^{\ominus}$ (refluxing *t*BuOH), $H^{\ominus}$

Whereas 1,3-di-*tert*-butylaziridinone (an α-lactam!) is not reducible electrochemically, *(49)* is cleanly converted into 1,3-di-*tert*-butylurea by electrochemical reduction[57]. Reduction of *(49)* is also achieved with hydrogen on palladium, sodium naphthalenide, *tert*-butyllithium, as well as with a number of other reducing agents summarized in eq. (l)[50].

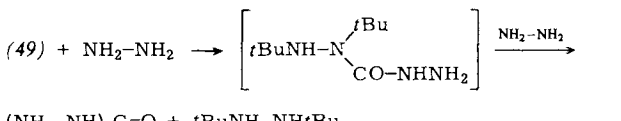


(49) → *t*BuNH—CO—NH*t*Bu (l)

|2H| = H_2/Pd/C, $PhNHNH_2$ (→ $C_6H_6 + N_2$), RNHNHR (→ RN=NR), EtSH (→ EtSSEt), *t*BuNHOH (→ *t*BuN=O), PhOH, Ph_2CHOH (→ Ph_2C=O)

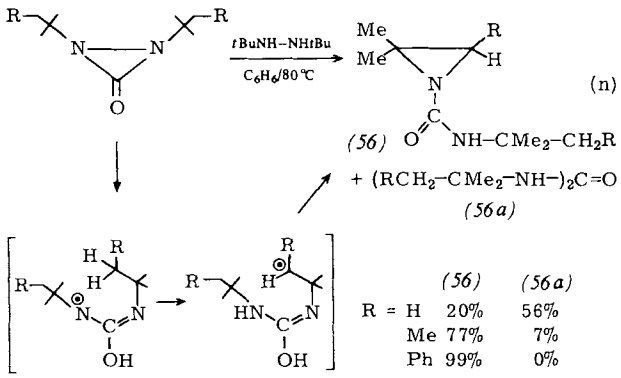
Hydrazines can react in three different ways; as reducing agents [eq. (l)], as nucleophiles [eq. (m)], or as catalysts of the rearrangement of diaziridinones into aziridinecarboxamides *(56)* by a radical mechanism [eq. (n)][50,58]. From the yields reported in eq. (n) it is evident that the rearrangement is favored by increasing the lability of hydrogen β to nitrogen in the diaziridinone. Furthermore, low hydrazine concentrations favour rearrangement over reduction of diaziridinone.

Tervalent phosphorus compounds, *e.g.* $(EtO)_3P$, effect the deoxygenation of *(49)* to give di-*tert*-butylcarbodiimide and ethyl phosphate [eq. (o)][52]. This reaction proceeds *via* an isocyanate and iminophosphorane; the former was shown to accumulate in the course of the reaction.



(NH2–NH)2C=O + *t*BuNH–NH*t*Bu (m)

+ *t*BuNH–N(*t*Bu)–CO–NHNH–CO–NHNH2

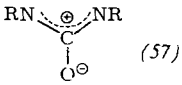


(56) + (56a) (n)

	(56)	(56a)
R = H	20%	56%
Me	77%	7%
Ph	99%	0%

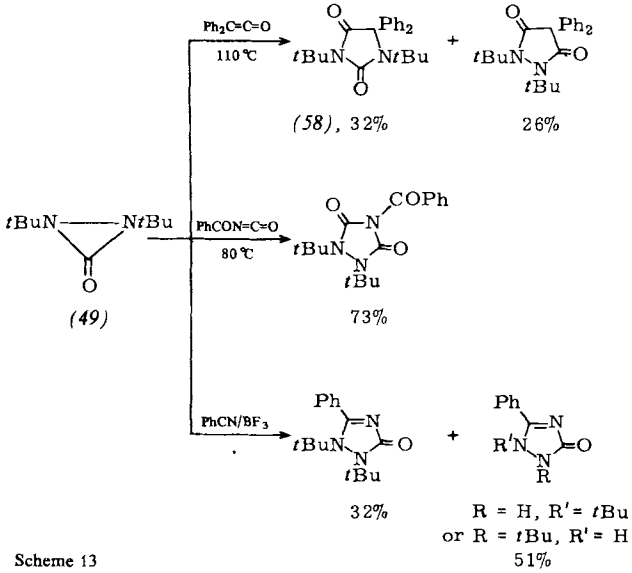
(49) + $(EtO)_3P$ → [*t*BuN=C=O + $(EtO)_3P$=N*t*Bu] → *t*BuN=C=N*t*Bu + $(EtO)_3P$=O (o)

Thermal decomposition of diaziridinones occurs at high temperatures [at 180 °C for *(49)*], resulting in decarbonylation as well as fragmentation into isocyanate and imine. The latter arises from rearrangement of a nitrenoid species[56,59]. Other products are also formed in minor amounts and are accounted for by radical mechanisms.



(57)

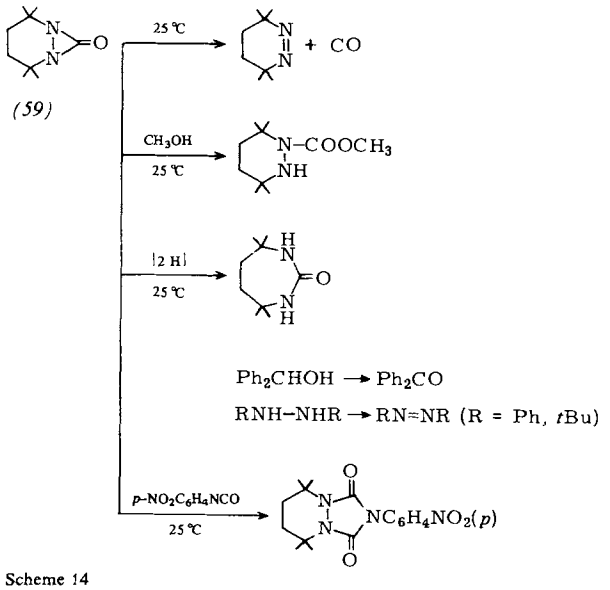
Since the open-chain dipolar form *(57)* of a diaziridinone should be less stable than that of α-lactones or α-lactams[31], cycloaddition reactions involving this intermediate cannot be expected. *Greene et al.*[50–52] stressed the lack of reactivity of di-*tert*-butyldiaziridinone *(49)* towards cyclohexene, cyclo-



Scheme 13

pentadiene, norbornene, maleic anhydride, isocyanides, and phenyl isocyanate. Successful cycloadditions were carried out with diphenylketene, acyl- and sulfonyl isocyanates, and benzonitrile in the presence of boron trifluoride (Scheme 13)[59-61]. In all but one case, *i.e. (58)*, the mode of addition is the result of sp^2C—N bond cleavage, which is also the mode of scission when the three-membered ring is treated with electrophiles and nucleophiles [cf. eq. (k)].

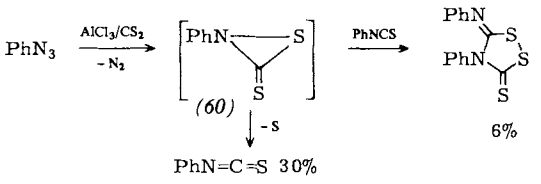
Finally, it is worth mentioning that a *cis*-fused diaziridinone *(59)* has been prepared by dehydrochlorination of the corresponding *N*-chlorourea (yield 14–23%)[61]. This compound undergoes quantitative decarbonylation on standing at room temperature and reacts with nucleophiles, reducing agents, and activated isocyanates much faster than *(49)*, although in a similar manner (Scheme 14).



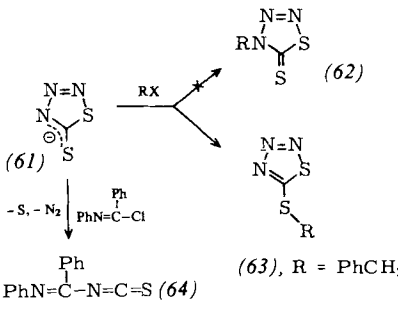
Scheme 14

4. Thioketone Derivatives. There are None!

Borsche[62] first proposed thiaziridinethione *(60)* as a reactive intermediate in the $AlCl_3$ catalyzed decomposition of phenyl azide in CS_2. This intermediate was also postulated for the reactions of oxaziridines with CS_2, giving isothiocyanates in high yields[63]. In both cases, however, no direct evidence for the presence of *(60)* is available and its formation was only assumed in order to rationalize the reaction course.



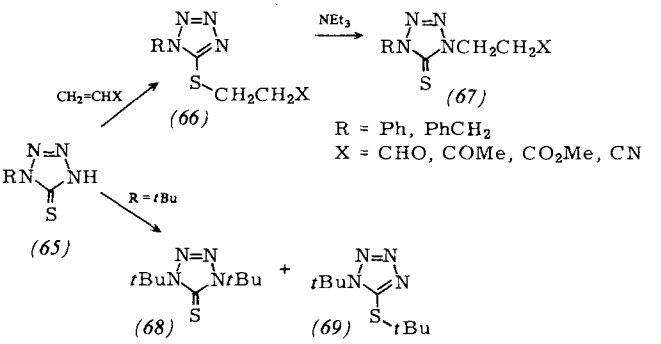
The possibility that 4-substituted thiatriazolinethiones *(62)* would yield thiaziridinethiones has been considered in our laboratory. However, all attempts to prepare the starting materials were unsuccessful since alkylation and acylation of sodium thiatriazolinethiolate *(61)* (obtained from CS_2 and



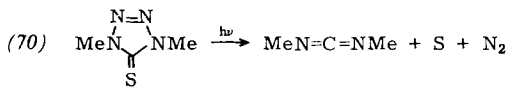
NaN_3)[64] furnished the *S*-substituted derivatives *(63)* in all cases[65]. Treatment of the triethylammonium salt of *(61)* with phenylbenzimidoyl chloride in tetrahydrofuran resulted in elimination of nitrogen and sulfur, and formation of the imidoyl isothiocyanate *(64)*[66].

In contrast with the corresponding ketones, diaziridinethiones cannot be obtained by treatment of thioureas with *tert*-butyl hypochlorite and potassium *tert*-butoxide; instead, desulfurization occurs to yield carbodiimides[66,67].

Thermolysis of 1,4-disubstituted tetrazoline-5-thiones, *e.g. (67)* and *(68)*, also failed to give diaziridinethiones. The starting materials of type *(67)* were prepared by Michael additions of *(65)* (obtained from isothiocyanates and NaN_3)[68] to electron-poor olefins in basic medium[69]. In the absence of base, *S*-substituted derivatives *(66)* are formed which, however, isomerize to *(67)* upon addition of a base[69]. 1,4-Di-*tert*-butyltetrazoline-5-thione *(68)* is prepared from *(65)*, R = *t*Bu, by *tert*-butylation with a mixture of *tert*-butyl alcohol, dicyclohexylcarbodiimide and cuprous chloride as described by *Henry*[70]. Besides *(68)* (65%), the *S*-substituted derivative *(69)* is formed in smaller amount (15%)[66]. The thiones *(67)* and *(68)* remain unchanged when heated at 120—150 °C[66,69], thus resembling the corresponding ketones in their thermal stability[53].



Also photolysis of *(70)* does not produce the three-membered ring but, instead, furnishes a carbodiimide after loss of nitrogen and sulfur[55].



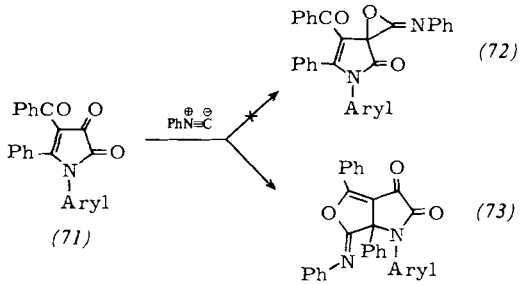
5. Imino Derivatives

In this series, thiiranimines, aziridinimines, and diaziridinimines have been isolated whereas oxiranimines and thiazir-

idinimines have been demonstrated only as elusive intermediates.

5.1. Oxiranimines

We have previously mentioned that oxiranimines (iminolactones) are postulated as reactive intermediates in the thermal decomposition of α-lactams into carbonyl compounds and isocyanides [eq. (h)]. The reverse reaction was reported by *Ziegler et al.*[71] for the heterocyclic diones *(71)* and phenyl isocyanide at 100 °C, but a careful reinvestigation indicated that *(73)* is formed instead of *(72)*[72].

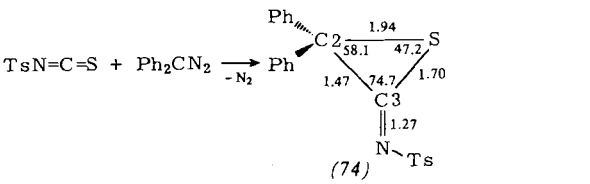


(71) *(72)* *(73)*

Also, the claim[40] that an oxiranimine has been detected as side product (3—5%) during the synthesis of 1-*tert*-butyl-3-adamantylaziridinone should be regarded with much reservation until more evidence is given for its structure.

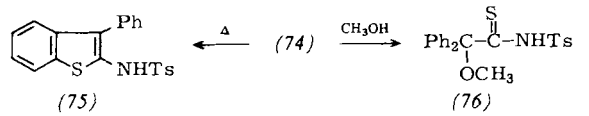
5.2. Thiiranimines

The first member of the class of thiiranimines, *i.e. (74)*, was synthesized in 1978 by reaction of tosyl isothiocyanate with diphenyldiazomethane [eq. (p)][73]. X-Ray analysis revealed the presence of an unusually long C^2—S bond which is broken in chemical reactions. Thus *(74)* isomerizes into benzothiophene *(75)* upon warming, and its reaction with methanol furnishes the thioxosulfonamide *(76)*.



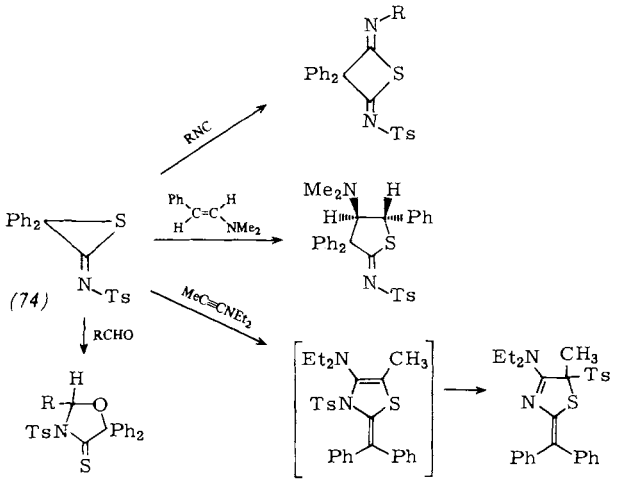
(p)

(74)



(75) *(76)*

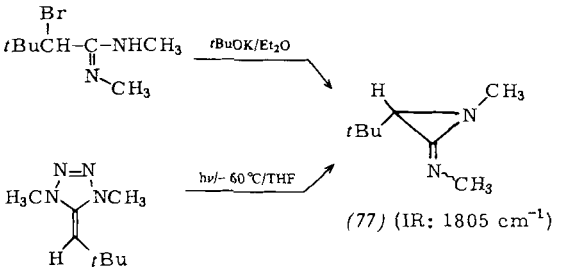
In cycloaddition reactions the C^2—S bond is also cleaved and adducts are formed which involve participation of either the C^2 and S, or the N and S, or the C^2 and N atoms depending on the nature of the co-reagent. The results are summarized in Scheme 15[74,75]. In the case of ynamines, exemplified with *N*-diethylaminopropyne, the primary cycloadduct (addition along the N,S part of the molecule) undergoes a sulfonyl migration from N^3 to C^5 during the reaction.



Scheme 15

5.3. Aziridinimines

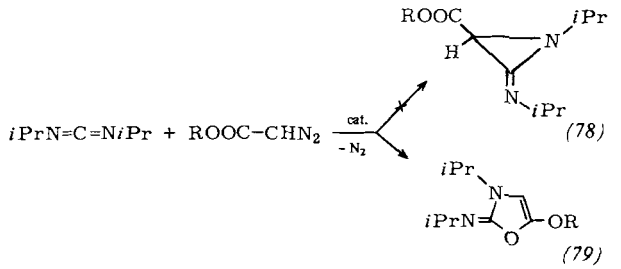
Stable aziridinimines, *e.g. (77)*, were prepared in *Quast*'s laboratory by dehydrohalogenation of α-bromoamidines[76] and by photolysis of alkylidenetetrazolines[55] (see Scheme 16).



(77) (IR: 1805 cm^{-1})

Scheme 16

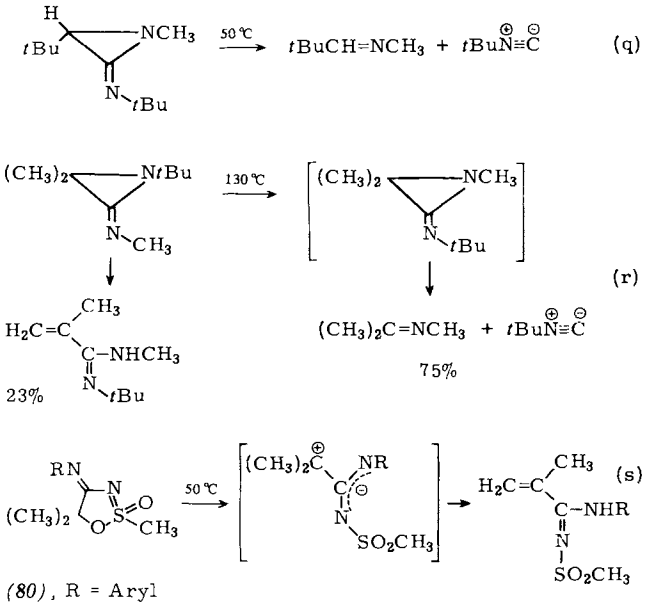
In a preliminary communication, *Teyssié* and co-workers[77] reported the synthesis of *C*-alkoxycarbonyl-substituted aziridinimines *(78)* from diisopropylcarbodiimide and alkyl diazoacetates in the presence of transition metal salts. A more detailed reexamination of this reaction, however, indicated that the products are in fact oxazoline derivatives *(79)*[78].



(78) *(79)*

The aziridinimines exhibit *syn-anti* isomerization of the imino group at ambient temperature[76]. They decompose thermally into imines and isocyanides [eq. (q)]; in some cases the fragmentation products are interpretable in terms of a valence isomerization occurring during thermolysis [eq. (r)][79]. When methyl substituents are present on the ring C-atom, rearrangement into α,β-unsaturated amidines is also observed [eq. (r)]. This isomerization is analogous to that

found for α-lactam *(41)* [eq. (i)], and is also comparable with the thermal rearrangement of the 1,2λ⁶,3-oxathiazolines *(80)* (first thought to be isopropylidenediaziridines!)[80] to methacrylic amidines [eq. (s)][81]. The latter may possibly proceed *via* a ring-opened aziridinimine.



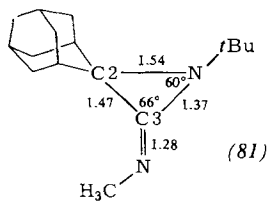
(q)

(r)

(s)

(80), R = Aryl

The spiroaziridinimine *(81)* has been subjected to an X-ray diffraction analysis and the bond lengths and internal angles are shown with the structure[82]. Here again, the same general features are found as with other three-membered rings; *i.e.* long C^2—N bond and short C^3—N and C^2—C^3 bond distances.

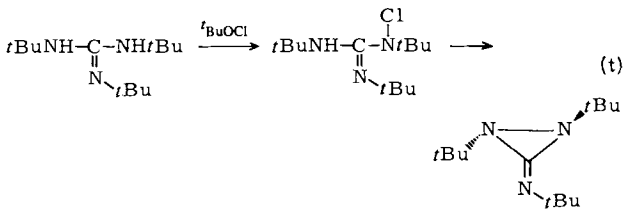


(81)

5.4. Diaziridinimines

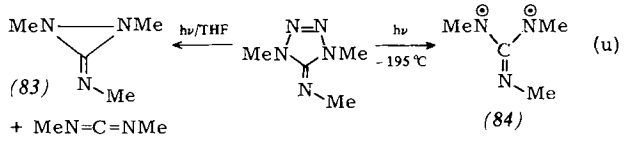
Quast and co-workers developed two methods for the synthesis of stable diaziridinimines. The first method consists in reacting *tert*-butylguanidines with *tert*-butyl hypochlorite (molar ratio 2:1); this reaction involves the intermediacy of an *N*-chloroguanidine [eq. (t)]. The reaction, however, is most conveniently carried out with the respective guanidinium perchlorate and *tert*-butyl hypochlorite in the presence of potassium *tert*-butoxide[83]. The second preparative method is photolysis of trisubstituted tetrazolin-5-imines [eq. (u)][55]. Here, dimethyl carbodiimide is obtained alongside *(83)*. When the irradiation was carried out at low temperature (−195 °C), tris(imino)methane *(84)* was identified by ESR[84]. This is the nitrogen analogue of the better known trimethylenemethane[85].

No formation of diaziridinimines by thermal decomposition of trisubstituted tetrazolin-5-imines has been reported,



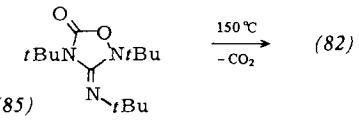
(t)

(82) (IR: 1790 cm^{-1})



(u)

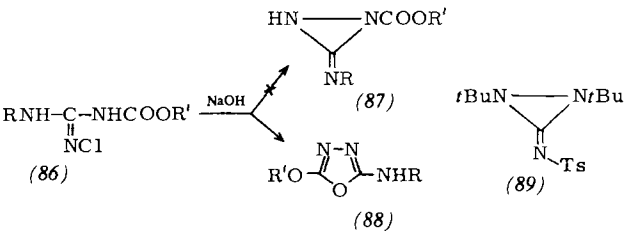
but a closely related reaction *(85)*→*(82)* was observed by *Greene*'s group[86].



(82)

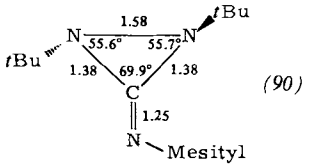
(85)

In a Japanese patent the synthesis of 1-alkoxycarbonyl-substituted diaziridinimines *(87)* was claimed by dehydrohalogenation of *N*-chloroguanidines *(86)*[87]. No spectral data were given to substantiate the structure and a reinvestigation of the reaction products by spectral and X-ray analyses established that 1,3,4-oxadiazoles *(88)* are formed instead[88]. The only functionalized diaziridinimine isolated so far is *(89)*, prepared in our laboratory by utilizing the first method of *Quast*[81].



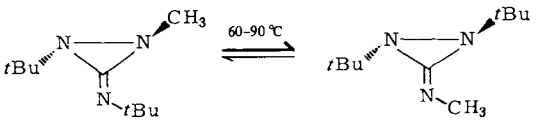
(86) *(87)* *(88)* *(89)*

All the diaziridinimines isolated so far most probably exist in the *trans* configuration. This was ascertained for *(90)* by an X-ray structure analysis[89]. The molecule features a long N—N bond length and short C—N distances (compare the indicated values with the sum of the covalent radii for N—N, 1.50 Å, and C—N, 1.46 Å). In the crystalline state, the aromatic ring is twisted 58.6° out of the plane of the three-membered ring.



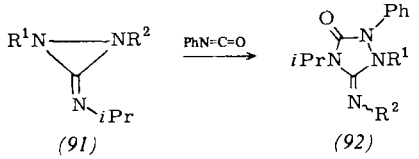
(90)

Diaziridinimines decompose thermally into azo compounds and isocyanides[83]. Those substituted with different groups are also susceptible to thermal valence isomerization, favoring the isomer with the less bulky group at the imino nitrogen [eq. (v)][90].



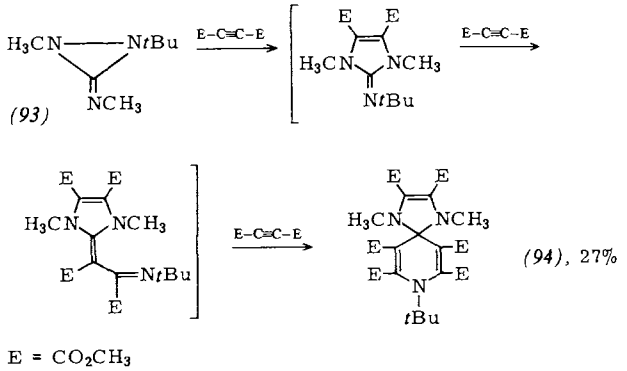
(v)

Diaziridinimines undergo cycloaddition reactions initiated by nucleophilic attack of the imino function on the electrophilic center of the reaction partner. Thus, reaction of *(91)* with phenyl isocyanate occurs readily at low temperature to give iminotriazolinones *(92)*, in which the exocyclic nitrogen of *(91)* becomes part of the five-membered ring[91].



(91) *(92)*

Another beautiful example from *Quast*'s group is the reaction of *(93)* with dimethyl acetylenedicarboxylate at room temperature to give the spiro adduct *(94)*, whose structure was confirmed by X-ray analysis[92]. The mechanism involves three consecutive cycloaddition steps.

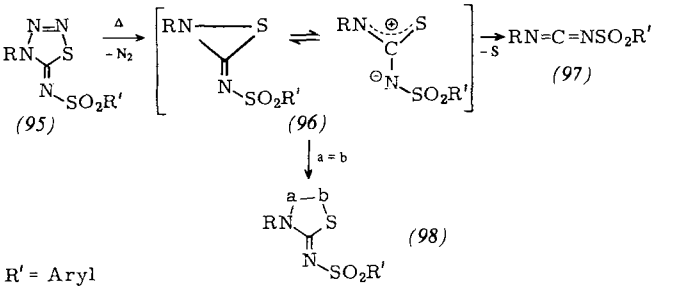


(93) *(94)*, 27%

E = CO_2CH_3

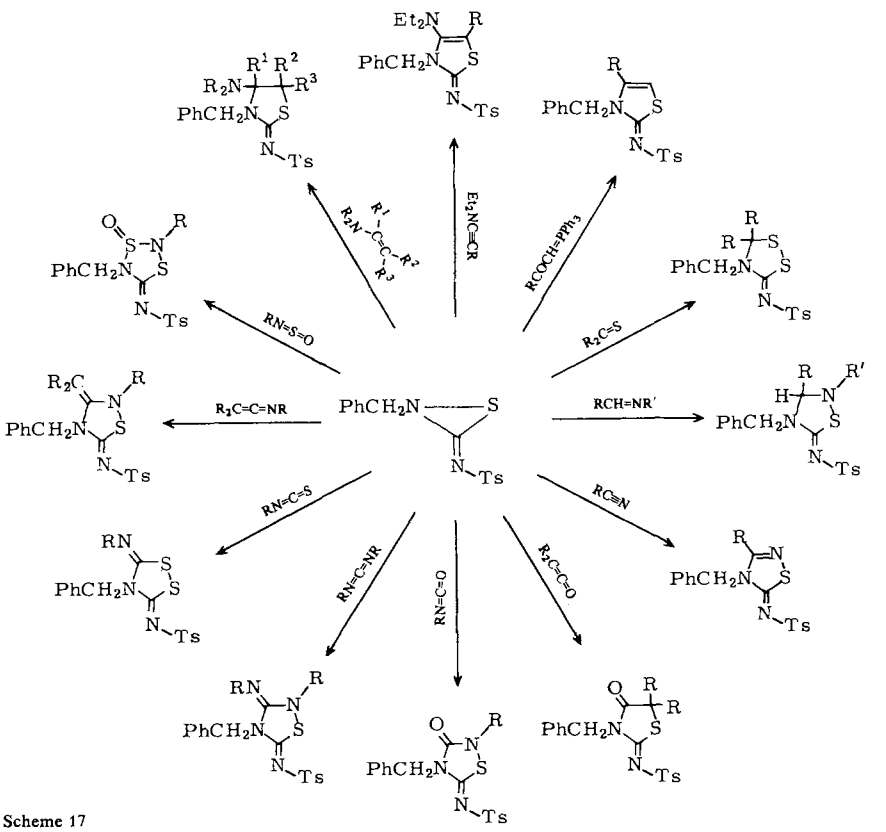
5.5. Thiaziridinimines

4-Alkyl-5-arylsulfonylimino-1,2,3,4-thiatriazolines *(95)* (obtained from alkyl azides and arylsulfonyl isothiocyanates) are thermally converted into sulfonylcarbodiimides *(97)* by loss of nitrogen and sulfur[93]. A thiaziridinimine and/or its ring-opened dipolar species *(96)* is postulated as intermediate, since it can be trapped by a large number of unsaturated systems (a=b and a≡b), including enamines, ynamines, carbonyl-stabilized phosphorus ylides, thiocarbonyl compounds, imines, nitriles, heterocumulenes, and *N*-sulfinylamines[93,94]. The adducts of type *(98)* formed from 4-benzyl-5-tosylimino-1,2,3,4-thiatriazoline *(95)*, R = benzyl, R′ = *p*-tolyl, are listed in Scheme 17.



(95) *(96)* *(97)* *(98)*

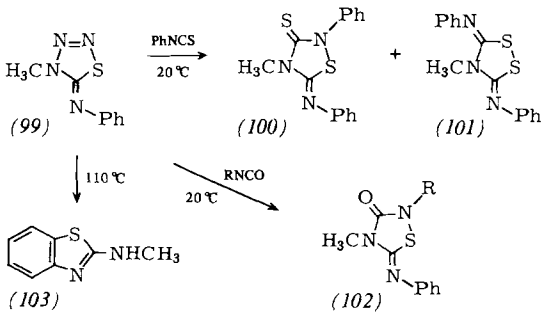
R′ = Aryl



Scheme 17

All the reactions occur at 60—70 °C, *i.e.* the decomposition temperature of *(95)*, R = benzyl, R′ = tolyl, thus being independent of the nature and concentration of the trapping reagent. Furthermore, the additions are regiospecific, and even stereospecific in the few cases studied so far. We can only speculate about the mechanism of these cycloadditions; *i.e.* concerted with participation of sulfur d-orbitals, or nonconcerted. Much evidence, however, points to a stepwise mechanism. Indeed, *(96)* does not react in a Diels-Alder fashion with furan, 1,3-diphenylisobenzofuran, or 1,2,3,4-tetraphenyl-1,3-cyclopentadiene[95], although this is a characteristic symmetry-allowed behavior of cyclopropanones[6]. The nature of the reaction partners which are polar molecules, also suggests that *(96)* reacts preferentially *via* a polar open-chain betaine[96].

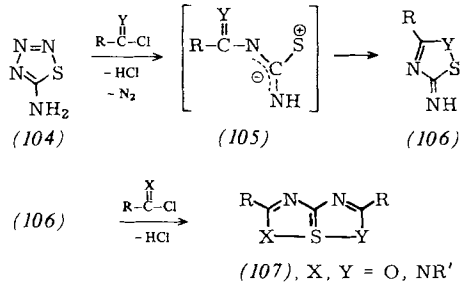
When the arylsulfonyl substituent in *(95)* is replaced by an aryl substituent the behavior towards heterocumulenes is drastically altered. Compound *(99)* now reacts with phenyl isothiocyanate at room temperature to give thiadiazolidine *(100)* as main product in addition to a smaller amount of *(101)* [formed from *(100)* by a Dimroth rearrangement][97].



(99) *(100)* *(101)* *(103)* *(102)*

Also, the reaction with isocyanate occurs at 20 °C to give *(102)* in excellent yield[98]. Since *(99)* only decomposes thermally in refluxing toluene to yield benzothiazole *(103)*[99], the reactions with heterocumulenes must be bimolecular processes, not proceeding *via* the intermediacy of the desired thiaziridinimine.

Our research in this field has led to the discovery of an interesting application of undoubtedly widespread interest; namely the synthesis of λ^4-thiapentalenes *(107)* by treating 5-amino-1,2,3,4-thiatriazole *(104)* with acyl chlorides and imidoyl chlorides[100]. The ring-opened thiaziridinimines *(105)* are believed to be the key intermediates in this reaction. They undergo cyclization into *(106)* and reaction with a second molecule of electrophilic reagent to give *(107)*. Since the hydrochloride of *(106)*, Y = NR′, can be isolated, unsymmetrical thiapentalenes *(107)*, X ≠ Y, are also accessible.

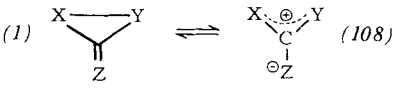


(104) *(105)* *(106)*

(106) *(107)*, X, Y = O, NR′

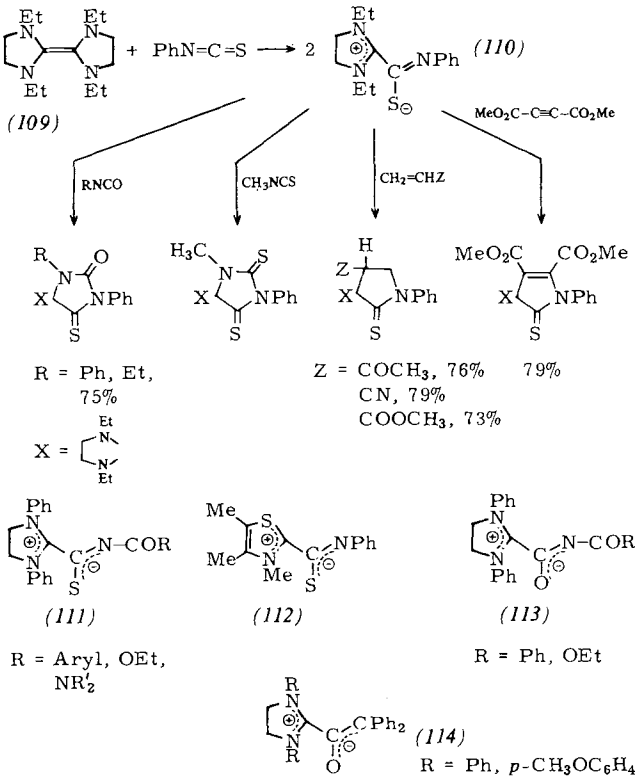
6. Externally Stabilized 1,3-Dipoles

In the previous sections, I have suggested that some heterocycles of type *(1)* may possibly react as dipolar systems of type *(108)* in cycloadditions[101]. These reactive species differ from the classical 1,3-dipoles studied by *Huisgen*[102], and also from the 1,3-dipoles which result from thermal or photochemical C—C bond cleavage of aziridines, oxiranes, and thiiranes[103]. Hence, it is appropriate here to mention briefly the literature on this subject.



(1) *(108)*

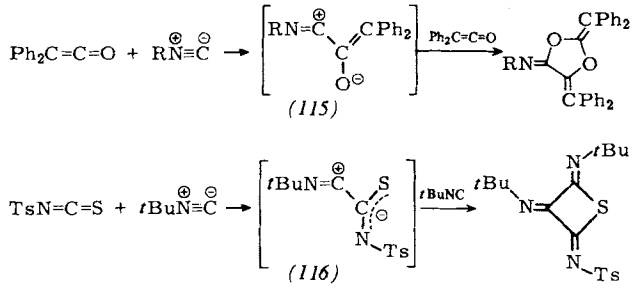
In 1965, *Winberg* and *Coffman*[104] reported the reaction of biimidazolidinylidene *(109)* with phenyl isothiocyanate to give the stable inner salt *(110)* under mild conditions. This yellow-colored dipole undergoes cycloadditions with isocyanates, isothiocyanates, electron-poor olefins, and dimethyl acetylenedicarboxylate (see Scheme 18). Extensions to other electron-rich olefins and nucleophilic carbene progenitors, as well as to other heterocumulenes, were made by several investigators[105]. In many cases, the dipoles were only postulated as reactive intermediates, whereas in other experiments, stable dipoles were isolated and subsequently reacted with isocyanates and substituted acetylenes. Examples of the latter are *(111)*—*(114)*.



(109) *(110)* *(111)* *(112)* *(113)* *(114)*

Scheme 18

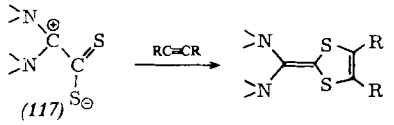
The combination of isocyanides with heterocumulenes would also lead initially to resonance-stabilized zwitterionic adducts[106]. The only two zwitterions of this kind to have been trapped so far are *(115)* and *(116)*[107,108].



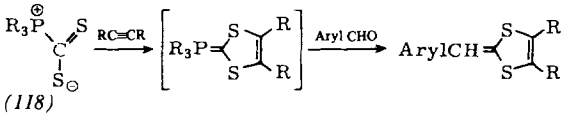
(115)

(116)

The stable dipoles *(117)* and *(118)* are prepared from carbon disulfide and peraminoethylenes[104] or triethylphosphanes[109] respectively. They react with acetylenes to give 1,3-dithiol derivatives[110,111].

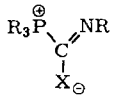


(117)



(118)

Finally, it is worth mentioning that stable adducts of type *(119)* are also formed from tertiary phosphanes and isothio-



(119), X = S, O

cyanates[112], or isocyanates in some cases[113], but no cycloadditions have been reported thus far[114].

I am grateful to my co-workers, whose names are quoted in the references for their enthusiastic collaboration in this field. I am also indebted to Prof. M. Quast (Würzburg) and Prof. G. Smets (Leuven) for stimulating discussions.

Received: March 15, 1979 [A 313 IE]
German version: Angew. Chem. *92*, 277 (1980)

[1] *R. L. Camp, F. D. Greene,* J. Am. Chem. Soc. *90*, 7349 (1968); *J. K. Crandall, W. H. Machleder,* J. Heterocycl. Chem. *6*, 777 (1969); *J. K. Crandall, W. W. Conover, J. B. Komin, W. H. Machleder,* J. Org. Chem. *39*, 1723 (1974).

[2] *T. H. Chan, B. S. Ong, W. Mychajlowskij,* Tetrahedron Lett. *1976*, 3253; *T. H. Chan, B. S. Ong,* J. Org. Chem. *43*, 2994 (1978).

[3] *J. K. Crandall, W. H. Machleder,* J. Am. Chem. Soc. *90*, 7292 (1968); *J. K. Crandall, W. H. Machleder, M. J. Thomas, ibid. 90*, 7346 (1968); *J. K. Crandall, W. H. Machleder, ibid. 90*, 7347 (1968); *J. K. Crandall, W. H. Machleder, S. A. Sojka,* J. Org. Chem. *38*, 1149 (1973).

[4] *J. K. Crandall, W. W. Conover,* J. Chem. Soc. Chem. Commun. *1973*, 340; *Y.-N. Kuo, M. J. Nye,* Can. J. Chem. *51*, 1995 (1973).

[5] *H. M. R. Hoffmann, R. H. Smithers,* Angew. Chem. *82*, 43 (1970); Angew. Chem. Int. Ed. Engl. *9*, 71 (1970); *H. M. R. Hoffmann, K. E. Clemens, E. A. Schmidt, R. H. Smithers,* J. Am. Chem. Soc. *94*, 3201 (1972).

[6] Reviews: *N. J. Turro,* Acc. Chem. Res. *2*, 25 (1969); *H. H. Wasserman, G. M. Clark, P. C. Turley,* Fortschr. Chem. Forsch. *47*, 73 (1974).

[7] a) *E. Jongejan, Th. S. V. Buys, H. Steinberg, Th. J. de Boer,* Recl. Trav. Chim. Pays-Bas *97*, 214 (1978); b) *E. Block, R. E. Penn, M. D. Ennis, T. A. Owens, S.-L. Yu,* J. Am. Chem. Soc. *100*, 7436 (1978).

[8] *W. J. Middleton,* J. Org. Chem. *34*, 3201 (1969).

[9] *A. G. Hortmann, A. Bhattacharjya,* J. Am. Chem. Soc. *98*, 7081 (1976).

[10] *A. T. Bottini, R. E. Olsen,* Org. Synth. Coll. Vol. V, 544 (1973).

[11] *C. B. Pollard, R. F. Parcell,* J. Am. Chem. Soc. *73*, 2925 (1951).

[12] *M. G. Ettlinger, F. Kennedy,* Chem. Ind. (London) *1956*, 166.

[13] *A. T. Bottini, J. D. Roberts,* J. Am. Chem. Soc. *79*, 1462 (1957).

[14] *A. T. Bottini, R. E. Olsen,* J. Am. Chem. Soc. *84*, 195 (1962).

[15] *H. Quast, W. Risler,* Angew. Chem. *85*, 411 (1973); Angew. Chem. Int. Ed. Engl. *12*, 414 (1973).

[16] *H. Quast, C. A. Weise Vélez,* Angew. Chem. *86*, 380 (1974); Angew. Chem. Int. Ed. Engl. *13*, 342 (1974).

[17] *E. M. Binghan, J. C. Gilbert,* J. Org. Chem. *40*, 224 (1975).

[18] *R. S. Atkinson, J. R. Malpass,* Tetrahedron Lett. *1975*, 4305.

[19] *I. E. Den Besten, C. R. Wenger,* J. Am. Chem. Soc. *87*, 5500 (1965).

[20] *A. T. Bottini, J. D. Roberts,* J. Am. Chem. Soc. *80*, 5203 (1958).

[21] For the chemistry of stable cyclopropanimines, see *H. Quast, E. Schmitt, R. Frank,* Angew. Chem. *83*, 728 (1971); *84*, 316 (1972); Angew. Chem. Int. Ed. Engl. *10*, 651 (1971); *11*, 329 (1972).

[22] *J. K. Crandall, J. B. Komin,* J. Chem. Soc. Chem. Commun. *1975*, 436; *J. K. Crandall, L. C. Crawley, J. B. Komin,* J. Org. Chem. *40*, 2045 (1975).

[23] a) *E. Jongejan, H. Steinberg, Th. J. de Boer,* Recl. Trav. Chim. Pays-Bas *97*, 145 (1978); b) *E. Jongejan, H. Steinberg, Th. J. de Boer, ibid. 98*, 66 (1979)

[24] *H. Quast, C. A. Weise Vélez,* Angew. Chem. *90*, 224 (1978); Angew. Chem. Int. Ed. Engl. *17*, 213 (1978).

[25] *R. C. Cookson, B. Halton, I. D. R. Stevens, C. T. Watts,* J. Chem. Soc. *C 1967*, 928.

[26] *N. G. Moll, D. R. Clutter, W. E. Thompson,* J. Chem. Phys. *45*, 4469 (1966); *M. E. Jacox, D. E. Milligan, ibid. 54*, 919 (1971).

[27] See, for instance, *J. K. Crandall, S. A. Sojka, J. B. Komin,* J. Org. Chem. *39*, 2172 (1974), and references cited therein.

[28] *R. Wheland, P. D. Bartlett,* J. Am. Chem. Soc. *92*, 6057 (1970).

[29] For a discussion of the mechanism of ozonolysis of ketenes, see *R. M. Moriarty, K. B. White, A. Chin,* J. Am. Chem. Soc. *100*, 5582 (1978).

[30] *O. L. Chapman, P. W. Wojtkowski, W. Adam, O. Rodriguez, R. Rucktäschel,* J. Am. Chem. Soc. *94*, 1365 (1972); *W. Adam, J.-C. Liu, O. Rodriguez,* J. Org. Chem. *38*, 2269 (1973).

[31] *J. F. Liebman, A. Greenberg,* J. Org. Chem. *39*, 123 (1974).

[32] *E. U. Elam, F. H. Rash, J. T. Dougherty, V. W. Goodlett, K. C. Brannock,* J. Org. Chem. *33*, 2738 (1968); *E. Schaumann, W.-R. Klein,* Tetrahedron Lett. *1977*, 3457.

[33] *E. Schaumann, U. Behrens,* Angew. Chem. *89*, 750 (1977); Angew. Chem. Int. Ed. Engl. *16*, 722 (1977).

[34] *A. Gomes, M. M. Joullié,* J. Heterocycl. Chem. *6*, 729 (1969); *J. M. Bohen, M. M. Joullié,* J. Org. Chem. *38*, 2652 (1973); *Z. Lysenko, M. M. Joullié, ibid. 41*, 3925 (1976). Note that the structure of *(36)* has been questioned by *K. Schank, F. Werner,* Tetrahedron Lett. *1977*, 2567; see also *I. R. Dunkin, J. G. MacDonald,* J. Chem. Soc. Chem. Commun. *1978*, 1020.

[35] *H. E. Baumgarten,* J. Am. Chem. Soc. *84*, 4975 (1962); *H. E. Baumgarten, J. F. Fuerholzer, R. D. Clark, R. D. Thompson, ibid. 85*, 3303 (1963).

[36] Review: *I. Lengyel, J. C. Sheehan,* Angew. Chem. *80*, 27 (1968); Angew. Chem. Int. Ed. Engl. *7*, 25 (1968).

[37] *M. Miyoshi,* Bull. Chem. Soc. Jpn. *43*, 3321 (1970); *46*, 212, 1489 (1973).

[38] *J. H. Jones, M. J. Witty,* J. Chem. Soc. Chem. Commun. *1977*, 281. Distinction between *(39)* and *(40)* can be made by considering the C^{13}–H coupling constant for the ring C atom and the H atom linked to it. The value found by us ($^1J_{CH} = 147.5$ Hz) is in agreement with structure *(40)*, R = $PhCH_2$, and not with *(39)* for which a $^1J_{CH}$ value of about 168 Hz should be expected (see ref. [35]).

[39] *J. C. Sheehan, I. Lengyel,* J. Am. Chem. Soc. *86*, 1356 (1964); *J. C. Sheehan, J. H. Beeson, ibid. 89*, 362 (1967); *K. Bott,* Angew. Chem. *79*, 943 (1967); Angew. Chem. Int. Ed. Engl. *6*, 946 (1967); *E. R. Talaty, A. E. Dupuy, A. E. Cancienne,* J. Heterocycl. Chem. *4*, 657 (1967); *E. R. Talaty, A. E. Dupuy,* Chem. Commun. *1968*, 790; *E. R. Talaty, C. M. Utermoehlen, ibid. 1970*, 473; Tetrahedron Lett. *1970*, 3321; *I. Lengyel, D. B. Uliss,* Chem. Commun. *1968*, 1621; *S. Sarel, B. A. Weissman, Y. Stein,* Tetrahedron Lett. *1971*, 373.

[40] *K. Bott,* Tetrahedron Lett. *1968*, 3323.

[41] *E. R. Talaty, A. E. Dupuy, T. H. Golson,* Chem. Commun. *1969*, 49; *J. C. Sheehan, M. Mehdi Nafissi-V,* J. Am. Chem. Soc. *91*, 1176 (1969).

[42] *H. E. Baumgarten, D. G. McMahan, V. J. Elia, B. I. Gold, V. W. Day, R. O. Day,* J. Org. Chem. *41*, 3798 (1976), and references cited therein.

[43] *H. E. Baumgarten, R. D. Clark, L. S. Endres, L. D. Hagemeier, V. J. Elia,* Tetrahedron Lett. *1967*, 5033.

[44] *M. Kakimoto, S. Kajigaeshi, S. Kanemasa,* Chem. Lett. *1976*, 47.

[45] *S. Toppet, G. L'abbé, G. Smets,* Chem. Ind. (London) *1973*, 1110.

[46] *M. Komatsu, Y. Ohshiro, H. Hotta, M. Sato, T. Agawa,* J. Org. Chem. *39*, 948 (1974).

[47] *G. L'abbé, A. Van Asch, S. Toppet,* Bull. Soc. Chim. Belg. *87*, 929 (1978).

[48] *E. R. Talaty, A. E. Dupuy, C. M. Utermoehlen, L. H. Stekoll,* J. Chem. Soc. Chem. Commun. *1973*, 48.
[49] *A. H.-J. Wang, I. C. Paul, E. R. Talaty, A. E. Dupuy,* J. Chem. Soc. Chem. Commun. *1972*, 43.
[50] *F. D. Greene, J. C. Stowell,* J. Am. Chem. Soc. *86*, 3569 (1964); *F. D. Greene, J. C. Stowell, W. R. Bergmark,* J. Org. Chem. *34*, 2254 (1969).
[51] *F. D. Greene, J. F. Pazos,* J. Org. Chem. *34*, 2269 (1969).
[52] *F. D. Greene, W. R. Bergmark, J. F. Pazos,* J. Org. Chem. *35*, 2813 (1970).
[53] *J.-M. Vandensavel, G. Smets, G. L'abbé,* J. Org. Chem. *38*, 675 (1973).
[54] *G. Denecker, G. Smets, G. L'abbé,* Tetrahedron *31*, 765 (1975); *N. W. Rokke, J. J. Worman, W. S. Wadsworth,* J. Heterocycl. Chem. *12*, 1031 (1975).
[55] *H. Quast, L. Bieber,* Angew. Chem. *87*, 422 (1975); Angew. Chem. Int. Ed. Engl. *14*, 428 (1975).
[56] *P. E. McGann, J. T. Groves, F. D. Greene, G. M. Stack, R. J. Majeste, L. M. Trefonas,* J. Org. Chem. *43*, 922 (1978).
[57] *A. J. Fry, W. E. Britton, R. Wilson, F. D. Greene, J. G. Pacifici,* J. Org. Chem. *38*, 2620 (1973).
[58] *F. D. Greene, W. R. Bergmark, J. G. Pacifici,* J. Org. Chem. *34*, 2263 (1969).
[59] *F. D. Greene, R. L. Camp, L. Kim, J. F. Pazos, D. B. Sclove, C. J. Wilkerson,* XXIII. Int. Congr. Pure Appl. Chem. *2*, 325 (1971).
[60] *Y. Oshiro, M. Komatsu, Y. Yamamoto, K. Takaki, T. Agawa,* Chem. Lett. *1974*, 383.
[61] *C. A. Renner, F. D. Greene,* J. Org. Chem. *41*, 2813 (1976).
[62] *W. Borsche,* Ber. Dtsch. Chem. Ges. *75*, 1312 (1942).
[63] *M. Komatsu, Y. Ohshiro, K. Yasuda, S. Ichijima, T. Agawa,* J. Org. Chem. *39*, 957 (1974).
[64] *E. Lieber, E. Oftedahl, C. N. R. Rao,* J. Org. Chem. *28*, 194 (1963).
[65] *G. L'abbé, S. Toppet, G. Verhelst, C. Martens,* J. Org. Chem. *39*, 3770 (1974); see also *C. Christophersen, A. Holm,* Acta Chem. Scand. *25*, 2015 (1971).
[66] *G. L'abbé, J. Flémal,* unpublished results.
[67] *H. G. Khorana,* Chem. Rev. *53*, 145 (1953); *F. Kurzer, K. Douraghi-Zadeh, ibid. 67*, 107 (1967).
[68] *E. Lieber, J. Ramachandran,* Can. J. Chem. *37*, 101 (1959).
[69] *G. L'abbé, G. Vermeulen, J. Flémal, S. Toppet,* J. Org. Chem. *41*, 1875 (1976).
[70] *R. A. Henry,* J. Heterocycl. Chem. *13*, 391 (1976).
[71] *E. Ziegler, G. Kollenz, W. Ott,* Justus Liebigs Ann. Chem. *1976*, 2071.
[72] *E. Ziegler, G. Kollenz, W. Ott, H. G. von Schnering, K. Peters, H. Quast,* Justus Liebigs Ann. Chem., in press.
[73] *G. L'abbé, J.-P. Dekerk, J.-P. Declercq, G. Germain, M. Van Meerssche,* Angew. Chem. *90*, 207 (1978); Angew. Chem. Int. Ed. Engl. *17*, 195 (1978).
[74] *G. L'abbé, J.-P. Dekerk, S. Toppet, J.-P. Declercq, G. Germain, M. Van Meerssche,* Tetrahedron Lett. *1979*, 1819.
[75] *G. L'abbé, J.-P. Dekerk, J.-P. Declercq, G. Germain, M. Van Meerssche,* Tetrahedron Lett. *1979*, 3213.
[76] *H. Quast, E. Schmitt,* Angew. Chem. *82*, 395 (1970); Angew. Chem. Int. Ed. Engl. 9, 381 (1970).
[77] *A. J. Hubert, A. Féron, R. Warin, Ph. Teyssié,* Tetrahedron Lett. *1976*, 1317.
[78] *J. Drapier, A. Féron, R. Warin, A. J. Hubert, Ph. Teyssié,* Tetrahedron Lett. *1979*, 559.
[79] *H. Quast, P. Schäfer,* Tetrahedron Lett. *1977*, 1057.
[80] *G. L'abbé, C.-C. Yu, S. Toppet,* Angew. Chem. *89*, 492 (1977); Angew. Chem. Int. Ed. Engl. *16*, 475 (1977); *G. L'abbé, C.-C. Yu, J.-P. Declercq, G. Germain, M. Van Meerssche, ibid. 90*, 394 (1978) and *17*, 352 (1978), respectively.
[81] *G. L'abbé, A. Verbruggen,* Tetrahedron Lett. *1979*, 49.
[82] *H. Quast, P. Schäfer, K. Peters, H. G. von Schnering,* Chem. Ber., in press; *P. Schäfer,* Dissertation, Universität Würzburg 1977.
[83] *H. Quast, E. Schmitt,* Angew. Chem. *81*, 428 (1969); Angew. Chem. Int. Ed. Engl. *8*, 448 (1969).
[84] *H. Quast, L. Bieber, W. C. Danen,* J. Am. Chem. Soc. *100*, 1306 (1978).
[85] Reviews on trimethylenemethane: *P. Dowd,* Acc. Chem. Res. *5*, 242 (1972); *J. A. Berson, ibid. 11*, 446 (1978).
[86] *C. J. Wilkerson, F. D. Greene,* J. Org. Chem. *40*, 3112 (1975).
[87] *T. Konotsune, T. Yauchi, M. Suzuki,* Jap. Pat. 85565 (1973), Sankyo Co.; Chem. Abstr. *80*, 47968p (1974).
[88] *G. L'abbé, G. Verhelst, S. Toppet, J.-P. Declercq, G. Germain, M. Van Meerssche,* Bull. Soc. Chim. Belg. *87*, 493 (1978).
[89] *K. Peters, G. von Schnering,* Chem. Ber. *109*, 1384 (1976).
[90] *H. Quast, E. Schmitt,* Angew. Chem. *81*, 429 (1969); Angew. Chem. Int. Ed. Engl. *8*, 449 (1969); Chem. Ber. *103*, 1234 (1970).
[91] *H. Quast, E. Spiegel,* Angew. Chem. *89*, 112 (1977); Angew. Chem. Int. Ed. Engl. *16*, 109 (1977).
[92] *H. Quast, K.-H. Ross, E. Spiegel, K. Peters, H. G. von Schnering,* Angew. Chem. *89*, 202 (1977); Angew. Chem. Int. Ed. Engl. *16*, 177 (1977); see also *H. Quast, E. Spiegel,* Tetrahedron Lett. *1977*, 2705.
[93] *G. L'abbé, E. Van Loock, R. Albert, S. Toppet, G. Verhelst, G. Smets,* J. Am. Chem. Soc. *96*, 3973 (1974).
[94] *G. L'abbé,* Bull. Soc. Chim. Fr. *1975*, 1127; *G. L'abbé, G. Verhelst, C. C. Yu, S. Toppet,* J. Org. Chem. *40*, 1728 (1975); *G. L'abbé, C. C. Yu,* J. Heterocycl. Chem. *13*, 883 (1976); *G. L'abbé, G. Verhelst, S. Toppet, G. S. D. King, J. Briers,* J. Org. Chem. *41*, 3403 (1976); *G. L'abbé, C. C. Yu,* Chem. Ind. (London) *1977*, 312; *G. L'abbé, A. Van Asch, J.-P. Declercq, G. Germain, M. Van Meerssche,* Bull. Soc. Chim. Belg. *87*, 285 (1978); see also *R. Neidlein, K. Salzmann,* Synthesis *1975*, 52.
[95] *G. L'abbé, D. Sorgeloos,* unpublished results.
[96] Review: *R. Gompper,* Angew. Chem. *81*, 348 (1969); Angew. Chem. Int. Ed. Engl. *8*, 312 (1969).
[97] *G. L'abbé, G. Verhelst, S. Toppet,* J. Org. Chem. *42*, 1159 (1977); see also *G. L'abbé, A. Timmermann, C. Martens, S. Toppet, ibid. 43*, 4951 (1978); *N. H. Toubro, A. Holm,* J. Chem. Soc. Perkin I, *1978*, 1440.
[98] *G. L'abbé, G. Verhelst,* Angew. Chem. *88*, 510 (1976); Angew. Chem. Int. Ed. Engl. *15*, 489 (1976).
[99] *R. Neidlein, J. Tauber,* Arch. Pharm. (Weinheim) *304*, 687 (1971).
[100] *G. L'abbé, G. Verhelst, G. Vermeulen,* Angew. Chem. *89*, 420 (1977); Angew. Chem. Int. Ed. Engl. *16*, 403 (1977); see also *R. J. S. Beer, I. Hart,* J. Chem. Soc. Chem. Commun. *1977*, 143.
[101] Review on cycloadditions of allyl cations: *H. M. R. Hoffmann,* Angew. Chem. *85*, 877 (1973); *Angew. Chem. Int. Ed. Engl. 12*, 819 (1973).
[102] Reviews: *R. Huisgen,* Angew. Chem. *75*, 604, 741 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565, 633 (1963); J. Org. Chem. *33*, 2291 (1968); *41*, 403 (1976).
[103] Reviews: *R. M. Kellogg,* Tetrahedron *32*, 2165 (1976); *R. Huisgen,* Angew. Chem. *89*, 589 (1977); Angew. Chem. Int. Ed. Engl. *16*, 572 (1977).
[104] *H. E. Winberg, D. D. Coffman,* J. Am. Chem. Soc. *87*, 2776 (1965).
[105] *A. Takamizawa, K. Hirai, S. Matsumoto,* Tetrahedron Lett. *1968*, 4027; *H. J. Schönherr, H. W. Wanzlick,* Chem. Ber. *103*, 1037 (1970); *M. Regitz, J. Hocker,* Synthesis *1970*, 301; *M. Regitz, J. Hocker, B. Weber,* Angew. Chem. *82*, 394 (1970); Angew. Chem. Int. Ed. Engl. *9*, 375 (1970); *M. Regitz, J. Hocker, W. Schössler, B. Weber, A. Liedhegener,* Justus Liebigs Ann. Chem. *748*, 1 (1971); *W. Schössler, M. Regitz,* Chem. Ber. *107*, 1931 (1974); *J. Hocker, R. Merten,* Justus Liebigs Ann. Chem. *751*, 145 (1971); *R. Richter, H. Ulrich,* J. Org. Chem. *36*, 2005 (1971); *R. W. Hoffmann, K. Steinbach, B. Dittrich,* Chem. Ber. *106*, 2174 (1973); *R. W. Hoffmann, W. Lilienblum, B. Dittrich, ibid. 107*, 3395 (1974); *R. W. Hoffmann, M. Reiffen, ibid. 109*, 2565 (1976); *R. W. Hoffmann, B. Hagenbruch, D. M. Smith, ibid. 110*, 23 (1977); *M. Reiffen, R. W. Hoffmann, ibid. 110*, 37, 49 (1977).
[106] *J. H. Boyer, V. T. Ramakrishnan,* J. Org. Chem. *37*, 1360 (1972).
[107] *I. Ugi, K. Rosendahl,* Chem. Ber. *94*, 2233 (1961); *T. ElGomati, J. Firl, I. Ugi, ibid. 110*, 1603 (1977).
[108] *G. L'abbé, L. Huybrechts, J.-P. Declercq, G. Germain, M. Van Meerssche,* J. Chem. Soc. Chem. Commun. *1979*, 160.
[109] *T. N. Margulis, D. H. Templeton,* J. Am. Chem. Soc. *83*, 995 (1961), and references cited therein.
[110] *H. Behringer, J. Falkenberg,* Tetrahedron Lett. *1967*, 1895.
[111] *H. D. Hartzler,* J. Am. Chem. Soc. *93*, 4961 (1971).
[112] *U. Anthoni, O. Dahl, C. Larsen, P. H. Nielsen,* Acta Chem. Scand. *23*, 943 (1969); *K. Akiba, T. Yoneyama, H. Hamada, N. Inamoto,* Bull. Chem. Soc. Jpn. *49*, 1970 (1976).
[113] *H. W. Roesky, G. Sidiropoulos,* Angew. Chem. *88*, 759 (1976); Angew. Chem. Int. Ed. Engl. *15*, 693 (1976).
[114] For di- and trimerization of isocyanates under the catalytic influence of trialkylphosphanes, see *H. Ulrich:* Cycloaddition Reactions of Heterocumulenes. Academic Press, New York 1967, pp. 6, 123.

Polarized Low-Temperature Crystal Spectra of Inorganic Complexes

By Peter Day[*]

The electronic spectra of complexes are especially informative if they are recorded for crystals at low temperature or at varying temperature with polarized light. This straightforward technique frequently permits reliable band assignment. Such assignments, being independent of the assumptions of any particular theoretical model, then provide a basis for testing theories of electronic structure.

1. Introduction

When chemists want to measure the electronic spectrum of a molecular complex ion or molecule in the visible or ultraviolet, they usually dissolve it in some suitable solvent and run the spectrum of the solution at room temperature. Under these circumstances, absorption bands are generally broad (rarely less than 10^3 cm^{-1}) and unstructured. In that case, the experimental information content of each band consists of its energy at the absorption maximum, its intensity (often defined as the maximum molar extinction coefficient, but better taken as the integrated band area) and its halfwidth or shape function. We can use all three of these observables to help assign the band, for example to a charge transfer or a ligand field transition, and by matching its energy to the results of some calculation to try and define the electronic symmetry of the excited state. However, even with such a well established procedure as ligand-field theory, the results are often ambiguous. Many generalizations about electronic structures of metal complexes have foundered because of wrongly assigned spectra.

A simple illustration of this fact is the case of the purple permanganate ion, MnO_4^-. Across the visible and near ultraviolet it has four main absorption bands, plus another much weaker one in the near infrared. Since the oxidation state of the manganese is +7, with an effective electron configuration $3d^0$, they cannot be d-d (ligand field) transitions but must be of charge transfer type, *i.e.* excitations of electrons from molecular orbitals mainly localized on the oxygen atoms into the empty d orbitals. In the tetrahedral ion the d orbitals are split into two-fold (e) and three-fold (t_2) degenerate subsets, while the eight 2p orbitals of π-symmetry on the four oxygen atoms are also split into sets labeled e, t_1, and t_2, with degeneracies 2, 3, and 3. In principle, therefore, we could have electronic transitions of any of the filled levels to either of the empty ones, giving a total of six possibilities, even without taking into account splitting of the excited configurations by electron repulsion. From 1952 up to the present, at least a dozen attempts have been made, using various kinds of molecular orbital calculation, to assign the five observed bands to permutations of these orbital excitations. The point I wish to make here is that the seven assignments reported between 1952 and 1970 were all different! Yet the low temperature polarized crystal spectrum described in Section 6.1 contains experimental evidence which uniquely assigns most of the observed bands.

In this article, I want to show how much more information, often of a very precise and unambiguous kind, one can get about the electronic excited states of inorganic molecules and complexes by measuring the spectra of single crystals using polarized light and low temperatures. Figure 1 is a dramatic illustration of the extra information gained by lowering the sample temperature.

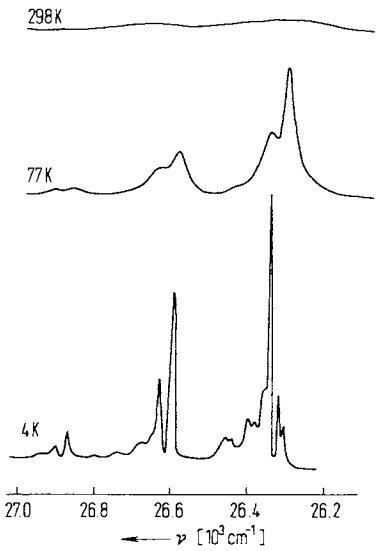


Fig. 1. A ligand field transition in Cs_3CoCl_5 at room temperature, 77 K, and 4 K.

Most of the examples come from our own work, but they are quite representative of many now found in the literature. Also, I shall only deal with complexes, by which I mean molecular species, whether charged or not, which retain their chemical integrity when isolated in dilute solution just as when they are placed in a crystal lattice. Electronic spectroscopy of transition metal ions in continuous lattice solids, like Ni^{2+} in MgO or pure NiO for example, forms a large subject of its own, traditionally closer to solid state physics, although many of the principles I shall describe here apply equally to continuous lattices. There is a very large literature on the electronic spectra of inorganic compounds. Thus, no attempt is made here to treat the theoretical background of the subject, for which reference should be made to textbooks[1] and review articles[2]. Rather, I wish to give an overview, albeit

[*] Dr. P. Day
Oxford University, Inorganic Chemistry Laboratory
South Parks Road, Oxford OX1 3QR (England)

 © Verlag Chemie, GmbH, D-6940 Weinheim, 1980 0570-0833/80/0404-0290 $ 02.50/0 Angew. Chem. Int. Ed. Engl. 19, 290-301 (1980)

brief, of some of the methods used to obtain precise and experimentally based assignments of ligand field and charge transfer states on which, ultimately, the tests for theories of electronic structure depend.

2. Why Measure the Spectra of Single Crystals?

There are several answers to this question. The most straightforward is that one may wish to know about the spectrum of a complex which does not exist in solution, perhaps because it is hydrolyzed or transformed to a complex with a different stoichiometry or stereochemistry. A simple example is $CuCl_5^{3-}$. However large an excess of chloride ions one puts into a solution of $CuCl_2$ either in water or dipolar aprotic solvents, the highest complex formed in any appreciable amount is $CuCl_4^{2-}$. Because of lattice energy considerations though, use of a tripositive counterion like $[Co(NH_3)_6]^{3+}$ allows one to crystallize the pentachlorocuprate. Its ligand field spectrum has been recorded for comparison with that of tetrachlorocuprate[3].

Another reason which motivates much work on inorganic crystal spectra is that one may be interested in the interactions between complex ions, due either to magnetic exchange or to charge transfer. For instance, the color of Magnus' Green Salt, $[Pt(NH_3)_4]PtCl_4$, tells one at once that molecular interactions are present in the crystal since the constituent ions $[Pt(NH_3)_4]^{2+}$ and $PtCl_4^{2-}$ are respectively colorless and red[4]. Mixed valency is another frequent source of "non-additive" colors[5]. Several examples of fine structure due to magnetic exchange and the much broader intervalence charge transfer transitions are given later (cf. Sections 6.4 and 4).

Probably the most valuable consequence of building complex ions into a crystal is that the orientations and geometries of the molecules are thereby fixed, so that the polarization vector of the incident light can be defined with respect to the molecular axes. For the detailed quantum mechanics of the interaction between electromagnetic radiation and molecules, reference should be made to the standard quantum chemistry textbooks such as *Eyring, Walter,* and *Kimball*[6]. Suffice it to say here that when an electromagnetic wave passes by, the molecule is subjected to simultaneous electric and magnetic fields, oscillating with the frequency ν of the radiation. If this frequency coincides with the energy difference between the ground state 0 and an excited state n of the molecule through the relationship $E_{0n}=h\nu_{0n}$, the resulting time-dependent perturbation can be thought of as "mixing together" the two wavefunctions ψ_0 and ψ_n. Integrating over time one finds that radiation is absorbed and the molecule undergoes a transition from ψ_0 to ψ_n. The probability of light absorption, represented experimentally by the peak molar extinction coefficient or the oscillator strength, is related theoretically to the magnitude of the off-diagonal matrix element of the appropriate perturbation operator between the two states 0 and n. Now the transition may be brought about by the oscillations of either the electric or the magnetic component of the radiation. In the former case the perturbation operator is the electric dipole operator $\boldsymbol{m}=\sum_i e\boldsymbol{r}_i$ where the summation goes over all the electrons, and in the latter it is the magnetic dipole operator $\boldsymbol{\mu}=(e/2m)\sum_i \boldsymbol{l}_i$. In principle, matrix elements like $\int\psi_n^*\boldsymbol{m}\psi_0 d\tau$ and $\int\psi_n^*\boldsymbol{\mu}\psi_0 d\tau$ are observable properties of the molecule, like the ground state dipole moment $\int\psi_0^*\boldsymbol{m}\psi_0 d\tau$. Consequently, their absolute values have to be independent of the molecular coordinates used to define the wave functions ψ. Put another way, the matrix elements must be totally symmetric to all transformations of the molecular coordinate system or, in the language of group theory, they must span the totally symmetric representation A_{1g} within the point group of the molecule (for nomenclature see ref. [7]; a very useful compilation of group theoretical tables is ref. [8]). In a cubic system the vector $\boldsymbol{r}$ appearing in the electric dipole operator is three-fold degenerate: $\boldsymbol{r}=x+y+z$, for example T_{1u} in the group O_h. Light absorption is then isotropic. However, when the symmetry is lowered from cubic to tetragonal one axis, *e.g.*, z is no longer equivalent to x and y. In the D_{4h} point group z transforms as A_{2u} and x, y as E_u.

A particularly simple example of the assignment of an absorption band using polarized light is provided by the square planar $PtCl_4^{2-}$ ion. This is a low spin d^8 ion with a diamagnetic closed shell ground state, which therefore transforms as A_{1g} in D_{4h}. The crystal K_2PtCl_4 contains stacks of $PtCl_4^{2-}$ ions with their planes all parallel or perpendicular to the planes of the ions (Fig. 2a). For a transition to take place, the arguments just given lead to the general rule

$$\Gamma_0 \times \Gamma_{op} \times \Gamma_n \subset A_{1g} \qquad (1)$$

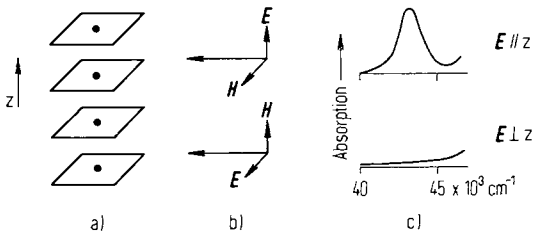


Fig. 2. a) Arrangement of $PtCl_4^{2-}$ ions in the K_2PtCl_4 crystal (schematic); b) directions of polarization of incident light; c) polarized absorption spectra.

where the Γ's are irreducible representations of the ground state, the electronic or magnetic dipole operator and the excited state, respectively. For the two orientations of the electric vector of the incident light, shown in Figure 2b, we therefore have

$$\begin{aligned} &A_{1g} \times A_{2u} \times \Gamma_n \subset A_{1g} \\ &A_{1g} \times E_u \times \Gamma_n \subset A_{1g}. \end{aligned} \qquad (2)$$

The former is satisfied for $\Gamma_n = A_{2u}$, the latter for $\Gamma_n = E_u$. Experimentally one finds[9] that in the ultraviolet there is a very intense band in the crystal spectrum of K_2PtCl_4 at 42500 cm^{-1} when the electric vector of the incident light is parallel to z, but which is absent when $\boldsymbol{E}\|x,y$ (Fig. 2c). Thus, the upper state in question is $^1A_{2u}$, and probably results from a $5d_{z^2}\rightarrow 6p_z$ transition. On the other hand, the first intense band in the spectrum of the isostructural crystal K_2PdCl_4 only appears in $\boldsymbol{E}\|x,y$ so it has to be assigned to a ^1E_u state, most likely a $Cl(p\pi)\rightarrow Pt5d_{x^2-y^2}$ charge transfer transition. Such information could never have been found from a solution spectrum.

Strictly speaking, in the example we have just given, no definitive judgment could be made from the two polarized

spectra as to whether the transition was being allowed by the electric or magnetic dipole mechanism. However, because of the relative magnitudes of the electronic charge and the Bohr magneton, it turns out that even fully allowed magnetic dipole transitions are many orders of magnitude weaker than electric dipole transitions. For uniaxial crystals though, there is a simple test to determine whether a transition is allowed by the electric or magnetic dipole operator. As shown in Figure 3, we measure three polarized spectra, one called the axial (α) spectrum, with the light incident parallel to the unique crystal axis (in which case both electric and magnetic vectors are perpendicular to the axis) and two with the incident light perpendicular. In the latter case, one has the choice of placing the electric vector parallel or perpendicular to the axis (called respectively the π and σ spectra). Compare the three spectra: two will be similar, the other different. Depending on whether the transition is induced by the oscillating electric or magnetic component of the light, the axial spectrum coincides with the σ- or with the π-spectrum, because then these two vectors are parallel. An example, shown in Figure 4, is one of the ligand field transitions of the $CoCl_4^{2-}$ ion in Cs_3CoCl_5. In this tetragonal crystal we see clearly that the axial and σ-spectra coincide, demonstrating the electric dipole character of the transition.

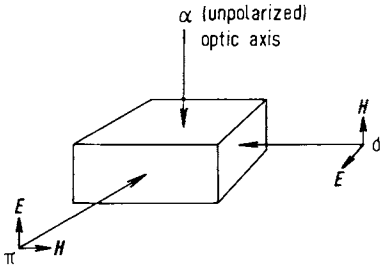


Fig. 3. Measurement of polarized spectra for a uniaxial crystal.

A final reason for measuring the spectra of crystals is that it gives us much the most convenient way of examining the spectra at low temperatures.

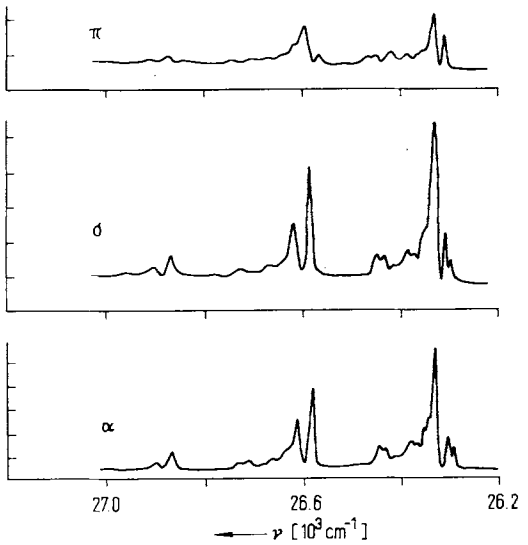


Fig. 4. Axial (α), σ- and π-polarized spectra of a ligand field transition in Cs_3CoCl_5.

3. Why Measure the Spectra of Crystals at Low Temperatures?

A fundamental problem with any kind of spectroscopy is that information about two states, ground and excited, is convoluted into one observable, the energy of the transition between them. How can one uncouple that information and find out about the two states separately? The simplest experiment along these lines is to change the temperature because changes of thermal population among closely spaced sublevels only affect the ground state. In the limit, as we approach absolute zero, all the molecules in the ensemble are in their lowest states and any fine structure observed in the spectrum relates to sublevels of the excited state. There are many sources of sublevels within the electronic ground states of inorganic complexes which, if thermally populated, confuse and broaden the optical spectrum. Bearing in mind that the thermal energy kT corresponding to room temperature is about 200 cm^{-1}, we can cite the following:

1) Skeletal vibrations in the range 100—300 cm^{-1}, (ν(CoN) is about 350 cm^{-1} in $Co(NH_3)_6^{3+}$ and ν(Hg—I) is about 120 cm^{-1} in HgI_4^{2-});
2) Lattice vibrations and librations of complex ions in the range 20—100 cm^{-1};
3) Low symmetry splittings due to the distortion of the complex when placed in the crystal, usually in the range 1—10 cm^{-1} (usually referred to by ESR spectroscopists as "zero-field splittings");
4) Splittings of the order of 5—50 cm^{-1} due to magnetic exchange interactions in dimeric or cluster complexes.

At liquid helium temperature (4.2 K), kT is only about 3 cm^{-1}, so broadening due to the population of these kinds of sublevels is almost entirely eliminated, often with dramatic effects on the resolution and hence on the information content of the spectrum. An example, shown in Figure 5, is a

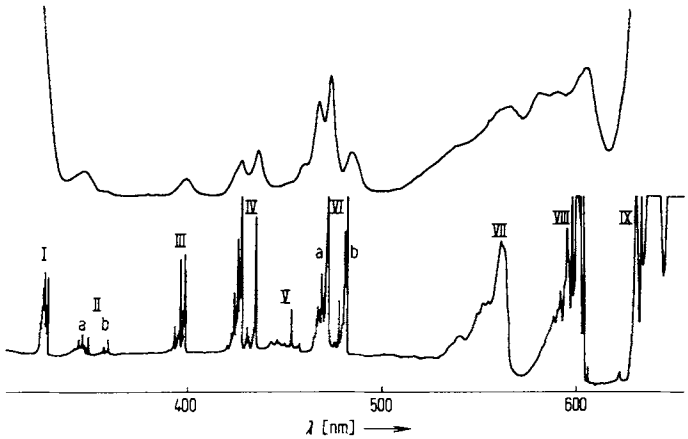


Fig. 5. The spin-forbidden ligand field bands of Cs_3CoBr_5 at room temperature (top) and 4.2 K (bottom) (after [10]).

portion of the ligand field spectrum of $CoBr_4^{2-}$ in Cs_3CoBr_5[10]. In favorable cases such as this one, even very small perturbations of a few cm^{-1} can be used as assignment methods.

Apart from cooling the sample to the lowest available temperature, another approach is to measure the spectrum as a

function of temperature and monitor the changing populations of the ground state sublevels. This can be done in two different ways: if the spectrum is well resolved one can simply monitor the areas of the separate peaks and fit the results to a Boltzmann distribution equation to extract the energy separation between the ground state sublevels directly. For example in $CoCl_4^{2-}$ the ground state of the Co^{II} is $^4A_2$, but in the crystal of Cs_3CoCl_5 the anion is slightly distorted in such a way that the fourfold degeneracy (U' in the double group T_d^*) is lifted and two doublet states result, split apart by 8.4 cm^{-1}. Looking at some of the ligand field bands under high resolution, one sees pairs of bands with just this separation, one member of each pair increasing in intensity with increasing temperature and the other decreasing. On fitting the intensities to the Boltzmann populations in a two-level model an estimate of the separation of the two levels is easily made (Fig. 6)[11].

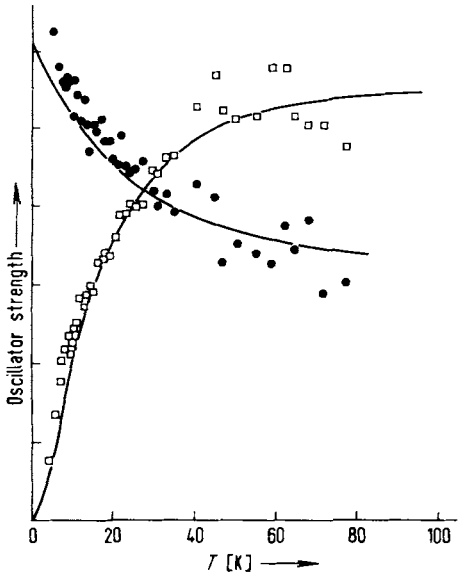


Fig. 6. Temperature dependence of the intensity (oscillator strength, arbitrary units) of a pair of ligand field bands in Cs_3CoBr_5 [11]. The full line is fitted to 11 cm^{-1} separation between the ground state levels.

4. Band Shapes of Broad Absorption Bands

Unfortunately, it sometimes happens that absorption bands remain broad and unstructured, even at very low temperatures. In such cases it may still be possible to extract useful information from the spectrum by measuring it as a function of temperature. For example, Figure 7a shows the first transition of HgI_4^{2-} doped in a crystal of $[(C_2H_5)_4N]_2ZnI_4$ from room temperature to 4.2 K[12]. On cooling it shifts somewhat and narrows, but otherwise remains featureless. What we can measure, though, is its shape or, more particularly, its halfwidth. As we shall describe in more detail below, the band is broadened because the electronic excitation couples to molecular vibrations: the transition obeys the Franck-Condon principle, *i.e.*, it is vertical on a potential energy diagram because the nuclei remain at the same positions in space as an electron is transferred from an occupied to an unoccupied orbital. If the equilibrium geometry of the excited state differs substantially from that of the ground state when it is formed by absorbing a photon it must be in a strongly vibrationally excited state.

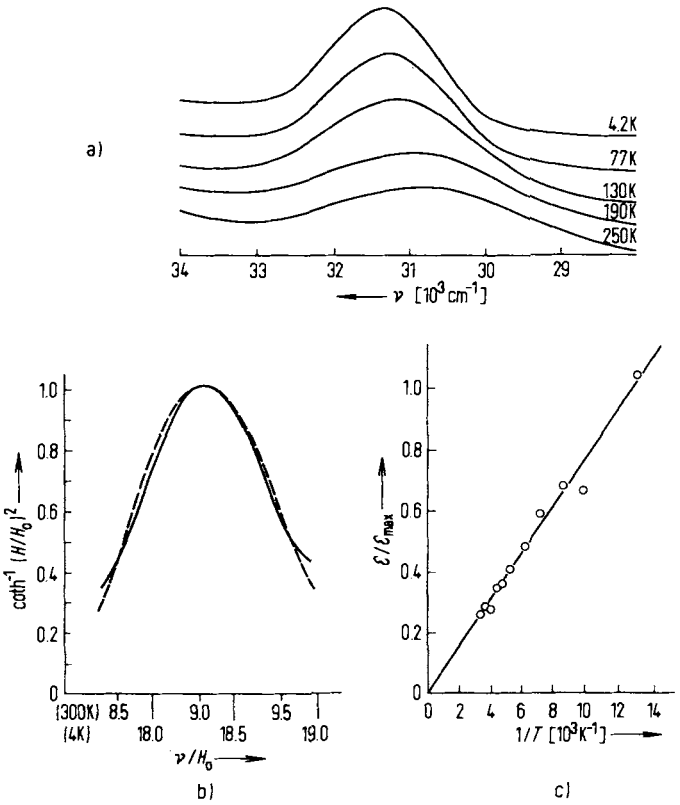


Fig. 7. Treatment of broad absorption bands: HgI_4^{2-} doped into a crystal of $[N(C_2H_5)_4]_2ZnI_4$. a) Axial absorption spectrum at temperatures from 300 to 4.2 K; b) band shape at 300 and 4.2 K; c) halfwidth as a function of temperature [12].

If the motions of the electron and the nuclei are not coupled (*i.e.*, the Born-Oppenheimer approximation is valid) the total wavefunctions of the ground and excited states may be factored into products of electronic and vibrational wavefunctions: *e.g.*, $\psi_n = \psi_n \chi_v$, where χ is a vibrational function. If, as suggested above, we get the total oscillator strength of the band by integrating the band area, this amounts to summing over all transitions from the thermally populated vibrational levels of the ground state to each vibrational level of the excited state:

$$f_{0n} \propto |\langle \psi_n | e\boldsymbol{r} | \psi_0 \rangle|^2 \propto \sum_{v,v'} |\langle \psi_n \chi_{v'} | e\boldsymbol{r} | \psi_0 \chi_v \rangle|^2 \quad (3)$$

Given that the electric dipole operator operates only on the electronic part of the wavefunction, the shape function $G(\nu)$ of the band envelope is obtained by summing over the set of overlap integrals between the vibrational wavefunctions χ_v and $\chi_{v'}$ the purely electronic matrix element $\langle \psi_n | e\boldsymbol{r} | \psi_0 \rangle$ acting as a constant multiplier:

$$G(\nu) \propto \sum_{v,v'} |\langle \psi_n | e\boldsymbol{r} | \psi_0 \rangle|^2 |\langle \chi_{v'} | \chi_v \rangle|^2 P(v) \cdot \delta(\nu - (E_{v'} - E_v)/h) \quad (4)$$

In Eq. (4) P(v) represents the probability that the vth vibrational level of the electronic ground state is occupied. Of course, there are many different modes i with frequencies ω_i.

Then

$$P(v) = \prod \{\exp(-v_i h\omega_i/kT)/[1-\exp(-h\omega_i/kT)]\} \quad (5)$$

For any general case $G(\nu)$ cannot easily be computed. However, by making some rather drastic simplifying assumptions, a tractable expression results. In particular, one assumes that all the modes i have the same frequency or alternatively, and more realistically, that only one mode contributes to the broadening. Furthermore, one supposes that the ground and excited state potential energy surfaces are both harmonic, and merely displaced Δq from one another as shown in Figure 8. The shape function $G(\nu)$ then simplifies to a Gaussian with a halfwidth H which is quite a simple function of temperature

$$H^2 \propto (h\omega)^2 S \coth(h\omega/2kT) \quad (6)$$

where ω is the "effective" vibrational frequency in the ground state and S, called the Huang-Rhys factor[13], is the ratio of the vibrational energy excited in the upper state to the energy of a single vibrational quantum, *i.e.*, $(1/2)\omega^2\Delta q^2/h\omega$. Measuring H as a function of T is thus a means of determining ω, whilst the value of H at $T=0$ gives S and hence Δq, the expansion of the excited state compared with the ground state.

To test Eq. (6) we first have to be sure that the band is well represented by a Gaussian and that the shape does not change with temperature. This is done by plotting $\varepsilon/\varepsilon_{max}$, the ratio of the absorption constant to its maximum value, against ν/H. A Gaussian curve converts to a parabola, as shown in Figure 7b, which also shows that for HgI_4^{2-} the shape is indeed constant with temperature. To obtain ω one then plots $\coth^{-1}(H/H_0)^2$ against $1/T$, giving a straight line passing through the origin, from whose slope ω is found (Fig. 7c). For HgI_4^{2-} the value of ω found in this way is 116 cm^{-1}, remarkably close to the frequency of the totally symmetric Hg—I stretching vibration as found by Raman spectroscopy. The charge transfer spectrum of the ion CoI_4^{2-} behaves in exactly the same way[14].

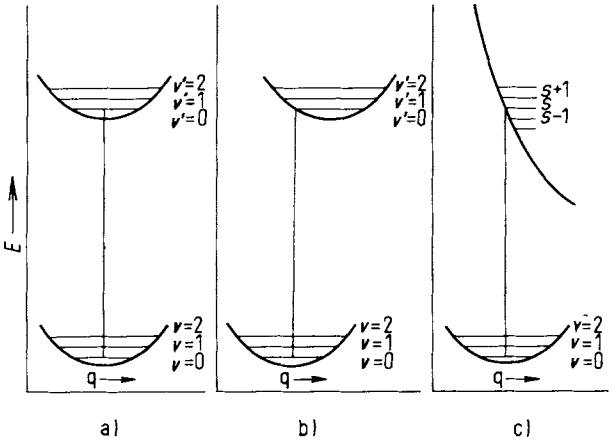


Fig. 8. Ground and excited state potential energy surfaces. a) No change of dimensions in the excited state; b) small change; c) large change.

The ultraviolet spectrum of HgI_4^{2-} remains broad because it results from transfer of an electron from non-bonding orbitals localized on the halogen atoms to the highly antibonding empty 6s orbital on Hg. Even broader are the bands which, in mixed valency compounds, arise from electron transfer between two complex ions containing metals in different oxidation states. For instance, compounds containing the two complex ions $SbCl_6^-$ and $SbCl_6^{3-}$ are dark blue because of an absorption band which does not occur in compounds containing either ion separately[15]. The new band is a charge transfer $Sb^{III} \rightarrow Sb^{V}$. As can be seen from Figure 9a, it is at least 5000 cm^{-1} wide[16]. This is because we are removing an electron completely from one complex ion and placing it on another, a process which must lead to an excited state having an equilibrium geometry very different from that of the ground state. In Figure 9b the variation of halfwidth with temperature is compared with that calculated from eq. (6) with $\omega = 210$ cm^{-1} and $S = 130$[16]. The fit, which is quite good, corresponds to the bond length change (about 0.2 Å) expected on going from MCl_6^{3-} to MCl_6^{2-}. On the other hand, the frequency is not that of either $SbCl_6^{3-}$ or $SbCl_6^-$.

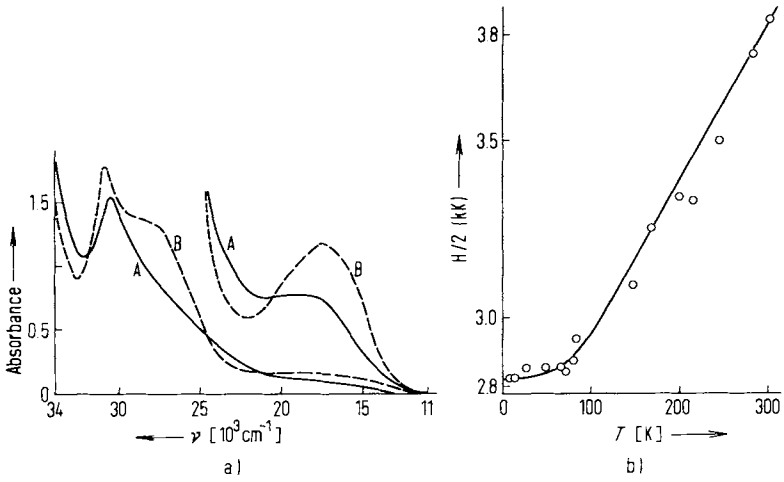


Fig. 9. Intervalence $Sb^{III} \rightarrow Sb^{V}$ absorption band in $[CH_3NH_3]_2Sb_xSn_{1-x}Cl_6$ [16]. a) Transmission spectra of two crystals of different thickness, A at 300 K, B at 6 K; b) observed and calculated half-width of the intervalence band as a function of temperature.

5. How to Measure the Spectra of Crystals at Low Temperatures

We have discussed some of the types of information which are potentially accessible by measuring crystal spectra at low temperatures. How then does one go about it? Technical details of optical spectroscopy are given in a number of books[17]; here I will describe some general principles.

5.1. Cryostats

Liquid helium is now found much more often in chemistry laboratories than it was a few years ago, so we shall not consider any other cryogenic fluids such as liquid nitrogen (b.p. 77 K) or liquid hydrogen (b.p. 20 K). Cryostats for optical spectroscopy are of two main types: static or flow. Also available, though more expensive than cryostats, are various types of closed-cycle or open-cycle refrigerators which are usually based on the Joule-Thomson effect. However, they are much cheaper than conventional cryostats to operate, since they only need gas or, in the case of the closed-cycle systems, only electricity, and are very suitable for laboratories where supply of liquid refrigerants is a problem. On the other hand, they rarely work below about 10 K, and have only a limited cooling capacity.

Static cryostats, nowadays mostly made of metal, consist of an outer vacuum casing within which the can containing the liquid helium is further isolated from heat entry by surrounding it with a copper radiation shield cooled by liquid nitrogen. The sample is then suspended on a rod so that it is immersed in the liquid helium for experiments at 4 K, or in cold flowing gas for work above 4 K. The sample rod usually contains a small heating element, as well as a temperature sensor such as a carbon resistor or a gold/0.03 atomic percent iron *vs.* chromel thermocouple, to enable the temperature to be controlled by a feed-back device. A typical form of static cryostat is shown in Figure 10a. To reach temperatures below 4 K, a second liquid helium container is placed within the main container, insulated from it by another vacuum space but connected to it by a siphon tube. The inner chamber is filled through the siphon from the outer, then closed off, and the pressure above the liquid is reduced by a rotary pump. In this way, temperatures down to about 1.4 K are accessible. To go lower, more specialized methods are needed.

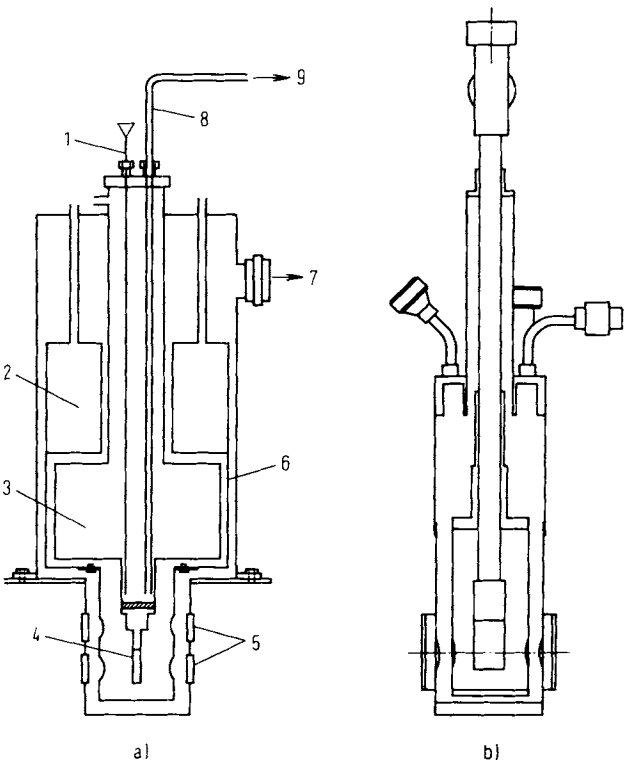


Fig. 10. a) Static cryostat. 1, helium level indicator; 2, liquid nitrogen reservoir; 3, liquid helium container; 4, copper block; 5, quartz windows; 6, copper radiation shield; 7, to vacuum pump; 8, transfer tube; 9, to helium Dewar. b) Flow cryostat [18].

A very convenient form of small cryostat for carrying out short experiments down to about 3.6 K is the continuous flow system shown in Figure 10b[18]. Here the liquid helium is sucked from a storage vessel through the cryostat by a small pump, the flow rate being controlled by a needle valve.

5.2. Sample Mounting

Unless condensing optics are used to focus the light onto the crystal, the minimum crystal dimensions for optical spectroscopy are about 1 mm^2 in area. Of course, the thickness depends upon the extinction coefficients of the bands being measured and the concentration of active chromophore in the crystal. Most conventional double beam spectrophotometers can measure an optical density of about 3 without the effects of stray light becoming too noticeable. Pure solids may have an effective concentration of light absorbing species as high as 5—10 M, so if the molar extinction coefficient of the band in question is 10 l mol^{-1} cm^{-1} the crystal should not be thicker than about 0.2 mm. On the other hand, if one wishes to measure a charge transfer transition, with a molar extinction coefficient of several thousands, the best way is to dilute the chromophore by making a solid solution with an isomorphous but non-absorbing host lattice, for example MnO_4^- in $KClO_4$. If necessary, crystals can be thinned either on a lapping wheel using diamond paste, or with successively finer grades of emery paper, followed by polishing with talc.

After determining its orientation by taking an oscillation or a Laue back-reflection X-ray photograph, the crystal is usually mounted in the cryostat by fixing it over a hole in a copper plate with a small amount of silicone grease, taking care that it is not strained, and that no light passes around its edges.

5.3. Spectrophotometers

Commercial double beam ratio recording spectrophotometers are quite suitable for all except the most sophisticated measurements of polarized low temperature crystal spectra. Important factors to bear in mind are the resolution of the monochromator, determined by the length and the number of lines/mm of the grating; the stray light level, which determines the maximum optical density which can be measured, and the sensitivity and wavelength range of the detection system, which governs the slit width at which one can work, and hence the ultimate resolution possible with a crystal of given size. Taking the Cary 14 or 17 as an example, these in-

struments have monochromators containing both a prism and a grating. The quality of the monochromation is usually expressed as the reciprocal dispersion, in this case about 30 Å mm^{-1} in the visible. The ability of the instrument to resolve closely spaced peaks depends on the width of the entrance and exit slits: at the minimum values usually employed in the Cary (about 0.02—0.05 mm) it has a resolution, or spectral band-pass, of about 1 Å. Normally visible-ultraviolet spectra are expressed in wavenumbers (cm^{-1}), so it is of interest to note that at 4000 Å, on the edge of the ultraviolet, 1 Å is equivalent to about 6 cm^{-1}, while in the red, at 7000 Å, it is about 3.5 cm^{-1}.

More sophisticated monochromators may do considerably better than this. For example, a standard 1 m Czerny-Turner monochromator with a grating having 1200 lines mm^{-1} has a reciprocal dispersion of 8.3 Å mm^{-1} in first order, and can be used to obtain spectral bandpass nearer 0.1 Å, *i.e.*, about 0.5 cm^{-1} in the visible. Quite a different way of obtaining highly monochromatized radiation, now having a large impact on many fields of spectroscopy, is the tunable dye laser. With a given dye one can usually tune the radiation over about 300 Å but dyes are now available to cover the whole range from the near infrared (9500 Å) to the ultraviolet (3500 Å) or, with frequency doubling, to about 2200 Å. As in a monochromator the spectral bandpass of the radiation depends upon the size and quality of the grating used in the laser cavity, but around 0.1 Å is quite readily obtained. Further, by fitting an etalon in the cavity this may be reduced by a further factor of 100. The uses of such very narrow bandpass radiation for inorganic spectroscopy are only now beginning to be explored.

6. Fine Structure in Low Temperature Crystal Spectra

Earlier on in Section 3 we listed some of the sublevels within the electronic ground state which, by becoming thermally populated at room temperature, serve to confuse the absorption spectrum. It is important to realize that such sublevels exist for every excited state, so at low temperatures the fine structure we see in the spectra reflects the sublevel structure of the excited state, and is extremely valuable for assigning the transition. Let us now consider some sources of fine structure, and the kind of information that we can get from them. First of all, we take the fine structure which comes from co-excitation of molecular vibrations.

6.1. Vibrational Structure

The three parts of Figure 8 indicate the three broad subdivisions of behavior when a transition occurs between a ground state and excited state potential energy surface. They correspond to increasingly strong coupling between the electron being excited and the nuclear framework of the complex, a distinction which was originally made a long time ago by *Herzberg* in the spectra of small molecules in the gas phase[19]. We have already discussed in Section 4 the extreme form of case c, when only a broad unstructured envelope is seen. In the other limiting case, when the equilibrium dimensions and the force constants of the molecule are unchanged by the electronic transition, one would anticipate only a single sharp line corresponding to $v=0 \rightarrow v'=0$, because the vibrational wave functions form an orthonormal set. Only when $v=v'$ is the vibrational overlap integral in Eq. (4) nonzero. Case a of Figure 8 applies when the electrons involved in the transition scarcely influence the molecular binding; an extreme example would be an f→f transition in a lanthanoid or actinoid complex. However, there is a complicating factor here because the electronic transition itself is not electric dipole-allowed if the complex is centrosymmetric, owing to the fact that ψ_0 and ψ_n share the same parity. For an electric dipole transition to be observed, the electronic excitation has to be accompanied by creation ($\chi_0 \rightarrow \chi_i'$) or annihilation ($\chi_1 \rightarrow \chi_0'$) of a quantum of some non-totally symmetric vibrational mode. An extension of Eq. (1) is then

$$\Gamma_0 \times \Gamma_0^{vib} \times \Gamma_{op} \times \Gamma_n \times \Gamma_n^{vib} \subset A_{1g}. \quad (7)$$

Applying Eq. (7) to an octahedral complex of an f-block element, for example, Γ_0 and Γ_n would both be u-functions, Γ_{op} is the u while if the temperature is low enough for all the molecules in the crystal to be in their vibrational ground states Γ_0^{vib} is g. Hence, Γ_n^{vib} has to be u.

Just such a situation, which represents a particularly neat example of these arguments, is the UCl_6^{2-} ion, whose spectrum was measured some years ago by *Satten* and his colleagues[20]. The electron configuration of the ion is $5f^2$ and the ground term is $^3H_4$. Fine structure of one of the f→f transitions in $[N(CH_3)_4]_2UCl_6$, in which the UCl_6^{2-} occupies a centrosymmetric site, is shown in Figure 11. There is a clear symmetry about this band system, corresponding components lying at equal frequency intervals on either side of a central point, marked with the arrow. The latter represents the frequency of the purely electronic f→f transition which, because it is u→u, does not appear. What we do see, though, are narrow bands corresponding to the frequency of the purely electronic transition plus or minus the frequencies of single quanta of each of the odd-parity vibrational modes of the octahedral complex. Sum and difference bands are easily distinguished by varying the temperature because the $\chi_1 \rightarrow \chi_0'$ bands lose intensity when the crystal is cooled and the $v=1$ levels become depopulated. The way their intensities vary with the temperature provides an additional check on the ground state vibrational frequencies *via* the Boltzmann population expression [Eq. (5)].

Usually, d-electrons in transition metal complexes are thought of as more heavily engaged in molecular binding than f-electrons in complexes of the lanthanoids and actinoids. In analyzing vibrational fine structure accompanying the d-d transitions of centrosymmetric transition metal complexes we meet the same problem we have just described for UCl_6^{2-}, namely that the absorption is electric dipole-forbidden, this time because it is g→g. However, we can avoid this complication by looking at the spectrum of a tetrahedral complex. If the equilibrium position along a vibrational coordinate in the excited state is slightly (but only slightly) displaced from its position in the ground state, or if the force constant is slightly altered by the excitation, the ground and excited state vibrational wavefunctions no longer form a strictly orthonormal set so that transitions other than $v=v'$ become allowed. On the other hand, the vibrational overlap

integrals $\langle\chi_0'|\chi_v\rangle$, whose squares are called Franck-Condon factors, fall off rapidly in magnitude as v and v' diverge. At low temperature then, we find the $\chi_0 \rightarrow \chi_0'$ band strongest, but followed by a "progression" of increasingly weaker bands from excitation to χ_1', χ_2', ... *etc.* If the potential energy surface remains reasonably harmonic in the excited state, the intervals between its vibrational levels are constant. The progression then manifests itself in a very obvious way, as a series of equally spaced bands. In fact, one of the first things which a spectroscopist does when confronted by a highly structured band system is to search for some constant energy intervals.

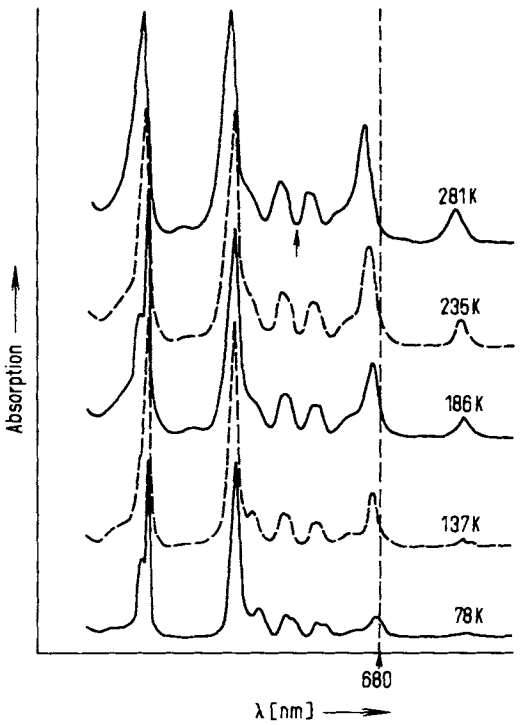


Fig. 11. Part of the f→f spectrum of $[(CH_3)_4N]_2UCl_6$ at various temperatures, showing fine structure due to odd-parity vibrational modes [20].

He is often aided by the fact that the vibrational frequencies in the excited state are not more than 10% or so different from those of the ground state. Consequently, a good knowledge of the crystal's infrared and Raman spectra is a great help.

Nevertheless, even such a simple molecule as a tetrahedron has four intramolecular vibrational modes (a, e, t_1, and t_2), not to mention vibrations of the molecules against one another, or against the counterions in the crystal. Which of them are likely to show up as progressions? The answer is mostly the totally symmetric ones. This is because of the operation of the Born-Oppenheimer approximation. Even if we remove the orthonormality requirement from the vibrational wavefunctions, only multiple quanta can be excited of those modes which are totally symmetric in the point group both of the ground and the excited electronic state. Should the complex change shape on excitation, *i.e.* if the point group of the excited complex, at its equilibrium geometry, is different from the ground state, one may find co-excited modes which, while non-totally symmetric in the ground state's point group, become totally symmetric in that of the excited state. The most common consequence of the breakdown of the Born-Oppenheimer approximation is the Jahn-Teller effect: as *Liehr* remarked[21] many years ago "observation of a progression in a non-totally symmetric mode is a sure sign of Jahn-Teller funny business". However, in this short article, I do not want to consider this particular complication.

An illustration representative of the vibrational fine structure often seen in ligand field spectra is the band system of Figure 4. Three sets of repeating bands are observed; they are separated by intervals of 275 cm^{-1}, very close to the a_1 Co—Cl stretching frequency in the ground state of $CoCl_4^{2-}$ (285 cm^{-1}). Further subsidiary intervals correspond to excitation of single quanta of the e molecular mode, and also various lattice modes. After the vibrational sidebands have been assigned in this particular case, there remain four closely spaced electronic origin bands. These originate from the lowering of symmetry in the ground and excited states as a result of the crystal lattice environment. We shall discuss them further below.

When the molecule changes its dimensions by a larger amount on excitation, as for example in a charge transfer transition when an electron is transferred from an orbital localized on the ligands to one localized on the metal, the first member of the vibrational progression is no longer necessarily the most intense: as a function of v' the vibrational overlap integral $\langle\chi_0|\chi_{v'}'\rangle$ may have its maximum value for $v'>0$. Figure 12 shows a particularly well resolved progression in the visible spectrum of the MnO_4^- ion doped into the tetragonal lost lattice KIO_4[22]. The frequency of the repeat interval is 764 cm^{-1}, which should be compared to the a_1 Mn—O stretching frequency in the ground state, 850 cm^{-1}. Note that this excited state frequency is reduced by a much larger factor than was the case for the ligand field band of $CoCl_4^{2-}$. By assuming that the potential energy surfaces of the two states are harmonic, one can use the set of Franck-Condon factors to calculate how much the molecule is expanded in the excited state: from the very similar spectra of MnO_4^- in the orthorhombic host crystal $KClO_4$, a figure of 0.10 Å has been estimated[23].

Sometimes the nature of the vibration co-excited with the electronic transition can be used to diagnose the type of transition. An interesting set of examples of this way of using vibrational fine structure are the metal-metal bonded dimers such as $Re_2Cl_8^{2-}$, whose structures consist of two planar $ReCl_4$ moieties placed face-to-face with a very short Re—Re distance. Two kinds of electronically excited state can be envisaged in this kind of complex. Either electrons are excited

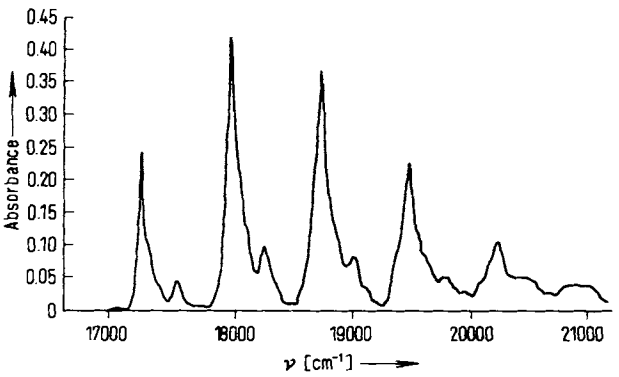


Fig. 12. Part of the axial spectrum of MnO_4^- in tetragonal KIO_4 [22].

from Cl orbitals to empty Re orbitals (charge transfer) or the excitation is from metal-metal bonding orbitals to antibonding ones, in which case the transition is localized within the Re_2 part of the molecule. If the transition were of charge transfer type the vibrational coordinate q in Figure 8 along which the molecule is displaced on going from the ground to the excited state is that of an Re—Cl normal mode. On the other hand if the electron remains within the Re_2 unit, while reducing the Re—Re bond order, then it is the Re—Re distance which is most altered on excitation. In the event (Fig. 13) the vibrational mode co-excited with the 680 nm band in $Re_2Cl_8^{2-}$ is the Re—Re stretching mode (350 cm^{-1}), so the band is assigned to the $\delta-\delta^*$ transition of the Re—Re quadruple bond[24]. Similar conclusions were reached about the visible absorption bands of several complexes containing the Mo_2^{4+} unit, though here there is an interesting complication because much of the intensity appears to arise from vibronic coupling[25].

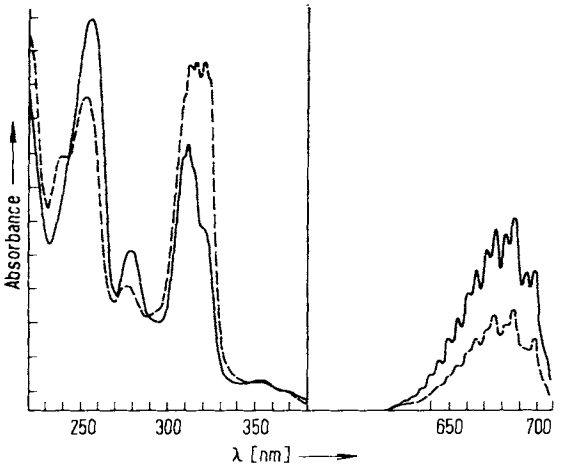


Fig. 13. Polarized absorption spectra of $[N(C_4H_9)_4]_2[Re_2Cl_8]$ at 5 K [24].

6.2. Isotope Vibrational Splittings

A special case of vibrational fine structure occurs when the ligands can exist in more than one isotopic form. Frequencies of metal-ligand vibrations depend on the masses of the vibrating atoms and on the force constant of the bond, which, of course, is unaffected by substituting one isotope for another. Shifts in the frequencies on isotope substitution therefore result from the changed reduced mass alone. Sometimes isotope substitutions are made deliberately to assign vibrational fine structure: for example D for H in aquo-complexes[26] or O^{18} for O^{16} in complexes of the uranyl (UO_2^{2+}) ion[27]. Sometimes, too, one may simply find two isotopes present in ordinary natural abundance. An instance of this effect is shown in Figure 14. One of the ligand field bands of $MnCl_4^{2-}$ in the tetragonal crystal Cs_3MnCl_5 [actually one of the spin-orbit components of $^4T_2(D)$] is accompanied by a progression in the a_1 Mn—Cl stretching mode, much as in the band of $CoCl_4^{2-}$ in Figure 4. However, in the Mn case the bands are particularly sharp and well resolved, so that further substructure becomes apparent[28]. In the first vibrational sideband (*i.e.*, one quantum of the a_1 mode) we see an envelope of at least three bands, each separated from the next by 2.1 cm^{-1}. Chlorine occurs as ^{35}Cl and ^{37}Cl with natural abundances 75.4% and 24.6%, respectively. The tetrachloromanganate complexes in our crystal therefore consist of $[Mn^{35}Cl_4]^{2-}$, $[Mn^{35}Cl_3{}^{37}Cl]^{2-}$, $[Mn^{35}Cl_2{}^{37}Cl_2]^{2-}$, ...*etc.* in

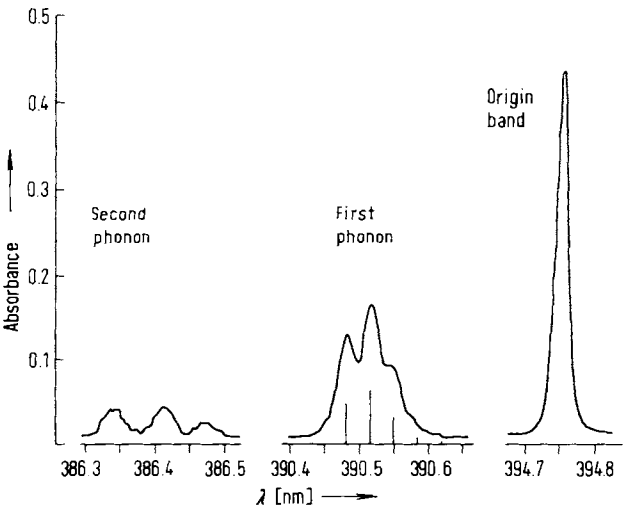


Fig. 14. Isotope fine structure in the vibrational sidebands of a ligand field transition of $MnCl_4^{2-}$ in Cs_3MnCl_5 [28].

statistically determined proportions. Each Cl_4 unit has a slightly different reduced mass (in the a_1 mode the Mn remains stationary) and so gives a sideband at a slightly different frequency. The calculated frequencies and abundances are shown as sticks in Figure 14: agreement with the experimental spectrum is clearly excellent.

6.3. Site Group Splittings

Although complex ions like $CoCl_4^{2-}$ and MnO_4^- may be regular tetrahedral in solution, when they are incorporated into a crystal lattice they will almost certainly occupy sites with lower point symmetry than T_d. Taking the absorption band in Figure 4 as an example, we noticed that after the vibrational sidebands were all accounted for there remained a group of bands constituting the electronic origin. This is shown in greater detail in Figure 15. As noted earlier, the ground state ($^4A_2$ in T_d) is split in the crystal of Cs_3CoCl_5 by a combination of spin-orbit coupling and a small tetragonal distortion to give two doublets (E′ and E″ in D_{2d}^*). Ligand field calculations[11] suggest that the band system in Figures 4 and 15 might be assigned as a transition to a $^2E(T_d)$ state which, like the ground state, would transform as U′ in the double group T_d^*. Also like the ground state, this excited U′ state would be split by the tetragonal site distortion, similarly giving two doublets, E′+E″. In principle, therefore, four transitions are possible, and they can all be assigned by combining temperature dependence and polarization data as shown in Figure 16[11]. Eq. (1) applied to the double point group D_{2d}^* tells us that E′→E′ and E″→E″ are allowed only in *xy*-polarization while E′→E″ and E″→E′ are allowed for both *xy*- and *z*-polarizations. In Figure 15a we see that the lowest energy band A only appears in the *xy*-spectra while temperature variation experiments indicate that it is a "hot" band; 8.4 cm^{-1} to higher energy the next band B has mixed polarization and behaves as a "cold" band. Figure 15b shows

bands A and B in the *xy* polarization at even higher resolution and lower temperature. At 1.3 K band A has disappeared completely. The temperature variation experiments also

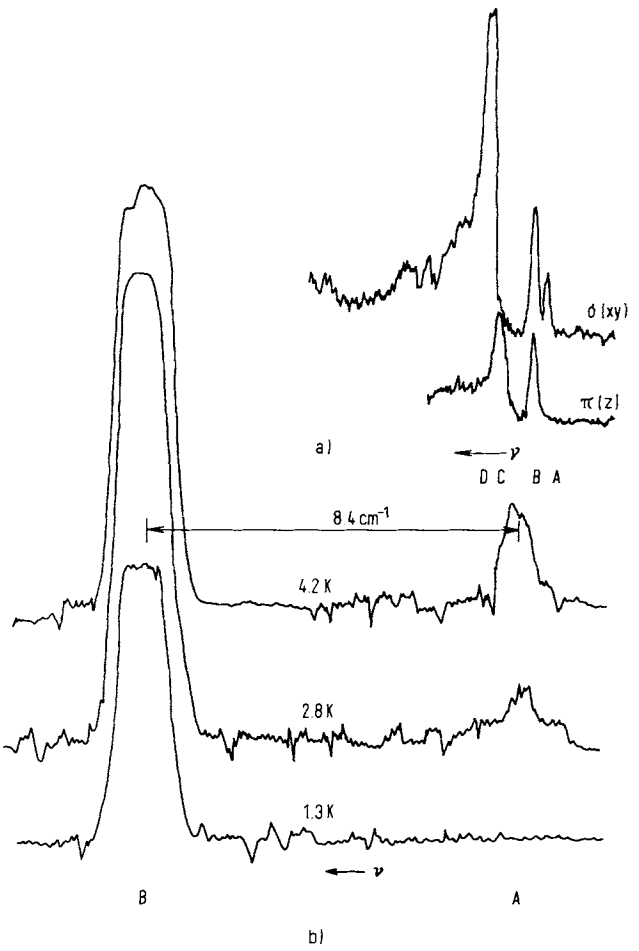


Fig. 15. Electronic origin region of the $^4A_2 \rightarrow {}^2E(D)$ transition of $CoCl_4^{2-}$ in Cs_3CoCl_5: a) under medium resolution; b) under high resolution. Bands A—D refer to Fig. 16.

tell us that the hot band A originates from a level 8.4 cm^{-1} above the lowest, hence the first two bands come from transitions to the same upper level from the two components of the ground state. The third band C, which is also "hot", is of mixed polarization while the fourth D, again "cold", is only seen in the *xy*-spectrum. ESR spectroscopy[30] tells us that the E′ level lies 8.4 cm^{-1} below the E″ in the ground state so the optical data show quite unambiguously that the two levels of the upper state lie in the opposite sequence. The two cold bands are 33 cm^{-1} apart, which is therefore the site-group splitting of the upper ^2E state. By applying the same kind of arguments most of the other dozen or so doublet ligand field states of $CoCl_4^{2-}$ and $CoBr_4^{2-}$ were definitively located and assigned[10,11].

Charge transfer spectra too show many nice examples of site-group splittings which constitute a most valuable assignment tool for this type of transition. Again the MnO_4^- ion provides a good illustration. When doped in the orthorhombic crystal $KClO_4$ the MnO_4^- occupies the ClO_4^- sites, having only C_S point symmetry, *i.e.*, only one remaining element of symmetry, a mirror plane passing through the Cl and two oxygen atoms. Actually in the unit cell of $KClO_4$ there are four ClO_4^- groups but fortunately their mirror planes are all parallel. Permanganate has a closed shell ground state, transforming as $^1A'$. Transitions are allowed to $^1A'$ when the electric vector is parallel to the mirror plane and to $^1A''$ when it is perpendicular. When one examines the electronic origin of the visible band at 4 K for these two polarizations[29] one finds that there are two $^1A'$ bands and one $^1A''$. Since T_2 in T_d is decomposed into $2A' + A''$ in C_S, the experiment clearly defines the tetrahedral parentage of the excited state as $^1T_2$.

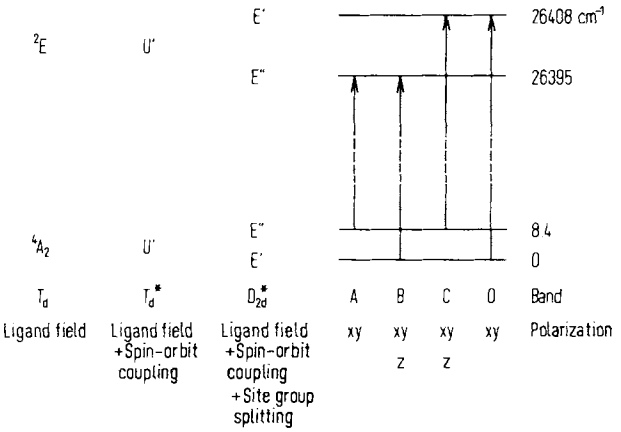


Fig. 16. Site splitting of the $^4A_2 \rightarrow {}^2E$ transition of $CoCl_4^{2-}$ in Cs_2CoCl_5. Labels A—D refer to Fig. 15.

A very similar example is MnO_4^{2-}, a $3d^1$ ion, whose low temperature charge transfer spectrum in a Cs_2SO_4 host crystal is shown in Figure 17[31]. The site group in this lattice is again C_S, which splits the $^2E(T_d)$ ground state into $^2A'$ and $^2A''$. From ESR spectroscopy[32] it is found that the latter lies lower by some 200—300 cm^{-1}. Because of the extra electron the situation is now more complicated than for MnO_4^- and in the T_d point group transitions would be electric dipole-allowed from ^2E to either $^2T_1$ or $^2T_2$ states. Our task is thus to discover which in fact appear in the charge transfer spectrum, and in what order. Selection rules in the Cs_2SO_4 lattice are the same as the ones we have just given for $KClO_4$. Notice that the origin region of the first charge transfer band in Figure 1 consists of two bands in the $\boldsymbol{E}\|\boldsymbol{b}$ spectra and one in the $\boldsymbol{E}\|\boldsymbol{a}$; in the former the electric vector is parallel to the mirror planes through the Mn atoms, in the latter it is perpendicular. Consequently we have the same result as for MnO_4^- in $KClO_4$, namely two A′ and one A″ origin, and the tetrahedral parentage of the first charge transfer band is

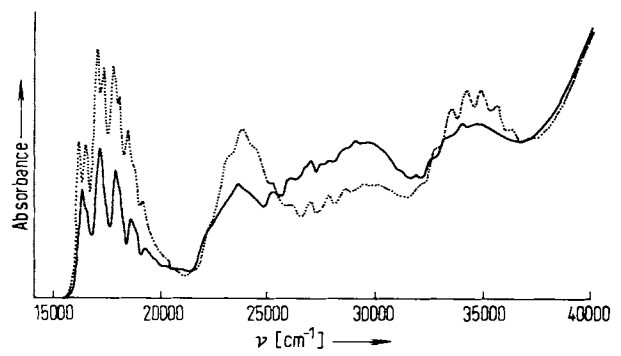


Fig. 17. The polarized charge transfer spectrum of MnO_4^{2-} in Cs_2SO_4 at 4 K [31]. —, $\boldsymbol{E}\|\boldsymbol{a}$; ·····, $\boldsymbol{E}\|\boldsymbol{b}$.

again T_2. As can be seen from Figure 1 the higher energy bands are not sufficiently resolved, even at 4 K, for this means of assignment to be used, but the relative intensities in the two polarizations give a clue to the fact (confirmed by more detailed arguments which we shall not reproduce here) that all except the band near 30000 cm^{-1} also have T_2 parentage.

6.4. Magnetic Interactions

Most metal complexes are monomeric, but a number of classical examples such as the acid and basic "rhodo-" and "erythro"-chromium(III) salts contain pairs or larger clusters of transition metal ions, and in recent years an increasing number of others have been synthesized. If the individual metal ions in the cluster have unpaired electrons there will be some magnetic exchange interaction between them, either ferro- or antiferromagnetic. The ground state of the cluster then consists of a series of sublevels characterized by various values of S_T, the total spin quantum number of the cluster. Consider, for example, a dimeric chromium(III) complex. In the ground state, each Cr atom ($3d^3$, $^4A_{2g}$ in an octahedral ligand field) labeled 1 and 2 carries a net spin of $S_1 = S_2 = 3/2$ so the total spin quantum number of the complex can take integral values from $S_1 - S_2$ to $S_1 + S_2$, *i.e.* from 0 to 3. The sublevels with different S_T have different energies, often described to a good approximation by the Heisenberg hamiltonian

$$H = -J_{12} S_1 \cdot S_2 \qquad (8)$$

which predicts energy intervals between successive levels with increasing S_T of J, $2J$, $3J$. If J in eq. (8) is negative (antiferromagnetic) the $S_T = 0$ sublevel lies lowest while if it is positive (ferromagnetic) $S_T = 3$ is lowest. In the ligand field spectra of dimeric chromium(III) complexes therefore we expect to see groups of bands representing transitions from each of the S_T sublevels of the ground state to various S_T^* sublevels of the excited state. The selection rule $\Delta S_T = 0$ is usually obeyed quite well[33]. Changing the temperature will alter the populations of the S_T sublevels and hence the relative intensities of the bands. A quantitative intensity measurement as a function of temperature serves to identify which S_T sublevel the transition originates from, and, in combination with the observed energy of the band, enables one to map the ground and excited state exchange sublevels.

A good example[34] is the acid "rhodo"-chloride $[(NH_3)_5Cr(OH)Cr(NH_3)_5]Cl_5 \cdot 3H_2O$ in which the hydroxyl ion forms a bent bridge between the two Cr atoms. Figure 18 shows the temperature variation of the two most intense bands in the 680 nm ($^4A_2 \rightarrow {}^2E$) region of the ligand field spectrum fitted to fractional populations calculated for the separations of S_T sublevels shown. A value of J of about -33 cm^{-1} gives quite a good fit to the experimentally observed energy levels, with the ratio of the intervals between the sublevels very close to 1:2:3. Comparable experiments have been done with several other dimeric[35] and trimeric[36] chromium(III) complexes, as a testing ground for theories of magnetic exchange.

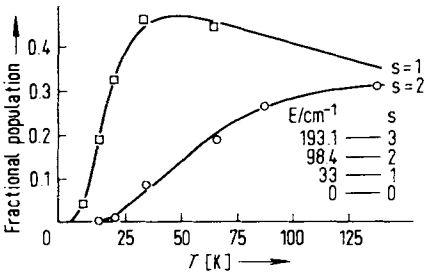


Fig. 18. Temperature dependence of intensity of two exchange-split ligand field bands in $[(NH_3)_5Cr(OH)Cr(NH_3)_5]Cl_5 \cdot 3H_2O$ fitted to the ground state exchange splitting shown inset [34].

7. Conclusion

Electronic absorption spectroscopy is one of the most widely used tools of the inorganic and coordination chemist who wants to learn something about the electronic structures of molecular complexes containing not only transition metal but also B-subgroup cations. By orienting the complex in a crystal and then lowering the temperature the amount of information contained in the visible absorption spectrum is enormously enhanced. Not just the overall polarization of the bands, but the various kinds of fine structure only resolved at low temperature, contribute to a refined view of the excited state's electronic structure. In particular in this article we have tried to show how various observable features in low temperature polarized crystal spectra can give unambiguous symmetry assignments to transitions using only our knowledge of the crystal structure and the group theoretical selection rules and, further, give information about the equilibrium geometry of the excited state. However, the beauty of selection rules based only on symmetry requirements is that they do not depend for their validity on the results of detailed quantum mechanical calculations containing approximations which may or may not be well founded.

It will be clear that such experimentally based assignments, not relying for their validity on the assumptions of any particular theoretical model, are the only possible starting point for assessing how valid these assumptions are. Fitting absorption band energies to the results of ligand field calculations is a long standing sport among inorganic chemists, but it is always wise to be sure, from some other experiment, that the bands being being fitted actually have the assignment which is being put on them. Such advice is doubly necessary in the field of charge transfer spectra, for which no reliably predictive model exists yet. Only by amassing the results of many experiments of the kind described here on the widest possible variety of complexes can we arrive at the experimental basis on which a predictive model must be founded. Basic equipment for measuring low temperature polarized crystal spectra is readily available commercially, and is not difficult to use. In our laboratory we have measured temperature dependent spectra down to as low as 0.8 K using a specially designed cryostat, and spectral bandwidths as small as 0.001 Å could be obtained using a tunable dye laser containing an intracavity etalon. However, very little work on the spectra of inorganic complexes has been reported yet with such low temperatures and high resolving power. More important for the chemist wanting to correlate his results with structural theories is the accumulation of a large body of securely assigned spectra. For the simplest tetra- and hexahalide and tetroxo-complexes the information is

at hand, for mixed complexes and complexes of more elaborate ligands it is only now beginning to be accumulated.

Most of this article was written while a Visiting Scientist at the Xerox Corporation Webster Research Center. I am grateful for the hospitality extended to me by members of the Center.

Received: December 22, 1978;
supplemented: November 12, 1979 [A 314 IE]
German version: Angew. Chem. *92*, 290 (1980)

[1] *C. J. Ballhausen:* Introduction to Ligand Field Theory. McGraw-Hill, New York 1962; *A. B. P. Lever:* Inorganic Electronic Spectroscopy. Elsevier, Amsterdam 1967; *D. S. McClure:* Electronic Spectra of Molecules and Ions in Crystals. Academic Press, New York 1964; *P. Day:* Electronic States of Inorganic Compounds: New Experimental Techniques. D. Reidel, Dordrecht 1975.

[2] *J. Ferguson*, Prog. Inorg. Chem. *12*, 359 (1970); *C. K. Jørgensen, ibid. 12*, 101 (1970).

[3] *P. Day*, Proc. Chem. Soc. *1964*, 18.

[4] *P. Day, A. F. Orchard, A. J. Thomson, R. J. P. Williams*, J. Chem. Phys. *42*, 1973 (1965).

[5] *M. B. Robin, P. Day*, Adv. Inorg. Chem. Radiochem. *10*, 247 (1967); *N. Hush*, Prog. Inorg. Chem. *8*, 391 (1967).

[6] *H. Eyring, J. Walter, G. E. Kimball:* Quantum Chemistry. Wiley, New York 1944.

[7] *F. A. Cotton:* Chemical Applications of Group Theory. Interscience, New York 1967.

[8] *G. F. Koster, J. O. Dimmock, R. G. Wheeler, H. Statz:* Properties of the Thirty Two Point Groups. M.I.T. Press, Cambridge, Mass. 1963.

[9] *B. G. Anex, N. Takeuchi*, J. Am. Chem. Soc. *96*, 4411 (1974).

[10] *P. N. Quested, J. Tacon, P. Day, R. G. Denning*, Mol. Phys. *27*, 1553 (1974).

[11] *B. D. Bird, E. A. Cooke, P. Day, A. F. Orchard*, Phil. Trans. R. Soc. London *A 276*, 278 (1974).

[12] *P. Day, P. J. Diggle, G. A. Griffiths*, J. Chem. Soc. Dalton Trans. *1974*, 1446.

[13] *J. J. Markham:* F-Centres in Alkali Halides. Solid State Phys. Suppl. *8*. Academic Press, New York 1966.

[14] *P. Day, E. A. Grant*, Chem. Commun. *1969*, 123.

[15] *P. Day*, Inorg. Chem. *2*, 452 (1963).

[16] *L. Atkinson, P. Day*, J. Chem. Soc. *A 1969*, 2423.

[17] *E. A. White:* Experimental Techniques in Low Temperature Physics. Oxford University Press, Oxford 1959.

[18] Modell CF100, Oxford Instrument Co., Osney Mead, Oxford (England).

[19] *G. Herzberg:* Electronic Spectra of Diatomic Molecules. Van Nostrand, Princeton 1950.

[20] *R. A. Satten, E. Y. Wong*, J. Chem. Phys. *43*, 3025 (1965).

[21] *A. D. Liehr*, Prog. Inorg. Chem. *4*, 455 (1962).

[22] *P. A. Cox, D. J. Robbins, P. Day*, Mol. Phys. *30*, 405 (1975).

[23] *C. J. Ballhausen*, Theor. Chim. Acta *1*, 285 (1963).

[24] *A. P. Mortola, J. W. Moskowiitz, N. Roesch, C. D. Cowman, H. B. Gray*, Chem. Phys. Lett. *32*, 203 (1975).

[25] *F. A. Cotton, D. S. Martin, T. R. Webb, T. J. Peters*, Inorg. Chem. *15*, 1199 (1976).

[26] *J. Ferguson, T. E. Wood*, Inorg. Chem. *14*, 184 (1975).

[27] *R. G. Denning, T. R. Snellgrove, D. R. Woodward*, Mol. Phys. *32*, 419 (1974).

[28] *J. Tacon, P. Day, R. G. Denning*, J. Chem. Phys. *61*, 251 (1974).

[29] *S. Holt, C. J. Ballhausen*, Theor. Chim. Acta *7*, 313 (1967).

[30] *R. P. Van Stapele, H. G. Belgers, P. F. Bongers, H. Zijlstra*, J. Chem. Phys. *44*, 3719 (1966).

[31] *P. Day, L. DiSipio, C. Ingletto, L. Oleari*, J. Chem. Soc. Dalton Trans. *1973*, 2595.

[32] *A. Carrington, D. J. E. Ingram, K. A. K. Lott, D. Schonland, M. C. R. Symons*, Proc. R. Soc. *A 254*, 101 (1960).

[33] *J. Ferguson, H. J. Guggenheim, Y. Tanabe*, J. Phys. Soc. Jpn. *21*, 692 (1966).

[34] *J. Ferguson, H. U. Gudel*, Aust. J. Chem. *26*, 505 (1973).

[35] *L. Dubicki*, Aust. J. Chem. *25*, 739 (1972).

[36] *L. Dubicki, P. Day*, Inorg. Chem. *11*, 1868 (1972).

COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

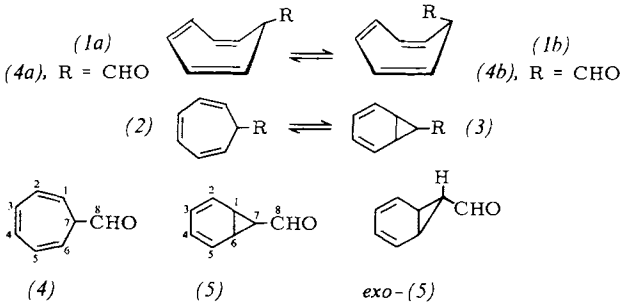
The Dynamic Behavior of 2,4,6-Cycloheptatriene-1-carbaldehyde[**]

By *Metin Balci, Hartmut Fischer*, and *Harald Günther*[*]

Ring inversion and valence tautomerism are well-known dynamic processes in cycloheptatrienes[1]. While steric effects, besides possible electronic factors, play a major role[2] in determining the position of the conformational equilibrium *(1a)*⇌*(1b)* in C^7-substituted derivatives, the cycloheptatriene-norcaradiene equilibrium *(2)*⇌*(3)* is largely controlled by the acceptor properties of the substituents R[3]. According to MO calculations[4] this influence should increase

[*] Dr. M. Balci, Dipl.-Chem. H. Fischer, Prof. Dr. H. Günther
Gesamthochschule Siegen, FB8, OC II
Postfach 210209, D-5900 Siegen 21 (Germany)

[**] This work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen.



along the series CN < COOH < CHO; so far, this prediction has been confirmed experimentally for R = CN and COOH[5]. We have now examined the influence of the aldehyde group for cycloheptatrienecarbaldehyde[6] *(4)* by high-field NMR spectroscopy (^{1}H: 400 MHz, ^{13}C: 100 MHz) and have found that the dynamics of the molecule are more complicated than expected.

Already at room temperature the highfield position of the H(1,6) signal ($\delta = 5.28$) would suggest that a considerable proportion of 7-norcaradienecarbaldehyde *(5)* is present at equilibrium. In agreement with this, strong broadening of the H(7) and H(1,6) signals takes place on cooling, until at $-100\,^\circ$C, the spectra of *(4)* and *(5)* are observed (Table 1). Further lowering of the temperature then leads—at first surprisingly—to renewed line-broadening in the spectrum of *(4)*, which after signal splitting finally shows two signals of similar intensity each for both H(7) as well as H(8). Consequently, in the system investigated a conformational equilibrium *(4a)*⇌*(4b)* must also exist besides the valence tautomerism *(4)*⇌*(5)* (Fig. 1).

The interpretation of the ^{1}H-NMR spectrum is confirmed by the temperature-dependence of the ^{13}C-NMR spectrum (Table 1). Here also, the signals of C(1,6,7)—particularly sensitive for the valence tautomerism[7]—show the strongest temperature effect. Below $-134\,^\circ$C the ring inversion is documented by the renewed broadening of the signal due to C(7), and in particular of the CHO signal, until superposition of the ^{13}C spectra of *(4a)*, *(4b)*, and *(5)* is reached at $-156\,^\circ$C; thus, to our knowledge, *(4)* is the first monosubstituted cycloheptatriene in which ring inversion has been demonstrated to accompany valence tautomerism.

As integration of the ^{1}H-NMR low-temperature spectrum shows, at $-145\,^\circ$C *ca.* 7% of *(5)* is present besides the cyclo-

Table 1. ^{1}H- and ^{13}C-NMR data [a] of the system *(4b)*⇌*(4a)*⇌*(5)* (δ values rel. to TMS [b]). For numbering of the atoms see formulas in text.

^{1}H-NMR (400.16 MHz)							
T [°C]	Cpd.	H(1,6)	H(2,5)	H(3,4)	H(7)	H(8)	Solv./ Concn.
20	mean spectrum	5.28	6.17—6.74		2.79	9.73	[c]
−148	*(5)*	2.41	—	—	0.48	10.00	[d]
−148	*(4a)*	—	—	—	2.25 [e]	9.59	[d]
−148	*(4b)*	—	—	—	3.57 [f]	8.62	[d]
^{13}C-NMR (100.61 MHz)							
T [°C]	Cpd.	C(1,6)	C(2,5)	C(3,4)	C(7)	C(8)	Solv./ Concn.
20	mean spectrum	111.1	127.8	130.9	49.8	200.1	[g]
−156	*(5)*	—	—	—	35.5	—	[d]
−156	*(4a)*	119.3	127.8	129.8	50.4	200.4	[d]
−156	*(4b)*		126.0	131.0	49.9	199.4	[d]

[a] PFT high-field spectrometer WH 400 E (Bruker Analytische Messtechnik, Karlsruhe). [b] The shifts are referred to the δ_{TMS} values of the solvent ($C^1H_2Cl_2$ 5.32, $^{13}CD_2Cl_2$ 53.8). [c] CD_2Cl_2; 0.1 M. [d] CD_2Cl_2/vinyl chloride (1:2); 0.3 M. [e] $J < 5$ Hz. [f] $J = 9.2$ Hz. [g] CD_2Cl_2; 0.3 M.

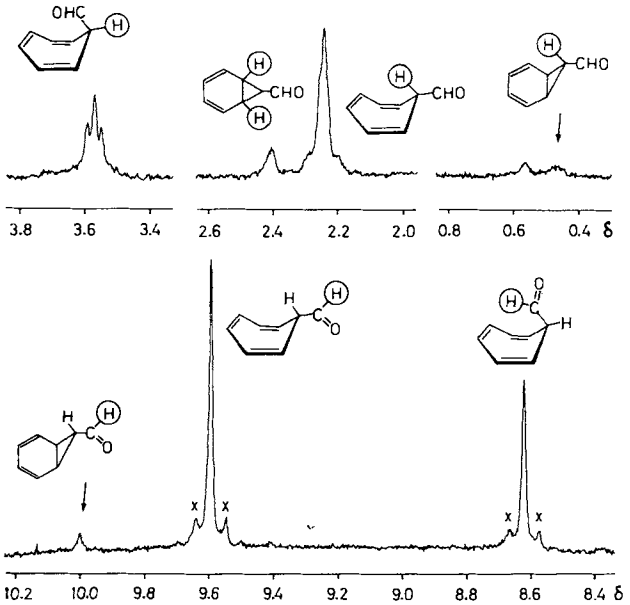


Fig. 1. ^{1}H-NMR spectrum of the system *(4b)*⇌*(4a)*⇌*(5)* at $-152\,^\circ$C in $CDCl_2$/vinyl chloride (1:2); spectrometer frequency 400.16 MHz, δ values ref. to TMS. Rotational sidebands at (×).

heptatrienes *(4a)* and *(4b)*. For the equilibrium *(4a)*⇌*(5)* we obtained $K = 8.9$ and hence ΔG^0 ($-145\,^\circ$C) = 2.3 kJ/mol in favor of *(4a)*. If we ignore possible complications by the entropy factor[8], then the above-mentioned sequence for the substituent effect is confirmed, for we found only 3% of the Buchner acid *(3)*, R = COOH, in equilibrium [ΔG^0 ($-150\,^\circ$C) = 3.8 kJ/mol in favor of *(2)*, R = COOH][5], and 7-norcaradienecarbonitrile could still not be detected. In contrast to the α-proton in the cyclopropanecarbaldehyde, H(7) is shielded in *(5)* by $\Delta\delta = -1.35$, so that *(5)*, like the Buchner acid, must be present in the *exo* configuration. Apparently, only this configuration allows the bisected geometry of the aldehyde group and thus optimum electronic interaction with the three-membered ring.

The difference in the free enthalpy between the conformers *(4a)* and *(4b)* is only 0.5 kJ/mol at $-145\,^\circ$C and is thus smaller than in the case of the nitrile (ΔG^0 ($-133\,^\circ$C) = 1.6 kJ/mol[5]). According to the ^{1}H-NMR data the *exo* configuration *(4a)* likewise predominates in *(4)*, with H(7) being shielded and H(8) deshielded. In agreement with this the H(7) signal of the *endo* conformer *(4b)* at $\delta = 3.57$ shows the typical *cis*-coupling $J(1,7)$[9] for the cycloheptatriene with $J = 9.2$ Hz. However, no report can be made on the stabilization of *(1a)* relative to *(1b)* by the substituents CN, COOH, and CHO until the ΔH^0 values are known since the entropy term may be important.

Received: September 28, 1979 [Z 420 IE]
German version: Angew. Chem. *92*, 316 (1980)

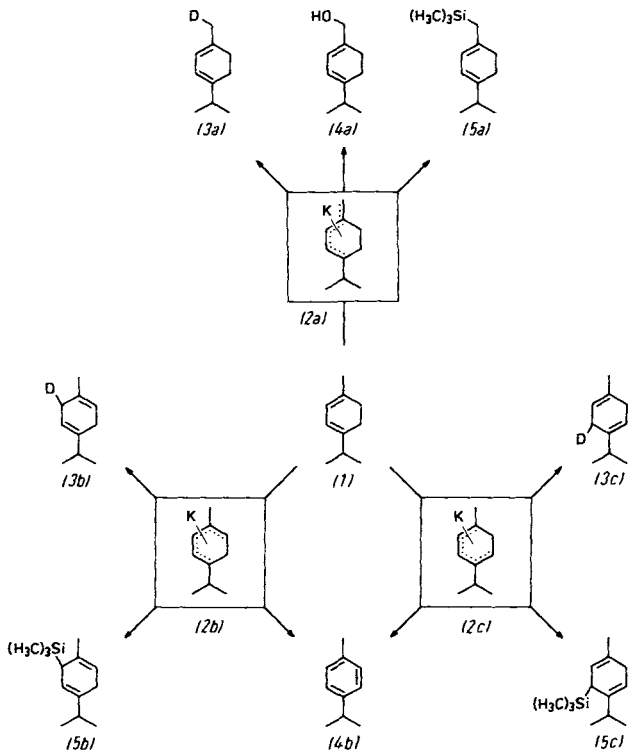
[1] *H. Kessler* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Vol. 5/1d. Thieme, Stuttgart 1972, pp. 300 ff.; *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew. Chem. Int. Ed. Engl. *6*, 402 (1967).
[2] *H. Günther, M. Görlitz, H.-H. Hinrichs*, Tetrahedron *24*, 5665 (1968); *W. E. Heyd, C. A. Cupas*, J. Am. Chem. Soc. *91*, 1559 (1969).
[3] *R. Hoffmann*, Tetrahedron Lett. *1970*, 2907; *H. Günther, ibid. 1970*, 5173.
[4] *R. Hoffmann, W.-D. Stohrer*, J. Am. Chem. Soc. *93*, 6941 (1971).
[5] *R. Wehner, H. Günther*, J. Am. Chem. Soc. *97*, 923 (1975).
[6] *R. Grigg, R. Hayes, A. Sweeney*, Chem. Commun. *1971*, 1248; the numbering used in the text corresponds to that in *(4)*.
[7] *H. Günther, T. Keller*, Chem. Ber. *103*, 3231 (1970).
[8] The sign of the entropy term for the equilibrium *(2)*⇌*(3)* should be independent of the nature of the substituents, so here the ΔG^0 values instead of the ΔH^0 values can be compared with the MO energies.
[9] *H. Günther, R. Wenzl*, Z. Naturforsch. *B 22*, 389 (1967).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0404-0302 $ 02.50/0

A Facile Route to a Sensitive Terpene Alcohol—Regio-unselective Metalation of α-Terpinene as Key Step[**]

By *Manfred Schlosser, Herbert Bosshardt, Annelis Walde,* and *Manfred Stähle*[*]

The monoterpene alcohol "anthemol" (4-isopropyl-1,3-cyclohexadienemethanol) *(4a)* has practically vanished from the scene since its debut in 1879[1]. We saw a challenge in the synthesis of this compound, providing an opportunity to test once more the efficiency of our novel access to allylic and dienylic primary alcohols. The one-pot method[2] consists of three reaction steps: metalation of a conjugated or homoconjugated diene, reaction with fluorodimethoxyborane, and oxidation with alkaline hydrogen peroxide solution. Terpinene *(1)* served as an inexpensive starting material. It was attacked by the butyllithium/potassium *tert*-butoxide reagent[3] with surprising ease (90 min, −45 °C, tetrahydrofuran). The borylation/oxidation reaction sequence afforded, however, only 44% of anthemol[4] together with 50% of *p*-cymene (4-isopropyl-1-methylbenzene) *(4b)*. While allylic methyl groups are generally deprotonated much faster than such methylene or even methine groups[5], the metalating agent attacks the allylic methyl and each of the methylene groups of α-terpinene with almost equal probability. Thus there arise the three pentadienylpotassium species: *(2a)*, with a serpent-like, partly exocyclic delocalization region, as well as *(2b)* and *(2c)*, in which delocalization involves a horseshoe-shaped, endocyclic region. After borylation with $FB(OCH_3)_2$, the intermediates formed from *(2b)* and *(2c)* apparently eliminate $HB(OCH_3)_2$ and are converted into the aromatic hydrocarbon *(4b)*. Addition of deuterium oxide to the organometallic intermediates *(2)* leads to deuterated α- and γ-terpinene [*(3a)*, 47% yield; *(3b)*, *(3c)*, each 24% yield], while reaction with chlorotrimethylsilane gives 4-isopropyl-1-(trimethylsilylmethyl)-1,3-cyclohexadiene [*(5a)*, 36%], 1-isopropyl-4-methyl-3-trimethylsilyl-1,4-cyclohexadiene [*(5b)*, 29%], and 4-isopropyl-1-methyl-3-trimethylsilyl-1,4-cyclohexadiene [*(5c)*, 29%][4].



Pentadienylpotassium compounds with horseshoe-shaped delocalization area ("U conformation") can form an *open-sandwich structure*[2b,6] and should therefore be energetically favored. The unexpected ease of formation of intermediates *(2b)* and *(2c)* is in full accord with this assumption.

Received: October 25, 1979 [Z 422 IE]
German version: Angew. Chem. *92*, 302 (1980)

[*] Prof. Dr. M. Schlosser, Dr. H. Bosshardt, A. Walde, M. Stähle
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project no. 2.128.0.78).

[1] *J. Köbig*, Justus Liebigs Ann. Chem. *195*, 92 (1879); structure proposal: *T. K. Devon, A. I. Scott:* Handbook of Naturally Occurring Compounds, Vol. II, p. 23, Academic Press, New York 1972.—According to a recent personal communication from Prof. *A. I. Scott*, Texas A & M University, this structure assignment has to be regarded as tentative. On the other hand, the "Dihydrocumin alcohol" obtained by *F. W. Semmler* [Ber. Dtsch. Chem. Ges. *33*, 1455 (1900)] might have been *(4a)*.

[2] a) *G. Rauchschwalbe, M. Schlosser*, Helv. Chim. Acta *58*, 1094 (1975); b) *M. Schlosser, G. Rauchschwalbe*, J. Am. Chem. Soc. *100*, 3528 (1978).

[3] *M. Schlosser*, J. Organomet. Chem. *8*, 9 (1967); *M. Schlosser, J. Hartmann*, Angew. Chem. *85*, 544 (1973); Angew. Chem. Int. Ed. Engl. *12*, 439 (1973).

[4] Elemental analyses as well as mass, IR, and NMR spectra confirm the purity and identity of all the reaction products. Anthemol *(4a)* proved unusually sensitive to acid and heat, and is not very stable towards bases either.—Commercially available α-terpinene contains small amounts of *p*-cymene *(4b)*. If these impurities are not removed, then the products mentioned are accompanied by 3—4% of electrophilically substituted cymenes, *viz.* 4-isopropyl[α-$^2H_1$]toluene, 4-isopropylbenzenemethanol, and 4-isopropyl(trimethylsilylmethyl)benzene.

[5] *M. Schlosser, J. Hartmann, V. David*, Helv. Chim. Acta *57*, 1567 (1974); *M. Schlosser*, Angew. Chem. *86*, 751 (1974); Angew. Chem. Int. Ed. Engl. *13*, 701 (1974).

[6] *M. Schlosser, P. Schneider*, Angew. Chem. *91*, 515 (1979); Angew. Chem. Int. Ed. Engl. *18*, 489 (1979); *H. Bosshardt, M. Schlosser*, Helv. Chim. Acta, in press.

α-Carbamoyloxymethyl-Substituted Lithium Enethiolates from 1-(*N,N*-Dimethylcarbamoylthio)-2-methyl-1-propenyllithium[**]

By *Dieter Hoppe, Ludger Beckmann,* and *Rainer Follmann*[*]

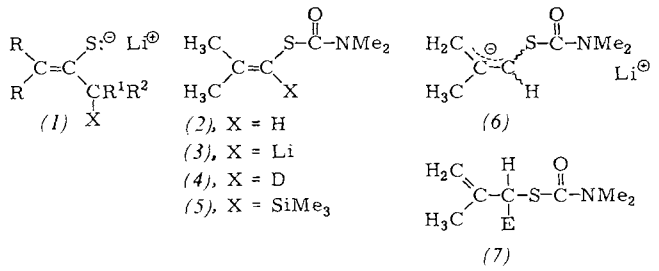
Owing to the kinetic instability of most thioaldehydes and thioketones[1], synthetic entry to the hitherto little investigated enethiolates *(1)*, X = H[2], is greatly restricted; enethiolates of type *(1)*, X = acyloxy or alkyloxy derived from thioketones are to our knowledge unknown. We now report on the synthesis of lithium α-(*N,N*-dimethylcarbamoyloxymethyl)enethiolates *(9)* from the readily accessible *S*-vinyl thiocarbamate *(2)*[3], which proceeds with concomitant chain lengthening. The key step is the vinyl deprotonation of the ester *(2)*[4] to the lithium compound *(3)*: The nucleophilic building block *(3)* transfers a latent enethiolate group, which is liberated in the carbonyl adducts *(8)* by intramolecular migration of the dimethylcarbamoyl group from the sulfur to the alkoxide oxygen.

The ester *(2)*[3] was deprotonated with lithium diisopropylamide (LDA), or better with *tert*-butyllithium, at −78 °C in

[*] Priv.-Doz. Dr. D. Hoppe, Dr. L. Beckmann, Dr. R. Follmann
Organisch-Chemisches Institut der Universität
Tammannstr. 2, D-3400 Göttingen (Germany)

[**] Metalated Nitrogen Derivatives of Carbonic Acid in Organic Synthesis, Part 14. This work was supported by a Postgraduate Grant from the Konrad-Adenauer-Stiftung for *L. B.*—Part 13: *D. Hoppe, L. Beckmann*, Justus Liebigs Ann. Chem. *1979*, 2066.

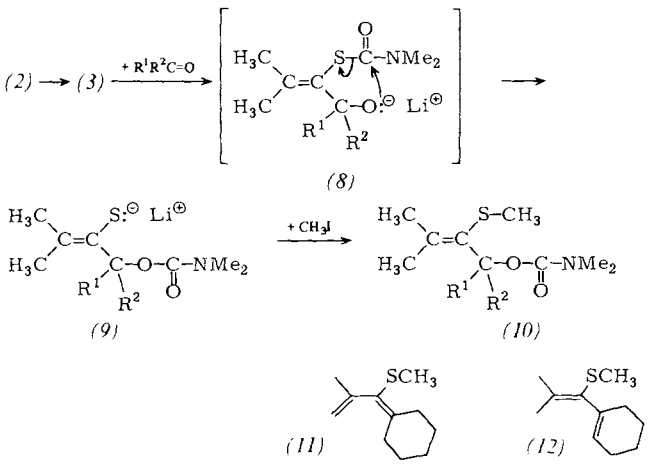
tetrahydrofuran (THF)/hexane and the product *(3)* detected as vinylsilane *(5)*[5] (yield 51 and 76%, resp.) after treatment with chlorotrimethylsilane. Reaction of *(3)*—generated with LDA—with CH_3OD gave 54% of the deuterium compound *(4)*[6], which on renewed lithiation and protonolysis lost 50% of the labeling. Hence, the presence of a resonance-stabilized allyl anion *(6)*[7] as intermediate[8] is ruled out.



(1) *(2)*, X = H; *(3)*, X = Li; *(4)*, X = D; *(5)*, X = $SiMe_3$

(6)

(7)



(8)

(9) *(10)*

(11) *(12)*

(8), *(9)*, *(10)*: *(a)*, $R^1 = H$, $R^2 = C_6H_5$; *(b)*, $R^1 = R^2 = CH_3$; *(c)*, $R^1 + R^2 = -(CH_2)_5-$

Reaction of *(3)* with benzaldehyde at −78 °C gave the lithium enethiolate *(9a)*, which we trapped as methyl vinyl thioether *(10a)* in 64% yield with methyl iodide, without the initial adduct *(8a)* being isolable. Acetone and cyclohexanone analogously afforded the compounds *(10b)*[5] and *(10c)*[5] in 26% and 44% yield, respectively. That the carbamate *(10)* is in fact present—and not the *O*-methylated isomer [from *(8)*]—follows from the carbonyl absorptions of *(10)* in the IR spectrum around 1690 cm^{-1} [*(2)*: $\nu_{S\ C\ O} = 1655\ cm^{-1}$], from the resonances of the SCH_3 groups in the ^{1}H-NMR spectrum between $\delta = 2.1$ and 2.2, and from the thermolysis of *(10c)* at 160—210 °C to a mixture[5] of the methylthiobutadienes *(11)* and *(12)* in the ratio 45:55, yield 82%.

Procedure

Solution of *(9a)*: 4.0 ml (5.6 mmol) of a 1.40 N solution of *tert*-butyllithium in *n*-hexane is added dropwise at −78 °C to a stirred solution of *(2)*[3] (0.80 g, 5.0 mmol) in 10 ml of anhydrous THF under N_2 and the mixture stirred for 1 h. After addition of 0.58 g (5.5 mmol) benzaldehyde in 5 ml THF, stirring is continued for a further 1.5 h.

(10a): A fine stream of methyl iodide (0.78 g, 5.5 mmol) is slowly pipetted into the solution of *(9a)* at −78 °C and the reaction mixture allowed to warm to 20 °C after 1 h. Removal of solvent by distillation, partition of the residue between diethyl ether (30 ml) and water (15 ml), drying over sodium sulfate, and removal of solvent afforded a colorless oil, which was purified by chromatography on silica gel (neutral) with ether/pentane (1:1); yield 0.89 g (64%) *(10a)*. $R_F = 0.33$; IR (film): 1690 (C=O), 1660 cm^{-1} (C=C); ^{1}H-NMR (CCl_4): $\delta = 7.2$ (m, C_6H_5), 6.87 (s, CH); 3.0, 2.9 (br, s, $N(CH_3)_2$), 2.08 (s, SCH_3), 2.08, 1.80 (s, CH_3).

Received: September 19, 1979 [Z 424 IE]
German version: Angew. Chem. *92*, 305 (1980)

[1] Thioketones and enethiols: *R. Mayer, J. Morgenstern, J. Fabian*, Angew. Chem. *76*, 157 (1964); Angew. Chem. Int. Ed. Engl. *3*, 277 (1964); *D. Paquer, J. Vialle*, Bull. Soc. Chim. Fr. *1969*, 3595; *P. Brandsma*, Recl. Trav. Chim. Pays-Bas *89*, 593 (1970).

[2] Enethiolates by reductive cleavage of alkylvinyl thioethers: *L. Brandsma, P. W. J. Schuijl*, Recl. Trav. Chim. Pays-Bas *88*, 513 (1969); deprotonation and alkylation of 2-thiocamphor: *G. E. Veenstra, B. Zwanenburg, ibid. 95*, 37 (1976); cf. also *N. H. Werstiuk, P. Andrews*, Can. J. Chem. *56*, 2605 (1978); intermediate enethiolates from doubly deprotonated 2-propenethiol: *K.-H. Geiss, D. Seebach, B. Seuring*, Chem. Ber. *110*, 1833 (1977), and earlier work cited therein.

[3] *D. Hoppe, R. Follmann*, Angew. Chem. *89*, 478 (1977); Angew. Chem. Int. Ed. Engl. *16*, 462 (1977).

[4] Lithiation of vinyl thioethers: *K. Oshima, K. Shimoji, H. Takahashi, Y. Yamamoto, H. Nozaki*, J. Am. Chem. Soc. *95*, 2694 (1973); *R. C. Cookson, P. J. Parson*, J. Chem. Soc. Chem. Commun. *1978*, 821 and earlier work cited therein; cf. also: *M. Braun*, Tetrahedron Lett. *1978*, 3695.

[5] The compound was analytically pure (C and H, ±0.3%).

[6] Determined ^{1}H-NMR spectroscopically.

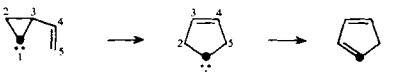
[7] Kinetic preference of the vinyl deprotonation in aryl-1-propenyl sulfoxides: *G. H. Posner, P.-W. Tang, J. P. Mallamo*, Tetrahedron Lett. *1978*, 3995; *H. Okamura, Y. Mitsuhira, M. Miura, H. Takei*, Chem. Lett. *1978*, 517.

[8] Anions of type *(6)* exclusively form *(7)*, E = $SiMe_3$, whose base-catalyzed isomerization would give *(5)*; *D. Hoppe, L. Beckmann*, unpublished.

1,5-Dihydropentalene by Tandem Carbene-Carbene Rearrangement[**]

By *Udo H. Brinker* and *Ilona Fleischhauer*[*]

Carbene-carbene rearrangements involving a 1,3-carbon shift *(1)*→*(2)* and subsequent 1,2-hydrogen shift open up a facile entry to cyclopentadienes[1].



(1) *(2)*

• = ^{12}C

Consecutive carbene-carbene rearrangements of the type *(1)*→*(2)* for the synthesis of multi-annelated, unsaturated cyclopentane structures[2] are not known.

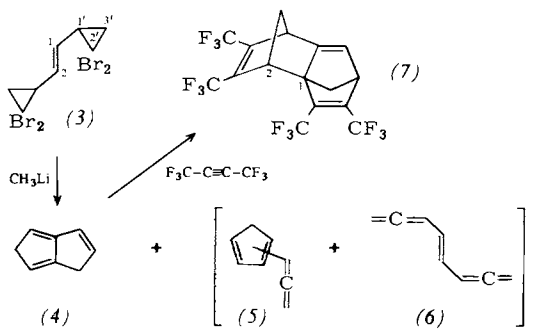
We have found that reaction of *trans*-1,2-bis(2,2-dibromocyclopropyl)ethene *(3)* with methyllithium gives 1,5-dihydropentalene *(4)*[3] as a main product.

Addition of dibromocarbene ($CHBr_3$, K-*tert*-butoxide) to *trans*-1,3,5-hexatriene (molar ratio 3:3:1) gives, besides the monoadduct[4] (15—20%), the *trans*-1,2-bis-(2,2-dibromocyclopropyl)ethene *(3)* [m.p. 92—93 °C (from methanol), ^{1}H-NMR (60 MHz, $CDCl_3$): $\delta = 5.45$—5.70 (dd, 2 olefinic H,

[*] Dr. U. H. Brinker, Dipl.-Chem. I. Fleischhauer
Abteilung für Chemie der Universität
Universitätsstr. 150, D-4630 Bochum 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. *I. F.* thanks the Studienstiftung des Deutschen Volkes for a study grant. We thank Dr. *W. Dietrich* and Priv.-Doz. Dr. *H. Duddeck* for recording the ^{13}C-NMR spectra.

$J_{1,1'}=5$ Hz, $J_{1',2}=2.5$ Hz), 1.45—2.60 (m, 6 cyclopropyl H)] in 40—50% yield. Reaction of *(3)* with methyllithium (molar ratio 1:2.2, ether) at −40 °C and −70 °C yields three major products. Since the reaction mixture already polymerizes at



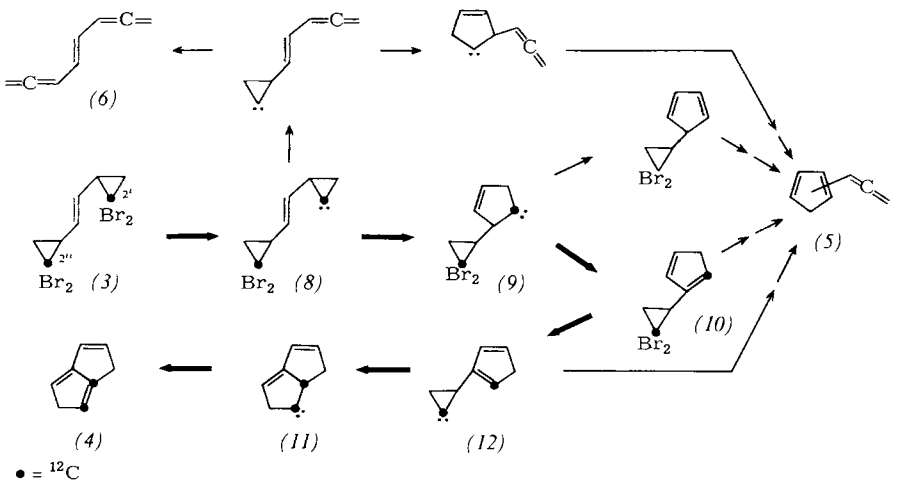
room temperature under argon, the crude mixture was directly hydrogenated (Pt/C, 10%; 1.5 h, −70 °C (−40 °C) to +25 °C). The resulting compounds[5] *cis*-bicyclo[3.3.0]octane, *n*-propylcyclopentane and *n*-octane suggest that 1,5-dihydropentalene *(4)*, propadienyl cyclopentadiene *(5)* and 1,2,4,6,7-octapentaene *(6)* are the major products of the reaction of *(3)*. The structure of 1,5-dihydropentalene *(4)* is further supported by the fact that *(4)* can be trapped with hexafluoro-2-butyne as main product (50—60%) from the crude reaction mixture[6]. The initial Diels-Alder adduct of *(4)* undergoes renewed reaction with the dienophile to give the 1:2 adduct *(7)*, which has already been synthesized *via* an independent route[6].

carbene rearrangement with 1,3-carbon shift to give *(9)* and subsequent 1,2-hydrogen shift to give *(10)*. Reaction of *(10)* with the second equivalent of methyllithium leads to *(12)*, which once again makes a structurally integrated vinylcyclopropylidene unit available. Renewed carbene-carbene rearrangement *(12)*→*(11)* and subsequent 1,2-hydrogen shift afford 1,5-dihydropentalene *(4)*. For consecutive carbene-carbene rearrangements of this type we propose the term tandem carbene-carbene rearrangement.

The reaction of *(3)* (C-2′, C-2″ = ^{12}C)[8] and subsequent treatment of the crude product mixture with hexafluoro-2-butyne under the given conditions confirm this mechanistic interpretation. Comparison of the ^{13}C-NMR spectra ($CDCl_3$) of labeled and unlabeled 3,4,9,10-tetrakis(trifluoromethyl)tetracyclo[6.2.1.1^{2,5}.0^{1,6}]dodeca-3,6,9-triene *(7)* reveals the absence of the signals at δ = 73.1 and 45.5, which were assigned to C-1 and C-2 in *(7)* with natural isotope distribution. C-2′ and C-2″, separated by five carbon-carbon bonds in the educt *(3)*, are directly connected in 1,5-dihydropentalene *(4)* after tandem carbene-carbene rearrangement.

Received: October 22, 1979 [Z 425 IE]
German version: Angew. Chem. *92*, 314 (1980)

[1] *W. M. Jones, U. H. Brinker* in *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions. Vol. I. Academic Press, New York 1977; *L. Skattebøl*, Tetrahedron *23*, 1107 (1967); *K. H. Holm, L. Skattebøl*, Tetrahedron Lett. *1977*, 2347; *W. W. Schoeller, U. H. Brinker*, J. Am. Chem. Soc. *100*, 6012 (1978).
[2] *L. A. Paquette*, Top. Curr. Chem. *79*, 41 (1979).
[3] *T. J. Katz, M. Rosenberger*, J. Am. Chem. Soc. *84*, 865 (1962); *T. J. Katz, M. Rosenberger, R. K. O'Hara, ibid. 86*, 249 (1964).
[4] *U. H. Brinker, I. Fleischhauer*, Angew. Chem. *91*, 424 (1979); Angew. Chem. Int. Ed. Engl. *18*, 396 (1979).



For the formation of *(4)*, *(5)*, and *(6)* in the reaction of *(3)* with methyllithium there are the following possibilities: 1,2,4,6,7-octapentaene *(6)* could be formed by twofold cyclopropylidene-allene rearrangement. Propadienylcyclopentadiene *(5)* can be regarded as the product of a carbene-carbene rearrangement[7] involving a 1,3-carbon shift followed by a 1,2-hydrogen shift and an additional cyclopropylidene-allene rearrangement. The sequence of these competing rearrangements cannot be established.

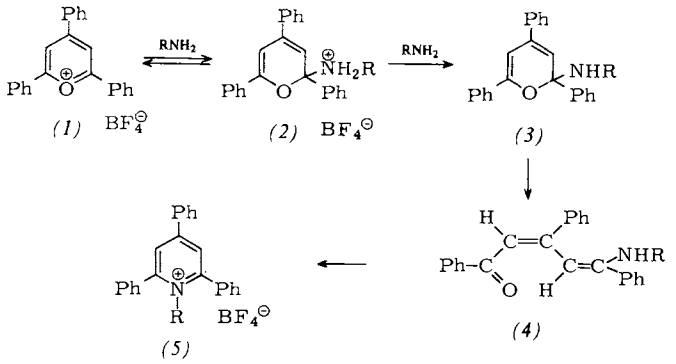
The formation of *(4)* can be conceived as the result of a sequence of carbene-carbene rearrangements[7] and 1,2 hydrogen shifts. Reaction of *(3)* with the first equivalent of methyllithium affords carbene *(8)*, which undergoes a carbene-

[5] Identified by comparison with the retention times of authentic compounds on two glass-capillary columns of different polarity.
[6] *P. J. van Vuuren*, Thesis, Cornell University, Ithaca 1970; Diss. Abstr. *31 B*, 7201 (1971). The additional adducts of 1,6a- and 1,4-dihydropentalene and hexafluoro-2-butyne ([2+2] and Diels-Alder adducts) described therein, which had been prepared by reaction of 8,8-dibromobicyclo[5.1.0]octa-2,4-diene with methyllithium, could not be detected in the reaction of *(3)*, either gas-chromatographically or ^{1}H-NMR spectroscopically.
[7] For the participation of carbenes or carbenoids in vinylcyclopropylidene-3-cyclopentenylidene rearrangements see *P. Warner, S.-C. Chang*, Tetrahedron Lett. *1978*, 3981; *U. H. Brinker, L. König*, J. Am. Chem. Soc. *101*, 4738 (1979), footnote 4.
[8] Synthesized by $^{12}CBr_2$-addition [9] to *trans*-1,3,5-hexatriene.
[9] $^{12}CDBr_3$, the source of $^{12}CBr_2$, was prepared from $^{12}CDCl_3$ (^{12}C-content >99.95%, E. Merck, Darmstadt, Germany); *H. H. Soroos, J. B. Hinkamp*, J. Am. Chem. Soc. *67*, 1642 (1945).

Mechanism of the Pyrylium/Pyridinium Ring Interconversion. Mild Preparative Conditions for Conversion of Amines into Pyridinium Ions

By *Alan R. Katritzky, Ruben H. Manzo, Jeremy M. Lloyd,* and *Ranjan C. Patel*[*]

^{13}C-NMR studies have demonstrated that excess *n*-butylamine reacts with 2,4,6-triphenylpyrylium tetrafluoroborate *(1)* by rapid ring-opening to the "vinylogous amide" *(4)* followed by slow reclosure to give the pyridinium salt[1]. Extensive spectrophotometric kinetic studies with a variety of amines and pyryliums have now clarified the reaction mechanism: the ultraviolet spectra of species *(1)*, *(4)*, and *(5)* are readily distinguished.



The sequence *(1)*→*(4)* is base catalyzed. For amines of $pK_a > 8$, excess of amine acts as base. For aniline, and for *m*- and *p*-nitroaniline, the sequence *(1)*→*(4)* becomes fast in the presence of NEt_3 as catalyst. For pyryliums possessing a 2- or 6-phenyl or 2- or 6-methyl group, the equilibrium of type *(1)*⇌*(4)* is displaced extensively towards *(4)*: however, if both the 2- and 6-positions are occupied by *tert*-butyl or by fused rings, appreciable quantities of the pyrylium salt remain in equilibrium.

The rate-determining step in the reaction of *(1)* with excess *n*-butylamine is the ring closure *(4)*, R = *n*Bu→*(5)*, R = *n*Bu which is found kinetically to be first order in *(1)* and zeroth order in $nBuNH_2$. The rate depends on the solvent (relative rates in dimethylformamide, acetonitrile, and dichloromethane were 1:20:270).

The rate of ring closure *(4)*→*(5)* varies strongly with the structure of the amine. Taking the rate for $nBuNH_2$ as unity, rates for amines RCH_2NH_2 were 1.3—0.7 and for amines $RR'CHNH_2$ were 0.01—0.002, while those for aniline and *m*-nitroaniline were respectively 0.02 and 0.0007 (obtained by extrapolation). Ring closure is clearly hindered both sterically and electronically by electron withdrawal.

The ring closure *(4)*→*(5)* is strongly acid catalyzed. Addition of two moles of AcOH to a mixture of *(1)* and $iPrNH_2$ [after the formation of the intermediate *(4)*] increased the rate 325 times; the rate for the $nBuNH_2$ reaction was too fast to measure under these conditions. Catalysis by AcOH of the reactions of *(1)* with $iPrNH_2$ and with $PhNH_2$ obey equations of the Michaelis-Menten type indicating a pre-equilibrium of vinylogous amide and catalyst to give protonated vinylogous amide which then reacts further by a unimolecular pathway[2].

The influence of successive basic and acidic catalysis of the reaction of *(1)* with aniline is shown in Figure 1. Such catalysis can dramatically improve preparative procedures for converting pyrylium into pyridinium. The pyrylium salt, amine, and triethylamine (equimolar quantities) are stirred in CH_2Cl_2 for 5 min to form the vinylogous amide, 2 mol of AcOH is added, the mixture kept 15 min and diluted with diethyl ether to yield the pyridinium.

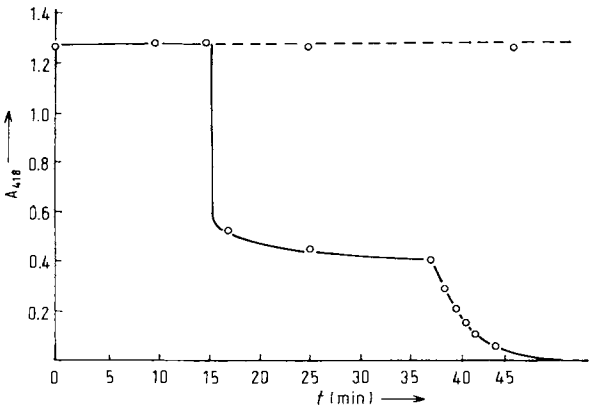


Fig. 1. Plot of absorption at 418 nm of a CH_2Cl_2 solution of 2,4,6-triphenylpyrylium perchlorate (6.1×10^{-3} M) and aniline (12.2×10^{-3} M). The solid line shows the variation when triethylamine (to bring to 6.1×10^{-3} M) was added after 16 min and acetic acid (to bring to 2.46×10^{-2} M) was added after 37 min. The dotted line shows the unchanged absorbance in the absence of NEt_3 (acetic acid was added as before after 37 min).

In this way the following improvements have been made:

(i) For amines RCH_2NH_2 reaction times have been reduced from *ca.* 12 h (*e.g.* ref. [3]) to 20 min, while at least maintaining the yield (≥80%).

(ii) For amines $RR'CHNH_2$ reaction times have been reduced from 12—30 h used to prepare iodides[4] to 20 min to obtain the more generally useful tetrafluoroborates in excellent yield (≥73%)[5].

(iii) Reaction of arylamines with 2,4,6-triphenylpyrylium previously required much stronger conditions: 80 °C for aniline[4] and *m*-nitroaniline[6] and refluxing dimethylformamide for *p*-nitroaniline[7]. Provided reagents are rigorously dried, the above procedure at 20 °C gives the 1-phenyl-, 1-(*m*-nitrophenyl)-, and 1-(*p*-nitrophenyl)pyridiniums in 77, 66, and 47% yield, respectively. The last two yields can be raised to 81 and 69% by slightly longer reaction times (at 20 °C).

(iv) Uncatalyzed reactions of even amines RCH_2NH_2 with more complex pyryliums can be very slow: thus at 20 °C the reaction of *n*-$BuNH_2$ with 2-*tert*-butyl-5,6-dihydro-4-phenylnaphtho[1,2-*b*]pyrylium is incomplete after 7 days at 20 °C: the catalyzed reaction leads to quantitative conversion at 20 °C in 15 min. Amines $RR'CHNH_2$ do not react with 5,6-dihydro-2,4-diphenylnaphthopyrylium in the absence of AcOH; the catalyzed reaction proceeds quantitatively at 20 °C in *ca.* 10 min.

Received: October 11, 1979 [Z 426 IE]
German version: Angew. Chem. *92*, 315 (1980)

[*] Prof. Dr. A. R. Katritzky, Dr. R. H. Manzo, J. M. Lloyd, Dr. R. C. Patel
School of Chemical Sciences, University of East Anglia
Norwich NR4 7TJ (England)

[1] *A. R. Katritzky, R. T. C. Brownlee, G. Musumarra,* Tetrahedron, in press.
[2] See, *e.g., K. B. Wiberg:* Physical Organic Chemistry. Wiley, New York 1964, p. 329.
[3] *A. R. Katritzky, U. Gruntz, D. H. Kenny, M. C. Rezende, H. Sheikh,* J. Chem. Soc. Perkin Trans. 1 *1979*, 430.
[4] *A. R. Katritzky, N. F. Eweiss, P.-L. Nie,* J. Chem. Soc. Perkin Trans. 1 *1979*, 433.
[5] Satisfactory analyses were obtained for all new compounds reported.
[6] *A. R. Katritzky, A. Krutošíková, C. A. Ramsden, J. Lewis,* Coll. Czech. Chem. Commun. *43*, 2046 (1978).
[7] *E. A. Zvezdina, M. P. Zhdanova, V. A. Bren', G. N. Dorofeyenko,* Khim. Geterotsikl. Soedin. *1974*, 1461.

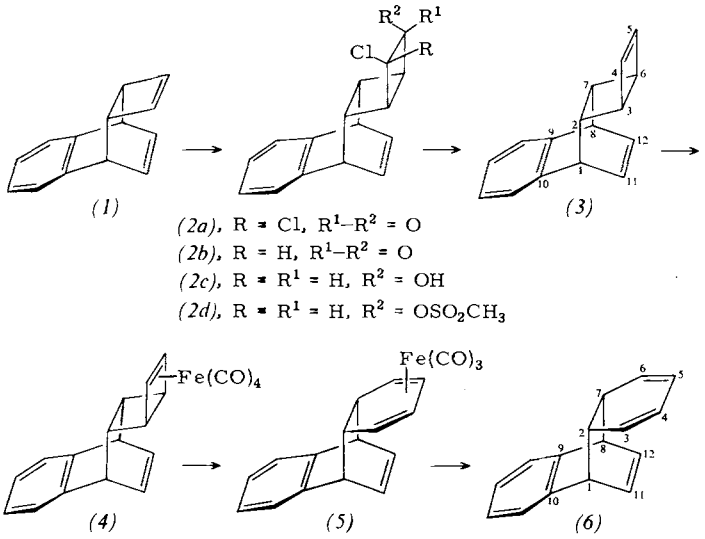
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0404-0306 $ 02.50/0*

9,10-Benzotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9,11-tetraene—A Diels-Alder Adduct of Benzene and Naphthalene[**]

By *Wolfram Grimme* and *Hans Günter Köser*[*]

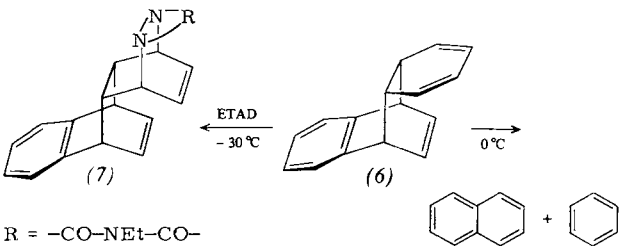
In Diels-Alder reactions benzene reacts neither as diene[1] nor as dienophile; however, its indirectly accessible [2+4]-cycloadducts are of interest regarding their retrocleavage. The decomposition is irreversible and exothermic, occurs already at low temperature, and can be easily measured both kinetically and calorimetrically. In the case of the Diels-Alder dimer of benzene, the "*o,p'*-dibenzene", whose tricarbonyliron complex is stable[2], retrocleavage occurs so readily that the free cycloadduct cannot be isolated, even at $-20\,^{\circ}C$. The Diels-Alder adduct of benzene and naphthalene, the title compound *(6)*, is more stable. It can be synthesized *via* the tricarbonyliron complex *(5)*, prepared analogously to the "*o,p'*-dibenzene"-tricarbonyliron[2].

[2+2]-Cycloaddition of dichloroketene, obtained by reaction of dichloroacetyl chloride with triethylamine, to the benzo-analog *(1)*[3] of *Nenitzescu*'s hydrocarbon furnished the dichlorocyclobutanone *(2a)* (37% yield; for physical data see Table 1), which on treatment with tri-*n*-butylstannane in boiling cyclohexane was partially dechlorinated to *(2b)* (81%). After reduction to the alcohol *(2c)* with $NaBH_4$ in 80% dioxane, reaction with methanesulfonyl chloride/trimethylamine in ether gave the ester *(2d)*. Subsequent elimination with sodium in liquid ammonia/ether afforded the valence isomer *(3)* of the title compound [57% from *(2b)*].



Opening of the bicyclohexane moiety in *(3)* was accomplished by heating with $Fe_2(CO)_9$ in hexane (20 min, 50 °C); subsequent chromatography on aluminum oxide (activity 2—3) with pentane as eluent afforded the tetracarbonyliron complex *(4)* (25%) followed, with ether, by the tricarbonyliron complex *(5)* of the title compound (25%). Further *(5)* could be obtained by thermolysis of *(4)* in boiling toluene. The higher temperature and migration of iron to the *exo* side of the cyclohexadiene moiety in *(5)* would indicate that *(4)* is not directly isomerized, but presumably first dissociates and is then opened by attack of a carbonyliron on the concave side of the bicyclohexene unit. For liberation of the benzene-naphthalene adduct *(6)*, *(5)* was oxidized at $-20\,^{\circ}C$ with ceric ammonium nitrate in acetone; after 20 minutes the reaction mixture was partitioned between pentane and saturated aqueous $CaCl_2$ solution. After drying and concentration of the pentane solution at $-20\,^{\circ}C$, 9,10-benzotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9,11-tetraene *(6)* was obtained as colorless crystals (92%), which were further purified by chromatography on silica gel (pentane, $-20\,^{\circ}C$).

Compound *(6)*, to our knowledge the first Diels-Alder adduct of two standard arenes, reacts with 4-ethyl-1,2,4-triazolinedione (ETAD) in chloroform at $-30\,^{\circ}C$ to give *(7)*, and already rapidly decomposes into its components benzene and naphthalene at 0 °C. The rate of retrocleavage was determined in *n*-hexane on the basis of the increasing naphthalene absorption at 311 nm at nine temperatures between 0 and 14.1 °C.



The reaction is of first order, the rate constant of which is given by the following Arrhenius equation[4]:

$$\log k = (12.07 \pm 0.60) - (19\,550 \pm 770)/2.303\,RT$$

We ascribe the enhanced stability of the benzene-naphthalene adduct *(6)* over that of "*o,p*-dibenzene" to the fact that in

Table 1. Physical data of the compounds *(2a)*, *(2b)*, *(3)*, *(4)*, *(5)*, *(6)*, and *(7)*. The ^{1}H-NMR spectra were recorded at 90 MHz in $CDCl_3$ [*(4)* and *(5)* in C_6D_6], the UV spectra in *n*-hexane.

(2a), M.p. 132 °C; ^{1}H-NMR: $\delta = 7.07$ (m, 4H), 6.62 (m, 2H), 4.12 (quint., H-1, 8), 3.12 (doubletted AX, $\Delta\nu = 54$ Hz, $J = 4.5$ Hz, H-3, 6), 2.50 (AB, $\Delta\nu = 32$ Hz, $J = 7.5$ Hz, H-2, 7); IR (KBr): $\nu_{CO} = 1795\ cm^{-1}$; UV: $\lambda_{max} = 258$ nm ($\varepsilon = 540$) sh, 263 (680), 272 (620), 316 (104), 328 (96) sh

(2b), M.p. 112 °C; ^{1}H-NMR: $\delta = 7.2$ (m, 4H), 6.63 (quint., $J = 3$ Hz, 2H), 5.03 (doubletted d, $J = 9$ Hz, H-4), 4.1 (m, H-1, 8), 3.2 (m, H-6), 2.8 (m, H-3, 7), 2.3 (m, H-2); IR (KBr): $\nu_{CO} = 1790\ cm^{-1}$; UV: $\lambda_{max} = 257$ nm ($\varepsilon = 375$) sh, 263 (480), 270 (450), 309 (165)

(3), M.p. 42 °C; ^{1}H-NMR: $\delta = 7.00$ (m, 4H), 6.47 (t, $J = 3.5$ Hz, H-11, 12), 6.07 (s, H-4, 5), 3.80 (m, H-1, 8), 2.83 (s, H-3, 6), 2.27 (m, H-2, 7); MS: $m/e = 206$ (M^+), 128 ($C_{10}H_8^+$, 100%), 78 ($C_6H_6^+$); UV: $\lambda_{max} = 251$ nm ($\varepsilon = 205$) sh, 256 (297), 263 (400), 270 (375)

(4), M.p. 82 °C; ^{1}H-NMR: $\delta = 7.10$ (m, 4H), 6.20 (t, $J = 3.5$ Hz, H-11, 12), 3.63 (m, H-1, 8), 3.33 (s, H-4, 5), 2.27 (s, H-3, 6), 2.03 (m, H-2, 7); MS: $m/e = 374$ (M^+), 290 (-3 CO), 262 ($-$CO), 184 ($-C_6H_6$), 128 ($-$Fe, 100%), 56 (Fe^+); IR (KBr): $\nu_{CO} = 2081\ cm^{-1}$, 1996, 1968, 1958; UV: $\lambda_{max} = 230$ nm ($\varepsilon = 27\,300$) sh, 275 (6500), 400 (80) end absorption

(5), Dec. p. 193 °C; ^{1}H-NMR: $\delta = 7.00$ (s, 4H), 6.40 (t, $J = 3.5$ Hz, H-11, 12), 4.32 (AA'XX'-half-spectrum, H-4, 5), 3.37 (m, H-1, 8), 2.75 (AA'XX'-half-spectrum, H-3, 6), 1.53 (s, H-2, 7); MS: $m/e = 318$ ($M^+ - CO$), 290 ($-$CO), 262 ($-$CO), 184 ($-C_6H_6$), 128 ($-$Fe), 78 ($C_6H_6^+$), 56 (Fe^+, 100%); IR (KBr): $\nu_{CO} = 2041\ cm^{-1}$, 1960, 1934; UV: $\lambda_{max} = 285$ nm ($\varepsilon = 2600$) sh, 400 (50) end absorption

(6), ^{1}H-NMR ($-30\,^{\circ}C$): $\delta = 7.17$ (AA'BB', 4H), 6.63 (A_2X_2-half-spectrum, $J = J' = 4$ Hz, H-11, 12), 5.63 (s, H-3, 4, 5, 6), 4.00 (A_2X_2-half-spectrum, H-1, 8), 2.83 (s, H-2, 7); UV ($-30\,^{\circ}C$): $\lambda_{max} = 264$ nm ($\varepsilon = 3400$), 271 (4000), 281.5 (3250), 293 (1550)

(7), M.p. 205 °C; ^{1}H-NMR: $\delta = 7.17$ (AA'BB', 4H), 6.10 (t, 2 olefinic H), 6.07 (t, 2 olefinic H), 4.8 (m, 2H), 3.87 (t, 2H), 3.48 (quart., CH_2), 2.57 (m, 2H), 1.13 (t, CH_3); MS: $m/e = 333$ (M^+), 205 ($-C_{10}H_8$), 128 ($C_{10}H_8^+$, 100%), 78 ($C_6H_6^+$)

[*] Dr. W. Grimme, Dipl.-Chem. H. G. Köser
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

[**] This work was supported by the Verein der Freunde und Förderer der Universität Köln and the Fonds der Chemischen Industrie.

both cycloreversions the gain in aromatic resonance energy is already utilized in the transition state; for *(6)* it is about 3.2 ± 1.0 kcal/mol smaller than for *"o,p*-dibenzene"[5]. Despite the highly negative heat of reaction of *ca.* -35 kcal/mol the transition state occurs late, *i.e.* it lies on the side of the components. The weakly negative entropy of activation, on the other hand, shows that the arenes are formed in a highly ordered transition state, which still has no new degrees of freedom. Hence, in the retrocleavage the adduct *(6)* passes through a reaction profile typical for Diels-Alder reactions in the reverse direction, and the frontier orbital model[8] developed for the forward reaction should hold here too.

Received: October 29, 1979 [Z 428 IE]
German version: Angew. Chem. *92*, 307 (1980)

[1] Exceptions are the reaction of benzene with dehydrobenzene [*R. G. Miller, M. Stiles*, J. Am. Chem. Soc. *85*, 1798 (1963)] and with dicyanoacetylene [*E. Ciganek*, Tetrahedron Lett. *1967*, 3321].
[2] *W. Grimme, E. Schneider*, Angew. Chem. *89*, 754 (1977); Angew. Chem. Int. Ed. Engl. *16*, 717 (1977).
[3] *L. A. Paquette, J. C. Howell*, Tetrahedron Lett. *1970*, 2259.
[4] The errors are the double standard deviations of the linear regression used for the kinetic analysis; $R = 1.986$ cal K^{-1} mol^{-1}.
[5] For equal strain energy in *"o,p'*-dibenzene" and in *(6)*, the difference in their heats of decomposition is equal to the negative difference in the heats of hydrogenation of benzene ($\Delta H_{hydr(l)} - 4.8 \pm 0.5$ kcal/mol) and naphthalene ($\Delta H_{hydr(l)} = 1.7 \pm 0.5$ kcal/mol) to their 1,4-dihydro compounds. The calculation was carried out using the data given in *J. D. Cox, G. Pilcher:* Thermochemistry of Organic and Organometallic Compounds. Academic Press, London 1970, and the standard heats of formation of cyclohexadienes [6] and tetralin [7].
[6] *R. B. Turner, B. J. Mallon, M. Tichy, W. von E. Doering, W. R. Roth, G. Schröder*, J. Am. Chem. Soc. *95*, 8605 (1973).
[7] *W. D. Good, S. H. Lee*, J. Chem. Thermodyn. *1976*, 643.
[8] a) *R. Sustmann*, Pure Appl. Chem. *40*, 569 (1974); b) *K. N. Houk*, Acc. Chem. Res. *8*, 361 (1975).

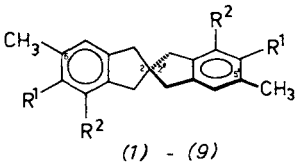
(+)-(2*R*)-5,5'-Dimethyl-2,2'-spirobi(2,3-dihydro-1*H*-cyclopenta[*a*]naphthalene)— A Chiral Spirohydrocarbon Containing Orthogonal Naphthalene Units[**]

By *Horst Neudeck* and *Karl Schlögl*[*]

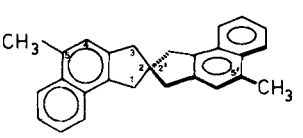
Optically active 2,2'-spirobiindanes of known chirality and enantiomeric purity—such as (+)-(2*R*)-*(1)*, $R^1 = R^2 = H$—are accessible *via* chiral tricarbonylchromium complexes of the corresponding 1-oxoindans[2]. This enables the synthesis of numerous 5,5'-di- and 5,5',6-trisubstituted 2,2'-spirobiindans[3,4], which are of particular interest for testing approximations for chirality functions[1,3].

We have now synthesized the title compound, a hitherto unknown spirosystem *(10)*[5] containing two mutually orthogonal naphthalene units, which should be of interest, *inter alia*, because of its chiroptic properties (cf. [6]).

Optically pure (2*R*)-*(1)* ($R^1 = R^2 = H$, $[\alpha]_D^{20} = +4.6°$ in acetone)[2] was acylated with succinic anhydride/$AlCl_3$ in nitrobenzene to the bis-oxo acid *(2)* (cf. Table 1) whose dimethyl ester *(3)* could be smoothly hydrogenated with H_2/Pd—C in 2-propanol to the bis-butyrate *(4)*. The corresponding dicarboxylic acid *(5)* could be cyclized with polyphosphoric acid (5 h, 100 °C) to the biscyclohexenone *(6)*. The hydrocarbon *(7)* was accessible from *(6)* by hydrogenation (H_2/Pd—C in propanol/benzene), and the diol *(8)* by reduction with $LiAlH_4$. *(8)* was dehydrated with *p*-toluenesulfonic



(1) - *(9)*



(+)- *(10)*

Table 1. Di- and tetra-substituted 5,5'-dimethyl-2,2'-spirobiindans [a].

Cpd.	R^1	R^2	Yield [%]	M.p. [°C]	$[\alpha]_D^{20}$ (in acetone)
(2)	$CO(CH_2)_2COOH$	H	58	159—163	—
(3)	$CO(CH_2)_2COOCH_3$	H	95	30—33	+ 8.7°
(4)	$(CH_2)_3COOCH_3$	H	98	72—73	+ 2.7°
(5)	$(CH_2)_3COOH$	H	95	192—196	—
(6)	$(CH_2)_3CO$		94	232—235	+ 39.5°
(7)	$(CH_2)_4$		98	156—157	+ 15.1°
(8)	$(CH_2)_3CHOH$		96	190—195	—
(9)	$(CH_2)_2CH{=}CH$		82	132—134	+ 45.0° ($CHCl_3$)
(10) [b]	$CH{=}CH$ $CH{=}CH$		90	185—189	+117.9°

[a] All compounds are thin-layer chromatographically pure; their structures are confirmed by ^{1}H-NMR and mass spectra. [b] ^{1}H-NMR ($CDCl_3$): $\delta = 8.01$ (m, 2H), 7.73 (m, 2H), 7.50 (m, 4H), 7.24 (s, 2H), 3.33 (s, 4H), 3.20 (s, 4H), 2.69 (s, 6H); UV (*n*-heptane): λ_{max} [nm] ($\lg \varepsilon$): 233 (5.30), 258 (4.43), 285 (4.37), 292 (4.38), 297 (4.34), 312 (3.95), 319 (3.72), 327 (4.03); $[\alpha]_D^{20} = +124.0$ ($c = 2.0$ in $CHCl_3$); CD (*n*-heptane): λ [nm] ($\Delta\varepsilon$): 231 (−312), 239 (+558), 267 (+2.89), 292 (−6.32), 311 (−0.92), 312 (−1.27), 321 (−0.66), 324 (−0.36), 328 (−1.81). $C_{27}H_{24}$ (348.5).

acid in benzene to the bishexadiene *(9)*, in which the two vinyl groups are essentially fixed in the orthogonal planes. Finally, catalytic dehydrogenation of *(9)* (Pd—C in boiling dioxane with passage of O_2) afforded the desired product *(10)* in 90% yield as colorless crystals of m.p. 185—189 °C (from benzene/methanol). *(9)* could also be dehydrogenated with dichlorodicyanobenzoquinone in benzene (3 h at 20 °C) to give *(10)* in 70% yield.

The configuration (2*R*) (cf. [2,3]) and the enantiomeric purity ($p = 100\%$) of (+)-*(10)* clearly follow from those of the educt (+)-(2*R*)-*(1)*[2].

Received: November 2, 1979 [Z 430 IE]
German version: Angew. Chem. *92*, 318 (1980)

[1] *H. Neudeck, B. Richter, K. Schlögl*, Monatsh. Chem. *110*, 931 (1979).
[2] *A. Meyer, H. Neudeck, K. Schlögl*, Chem. Ber. *110*, 1403 (1977).
[3] *H. Neudeck, K. Schlögl*, Chem. Ber. *110*, 2624 (1977).
[4] *H. Neudeck, K. Schlögl*, Monatsh. Chem. *110*, 541 (1979).
[5] *Note added in proof:* For the isomeric 1,1'-spirobi[benz[e]indan]-system, cf. *S. Imajo, A. Nakamura, K. Shingu, A. Kato, M. Nakagawa*, J. C. S. Chem. Commun. *1979*, 868.
[6] On the CD of 2,2'-spirobiindanes see: *E. Langer, H. Lehner, H. Neudeck, K. Schlögl*, Monatsh. Chem. *109*, 987 (1978); chiroptical properties of 1,1'-spirobiindans: *J. H. Brewster, R. T. Prudence*, J. Am. Chem. Soc. *95*, 1217 (1973), and references cited therein.

Carbon Monoxide/Water as a Reducing Agent: Formation of Selane from Selenium[1]

By *Noboru Sonoda, Kiyoshi Kondo, Kiyoyuki Nagano, Nobuaki Kambe, Fumihiko Morimoto*[*]

One of the striking applications of carbon monoxide in organic or inorganic chemistry is its use as reducing agent. In

[*] Prof. Dr. K. Schlögl, Dr. H. Neudeck
Institut für Organische Chemie der Universität
Währingerstrasse 38, A 1090 Wien (Austria)

[**] Optically Active Aromatic Spiranes, Part 10. This work was supported by the Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung (Project No. 3033).—Part 9: [1].

[*] Prof. Dr. N. Sonoda [+], Dr. K. Kondo, K. Nagano, N. Kambe, F. Morimoto
Department of Petroleum Chemistry, Faculty of Engineering,
Osaka University
Suita, Osaka 565 (Japan)
[+] Author to whom correspondence should be addressed.

this connection, there has been increasing interest in developing catalysts active at low temperature for the water gas shift reaction, and in establishing a convenient homogeneous hydrogenation system using carbon monoxide and water[2].

During the course of our studies on the selenium-catalyzed carbonylation of various compounds with carbon monoxide[3], we found that metallic selenium is readily reduced to selane (H_2Se) by carbon monoxide and water in the presence of base under mild conditions [eq. (1)].

$$Se + CO + H_2O \xrightarrow{Base} H_2Se + CO_2 \quad (1)$$

The yield of H_2Se is quantitative. The reaction proceeds at 25 °C/1 bar CO, but is accelerated at higher pressure and temperature. To obtain solvent-free H_2Se[4], water can be used as reaction solvent; in this case 60 °C and 5 bar were required. Acidification of the reaction mixture with sulfuric acid liberated H_2Se[5], which was trapped in a receiver cooled to −196 °C (see *Experimental*).

We assume that the reaction proceeds *via* carbonyl selenide[6] [eq. (2)].

$$Se + CO \xrightarrow{Base} Se{=}C{=}O \xrightarrow{H_2O} HSe{-}COOH \rightarrow H_2Se + CO_2 \quad (2)$$

It could prove possible to develop a catalytic cycle on this basis.

Experimental

Metallic selenium (0.400 g, 5 mmol), water (10 g), and *N*-methylpyrrolidine (1.04 ml, 10 mmol) are placed with a magnetic stirring bar in a 50-ml stainless steel autoclave, and the apparatus is then flushed several times with CO and finally charged with CO at 5 bar. The reaction is carried out at 60 °C for 7 h with vigorous stirring. On completion of the reaction (reaction mixture becomes pale yellow and homogeneous) the resulting gas (4.5 mmol CO_2) is collected in gas sampler and analyzed. Cautious addition of well degassed aqueous sulfuric acid (10 N; 10 ml, *ca.* 50 mmol) to the solidified solution mixture at −78 °C followed by distillation from the autoclave at −5 °C/10 torr directly into a tube cooled at −196 °C gives H_2Se containing CO_2. Trap-to-trap distillation at −41 to −39 °C/760 torr affords pure H_2Se (b.p. −41.3 °C). The yield (82%) was determined by gravimetry after oxidation of H_2Se with oxygen at room temperature in the presence of triethylamine (2.02 g, 20 mmol) in THF (10 ml) to give selenium (0.320 g, 4.1 mmol) and water.

Received: October 29, 1979 [Z 429 IE]
German version: Angew. Chem. *92*, 317 (1980)

[1] A new system of utilizing the reducing ability of carbon monoxide, Part 1.
[2] *H.-C. Kang, C. H. Mauldin, T. Cole, W. Slegeir, K. Cann, R. Pettit,* J. Am. Chem. Soc. *99*, 8323 (1977); *C.-H. Cheng, D. E. Hendriksen, R. Eisenberg, ibid. 99*, 2791 (1977); *R. M. Laine, R. G. Rinker, P. Ford, ibid. 99*, 252 (1977); *R. M. Laine, D. W. Thomas, L. W. Cary, S. E. Buttrill, ibid. 100*, 6527 (1978); *R. M. Laine, ibid. 100*, 6451 (1978); *C.-H. Cheng, R. Eisenberg, ibid. 100*, 5968 (1978); *P. C. Ford, R. G. Rinker, C. Ungermann, R. M. Laine, V. Landis, S. A. Moya, ibid. 100*, 4595 (1978); *K. Cann, T. Cole, W. Slegeir, R. Pettit, ibid. 100*, 3969 (1978); *T. Yoshida, Y. Ueda, S. Otsuka, ibid. 100*, 3941 (1978); *R. B. King, C. C. Frazier, R. M. Hanes, A. D. King, Jr., ibid. 100*, 2925 (1978); *J. W. Rathke, H. M. Feder, ibid. 100*, 3623 (1978).
[3] *N. Sonoda, T. Yasuhara, K. Kondo, T. Ikeda, S. Tsutsumi,* J. Am. Chem. Soc. *93*, 6344 (1971); *K. Kondo, N. Sonoda, S. Tsutsumi,* J. Chem. Soc. Chem. Commun. *1972*, 307; *K. Kondo, N. Sonoda, H. Sakurai,* Bull. Chem. Soc. Jpn. *48*, 108 (1975); *N. Sonoda, G. Yamamoto, K. Natsukawa, K. Kondo, S. Murai,* Tetrahedron Lett. *1975*, 1969; *K. Kondo, K. Murata, N. Miyoshi, S. Murai, N. Sonoda,* Synthesis *1979*, 735; *K. Kondo, N. Sonoda, H. Sakurai,* Chem. Lett. *1974*, 1429; *K. Kondo, N. Sonoda, S. Tsutsumi, ibid. 1972*, 373.
[4] In organic solvents such as acetonitrile and tetrahydrofuran, the reaction proceeded more smoothly than that in water.
[5] Production of H_2Se: *D. L. Klayman, T. S. Griffin,* J. Am. Chem. Soc. *95*, 197 (1973); *F. Fehér* in *G. Brauer:* Handbook of Preparative Inorganic Chemistry. Vol. 1. Academic Press, New York 1963, p. 418; *H. Reinboldt* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Vol. IX. Thieme, Stuttgart 1955, p. 953.
[6] *K. Kondo, S. Yokoyama, N. Miyoshi, S. Murai, N. Sonoda,* Angew. Chem. *91*, 760 (1979); Angew. Chem. Int. Ed. Engl. *18*, 691 (1979); *K. Kondo, S. Yokoyama, N. Miyoshi, S. Murai, N. Sonoda, ibid. 91*, 761 (1979) and *18*, 692 (1979), respectively.

X-Ray Structure Analysis of Bis(*O,O'*-diphenyldithiophosphato)tin(II), a Bicyclic Dimer Held Together by η^6-C_6H_5/Sn^{II} Interactions[**]

By *J. L. Lefferts, M. B. Hossain, K. C. Molloy, D. van der Helm,* and *J. J. Zuckerman*[*]

The tin(II) dithiophosphate ester $Sn[S_2P(OC_6H_5)_2]_2$, m.p. 125.5—126.5 °C, has been synthesized by the reaction of dimethoxytin(II) with *O,O'*-diphenyldithiophosphoric acid (molar ratio 1:2) in benzene:

$$Sn(OCH_3)_2 + 2\,HSP(S)(OC_6H_5)_2 \rightarrow 2\,CH_3OH + Sn[S_2P(OC_6H_5)_2]_2$$

and characterized by ^{119m}Sn Mössbauer [$I.S. = 3.78 \pm 0.02$; $Q.S. = 1.06 \pm 0.04$ mm/s] and mass [$m/e = 682$ (2.9%) M^+] spectrometry, as well as by elemental analysis. A triclinic single crystal of space group $P\bar{1}$ [$a = 10.499(5)$, $b = 13.948(7)$, $c = 9.291(4)$ Å; $\alpha = 99.18(6)°$, $\beta = 95.71(5)°$, $\gamma = 91.80(5)°$] was studied by $Mo_{K\alpha}$ X-radiation and refined to a final *R* value of 2.9% for 5517 reflections.

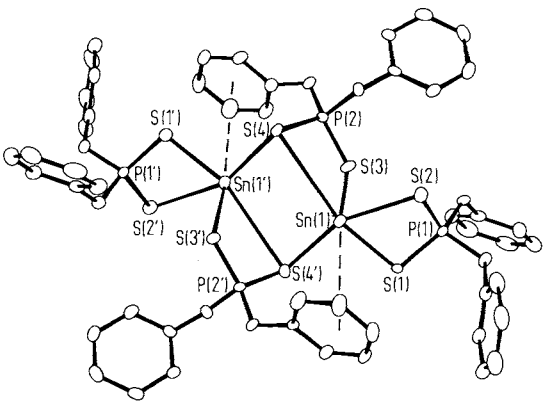


Fig. 1. Molecular structure of dimeric bis(*O,O'*-diphenyldithiophosphato)tin(II) $\{Sn^{II}[S_2P(OC_6H_5)_2]_2\}_2$ held together by bifurcated, three-coordinated sulfur atoms and η^6-C_6H_5 interactions with the tin(II) lone electron pairs.

[*] Prof. Dr. J. J. Zuckerman, Dr. M. B. Hossain, Dr. J. L. Lefferts, Dr. K. C. Molloy, Prof. Dr. D. van der Helm
University of Oklahoma, Department of Chemistry, Norman, OK 73019 (USA)

[**] Oxy- and Thio-Phosphorus Acid Derivatives of Tin, Part 3. Our work is supported by the U.S. Office of Naval Research and the National Science Foundation (Grant No. CHE-78-26584) (*J. J. Z.*) and the National Cancer Institute, U.S. D.H.E.W. through Grant No. CA-17562 (*D. v. d. H.*).—Part 2: *K. C. Molloy, M. B. Hossain, D. van der Shelm, J. J. Zuckerman,* Inorg. Chem. *18*, 3507 (1979).

The centrosymmetric dimer shown in Figure 1 contains one ligand bridging two tin atoms intermolecularly while simultaneously chelating one tin atom in an extremely anisobidentate fashion, *via* the three-coordinated (S4) and S(4′). A second ligand is involved in normal chelation as is found in the tin(II) dithiocarbamate $Sn[S_2CN(C_2H_5)_2]_2$[1] and dithiocarbonate $Sn[S_2COCH_3]_2$[2]. A planar Sn_2S_2 four-membered ring such as is found in Sn_2S_3[3] and $(CH_3Sn)_4S_6$[4] is circumscribed by an $[SnSPS]_2$ eight-membered ring in an arrangement reminiscent of the eight-membered centrosymmetric rings formed by the tin(IV) atoms and dichlorophosphate groups in the dimeric $[Cl_3SnPO_2Cl_2 \cdot POCl_3]_2$[5]. Our structure contrasts with those adopted by lead(II) diethyldithiophosphate in which the metal atoms are chelated in monomers[6a], and its diisopropyl analogue in which the metal atom is coordinated by six sulfur atoms, two of which are bonded intermolecularly to give a polymeric lattice[6b].

Unlike these structures, the dimeric title compound is held together by two coordinate bonds at 3.0248(7) emanating from S(4) and S(4′) atoms plus a long π-interaction at 3.655 Å along the S(3)—Sn(1) and S(3′)—Sn(1′) vectors to the center of one of the phenyl groups of an ester group of the bridging ligand of the second monomeric unit (Fig. 2). This phenyl group is oriented in a spatially significant position perpendicular to the assumed vector of the tin lone pair producing a distorted octahedral (ψ-6) geometry at the metal center. π-Interactions with tin(II) lone pairs are found in η^6-$C_6H_6Sn(AlCl_4)_2 \cdot C_6H_6$[7a] and η^6-$C_6H_6SnCl(AlCl_4)$[7b] where the distances to the center of the rings lie in the range 2.74 to 2.90 Å, long with respect to transition metal-arene distances. Our dimer is unusual, however, for two reasons. Firstly, to our knowledge[8] we have here the only example of an η^6-C_6H_5 main group π-bond; and secondly, the only known example of such an interaction contributing to the formation of a dimer from the constituent monomers.

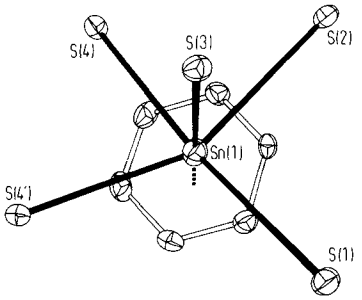


Fig. 2. The η^6-C_6H_5 Sn^{II} vector. The distance to the center of the ring is 3.655 Å.

The existence of the Sn_2S_2 ring is confirmed on close inspection of the phosphorus-sulfur distances. The more tightly bound to a metal the dithiophosphate sulfur is, then the longer its bond to phosphorus[9]. For example, in the purely chelating ligands in our structure atom S(1) makes a relatively short tin bond [S(1)—Sn(1) = 2.6230(6) Å] and a relatively long bond to phosphorus [S(1)—P(1) = 2.0016(8) Å]. Atom S(2) does the opposite [S(2)—Sn(1) = 2.8300(6), S(2)—P(1) = 1.9670(8) Å]. Thus we conclude that atom S(2) is double-bonded to P(1). However, comparison of the two ligands bonded to each tin atom reveals that although the bridging sulfur-tin bond is significantly longer [S(4)—Sn(1′) = 3.0248(7) Å] than the corresponding chelating bond [S(2)—Sn(1) = 2.8300(6) Å], the presumably P=S distances are quite similar [P(2)—S(4) = 1.9636(8), P(1)—S(2) = 1.9670(8) Å]. This unexpectedly long P(2)=S(4) distance must arise because of the electron withdrawal along the S(4)—Sn(1) vector at 3.3914(6) Å, thus confirming the interaction between these two atoms. In $\{Cu^I S_2P[OCH(CH_3)_2]_2\}_4$, on the other hand, the three-coordinated sulfur atoms that bridge two metal centers form equal or stronger sulfur-metal bonds than the sulfurs bonded to only one metal atom. In that case electron withdrawal from the bridging sulfur-phosphorus P=S bond so lengthens this distance that it actually becomes longer than the adjacent P–S single bond[10].

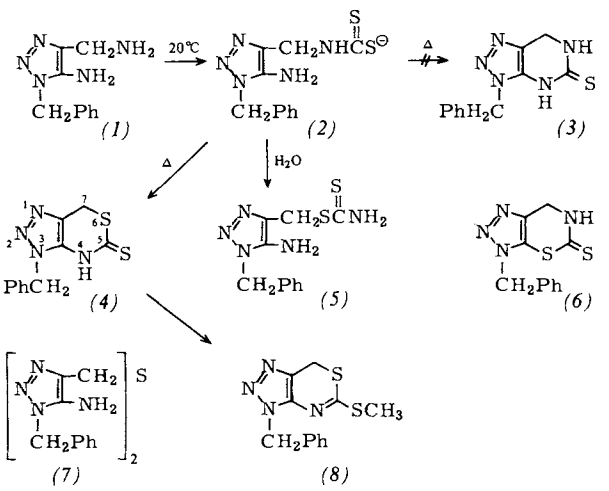
Received: September 17, 1979 [Z 431 IE]
German version: Angew. Chem. *92*, 326 (1980)

[1] *J. Potenze, D. Mastropaolo*, Acta Crystallogr. *B 29*, 1830 (1973).
[2] *P. R. R. Ewings, P. G. Harrison, T. J. King*, J. Chem. Soc. Dalton Trans. *1976*, 1399.
[3] *D. Mootz, R. Kunzmann*, Acta Crystallogr. *15*, 913 (1962); *23*, 471 (1967).
[4] *C. Dorfelt, A. Janeck, D. Kobelt, E. F. Paulus, H. Scherer*, J. Organomet. Chem. *14*, P22 (1968).
[5] *D. Moras, A. Mitschler, R. Weiss*, Acta Crystallogr. *B 25*, 1720, 1726 (1969).
[6] a) *T. Ito*, Acta Crystallogr. *B 28*, 1034 (1972); b) *S. L. Lawton, G. T. Kokotailo*, Nature *221*, 550 (1969).
[7] a) *Th. Auel, E. L. Amma*, J. Am. Chem. Soc. *90*, 5941 (1978); *H. Lüth, E. L. Amma, ibid. 91*, 7515 (1969); *P. F. Rodesiler, Th. Auel, E. L. Amma, ibid. 97*, 7405 (1975); b) *M. S. Weininger, P. F. Rodesiler, A. G. Gash, E. L. Amma, ibid. 94*, 2135 (1972); *M. S. Weininger, P. F. Rodesiler, E. L. Amma*, Inorg. Chem. *18*, 751 (1978).
[8] *J. A. Zubieta, J. J. Zuckerman*, Prog. Inorg. Chem. *24*, 251 (1978).
[9] *J. R. Wasson, G. M. Woltermann, H. J. Stoklosa*, Fortschr. Chem. Forsch. *35*, 65 (1973).
[10] *S. L. Lawton, W. J. Rohrbaugh, G. T. Kokotailo*, Inorg. Chem. *11*, 612 (1972).

1,2,3-Triazolo[4,5-*d*][1,3]thiazine, a New Heterocyclic System

By *Adrien Albert* and *Albert Dunand*[*]

When 4-amino-5-aminomethyl-3-benzyl-1,2,3-triazole *(1)* is stirred at 20 °C with carbon disulfide and ethanolic sodium ethoxide or methanolic ammonia, the expected (non-basic) dithiocarbamate [anion *(2)*] is formed exclusively (^{1}H-NMR evidence). Heating these mixtures does not lead to the expected[1] 9-benzyl-1,6-dihydro-8-azapurine-2-thione *(3)*, but instead to a compound richer in sulfur and poorer in nitrogen which could be a triazolothiazine of structure *(4)* or *(6)*. A single-crystal X-ray analysis of the *S*-methyl derivative *(8)* has now shown the parent to have the structure *(4)*.



[*] Prof. Dr. A. Albert, Dr. A. Dunand
Research School of Chemistry
Australian National University
P.O. Box 4, Canberra, Australia 2600

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0404-0310 $ 02.50/0

The methylthio group of *(8)* was easily displaced by nucleophiles and gave, for example, the 5-amino and 5-hydrazino derivatives, m.p. 165 and 159 °C, respectively. It appears that this new heterocycle, the substitution of which can be so easily modified, could provide many interesting new compounds as candidate drugs.

The transfer of the methylene group from nitrogen to sulfur in the reaction *(2)* → *(4)* is contrary to the usual direction of isomerism (*e.g.* thiocyanates → isothiocyanates). The same unusual shift furnished the (non-basic) by-product *(7)*. That this transfer may occur at the dithiocarbamate stage *(2)* is indicated by a change in the ^{1}H-NMR spectrum when water is added to the cold mixture of the diamine *(1)*, carbon disulfide, ammonia, and methanol. The initial spectrum of the *N*-alkyl dithiocarbamate *(2)* changes to that of the *S*-alkyl dithiocarbamate *(5)* (see Table 1).

Table 1. ^{1}H-NMR data of intermediates *(2)* and *(5)* and products *(4)* and *(8)*. δ values, in $(CD_3)_2SO$ [a].

(2), 8.30* (1H, NH), 7.22 (5H, Ph), 5.85* (2H, NH_2), 5.35 (2H, CH_2Ph), 4.58 (2H, d**, CH_2NH coupled with NH

(4), 7.19 (m, 5H, Ph), 5.60 (2H, CH_2Ph), 425 (2H, CH_2S)

(5), 7.99* (2H, SC NH_2), 7.22 (5H, Ph), 5.77* (2H, 4-NH_2), 5.27 (2H, CH_2Ph), 4.00 (2H, s, CH_2S)

(8), 7.31 (5H, Ph), 5.72 (2H, CH_2Ph), 4.40 (2H, CH_2S), 2.58 (3H, Me)

[a] *: vanishes on addition of D_2O; **: d becomes s on addition of D_2O.—For comparison, the CH_2S signal in the sulfide *(7)* is δ = 3.63.

The *S*-methyl derivative *(8)* of the thione forms triclinic crystals ($P\bar{1}$, $a = 8.742$, $b = 9.717$, $c = 9.823$ Å, $\alpha = 110.09°$, $\beta = 113.70°$, $\gamma = 102.17°$, $Z = 2$). The molecular configuration was determined by conventional crystal structure analysis (diffractometer data[2], $R = 5.1\%$) (see Fig. 1).

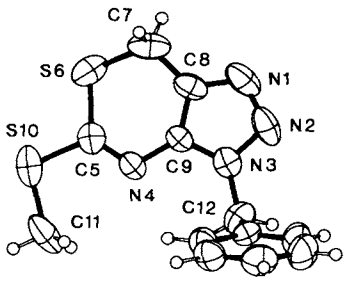


Fig. 1. Crystal structure of 3-benzyl-3,7-dihydro-5-methylthio-1,2,3-triazolo[4,5-*d*][1,3]thiazine *(8)* [2].

The 1,2,3-triazole ring is completely planar. The thiazine ring has a half-boat like conformation with the torsional angles C(9)—N(4)—C(5)—S(6) = 2.6(5)° and S(6)—C(7)—C(8)—C(9) = −30.4(5)°; C(7) and N(4) lie slightly above and below the triazole plane, respectively. While the C(sp^3)—S bonds are only marginally different, C(7)—S(6) (1.798(5) Å) and C(11)—S(10) (1.7811(7) Å), the two C(sp^2)—S bonds differ significantly by having C(5)—S(6) (1.779(4) Å) larger than C(5)—S(10) (1.733(4) Å) in relation with more N—C—S—C torsion around C(5)—S(6) (−24.6(4)°) than around C(5)—S(10) (−8.2(4)°). The methyl hydrogen atoms' observed locations are consistent with a staggered configuration around the S(10)—C(11) bond. The benzyl substituent also has an energetically favored configuration, the C(12)—C(phenyl) bond being almost perpendicular to the triazole ring, and the N(3)—C(12) bond is only 10° out of perpendicular to the benzene ring.

Procedure

(4) [and *(7)*]: The diamine *(1)*[3] (1.0 g, 0.005 mol), pyridine (20 ml), CS_2 (3.8 g, 10 equiv.), and triethylamine (1.0 g, 2 equiv.) are heated in a bath at 115 °C for 6 h. The mixture is taken to dryness *in vacuo* at 90 °C, and the residue shaken with 1 N KOH (12.5 ml). Filtration from the sulfide *(7)* [m.p. 173 °C (from 50% aqueous ethanol); MS, $m/e = 406$ (M^+)] and acidification of the filtrate to pH 3.5 gives *(4)* in 60% yield, crystals from 50% aqueous ethanol [m.p. about 190 °C with effervescence. MS: $m/e = 262$ (M^+)].

(8): Compound *(4)* (0.131 g), 1 N NaOH (0.6 ml), and CH_3I (0.085 g, 1.2 equiv.) are stirred for 15 min at 20 °C. After filtration, a 91% yield of *(8)* is obtained [m.p. 127 °C (from cyclohexane)].

Received: September 10, 1979 [Z 432 IE]
German version: Angew. Chem. *92*, 319 (1980)

[1] *M. Busch*, J. Prakt. Chem. *51* [2], 257 (1895); *W. L. F. Armarego*: Quinazolines. Wiley-Interscience, New York 1967, p. 276.
[2] *A. Dunand*, to be published.
[3] *A. Albert*, J. Chem. Soc. Perkin Trans. I *1973*, 1634.

Exceedingly Mild Desulfurization of Thiols by Sodium Triethylhydroborate and Transition Metal Chlorides[**]

By *Howard Alper* and *Trish L. Prince*[*]

Desulfurization reactions are of considerable current interest, particularly with reference to their possible application to the removal of sulfur from fuel oil, coke, and other energy sources. One of us has recently begun a search for new desulfurization processes[1]. We now wish to report a simple and exceedingly mild method for the desulfurization of thiols.

Mixed hydride/transition metal halide reagents have come into increased use in recent years[2]. Treatment of 2-naphthalenethiol *(1a)* with anhydrous ferrous chloride and sodium triethylhydroborate [molar ratio 1:2:4] in tetrahydrofuran at −78 °C gives naphthalene *(2a)* in 81—85% yield.

$$\underset{(1)}{RSH} + Na[(C_2H_5)_3BH] + MCl_n \rightarrow \underset{(2)}{RH} + \underset{(3)}{RR} + \cdots$$

2,2′-Binaphthyl *(3a)* appears as a reaction by-product if $CoCl_2$ is used instead of $FeCl_2$. VCl_3 gave less fruitful results. Table 1 lists examples.

Table 1. Desulfurization of thiols *(1)* to hydrocarbons *(2)* and didehydrodimers *(3)* with $Na[(C_2H_5)_3BH]/MCl_n$.

	R =	MCl_n	Yield [%] [a] *(2)*	*(3)*
a	2-Naphthyl	$FeCl_2$	81—85	
		$CoCl_2$	72	27
		VCl_3	23	
b	2,5-Dichlorobenzene	$CoCl_2$	84	
c	4-Methoxybenzyl	$FeCl_2$	63	
d	Triphenylmethyl	$FeCl_2$	59	8
e	1-Dodecyl	$FeCl_2$	78	

[a] Isolated yields. Products identified by comparison of analytical and spectral data with those of authentic materials.

[*] Prof. Dr. H. Alper, T. L. Prince
Department of Chemistry, University of Ottawa
Ottawa, Canada K1N 9B4

[**] We are indebted to the Natural Sciences and Engineering Research Council for support of this research.

This desulfurization reaction not only occurs with aromatic thiols, but with benzylic and nonaromatic thiols as well. Yields are good and product isolation is simple.

General procedure

The thiol *(1)* (1.5 mmol) in THF (2—3 ml) is added to anhydrous metal chloride (3.0 mmol) in THF (2 ml). After addition of THF (8 ml), the reaction mixture is stirred at room temperature for 15—25 min, cooled to −78 °C, and then a 1 M solution of $Na[(C_2H_5)_3BH]$ in THF (6.0—6.2 ml) is added by syringe. The solution is stirred for 15—20 min at −78 °C, and then allowed to warm to room temperature with stirring. Moist sodium sulfate is added, followed by water (10 ml), and the reaction mixture is filtered. The products are then extracted from the filtrate by methylene chloride or chloroform; further purification, if necessary, is by column chromatography.

Received: October 8, 1979 [Z 439 IE]
German version: Angew. Chem. 92, 321 (1980)

[1] *H. Alper, H. N. Paik,* J. Org. Chem. *42*, 3522 (1977).
[2] *E. C. Ashby, J. J. Lin,* J. Org. Chem. *43*, 1263, 2567 (1978); *F. Sato, Y. Mori, M. Sato,* Tetrahedron Lett. *1979*, 1405; *F. Sato* in *Y. Ishii, M. Tsutsui:* Fundamental Research in Homogeneous Catalysis. Vol. 2. Plenum Press, New York 1978, p. 81, and references cited therein.

General Method for Preparation of Multidentate Fluorophosphane Ligands[**]

By *Ernest R. Cromie, George Hunter,* and *David W. H. Rankin*[*]

Although fluorophosphanes are well known as monodentate ligands[1], very little work has been done with multidentate fluorophosphanes[2], and few suitable ligands are readily available. They are of interest because they can bond in a number of different ways: for example, $CH_3N(PF_2)_2$ may form two bonds to a single metal atom[3] or a bridge between two metal atoms[4]. We report here a reaction which may be used to prepare a wide variety of fluorophosphanes which may prove to be useful multidentate ligands.

We have observed that bis(difluorophosphino)sulfide *(1)*[5] reacts with organic and inorganic mono- and polyhydroxy compounds *(2)* to give difluorophosphane sulfides *(3)* and the desired difluorophosphinoxy compounds *(4)*.

$$\underset{(1)}{S(PF_2)_2} + \underset{(2)}{ROH} \rightarrow \underset{(3)}{SPF_2H} + \underset{(4)}{ROPF_2}$$

The product *(4)* is normally much less volatile than *(3)*, and may therefore easily be obtained in a pure form. Use of an excess of hydroxy compound *(2)* should be avoided, as a slow substitution reaction of *(3)* occurs, yielding less volatile products (SPFHR, $SPHR_2$).

The group R may be almost any organic group, such as primary, secondary, or tertiary alkyl, aryl or acyl, and inorganic "hydroxides" such as phosphoric acid may also be used. With 1,2-diols PF_3 is eliminated from the initial products to give 2-fluorodioxaphospholanes, which may also be of interest as ligands.

Similar reactions also occur with primary and secondary amines and, more slowly, with thiols. Thus, by choosing a suitable substrate, a product may be made with almost any desired spatial arrangement of fluorophosphino groups. Two typical syntheses are described, that of bis[2-(difluorophosphinoxy)ethyl]sulfide *(5)* and that of phosphoryltrioxytris(difluorophosphane) *(6)*.

(5) $S(CH_2CH_2OPF_2)_2$ $OP(OPF_2)_3$ *(6)*

Experimental

Preparation of *(5)*: Compound *(1)*[5] (4 mmol) is condensed into a glass ampoule (at −196 °C) containing $S(CH_2CH_2OH)_2$ (1.7 mmol) and the reagents are warmed to room temperature for 45 min. After the volatile products have been distilled out at −78 °C, *(5)* (1.4 mmol, 80% yield) is obtained in a pure form by distillation *in vacuo* at room temperature. Subsequent manipulation of *(5)* is by syringe in an inert atmosphere[6].

Preparation of *(6)*: Compound *(1)* (16.5 mmol) is condensed into a glass ampoule (at −196 °C) containing 100% H_3PO_4 (4.5 mmol). On warming to room temperature, effervescence occurs and the solid material disappears. After 30 min, the volatile products are removed, and *(6)* (4.3 mmol, 95% yield) is obtained as a clear liquid, involatile at −45 °C, by fractional condensation *in vacuo*[7].

Received: September 3, 1979 [Z 440 IE]
German version: Angew. Chem. 92, 323 (1980)

[1] *J. F. Nixon,* Adv. Inorg. Chem. Radiochem. *13*, 363 (1970), and references cited therein.
[2] *C. A. McAuliffe, W. Levason:* Phosphine, Arsine and Stibine Complexes of the Transition Elements. Elsevier, Amsterdam, 1979, 9. 310, and references cited therein.
[3] *R. B. King, J. Gimeno,* J. Chem. Soc. Chem. Commun. *1977*, 142.
[4] *M. G. Newton, R. B. King, M. Chang, N. S. Pantaleo, J. Gimeno,* J. Chem. Soc. Chem. Commun. *177*, 531.
[5] Preparation, see *D. E. J. Arnold, E. R. Cromie, D. W. H. Rankin,* J. Chem. Soc. Dalton Trans. *1977*, 1999.
[6] ^{1}H-NMR ($CDCl_3$): δ = 2.81 (4H, t, J = 7 Hz), 4.19 (4H, q, $J_{PH} = J_{HH} = 7$ Hz); ^{13}C-NMR: δ = 32.4 (d, $J_{PC} = 3$ Hz), 62.1 (t × d, $J_{FC} = 9$ Hz, $J_{PC} = 3$ Hz); ^{19}F-NMR: δ = −48 (d, $J_{PF} = 1294$ Hz); ^{31}P-NMR: δ = 112 (t × t, $J_{PF} = 1294$ Hz, $J_{PH} = 7$ Hz); IR (film): 2970, 2910, 1465, 1425, 1405, 1295, 1200, 1050, 1005, 965, 805, 760, 560 cm^{-1}.
[7] ^{31}P-NMR ($CDCl_3$): δ = 108 (3P, t × d, $J_{PF} = 1385$ Hz, $J_{PP'} = 28$ Hz), −41 (1P, m); ^{19}F-NMR: δ = −38 (d × d, $J_{PF} = 1384$ Hz, $J_{P'F} = 10$ Hz); IR (gas): 1345, 1042, 988, 867, 728, 529, 469, 399 cm^{-1}; m.p. −19 °C, vapor pressure at 0 °C, 1 torr.

^{195}Pt-NMR Spectroscopy of Catalytically Active Complexes. Extremely Large Spin-Spin Coupling between Platinum and Tin[**]

By *Karl-H. A. Ostoja Starzewski* and *Paul S. Pregosin*[*]

Platinum-phosphane complexes in combination with tin(II) chloride are excellent homogeneous catalysts for hydrogenation and hydroformylation reactions[1]. As part of our study[2] on the NMR characteristics of the active intermediates formed in these reactions, we found $^1J(^{195}Pt^{119}Sn)$ in *trans*-$[PtCl(SnCl_3)(PEt_3)_2]$ to be 28954 Hz, which represents the *largest one-bond spin-spin coupling constant* ever observed (cf. Table 1)[3].

[*] Dr. D. W. H. Rankin, E. R. Cromie, G. Hunter
Department of Chemistry, University of Edinburgh
West Mains Road, Edinburgh EH9 3JJ (Scotland)

[**] We thank the Science Research Council for research studentships (to *E. R. C.* and *G. H.*).

[*] Dr. P. S. Pregosin, Dr. K.-H. A. Ostoja Starzewski
Laboratorium für Anorganische Chemie, ETH-Zentrum
Universitätstrasse 6, CH-8092 Zürich (Switzerland)

[**] This work was supported by the Swiss National Science Foundation. We thank Prof. *L. M. Venanzi* for helpful discussions.

Table 1. ^{195}Pt-NMR data for some platinum-tin complexes [a].

Compound	$^1J(^{195}Pt^{119}Sn)$	$\delta(^{195}Pt)$	$\Delta\delta$ [b]
trans-[PtCl(SnCl$_3$)(PEt$_3$)$_2$] [c]	28954	−4780	−864
trans-[Pt(SnCl$_3$)$_2$(PEt$_3$)$_2$] [d]	20410	−5152	−618 [e]
trans-[PtH(SnCl$_3$)(PEt$_3$)$_2$] [f]	9067	−5302	−426
trans-[PtH(SnCl$_3$)(PPh$_2$CH$_2$Ph)$_2$] [f]	10955	−5322	−428
trans-[PtH(SnCl$_3$)(PPh$_3$)$_2$] [f]	11512	−5195	−354
trans-[Pt(C(CO$_2$Et)=CHCO$_2$Et)(SnCl$_3$)(PPh$_3$)$_2$] [g]	11320	−4771	−469

[a] Chemical shifts (δ values rel. to external Na_2PtCl_6) and coupling constants (in Hz). [b] $\Delta\delta = \delta[PtX(SnCl_3)(PR_3)_2] - \delta[PtX(Cl)(PR_3)_2]$. [c] In CD_2Cl_2 at −40 °C. [d] In $(CD_3)_2CO$ at −50 °C. [e] $\delta[PtCl_2(PEt_3)_2] - \delta[Pt(SnCl_3)_2(PEt_3)_2]$ divided by 2. [f] In CD_2Cl_2 at −70 °C. [g] In CD_2Cl_2 at room temperature.

The differences between the $^1J(^{195}Pt^{119}Sn)$ values for the series of complexes *trans*-[PtH(SnCl$_3$)(PEt$_3$)$_2$], *trans*-[Pt(SnCl$_3$)$_2$(PEt$_3$)$_2$], and *trans*-[PtCl(SnCl$_3$)(PEt$_3$)$_2$] may be understood in terms of the NMR *trans* influence series (H > SnCl$_3$ > Cl)[4]. There is some precedence for the similarity of *trans* influence in carbon and hydride ligands[4] so that the coupling constants of 11512 Hz for *trans*-[PtH(SnCl$_3$)(PPh$_3$)$_2$] and 11320 Hz for *trans*-[PtL(SnCl$_3$)(PPh$_3$)$_2$], L = C(CO$_2$Et)=CHCO$_2$Et, appear reasonable.

The large absolute value of $^1J(^{195}Pt^{119}Sn)$ can be understood in terms of the Fermi contact expression used by *Pople* and *Santry*[5]:

$$^1J(AB) \propto \gamma_A \gamma_B |\Psi_{ns_A}(0)|^2 |\Psi_{ns_B}(0)|^2 \pi_{A,B}$$

$$\pi_{AB} = \sum_{i}^{occ} \sum_{j}^{unocc} ({}^3\Delta E_{i\to j})^{-1} C_{iA} C_{jA} C_{iB} C_{jB}$$

The relatively large gyromagnetic ratios $\gamma_A \gamma_B$ for tin[6] and platinum combine with the relatively large expectation values $|\Psi(0)|^2$ for heavy metals[7] to afford a product which will be much larger than for most nuclei. Thus, typical $^1J(^{119}SnX)$ values are: for X = ^{1}H (Me_3SnH), 1744 Hz[8a]; ^{31}P (Me_3Sn—PRR′), 460—832 Hz[8b]; ^{207}Pb (Me_3Sn—$PbMe_3$), 3570 Hz[8a]. Furthermore, the presence of the three electron-withdrawing chlorine substituents on tin are recognized to result in an enhanced coupling constant[7]. This result stems from an increase in π_{AB}, presumably due to an enhanced amount of s-character in the metal-metal bond.

The values $\delta(^{195}Pt)$ are shifted to higher field by several hundred ppm when a Cl^- ligand is replaced by $SnCl_3^-$ *e.g.* from −3916 for *trans*-[PtCl$_2$(PEt$_3$)$_2$], to −4780 for *trans*-[PtCl(SnCl$_3$)(PEt$_3$)$_2$]$_2$. This is in keeping with the exceptional sensitivity of $\delta(^{195}Pt)$ to changes within the coordination sphere. It appears that ^{195}Pt-NMR spectroscopy will be an extremely sensitive probe for molecular structure in this catalytically active system.

Received: October 1, 1979 [Z 442 IE]
German version: Angew. Chem. *92*, 323 (1980)

[1] *H. Itatani, J. C. Bailar Jr.*, Int. Eng. Chem. Prod. Res. Develop. *11*, 146 (1972); *I. Schwager, J. F. Knifton*, J. of Catal. *45*, 256 (1976); *J. F. Knifton*, J. Org. Chem. *41*, 793 (1976).

[2] Cf. *P. S. Pregosin, S. N. Sze*, Helv. Chim. Acta *61*, 1848 (1978).

[3] We have recently learned that the complex (Ph$_3$MeP)$_2$[PtCl$_2$(SnCl$_3$)$_2$] shows a $^1J(^{195}Pt^{119}Sn)$ value of 27646 Hz: *J. H. Nelson, R. Rudolph*, personal communication, 1979. We find $\delta(^{195}Pt) = -4212$ (CD_2Cl_2) rel. to ext. Na_2PtCl_6, and $^1J(^{195}Pt^{119}Sn) = 27754$ Hz for $(Bu_4N)_2[PtCl_2(SnCl_3)_2]$.

[4] *T. G. Appleton, H. C. Clark, L. E. Manzer*, Coord. Chem. Rev. *10*, 335 (1973).

[5] *J. A. Pople, D. P. Santry*, Mol. Phys. *8*, 1 (1964); *9*, 311 (1965).

[6] Both the ^{119}Sn and ^{117}Sn one-bond coupling constants are observed in the ^{195}Pt-NMR spectrum. The ratio $^1J(^{195}Pt^{119}Sn)/^1J(^{195}Pt^{117}Sn)$ is in agreement with the ratio of their respective gyromagnetic constants.

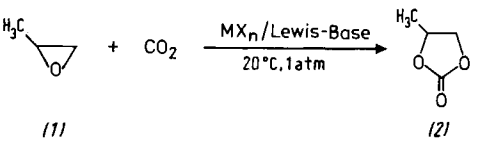
[7] *P. S. Pregosin, R. W. Kunz* in *P. Diehl, E. Fluck, R. Kosfeld:* NMR Basic Prnciples and Progress, Vol. 16. Springer-Verlag, Berlin 1979.

[8] a) *J. D. Kennedy, W. McFarlane, B. Wrackmeyer*, Inorg. Chem. *15*, 1299 (1976); b) *H. Schumann, H. J. Kroth*, Z. Naturforsch. *B 32*, 876 (1977).

Metal-Catalyzed Synthesis of Cyclic Carbonates from Carbon Dioxide and Oxiranes

By *Michael Ratzenhofer* and *Horst Kisch*[*]

The reactions of carbon dioxide are attracting renewed interest with regard to the use of readily available primary chemicals in organic synthesis[1]. Its reaction with methyloxirane *(1)* gives polycarbonates[2] or the monomeric carbonate 4-methyl-1,3-dioxolan-2-one *(2)*[3], depending upon the reaction conditions. All the catalytic processes known so far for the synthesis of *(2)* operate at elevated CO_2 pressure (5—200 atm) and elevated temperature (100—200 °C)[3,4]. We now wish to report catalysts that are active at room temperature and normal pressure.



(1) *(2)*

Addition of *(1)* to a mixture of a metal halide and a Lewis base under CO_2, is shown by IR spectroscopy to lead to the formation of *(2)*, $\nu(CO) = 1800$ cm^{-1} in *(1)*. Pure *(2)* is ultimately isolated directly from the reaction flask by simple vacuum distillation. Thus the $MoCl_5/PPh_3$ catalyst system gave the best conversions and yields at a molar ratio of 1:6 of the components and a 100 to 200-fold excess of *(1)* relative to $MoCl_5$ (see Procedure and Table 1).

The best catalysts were found to be mixtures of triphenylphosphane and the halides of aluminum, molybdenum, or iron. Neither of the catalyst components on its own is able to induce formation of *(2)*. Transition metal compounds in low oxidation states such as *trans*-$(N_2)_2$W(diphos)$_2$ or $CoCl(PPh_3)_3$ fail to catalyze the reaction; however, the latter compound does become active at high temperature and high pressure[3].

Preliminary mechanistic studies have been performed with the $AlCl_3$/Lewis base catalyst system: reaction of *(1)* with

[*] Priv.-Doz. Dr. H. Kisch, Dr. M. Ratzenhofer
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
Stiftstrasse 34—36, D-4330 Mülheim a. d. Ruhr 1 (Germany)

Table 1. Activity of some catalyst systems for the synthesis of *(2)* from carbon dioxide and *(1)* under normal conditions of pressure and temperature (7 d reaction time, in 10 ml of *(1)* as solvent).

MX_n/Lewis base [a]	$[MX_n]$ [mol/l]	Yield of *(2)* [b]	Turnover number [c]
$AlCl_3/PPh_3$	0.14	47	46
$AlCl_3/NEt_3$ (1:3)	0.23	52	32
AlI_3/PPh_3	0.1	46	67
$TiCl_4/PPh_3$	0.09	15	24
$CrCl_3/PPh_3$ (1:3)	0.19	< 1	< 1
$MoCl_5/PBu_3$	0.1	55	79
$MoCl_5/PPh_3$ (1:5)	0.15	78	76
$MoCl_3(C_4H_8O)_3/PPh_3$	0.063	13	31
$MoCl_5/NEt_3$	0.084	36	61
WCl_6/PPh_3	0.044	36	29
$FeCl_3/PPh_3$	0.185	75	58
$CoCl_2/PPh_3$ (1:5)	0.034	76	32
$NiBr_2/PPh_3$	0.16	20	18

[a] Molar ratio 1:6 unless stated otherwise. [b] Isolated product (% based on weigh-in of *(1)*). [c] mol *(2)*/mol MX_n.

$AlCl_3$ under argon is strongly exothermic and yields $[MeCH(Cl)CH_2O]_3Al$[5]. We found that this chloroalkoxide takes up CO_2 in the ratio of 1:1; the IR spectrum of the product (KBr) shows strong bands at 1610 and 1430 cm^{-1} which are probably due to a metal alkyl carbonate formed by insertion of CO_2 into one of the Al—O bonds of the alkoxide[6]. The dioxolanone *(2)* arises from the aluminum alkyl carbonate only after addition of PPh_3, pyridine, or NEt_3. The final reaction step occurs only in polar solvents such as tetrahydrofuran, oxetane, or methyloxirane.

The method described above is the simplest procedure available for the synthesis of cyclic carbonates from carbon dioxide and oxiranes. The disadvantage of the relatively long reaction time of about seven days is offset by the advantages of mild reaction conditions, very good yields (90—100% based on reacted oxirane), and recovery of unreacted oxirane. On use of a chiral base, the catalyst system could in principle permit a facile synthesis of chiral dioxolanones. Preliminary experiments with $MoCl_5$ and (*R*)-(+)-dimethyl-1-(phenylethyl)amine, (+)-brucine, (*R,R*)-(−)-1,2-bis(dimethylamino)cyclohexane, (−)-2-menthyldimethylphosphane, (+)-bis(2-menthyl)methylphosphane, and (+)-2,2-dimethyl-4,5-bis(diphenylphosphinomethyl)-1,3-dioxolane ("diop") have so far proved unsuccessful, however[7].

Procedure

Methyloxirane *(1)* (100 ml, 1430 mmol) is slowly added dropwise to molybdenum pentachloride (2.0 g, 7.3 mmol) and triphenylphosphane (11 g, 42 mmol) in a two-neck flask under CO_2 atmosphere. The solution is stirred for seven days at room temperature and then vacuum distilled: unreacted *(1)* (50 ml, 50%) distils over first, followed by the pure product *(2)* at b.p. 45—50 °C/0.1 torr; yield: 68.7 g (47% based on weigh-in of *(1)*, 94% based on reacted *(1)*); turnover number, 92 mol/mol $MoCl_5$. Experiments with other catalysts were performed analogously.

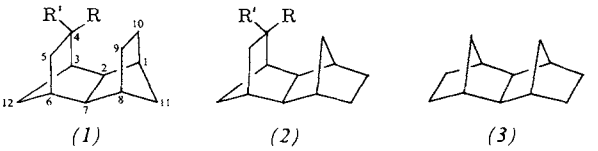
Received: April 4, 1979;
supplemented: October 22, 1979 [Z 423 IE]
German version: Angew. Chem. *92*, 302 (1980)

[1] Summary: *M. E. Volpin, J. S. Kolomnikov, Organomet. React. 5*, 313 (1975); Pure Appl. Chem. *33*, 567 (1973).
[2] *W. Kuran, S. Pasynkiewicz, J. Skupińska*, Makromol. Chem. *178*, 47 (1976).
[3] *H. Koinuma, H. Kato, H. Hirai*, Chem. Lett. *1977*, 517.
[4] *J. T. Dunn*, US-Pat. 2773881 (1953); *A. F. Millikan*, US-Pat. 2993908 (1958); *G. W. Crosby, A. F. Millikan*, US-Pat. 2994704, 2994705 (1958); *K. Shimomura, S. Yata, M. Gogo, C. Tsuno*, Jap. 70 38,534 (1970); *Y. Fujita, T. Morimoto*, Jap. 72 15,951 (1972); *J. Harada, A. Kimura, J. Takeshita, K. Watanabe, H. Sugahara*, Jap. Kokai 77 03,064 (1977).
[5] Cf. *F. Schmidt*, Brit. Pat. 716126 (1955).
[6] Cf. *M. Hidai, T. Hikita, Y. Uchida*, Chem. Lett. *1972*, 521.
[7] We are grateful to Dr. *I.-J. Wang* for experimental cooperation, and to Dr. *J. Neuffer* for providing chiral phosphanes.

Synthesis of the Epimeric 4-Methyl Derivatives of *endo-endo-* and *exo-endo-*Tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecane[**]

By *Dieter Lenoir* and *Robert M. Frank*[*]

The three isomeric tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecanes *(1)*, *(2)*, and *(3)* (R, R′ = H) were first used by *Winstein et al.* as test compounds for examining steric hindrance as a result of *trans*-annular H/H interactions[1]. Subsequently, strain energies were estimated for the hydrocarbons by force field calculations[2] and X-ray structure data were determined for derivatives of *endo-endo-(1)* and of the *exo-exo* compounds *(3)*[3].



(1) *(2)* *(3)*

Table 1. Calculated standard enthalpies of formation and strain energies [4] (values in parentheses) for the isomeric tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecanes and norbornane and their alkyl derivatives (values in kcal/mol). Inside, R = alkyl, R′ = H; outside, R = H, R′ = alkyl.

R	R′	*endo-endo* compound *(1)*	*exo-endo* compound *(2)*	Norbornane (inside ≙ *endo*) (outside ≙ *exo*)
H	H	6.12 (49.86)	− 2.92 (40.82)	−12.99 (16.98)
CH_3	H	4.82 (55.64) [a]	− 4.97 (45.85) [c]	−19.15 (17.90)
H	CH_3	− 0.57 (50.25) [b]	− 9.45 (41.37) [d]	−20.01 (17.04)
$CH(CH_3)_2$	H	− 6.64 (56.39)	−16.98 (46.05)	
H	$CH(CH_3)_2$	−11.42 (51.61)	−18.48 (44.55)	
$C(CH_3)_3$	H	− 7.34 (63.88)	−17.35 (53.87)	
H	$C(CH_3)_3$	−17.71 (53.51)	−26.04 (45.18)	

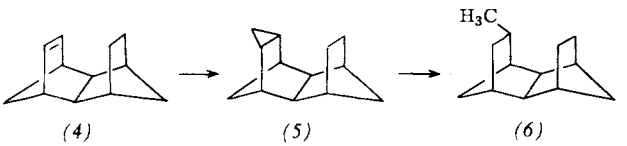
[a] Identical with compound *(12)*. [b] Identical with compound *(6)*. [c] Identical with compound *(15)*. [d] Identical with compound *(9)*.

[*] Priv.-Doz. Dr. D. Lenoir, Dr. R. M. Frank
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Results of Non-bonded Interactions, Part 1. This work was supported by the Deutsche Forschungsgemeinschaft.

Replacement of the inner hydrogen atom R (R′ = H) by an alkyl group is predicted by model studies to lead to a strong increase in strain energy; Table 1 lists the enthalpies of formation and strain energies calculated with the force field[2] (Bigstrin[4]) for *(1)* and *(2)*, R = CH_3, $CH(CH_3)_2$, and $C(CH_3)_3$, R′ = H, and for *(1)* and *(2)*, R′ = CH_3, $CH(CH_3)_2$, $C(CH_3)_3$, R = H. The calculated strain energy is larger for the "inside" compounds (R = alkyl) than for the "outside" compounds (R′ = alkyl); the energy difference is considerably greater than between 2-*exo*- and 2-*endo*-methylnorbornane[2] (see Table 1).

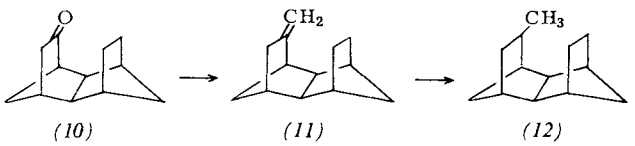
We have synthesized the epimeric 4-methyl derivatives of the *endo-endo- (1)* and *exo-endo* series *(2)*. Starting from *endo-endo*-tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-4-ene *(4)*[5] and the *exo-endo* isomer *(7)*[5] we obtained the cyclopropyl compounds *(5)* and *(8)*, respectively, by repeated treatment with



(4) *(5)* *(6)*

Analogously, *exo-endo*: *(7)* ⟶ *(8)* ⟶ *(9)*

CH_2N_2 in ether in the presence of CuCl (each in about 70% yield); they were purified by distillation (b.p. 119—120 °C/13 torr). *(5)* and *(8)* can be converted by treatment with hydrogen (60 atm) in glacial acetic acid into *(6)* and *(9)*, respectively (85%), which can be distilled (b.p. 110—111 °C/13 torr).



(10) *(11)* *(12)*

Analogously, *exo-endo*: *(13)* ⟶ *(14)* ⟶ *(15)*

The inside methyl compounds *(12)* and *(15)* are formed from the isomeric ketones *endo-endo- (10)*[6] and *exo-endo*-tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodecan-4-one *(13)*[6]. Wittig reaction with methyltriphenylphosphonium bromide/*n*-butyllithium in tetrahydrofuran at 175 °C over a period of 7 d affords the methylene compounds *(11)* (10%) and *(14)* (51%), respectively which were analytically pure after distillation (b.p. 60—62 °C/1 torr). Catalytic hydrogenation over Pd/C in ethanol (60 atm H_2 pressure, 50 °C, 17 h) gives the methyl isomers *(12)* (86%) and *(15)* (88%). *(12)* was purified by vacuum sublimation (m.p. 57—60 °C), while *(15)* was distilled (b.p. 50—60 °C/0.6 torr).

The new compounds *(5)*, *(6)*, *(9)*, *(11)*, *(12)*, *(14)*, and *(15)* have been completely characterized by elemental analysis and spectral data (mass, IR, and ^{1}H-NMR spectra)[7] (see Table 2). The methyl derivatives *(6)* and *(12)*, as well as *(9)* and *(15)*, which differ in their gas chromatographic retention times, are stereochemically pure within the detection limit of *ca.* 0.1%. This shows that cyclopropanation and hydrogenation occur exclusively from the outside direction. In contrast to 2-*endo*-methylnorbornane the inside isomers *(12)* and *(15)* cannot be equilibrated with Lewis acids to give the outside epimers since rearrangement to the thermodynamically more stable adamantane derivatives is much faster[7].

The NMR signals of the methyl protons of the inside and outside isomers differ by $\Delta\delta \approx 0.35$. Characteristic IR bands are observed above 3000 cm^{-1} (ν_{CH}); the shift from the normal position at 2950 cm^{-1} can be regarded as a measure of the intramolecular H...H contact distances which can be interpreted on the basis of quantum mechanical concepts in terms of an increase in the CH force constants as a result of compression[8]. These frequencies can be qualitatively correlated with the calculated H...H contact distances; this shows that the ethano bridge in the *endo-endo* skeleton is more strongly twisted in order to avoid steric hindrance by the inside methyl group.

Compounds with inside alkyl groups such as *(12)* and *(15)* are suitable as models for the quality of non-bonded interaction terms in force field calculations; the calculations are to be tested by X-ray structure analysis of suitable derivatives.

Received: October 12, 1979 [Z 427 IE]
German version: Angew. Chem. *92*, 306 (1980)

CAS Registry numbers:
(1) (R, R′ = H), 53862-33-2; *(1)* (R = CH_3, R′ = H), 57968-21-5; *(1)* (R = H, R′ = CH_3), 73307-18-3; *(1)* (R = $CH(CH_3)_2$, R′ = H), 73307-19-4; *(1)* (R = H, R′ = $CH(CH_3)_2$), 73307-20-7; *(1)* (R = $C(CH_3)_3$, R′ = H), 73274-94-9; *(1)* (R = H, R′ = $C(CH_3)_3$), 73307-21-8; *(2)* (R, R′ = H), 15914-95-1; *(2)* (R = CH_3, R′ = H), 73307-22-9; *(2)* (R = H, R′ = CH_3, 73307-23-0; *(2)* (R = $CH(CH_3)_2$, R′ = H), 73307-24-1; *(2)* (R = H, R′ = $CH(CH_3)_2$), 73307-25-2; *(2)* (R = $C(CH_3)_3$, R′ = H), 73307-26-3; *(2)* (R = H, R′ = $C(CH_3)_3$), 73307-27-4; *(5)*, 61140-68-9; *(8)*, 73307-28-5; *(10)*, 57968-22-6; *(11)*, 73307-29-6; *(13)*, 73307-30-9; *(14)*, 73346-46-0; norbornane, 279-23-2; 2-*endo*-methylnorbornane, 765-90-2; 2-*exo*-methylnorbornan, 872-78-6.

[1] a) *D. Kivelson, S. Winstein, P. Bruck, R. L. Hansen*, J. Am. Chem. Soc. *83*, 2938 (1961); b) *S. Winstein, P. Carter, F. A. L. Anet, A. J. R. Bourn, ibid. 87*, 5247 (1965).
[2] *E. M. Engler, J. P. Andose, P. v. R. Schleyer*, J. Am. Chem. Soc. *95*, 8005 (1973).

Table 2. Characteristic IR and ^{1}H-NMR data of the isomeric metyl derivatives *(6)*, *(9)*, *(12)*, and *(15)*.

Compound	IR [cm^{-1}] [a]		^{1}H-NMR [b]
	ν_{CH} (compr.)	$\delta_{(CH_3)}$	δ values for CH_3 (*J* [Hz])
(6) *endo-endo* outside	3060, 3012	1373	0.86 (6.8)
(9) *exo-endo* outside	3041	1373	0.88 (6.7)
(12) *endo-endo* inside	3043, 3000	1377	1.21 (6.5)
(15) *exo-endo* inside	3056, 3040	1377	1.21 (7.3)

[a] Conc. *ca.* 0.17 M in CCl_4; for comparison: *endo-endo* hydrocarbon 3031 cm^{-1}; *exo-endo* hydrocarbon 3040 cm^{-1}. [b] In $CDCl_3$, internal TMS.

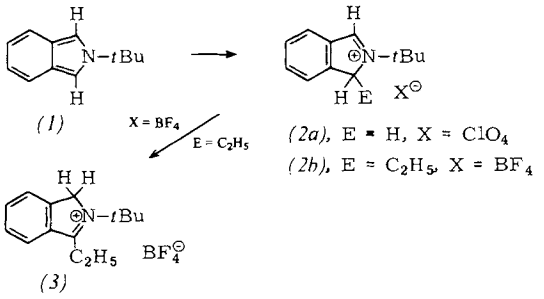
[3] *O. Ermer*, Angew. Chem. *89*, 833 (1977); Angew. Chem. Int. Ed. Engl. *16*, 798 (1977).
[4] Bigstrin, QCPE No. 348.
[5] *J. K. Stille, D. R. Witherell*, J. Am. Chem. Soc. *86*, 2188 (1964).
[6] *P. Bruck, D. Thompson, S. Winstein*, Chem. Ind. (London) *1960*, 405.
[7] *R. M. Frank*, Dissertation, Technische Universität München 1979.
[8] *A. T. Hagler, P. S. Stern, S. Lifson, S. Ariel*, J. Am. Chem. Soc. *101*, 813 (1979).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0404-0319 $ 02.50/0*

2-*tert*-Butyl-2*H*-isoindole: A Partner for Reactions with Electrophiles[**]

By *Richard Kreher* and *Götz Use*[*]

The *o*-quinonoid heteroarene *(1)* is readily accessible from *N*-*tert*-butyl-isoindoline *N*-oxide by reaction with acetic anhydride/triethylamine (6 h/0 °C)[1]. It shows remarkable thermal stability and is one of the few compounds in this series[2] which can be protonated, alkylated, and subjected to electrophilic substitution.



Reaction of *(1)* with 70% perchloric acid gives the crystalline perchlorate *(2a)* and that with triethyloxonium tetrafluoroborate affords the stable 2-*tert*-butyl-3-ethyl-1*H*-isoindolium tetrafluoroborate *(3)*. In this reaction, the 1*H*-isoindolium salt *(2b)* formed in a prior kinetically controlled process rearranges *via* a 1,3-proton shift into the more stable salt *(3)* (Table 1).

Table 1. Analytical data of compounds *(1)*, *(2a)*, and *(3)*.

(1), yield 90%; b.p. 97—98 °C/0.1 torr; ^{1}H-NMR ($CDCl_3$): $\delta = 7.19$ (s, H-1, H-3), 1.54 (s, *t*Bu); UV (methanol): $\lambda_{max} = 223$ ($\log \varepsilon = 4.68$), 266 (3.25), 270 (3.22), 277 (3.27), 289 (3.09), 329 nm (3.59)

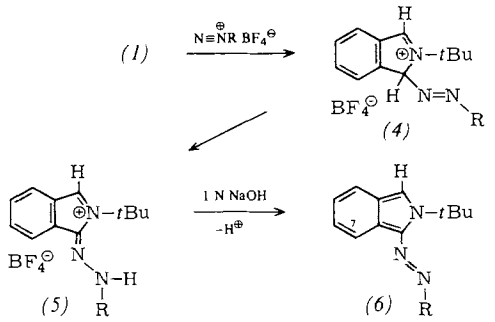
(2a), yield 99%; dec. pt. 241—243 °C; ^{1}H-NMR (CF_3CO_2H): $\delta = 9.46$ (t, $J = 2$ Hz, CH), 5.42 (d, $J = 2$ Hz, CH_2); UV (CH_3OH/1% $HClO_4$): $\lambda_{max} = 217$ ($\log \varepsilon = 3.98$), 224 (3.86), 275 nm (4.16)

(3), yield 96%; dec. pt. 160 °C; ^{1}H-NMR (CF_3CO_2H): $\delta = 5.37$ (s, CH_2), 3.58 (q, $J = 8$ Hz, CH_2), 1.88 (s, *t*Bu), 1.63 (t, $J = 8$ Hz, CH_3); UV (CH_3OH/1% $HClO_4$): $\lambda_{max} = 216$ ($\log \varepsilon = 3.96$), 223 (3.82), 272 nm (4.15)

Conditions for electrophilic substitution reactions of *(1)* therefore appear favorable, and it is indeed found to react *via* substitution with arenediazonium tetrafluoroborates. A cationic σ complex *(4)* is probably formed, which rearranges to the more stable isoindolium salt *(5)*.

The structure of the crystalline tetrafluoroborates *(5)* follows primarily from the ^{1}H-NMR and IR spectra (1 H singlet for CH=N, broadened singlet at $\delta = 10.2$—10.4 for NH; intense IR band at 3310 cm^{-1}) (Table 2).

The thermally stable and chemically reactive isoindolium salts *(5)* can be converted by 1 N NaOH into the crystalline, intensely colored azo compounds *(6)* with a long-wave absorption band between 480 and 530 nm. The coupling constant ($J_{ortho} = 8$ Hz) shows that the ^{1}H multiplet separated in the ^{1}H-NMR spectrum should be assigned to the *peri*-proton H-7 (Table 2).



(a), R = *p*-Cl–C_6H_4; *(b)*, R = *p*-C_2H_5OCO–C_6H_4; *(c)*, R = *p*-O_2N–C_6H_4

Table 2. Analytical data of compounds *(5a—c)* and *(6a—c)*. ^{1}H-NMR of *(5)* in CF_3CO_2H, of *(6)* in $CDCl_3$, UV of *(5)* in CH_3OH/1% $HClO_4$, of *(6)* in CH_2Cl_2.

(5a), yield 94%; dec. pt. 201—203 °C; ^{1}H-NMR: $\delta = 9.13$ (s, H-1), 2.08 (s, *t*Bu); UV: $\lambda_{max} = 243$ ($\log \varepsilon = 4.37$), 470 nm (4.05)

(5b), yield 88%; m.p. 202—203 °C; ^{1}H-NMR: $\delta = 9.24$ (s, H-1), 2.11 (s, *t*-Bu); UV: $\lambda_{max} = 266$ ($\log \varepsilon = 4.39$), 464 nm (3.82)

(5c), yield 99%; dec. pt. 212 °C; ^{1}H-NMR: $\delta = 9.32$ (s, H-1), 2.10 (s, *t*Bu); UV: $\lambda_{max} = 233$ ($\log \varepsilon = 4.23$), 264 (3.95), 325 (4.16), 458 nm (3.62)

(6a), yield 86%; m.p. 102 °C; ^{1}H-NMR: $\delta = 8.58$ (m, $J_{ortho} = 8$ Hz, H-7), 1.87 (s, *t*Bu); UV: $\lambda_{max} = 264$ ($\log \varepsilon = 3.92$), 310 (3.74), 482 nm (4.54)

(6b), yield 88%; m.p. 123 °C; ^{1}H-NMR: $\delta = 8.71$ (m, $J_{ortho} = 8$ Hz, H-7), 1.88 (s, *t*Bu); UV: $\lambda_{max} = 260$ ($\log \varepsilon = 3.86$), 295 (3.98), 492 nm (4.59)

(6c), yield 89%; m.p. 172 °C; ^{1}H-NMR: $\delta = 8.73$ (m, $J_{ortho} = 8$ Hz, H-7), 1.94 (s, *t*Bu); UV: $\lambda_{max} = 256$ ($\log \varepsilon = 3.92$), 319 (3.77), 530 nm (4.63)

Accordingly, 2*H*-isoindoles can be coupled, like substituted pyrroles[3] and indoles[4], with arenediazonium ions, provided that the reaction conditions can be adjusted to the reactivity of the 10π system.—2-*tert*-Butylpyrrolo[3,4-*b*]quinoxaline[5] also forms crystalline hydrazo compounds with arenediazonium salts.

Procedure

(5): Compound *(1)* (1.0 g, 5.77 mmol) in anhydrous acetone (10 ml) is stirred into an ice-cooled suspension of arenediazonium tetrafluoroborate (5.8 mmol) in anhydrous acetone (15 ml) under pure dry nitrogen over 15 min. After 2 h at 0 °C, the colored precipitate is filtered off under suction, washed with a little ice-cold anhydrous acetone and with ether and dried *in vacuo* over P_2O_5.

Received: October 1, 1979 [Z 433 IE]
German version: Angew. Chem. *92*, 309 (1980)

[*] Prof. Dr. R. Kreher, Dipl.-Ing. G. Use
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] Studies on the Chemistry of Isoindoles and Isoindolines, Part 15. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 14: *R. Kreher, K. J. Herd*, Heterocycles *11*, 409 (1978).

[1] *R. Kreher, J. Seubert*, Angew. Chem. *76*, 682 (1964); Angew. Chem. Int. Ed. Engl. *3*, 639 (1964).—Acetolysis of *N*-alkylisoindoline *N*-oxides gives the analytically and spectroscopically homogeneous 2-alkyl-2*H*-isoindoles if the reaction conditions are rigorously observed; cf. opposing report by *M. H. Palmer, S. M. F. Kennedy*, J. Chem. Soc. Perkin Trans. 2 *1976*, 81.

[2] *R. Livingstone* in Rodd's Chemistry of Carbon Compounds. Vol. 4*A*. 2nd Edit. Elsevier, Amsterdam 1973, pp. 470ff.; *J. D. White, M. E. Mann*, Adv. Heterocycl. Chem. *10*, 113 (1969).

[3] *A. Gossauer:* Die Chemie der Pyrrole. Springer, Berlin 1974, p. 37, 336; *R. A. Jones, G. P. Bean* in *A. T. Blomquist, H. H. Wassermann:* Organic Chemistry. Vol. 34. Academic Press, London 1977, p. 188.

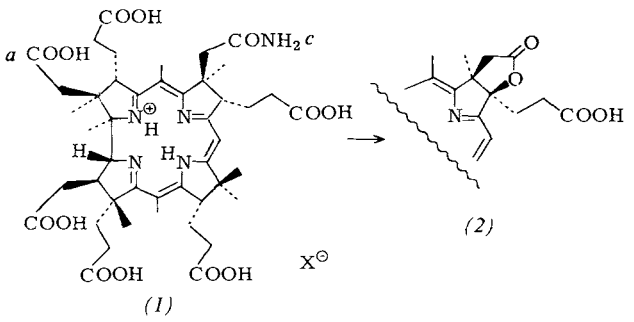
[4] *W. A. Remers* in *A. Weissberger, E. C. Taylor:* The Chemistry of Heterocyclic Compounds. *W. J. Houlihan:* Indoles. Vol. 1. Wiley-Interscience, New York 1972, p. 86; *A. R. Butler, P. T. Shepherd*, J. Chem. Res. (S) *1978*, 339; *A. H. Jackson, P. V. R. Shannon, A. C. Tinker*, J. Chem. Soc. Chem. Commun. *1976*, 796; *B. C. Challis, H. S. Rzepa*, J. Chem. Soc. Perkin Trans. 2 *1975*, 1209.

[5] *R. Kreher, G. Use*, Tetrahedron Lett. *1978*, 4671.

Structure of Metal-Free Corrinoids from *Rhodopseudomonas sphaeroides*

By *Bernd Dresow, Gerhard Schlingmann, William S. Sheldrick,* and *Volker B. Koppenhagen*[*]

Metal-free corrinoids are of interest as potential precursors in the biosynthesis of vitamin B_{12} and as starting materials for the preparation of vitamin B_{12} analogues containing other metals. So far they have mainly been obtained from the sulfur-containing purple bacterium *Chromatium vinosum,* but the yields are so low (*ca.* 1 mg/100 g wet bacteria, *i. e. ca.* 0.05 mg/l), that the preparation of larger amounts is extremely time consuming and expensive[1]. On investigating further phototrophic bacteria for their ability to form metal-free corrinoids we found that *Rhodopseudomonas sphaeroides* under cobalt-deficient conditions releases up to 3 mg/l of these compounds into the medium[2]. We thus succeeded for the first time in isolating this class of substance on a gram scale.



Unlike *Chromatium vinosum, Rhodopseudomonas sphaeroides* produces nucleotide-free polycarboxylic acids, which at this biogenetically early stage are probably recognized by the organism as "inappropriate products" and are excreted. From the culture medium of *Rhodopseudomonas sphaeroides* we isolated a mixture of isomer-free hydrogenobyrinic acid monamide *(1)* (20%) and hydrogenobyrinic acid diamide (80%). The position of the amide function in *(1)* was determined by conversion of *(1)* into hydrogenobyrinic acid *c*-lactone *(2)*[3]. *(2)* could be identified after incorporation of the central $Co(CN)_2$-group and esterification with methanol/sulfuric acid, as dicyanocobyrinic acid hexamethyl ester *c*-lactone.

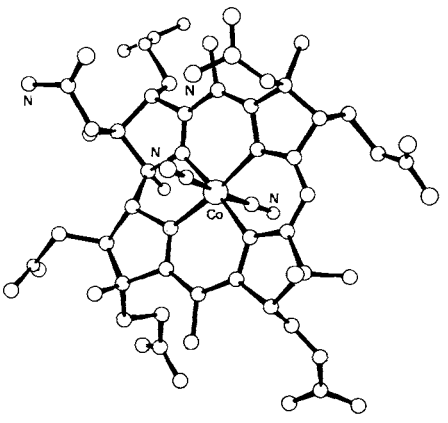


Fig. 1. Molecular structure of dicyanocobyrinic acid *a,c*-diamide *(3)* [4].

The two amide positions in the resulting biosynthetic hydrogenobyrinic acid diamide could be determined by X-ray structure analysis of the corresponding $Co(CN)_2$-containing product *(3)* and were assigned to the side chains *a* and *c* (Fig. 1). The *c*-amide function could also be determined independently by lactonization.

(3) crystallizes orthorhombically together with three water molecules[4]. Owing to the network of intermolecular hydrogen bonding, which stabilizes the crystal structure, the isotropic temperature factors of the O and N atoms of the potential OH- and NH_2-groups are relatively low (0.039—0.092 $Å^2$). In addition, the heteroatoms within a side chain have very similar temperature factors; the differences are 0.01 $Å^2$ or smaller. This facilitates an analysis of the isotropic temperature factors for placement of the OH- and NH_2-functions, thus leading to formulation as an *a,c*-diamide. This formulation is further supported by the lengths of the H bridges: on the side chains *a* and *c* they are 2.85—2.96 Å, as is typical for N...O bridges, on the remaining side chains they are 2.56—2.79 Å, which is typical for O...O bridges. The bond lengths and angles in *(3)* are similar to those in other metal-containing corrinoids.

Received: September 6, 1979 [Z 434a IE]
German version: Angew. Chem. *92*, 303 (1980)

CAS Registry numbers:
(1), 73367-49-4; *(2)*, 73367-50-7; *(3)*, 73367-45-0; dicyanocobyrinic hexamethyl ester *c*-lactone, 73367-46-1; hydrogenobyrinic acid diamide, 73367-51-8

[1] *J. I. Toohey,* Proc. Natl. Acad. Sci. *54*, 934 (1965); *V. B. Koppenhagen, E. Warmuth, F. Wagner,* 3. Symp. Tech. Microbiol., Berlin 1973, p. 323.
[2] *B. Dresow,* Dissertation, Technische Universität Braunschweig 1978.
[3] Obtainable by reaction of hydrogenobyrinic acid *c*-amide with *N*-iodosuccinimide in dilute acetic acid at room temperature.
[4] *(3)*·$3H_2O$, space group $P2_12_12_1$, $a = 15.191(3)$, $b = 22.578(3)$, $c = 14.656(3)$ Å, $Z = 4$, $\rho_{calc} = 1.38$ g cm^{-3}. The structure was refined to $R = 0.070$, $R_w = 0.065$ for 4306 independent reflections ($Cu_{K\alpha}$, $3.0 \leq 2\theta \leq 135.0°$) with $F^2 \geq 2.0\sigma(F^2)$. All atoms with anisotropic temperature factors. H atoms not taken into consideration.

Structure of Yellow Metal-Free and Yellow Cobalt-Containing Corrinoids

By *Gerhard Schlingmann, Bernd Dresow, Volker B. Koppenhagen, Wulf Becker,* and *William S. Sheldrick*[*]

All red metal-free corrinoids, which have hitherto been isolated from phototrophic bacteria, are irreversibly converted under alkaline conditions into a yellow form. Such yellow products also occur in larger amounts in the culture filtrate of fermentations with *Rhodopseudomonas sphaeroides* or *Rhodopseudomonas capsulata*[1]. Elucidation of the structure of the yellow corrinoids is of importance in view of their possible further use in the synthesis of vitamin B_{12} antimetabolites.

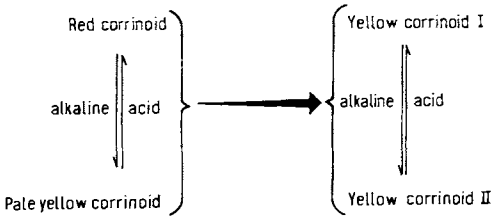
We have been able to demonstrate that on treatment with bases of any sort, red metal-free corrinoids are converted with initial change of color from red to yellow into a deprotonated form, which on immediate reneutralization is reconvertible into the red starting compound[2]. On prolonged treatment with alkali, a further irreversible transformation into a stable yellow corrinoid form takes place. Depending on the pH, this yellow corrinoid is either protonated (yellow

[*] Dr. V. B. Koppenhagen, Dr. B. Dresow, Dr. G. Schlingmann, Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[*] Dr. V. B. Koppenhagen, Dr. G. Schlingmann, Dr. B. Dresow, Dipl.-Chem. W. Becker, Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0404-0321 $ 02.50/0*

corrinoid I) or deprotonated (yellow corrinoid II) (Scheme 1).



Scheme 1. Transformation of metal-free corrinoids.

For the structure elucidation, the model compound hydrogenobyrinic acid *a,c*-diamide (150 mg) was converted with 0.2N KOH in the absence of oxygen into its yellow form. Subsequent incorporation of the $Co(CN)_2$-group and esterification with methanol/sulfuric acid afforded the yellow compound *(1)* as main product, which crystallizes from methanol/ether (Fig. 1).

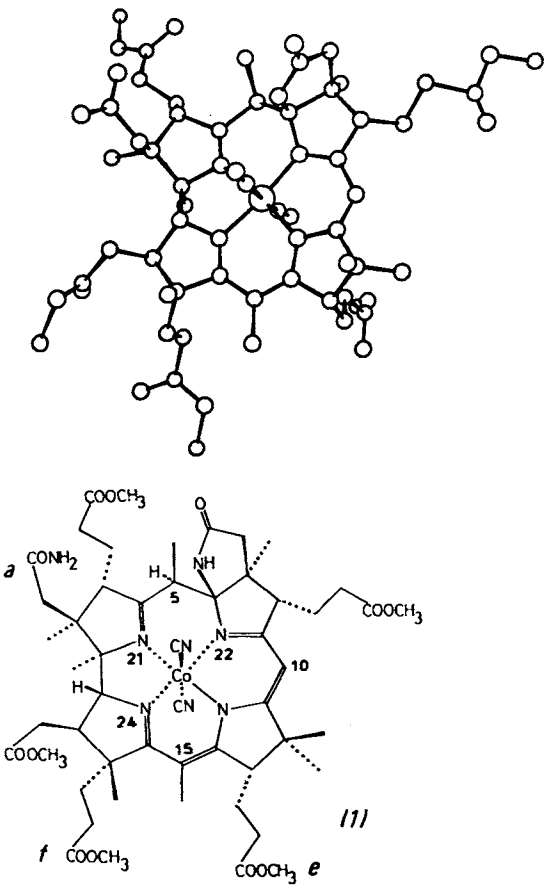


Fig. 1. 6-Aminodicyano-5,6-dihydrocobyrinic acid pentamethyl ester *a*-amide-*c*-lactam (gCoPSE) *(1)*.

(1)·0.5 H_2O ("gCoPSE") crystallizes triclinically with two independent molecules in the crystal lattice[3]. In both molecules the C-5 methyl group is located above the "plane" of the molecule. The *a*-amide and *f*-methoxycarbonyl functions of the first molecule, as well as the water molecule, are disordered. The conformation of the side chain *e* in the first molecule is very different from that in the second.

The chromophore in *(1)* consists of a conjugated system of four double bonds distributed over nine atoms between N-22 and N-24 of the macrocycle. The three bonds (C-10)—(C-11), (C-14)—(C-15), and (C-16)—(N-24) exhibit stronger double-bond character than the remaining bonds. (N-12)—(C-4) exists as an isolated double bond. Breakage of the corrin chromophore between C-5 and C-6 leads to no significant change in the bond angles with respect to the octahedral arrangement of the central cobalt atom. But the almost planar coordination of the four N atoms to the Co, observed in the other corrinoids, is here somewhat more tetrahedrally distorted (distances of the N atoms from the plane = ±0.06—0.08 Å); and the deviation of the macrocycle from the central plane through the four N atoms and the cobalt atom is more pronounced, not only in the region of the B ring but also in the region of the D ring. The B ring has an envelope conformation (cobyric acid: half-chair conformation)[4].

While yellow metal-free corrinoids are irreversibly formed from red metal-free corrinoids under alkaline conditions (Scheme 1), the compounds containing cobalt are readily converted into the corresponding red cobalt-containing compounds under the influence of bases. Here, deprotonation at C-5 and simultaneous opening of the lactam ring leads to reformation of the double bond between C-5 and C-6. *(1)* could be converted into dicyanocobyrinic acid pentamethyl ester *a,c*-diamide in this way by treatment with *t*-BuOK. Like hydrogenobyrinic acid *a,c*-diamide[5], on treatment with alkali and incorporation of cobalt, hydrogenobyric acid or hydrogenobalamin also form yellow cobalt-containing compounds, which once again are transformed into cobyrinic acid and cobalamin, respectively, on treatment with alkali (KCN).

These findings would suggest that the action of alkali on natural metal-free corrinoids leads to inerruption of the corrin chromophore between C-5 and C-6 through formation of a lactam ring as in *(1)*.

Received: September 6, 1979 [Z 434b IE]
German version: Angew. Chem. *92*, 304 (1980)

[1] *V. B. Koppenhagen, E. Warmuth, G. Schlingmann, B. Dresow* in Proceedings of 3rd European Symposium on Vitamin B_{12} and Intrinsic Factor, Zürich, March 1979.

[2] *G. Schlingmann*, Dissertation, Technische Universität Braunschweig 1979.

[3] *(1)*·0.05 H_2O, space group P1, $a = 13.218(7)$, $b = 23.563(11)$, $c = 9.619(5)$ Å, $\alpha = 97.21(4)$, $\beta = 111.32(3)$, $\gamma = 90.68(4)°$, $Z = 2$, $\rho_{calc} = 1.28$ g cm^{-3}. The structure was refined to $R = 0.122$, $R_w = 0.115$ (Co anisotropic, without H atoms) for 7041 reflections ($Cu_{K\alpha}$, $3.5 \le 2\theta \le 135.0°$, including Friedel pairs) with $F^2 \ge 2.0\sigma(F^2)$.

[4] *K. Venkatesan, D. Dale, D. C. Hodgkin, C. E. Nockolds, F. H. Moore, B. H. O'Connor*, Proc. R. Soc. *A 323*, 455 (1971).

[5] *B. Dresow, G. Schlingmann, W. S. Sheldrick, V. B. Koppenhagen*, Angew. Chem. *92*, 303 (1980); Angew. Chem. Int. Ed. Engl. *19*, 317 (1980).

A Pyrazine-Bridged Heme Dimer Absorbing at 800 nm

By *Jürgen-Hinrich Fuhrhop, Mohamed Baccouche,* and *Marlies Bünzel*[*]

Pyrazine takes up electrons from complexed redox-active metal ions (Co^{II}, Ru^{II}) in anti-bonding π-orbitals of one N atom, whereupon the basicity of the other N atom is so strongly enhanced that dinuclear complexes can be formed. If these complexes contain ions of different valency state (Ru^{II}/Ru^{III}) then charge transfer bands of modest intensity appear in the near IR (oscillator strength *ca.* 0.03)[1]. We

[*] Prof. Dr. J.-H. Fuhrhop, Dr. M. Baccouche, Dipl.-Chem. M. Bünzel
Institut für Organische Chemie der Freien Universität
Takustr. 3, D-1000 Berlin 33 (Germany)

have found that the electron-rich central ions of metal-porphyrins form similar electron donor-acceptor complexes with pyrazine, in which an efficient electron transfer takes place between two porphyrin ligands situated *ca.* 1 nm apart from each other. Such EDA complexes are of interest in connection with the synthesis of redox chains, in analogy to those of respiration and photosynthesis[2].

Hemin (iron(III)-protoporphyrin chloride) was dissolved in 0.1 N NaOH and reduced with dithionite in the presence of air to give the heme (iron(II)-protoporphyrin), which has a broad absorption band around 560 nm (see Fig. 1). The reduction could also be carried out with ascorbic acid acid or hydroquinone under inert gas. These heme solutions were titrated with pyrazine in 0.1 N NaOH. At a heme:pyrazine ratio of 2:1 the broad band at 560 nm was split into two narrower bands at 570 and 530 nm. The visible part of the spectrum almost corresponds to that of iron(II)porphyrin complexes with two axial pyridine ligands. In order to obtain such bis(pyridine) complexes in aqueous solution, however, the heme:ligand ratio must be about $1:10^5$[3]. In the case of pyrazine a semiequimolar amount suffices under the given reaction conditions.

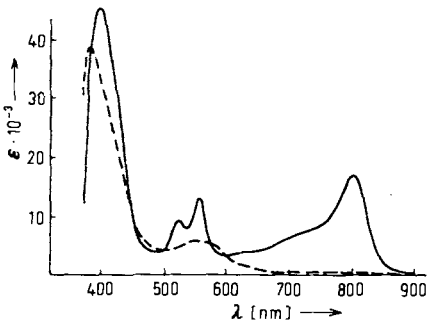


Fig. 1. Electron spectrum of heme in 0.1 N NaOH (---) and after addition of pyrazine (heme:pyrazine = 2:1) (—).

In addition, the heme-pyrazine solution showed an intense band in the near IR at 800 nm (oscillator strength *ca.* 0.1), which likewise reaches its maximum intensity at a heme:pyrazine ratio of 2:1. The solution was stable for several days and did not decompose even on irradiation with visible light (30 min; 1000 W halogen lamp, 30 cm). On warming to 60 °C, the band became broader but regained its original shape on cooling. On passage of carbon monoxide, or on addition of 10% methanol, acetone or hydrochloric acid, the band irreversibly disappeared. The heme could also be oxidized to hemin in this solution, and subsequently demetalated and esterified with diazomethane; dimethyl protoporphyrinate was isolated as sole product in 60% yield. From these experiments we conclude that the pyrazine is not covalently bonded to the porphyrin periphery in the 800-nm complex.

4,4′-Bipyridyl gave analogous changes in the visible spectrum, but no IR bands. No changes were observed in the spectrum with low concentrations of imidazole. Readily soluble iron(II) complexes of porphyrinsulfonic acids also showed no changes in the spectrum on titration with equimolar pyrazine or 4,4′-bipyridyl solutions.

Attempts to measure the NMR spectra and molecular weights of the pyrazine complexes met without success in the presence of the required excess of dithionite. The titration data with pyrazine, however, make the formation of a $(heme)_2$pyrazine complex very likely, for which we propose the structure of a cofacial pyrazine-bridged heme dimer (Fig. 2).

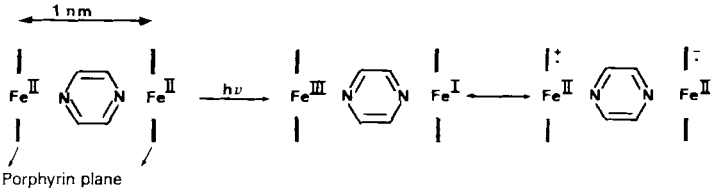


Fig. 2. Proposed structure for the pyrazine-bridged heme dimer and structures induced by excitation with light.

The electronic spectrum closely resembles that of dimeric metalporphyrin radicals; in these cases the bonds in the near IR were ascribed to the allowed direct electron transfer between two porphyrin chromophores[4]. According to *Briegleb*, the observed band shape is also indicative of a charge transfer origin[5]. Porphyrin π-radical anions also absorb in the neighborhood of 800 nm[6]. From the spectrum of the title compound it can be deduced that an aromatic double-bonded axial ligand to the iron(II) ion enables an efficient photoinduced electron transfer even over a distance of 0.8—1.0 nm.

We ascribe the extremely high formation constant of the dimer to a hydrophobic effect: The original iron(III)porphyrin derivative is present as μ-oxo dimer in aqueous solution. On reduction a cofacial heme dimer is most likely still retained, in which pyrazine is incorporated and provides further stabilization. The separation of the dimer by organic solvents or acids (protonation) is irreversible, because the formation constant of the iron-pyrazine bond in a heme monomer is just as low as in the case of pyridine, and therefore no complexation occurs.

The pyrazine-bridged heme dimer is a further example of the inner-sphere electron transfer of metal complexes of pyrazine[7], and, moreover, demonstrates for the first time the possibility of π electrons of the porphyrin ligand spreading over distances of up to 10 Å.—We are currently examining the possible exploitation of the photochemically induced charge separation in subsequent redox processes of the complex.

Received: October 5, 1979 [Z 435 IE]
German version: Angew. Chem. *92*, 320 (1980)

CAS Registry numbers:
Hemin, 15489-47-1; heme, 14875-96-3; $(heme)_2$ pyrazine, 73333-87-6

[1] *C. Creutz, H. Taube*, J. Am. Chem. Soc. *95*, 1086 (1973).
[2] *J.-H. Fuhrhop*, Struct. Bonding (Berlin) *18*, 1 (1974); Angew. Chem. *88*, 704 (1976); Angew. Chem. Int. Ed. Engl. *15*, 648 (1976).
[3] *K.-G. Paul, H. Theorell, H. Åkeson*, Acta Chem. Scand. *7*, 1284 (1953).
[4] *J.-H. Fuhrhop, P. Wasser, D. Riesner, D. Mauzerall*, J. Am. Chem. Soc. *94*, 7996 (1972).
[5] *G. Briegleb:* Elektronen-Donator-Akzeptor-Komplexe. Springer, Berlin 1961, p. 46.
[6] *G. Peychal-Heyling, G. S. Wilson*, Anal. Chem. *43*, 545, 550 (1971).
[7] *R. W. Callahan, F. R. Keene, T. J. Meyer, D. J. Salmon*, J. Am. Chem. Soc. *99*, 1064 (1977); *K. Wieghardt, H. Cohen, D. Meyerstein*, Angew. Chem. *90*, 632 (1978); Angew. Chem. Int. Ed. Engl. *17*, 608 (1978).

Matrix Isolation of OSiS: IR Spectroscopic Evidence for the Si=S Double Bond[**]

By *Hansgeorg Schnöckel*[*]

While the force constant $f(SiO)$ of monomeric SiO_2 isolated in an argon matrix[1] could not be unequivocally deter-

[*] Dr. H. Schnöckel
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. I am indebted to Prof. *H. J. Becher* for valuable discussions and to *H. J. Göcke* for experimental cooperation.

mined from the position of the asymmetric stretching vibration, it should be calculable for a substituted molecule OSiX on the basis of additional isotopic shifts. The OSiS molecule has now been prepared in an argon matrix and studied by IR spectroscopy.

Apart from the SiO bond, that between Si and S is of particular interest in this molecule. A true Si=S double bond has so far been found only in SiS ($f(SiS) = 4.94 \times 10^2$ N m^{-1})[2], which is only stable as a monomeric species at high temperature. OSiS, the first example of a compound of tetravalent silicon containing a Si=S double bond, is formed in an argon matrix by reaction of SiS[3] with atomic oxygen generated by microwave excitation[1]. A linear OSiS molecule would exhibit two stretching vibrations of equal symmetry and an orthogonal deformation mode[4]. In addition to strong absorption bands of unreacted SiS, the matrix spectrum of ^{16}OSiS shows two bands of medium intensity[5] between 1200 and 1300 cm^{-1}, which can be assigned to the fundamental vibration ν(SiO) and the overtone 2ν(SiS). Because of an interaction effect (Fermi resonance) the true frequency of these bands is shifted and the intensity of the fundamental is diminished in favor of the overtone. For the isotopic molecule ^{18}OSiS this effect is eliminated[6] and therefore the overtone 2ν(SiS) is no longer observed[7]. Thus,

Table 1. IR absorption of Ar matrix-isolated OSiS (cm^{-1}).

	ν(SiO)	ν(SiS)	2ν(SiS)
^{16}OSiS	1265.4	643.0	1290.2
^{18}OSiS	1232.9	632.7	—

since the accurately measurable ^{16}O/^{18}O shift of ν(SiO) is falsified as a result of Fermi resonance, the potential function can only be reliably determined by means of the ^{16}O/^{18}O splitting of the Si–S vibration. However, the intensity of this vibration is almost an order of magnitude less intense than the Si–O vibration and the ^{16}O/^{18}O shift of ν(SiS) therefore has a relatively large error of 10.4 ± 0.4 cm^{-1}. This splitting and the vibrational frequencies of ^{18}OSiS (Table 1) make it possible to calculate the following force constants:

f(SiS): 4.86 ± 0.06 [10^2 N m^{-1}]
f(SiO): 9.0 ± 0.1 [10^2 N m^{-1}]
f(SiS/SiO): 0.2 ± 0.1 [10^2 N m^{-1}]

The values for f(SiO/SiS) and f(SiO) confirm the force constants previously discussed for molecular SiO_2[1]. Since force constants of about 2.28×10^2 N m^{-1} have been calculated for Si–S single bonds in various other compounds[8a], corresponding to the predictions of the Siebert rule[8b] (2.22×10^2 N m^{-1}), a bond order of 1.9 results for the Si–S bond in OSiS; this value is almost identical to that of the CS bond in COS (1.93)[9].

Comparison of all the bond orders in the COS and OSiS molecules [CO (2.4), CS (1.93); SiO (2.01), SiS (1.9)] shows that the CO bond has a special position among the four bonds considered, exhibiting considerable strengthening relative to a double bond. In contrast, the multiple bonds between main group elements of the 3rd row (SiS) or between 2nd and 3rd row (CS, SiO) do not significantly exceed a bond order of 2 as a result of reduced orbital overlap.

Received: September 27, 1979 [Z 438 IE]
German version: Angew. Chem. 92, 310 (1980)

[1] *H. Schnockel*, Angew. Chem. *90*, 638 (1978); Angew. Chem. Int. Ed. Engl. *17*, 616 (1978); Z. Anorg. Allg. Chem. *460*, 37 (1980).
[2] *G. Herzberg*: Molecular Spectra and Molecular Structure, Vol. I, Spectra of Diatomic Molecules. Van Nostrand, New York 1950.
[3] SiS is formed in a Knudsen cell when a mixture of H_2S and Ar is passed over elemental Si at *ca.* 1500 K.
[4] A normal coordinate analysis with plausibly estimated force constants predicts the stretching vibrations of OSiS to lie in the regions ν(SiO) = 1300–1200 cm^{-1} and ν(SiS) = 700–600 cm^{-1}.
[5] A third absorption band at 1226 cm^{-1} arises from SiO; examination of our experiments with ^{18}O atoms suggests that it might have been formed in a matrix reaction SiS + O ⇌ SiO + S.
[6] Although more ^{16}O atoms than ^{18}O atoms reach the matrix in the experiment with enriched $^{18}O_2$ ($I_{Si^{16}O}/I_{Si^{18}O} = 1.4$), the intensity of the ν(SiO) bond (^{18}OSiS) is greater than that of the ν(SiO) bond (^{16}OSiS).
[7] Calculation of the Fermi shift from the frequency of ν(SiS) and the observed frequency of the overtone also shows that 2ν(SiS) of ^{18}OSiS must be masked by the fundamental ν(SiO) of ^{16}OSiS.
[8] a) *J. Goubeau, W. D. Hiersemann*, Z. Anorg. Allg. Chem. *290*, 292 (1957); b) *H. Siebert, ibid. 273*, 170 (1953).
[9] *W. H. Jones, W. J. Orville-Thomas, U. Opik*, J. Chem. Soc. *1959*, 1625; *P. H. Verdier, E. B. Wilson Jr.*, J. Chem. Phys. *30*, 1372 (1959).

Novel Selenoantimonate(III) Anions in $Ba_4Sb_4Se_{11}$[**]

By *Gerhard Cordier, Ralph Cook,* and *Herbert Schäfer*[*]

Preparative and structural investigations on alkali metal thioantimonates(III) have shown that the wide variety of structures of their highly-condensed anionic moieties arise from three basic units—ψ-SbS_3 tetrahedra, ψ-trigonal SbS_4 bipyramids, and ψ-SbS_5 octahedra[1]. However, there is no definite information available about the structures of corresponding compounds containing the higher homologues of sulfur. In $Ba_4Sb_4Se_{11}$, a compound of unusual stoichiometry and structure, besides the presence of Se_2^{2-} anions (Se–Se distance 236.7 pm), three different isolated anionic Sb–Se groups has been demonstrated by complete X-ray structure analysis on single crystals[2]. They are depicted in Figure 1 together with bond lengths and bond angles. Besides dis-

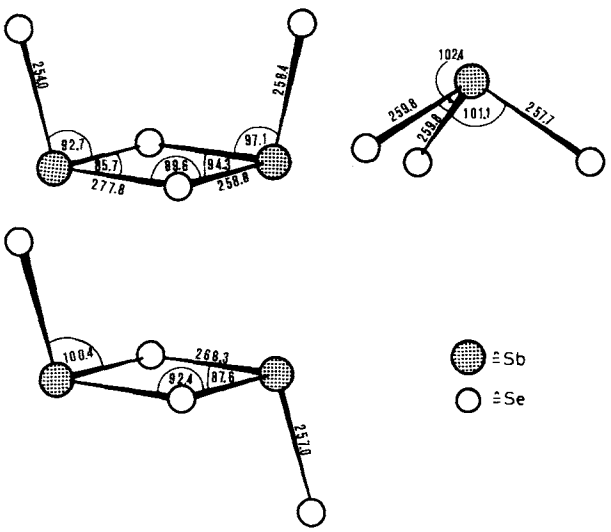


Fig. 1. The selenoantimonate(III) ions in $Ba_4Sb_4Se_{11}$. The unit cell contains one *trans*-$Sb_2Se_4^{2-}$, two *cis*-$Sb_2Se_4^{2-}$, two $SbSe_3^{3-}$ and two Se_2^{2-} ions together with eight Ba^{2+} ions.

[*] Prof. Dr. H. Schäfer, Dr. G. Cordier, R. Cook
Abteilung II für Anorganische Chemie im Eduard-Zintl-Institut der Technischen Hochschule
Hochschulstr. 4, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *Keulen*, Applications Laboratory for X-ray Diffraction N.V. Philips' Gloeilampenfabrieken, Almelo, for the single crystal measurements.

torted trigonal $SbSe_3$ pyramids, *i.e.* ψ-tetrahedra, two different dinuclear Sb_2Se_4 units are observed, representing the *cis*- and *trans*-configuration of two $SbSe_3$ pyramids linked to each other *via* a common edge. This simple linkage resulting in surprisingly small isolated units is so far unique in the structural chemistry of compounds of trivalent antimony.

Experimental

A mixture of anhydrous barium acetate, antimony, and selenium (molar ratio $Ba(CH_3COO)_2:Sb:Se = 1:1:10$) is fused at 600 °C under argon in an alumina crucible. After cooling, the sintered mass is finely ground in a mortar, then heated again to 650 °C, maintained at this temperature for 2 h, and finally allowed to cool slowly over a period of 12 h. The regulus is broken up and the excess of selenium removed by sublimation in a vacuum at 320 °C, leaving behind dark-gray prismatic crystals.

Received: September 27, 1979 [Z 437 IE]
German version: Angew. Chem. 92, 310 (1980)

CAS Registry number:
$Ba_4Sb_4Se_{11}$, 73377-52-3

[1] *H. A. Graf, H. Schäfer*, Z. Naturforsch. *B 27*, 735 (1972); Z. Anorg. Allg. Chem. *414*, 211 (1975); *G. Dittmar, H. Schäfer*, Z. Anorg. Allg. Chem. *437*, 183 (1977); *441*, 93, 98 (1978); *K. Volk, P. Bickert, R. Kolmer, H. Schäfer*, Z. Naturforsch. *B 34*, 380 (1979); *B. Eisenmann, H. Schäfer, ibid. B 34*, 383 (1979); *K. Volk, H. Schäfer, ibid. B 33*, 827 (1978); *B 34*, 172 (1979); *B 35*, in press.

[2] Orthorhombic, space group Pnnm, $a = 891.7(3)$, $b = 2797.6(7)$, $c = 927.6(3)$ pm, $Z = 4$, $\rho_{calc} = 5.47$, $\rho_{exp} = 5.45$ g/cm^3; four-circle diffractometer PW1100, ω scan, $\mu = 233.4$ cm^{-1}, no absorption correction, 3559 symmetry-independent reflections; solution by direct methods (Program SHELX-76, *G. M. Sheldrick*, Program for Crystal Structure Determination, University of Cambridge, England), refinement to $R = 0.0936$ for all observed reflections.

Dimerization of S_6O to $S_{12}O_2$: Crystal Structure Analysis of $S_{12}O_2 \cdot 2SbCl_5 \cdot 3CS_2$[1]

By *Ralf Steudel, Jürgen Steidel,* and *Joachim Pickardt*[*]

cyclo-Hexasulfur monoxide is formed on oxidation of S_6 with trifluoroperacetic acid[2]. However, it has not yet been obtained as crystals large enough to permit determination of its molecular structure. An attempt to prepare better crystalline adducts of S_6O with $SbCl_5$ by analogy with numerous sulfoxide-metal complexes[3] afforded (at −50 °C in CS_2) orange crystals of $S_{12}O_2 \cdot 2SbCl_5 \cdot 3CS_2$ *(1)*; their X-ray structure analysis[4] provides the first information about the structure of a *cyclo*-polysulfur dioxide.

On exposure to air, the initially clear crystals of *(1)* turn cloudy within 1 min as a result of efflorescence with liberation of CS_2, and ultimately form a yellow oil. In CS_2 at room temperature partial decomposition is already detectable after 10 min, yielding $SOCl_2$, SO_2, S_8, and $SbCl_3$ (SO_2 possibly by hydrolysis of $SOCl_2$).

The asymmetric SO stretching vibration of the $S_{12}O_2$ ligand was observed at 940 cm^{-1} in the IR spectrum (CS_2 solution); the symmetrical SO vibration expected in the Raman spectrum has not yet been detected.

The $S_{12}O_2 \cdot 2SbCl_5$ molecules occupy lattice sites of C_i symmetry. The conformation of their ring differs drastically from that of *cyclo*-dodecasulfur S_{12} (D_{3d} symmetry)[5], showing striking variations in the SS internuclear distances and a particularly striking value of 168° for two SSSS torsional angles, which exceeds the values found so far for sulfur homocycles by 45°. The principal molecular parameters are shown in Figure 1. The O atoms occupy axial positions relative to a mean plane through the S_{12} ring. The $SbCl_5$ groups and the bridging O atoms have an almost octahedral geometry. Only van der Waals interactions occur with the CS_2 molecules not shown in Figure 1.

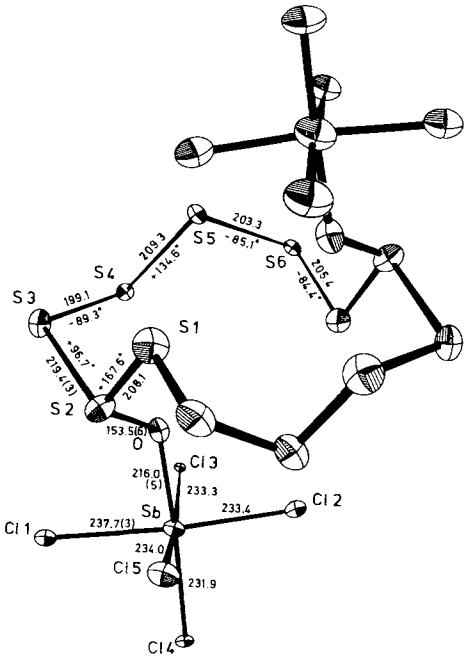
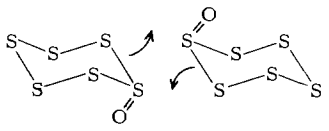


Fig. 1. Internuclear distances [pm] and torsional angles [°] of $S_{12}O_2 \cdot 2SbCl_5 \cdot 3CS_2$ *(1)*. The torsional angles to the O atom are S6′ S1 S2 O: 87.4° and S4 S3 S2 O: 9.6° (S6′ is obtained by reflection of S6 in the inversion center).

Valence angles [°]							
S2	S1	S6	100.3(1)	S4	S5	S6	101.6(1)
S1	S2	S3	94.4(1)	S1	S6	S5	107.5(1)
S2	S3	S4	103.9(1)	S1	S2	O	104.7(2)
S5	S4	S3	103.8(1)	S3	S2	O	103.4(2)

Formation of the centrosymmetric $S_{12}O_2$ molecule, which is still unknown in the free state, from S_6O can be explained in terms of a dipolar addition:



The chair conformation of the six-membered rings of the two S_6O components can still be seen in $S_{12}O_2$. Thus dimerization of a sulfur ring has now been observed for the first time.

Procedure

Freshly distilled $SbCl_5$ (0.5 ml) is added to a stirred solution of β-S_6O[2] (500 mg, 2.40 mmol) in dried CS_2 (100 ml) prepared at −10 °C, and the mixture is immediately cooled to −50 °C. After one week, crystals of *(1)* (150 mg; 10%) precipitate which are isolated at −30 °C on a glass frit, washed with pentane (−30 °C), and dried *in vacuo*. The crystals release CS_2 in the final step; they should therefore be stored in the mother liquor at −50 °C (where they can be kept for at least 5 weeks).

[*] Prof. Dr. R. Steudel, Dipl.-Chem. J. Steidel, Priv.-Doz. Dr. J. Pickardt
Institut für Anorganische und Analytische Chemie der Technischen Universität
Sekr. C 2, Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

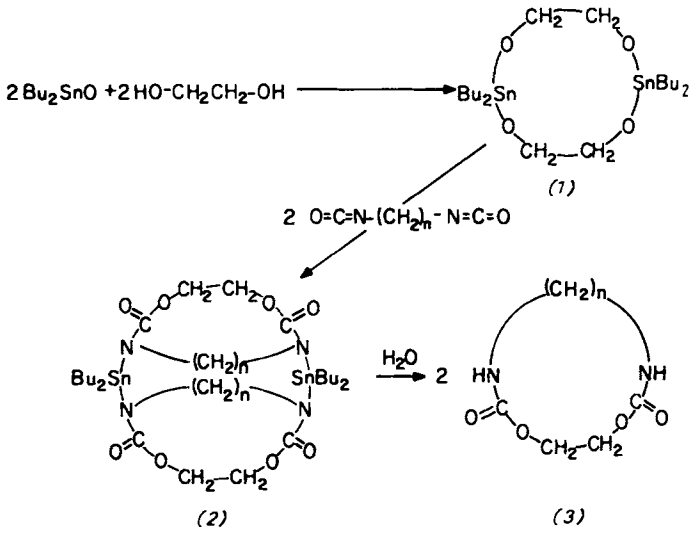
Received: October 19, 1979 [Z 421 IE]
German version: Angew. Chem. 92, 313 (1980)

[1] Sulfur Compounds, Part 64.—Part 63: *H.-J. Mäusle, R. Steudel*, Z. Anorg. Allg. Chem., in press.
[2] *R. Steudel, J. Steidel*, Angew. Chem. *90*, 134 (1978); Angew. Chem. Int. Ed. Engl. *17*, 134 (1978).
[3] *I. Lindqvist*: Inorganic Adduct Molecules of Oxo-Compounds. Springer-Verlag, Berlin 1963.
[4] Space group $P2_1/n$, $a = 1158.9(5)$, $b = 1833.3(9)$, $c = 935.9(5)$ pm, $\beta = 114.86(4)°$, $\rho_{calc.} = 2.29$ g·cm^{-3} (−115 °C), $Z = 2$. 3020 reflections measured at −115 °C (Syntex $P2_1$), $R = 0.046$ (anisotropic temperature factors).
[5] *A. Kutoglu, E. Hellner*, Angew. Chem. *78*, 1021 (1966); Angew. Chem. Int. Ed. Engl. *5*, 965 (1966).

Syntheses with Metalloid Derivatives: Preparation of Macrocyclic Dicarbamates

By *Abraham Shanzer, Nava Shochet, Dov Rabinovich,* and *Felix Frolow*[*]

The difficulty in directing condensation reactions to provide ring products in preference to polymeric materials represents the major barrier towards the efficient synthesis of macrocyclic structures[1]. In order to overcome this barrier various cyclization procedures have been recommended: dilution[2a] and double activation methods[2b], and the use of mercury salts[2c] or metal templates[2d]. We have found an alternative method, in which metalloid derivatives serve as covalent templates for the construction of ring compounds from acyclic precursors. Once the construction of the organic shell has been completed, the metalloid template is easily removed by mild hydrolytic cleavage of the weak metalloid-heteroatom bond. The feasibility of this approach will be demonstrated in this communication by the preparation of macrocyclic dicarbamates from ethylene glycol and diisocyanates using dibutyltin as covalent template.



The synthetic sequence involves condensation of ethylene glycol with dibutyltin oxide to give the known distannoxane derivative *(1)*[3]. Treatment of the latter with organic diisocyanates results in insertion[4] of the N=C group between the Sn –O bonds, affording the tricyclic intermediate *(2)*. Subsequent addition of a few drops of water cleaves the labile Sn –N bonds[5] and releases the macrocyclic dicarbamates *(3)*. Applying this procedure macrocyclic dicarbamates *(3a)*, $n = 6$[6], and *(3b)*, $n = 5$, have been prepared in a simple two step process. The compounds gave correct analyses and characteristic spectra in agreement with the assigned structures. Compound *(3a)* was in addition characterized by a single crystal X-ray structure analysis (Fig. 1).

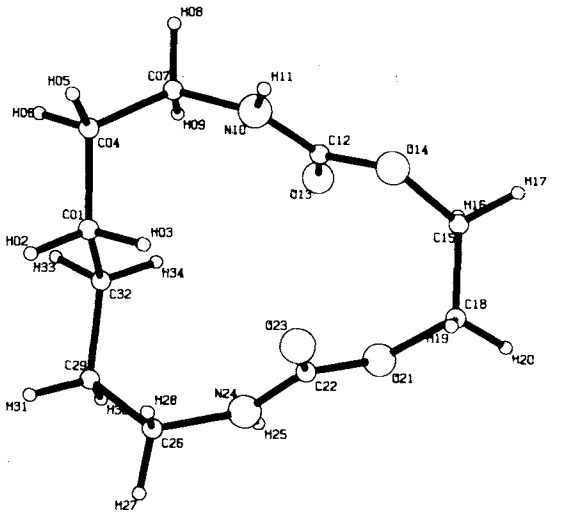


Fig. 1. Crystal structure of *(3a)*. The measurements were performed on an Enraf-Nonius CAD-4 diffractometer with $Mo_{K\alpha}$ radiation; space group C2/c, $a = 16.805(1)$, $b = 8.452(1)$, $c = 17.067(1)$ Å, $\beta = 104.88°$, $V = 2342.5$ Å^3, $Z = 8$, $\rho_{calc} = 1.32$ g/cm^3, $\rho_{obs} = 1.31$ g/cm^3; 2531 independent reflections ($\theta \leq 27°$), solution by direct methods (MULTAN), refinement to $R = 0.039$, torsion angles:

C32	CO1	CO4	CO7	62.4°	CO1	CO4	CO7	N10	− 53.1°
CO4	CO7	N10	C12	121.5°	CO7	N10	C12	O14	180.0°
N10	C12	O14	C15	171.5°	C12	O14	C15	C18	− 98.8°
O14	C15	C18	O21	71.4°	C15	C18	O21	C22	− 99.5°
C18	O21	C22	N24	−178.4°	O21	C22	N24	C26	−174.8°
C22	N24	C26	C29	−116.2°	N24	C26	C29	C32	− 58.7°
C26	C29	C32	CO1	− 58.6°	C29	C32	CO1	CO4	−172.6°

The two carbonyl oxygen atoms in *(3a)* are almost perpendicular to the equatorial plane of the molecule and their deviations above or below this plane are equal (1.48 Å). This arrangement of the carbonyl groups, which define an internal polar cavity, seems to be typical for such structures.

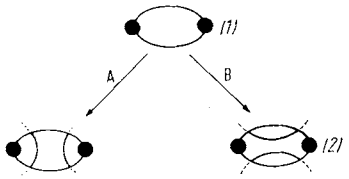
Likewise, in cyclic peptides such as enniatin[7] an alternating orientation of the carbonyl oxygen atoms above and below the plane of the ring is also observed.

The formation of the cyclic dicarbamates *(3)* from distannoxane *(1)* and diisocyanates indicates the dual function of the metalloid template as activating and guiding unit. Activation is achieved by the electropositive character of the tin, which increases the nucleophilicity of its attached functional groups[8]. Stereochemical guidance, on the other hand, is inferred by the rigidity of the ring structure. The latter directs condensation reactions to proceed intramolecularly and thereby reduces competitive polymerization processes. Direct condensation of ethylene glycol with hexamethylene diisocyanate (160—170 °C, 8—20 h, dilution technique) has been reported to yield less than 5% of the desired macrocyclic product *(3a)*[6].

The exclusive formation of the macrocyclic dicarbamate in preference to the tetracarbamate deserves particular attention. Insertion of diisocyanates into the distannoxane *(1)* could *a priori* occur by either of the two alternative pathways A or B (Scheme 1).

[*] Dr. A. Shanzer [†], Dipl-Chem. N. Shochet
Department of Organic Chemistry, The Weizmann Institute of Science
Rehovot (Israel)
Dr. D. Rabinovich, Dr. F. Frolow
Department of Structural Chemistry, The Weizmann Institute of Science
Rehovot (Israel)
[†] Author to whom correspondence should be addressed.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0404-0326 $ 02.50/0



Scheme 1.

The isolation of cyclic dicarbamates in favor of cyclic tetracarbamates implies predominant insertion *via* pathway B. This reaction mode may be attributed to a deactivation of the geminal Sn—O bond after completion of the first insertion process.

The use of dibutyltin as covalent template for the controlled condensation of acyclic substrates represent a systematic approach towards the preparation of macrocycles. The advantages of covalently bonded metalloid templates over metal templates, are ready removal of the metalloid after completion of the template reaction and broad range of applicability, as a large variety of organometalloid compounds may function as template.

Experimental

A solution of *(1)* (2.36 g, 4.0 mmol) in CCl_4 (30.0 ml) was treated under reflux dropwise with a solution of hexamethylene diisocyanate (1.29 ml, 8.0 mmol) in CCl_4 (9 ml). After the addition had been completed the reaction mixture was heated under reflux for one hour. 5.0 ml of aqueous THF (5%) was then added, and the resulting precipitate of dibutyltin oxide removed by filtration and the filtrate concentrated. Crystallization of the residue from benzene/petroleum ether (1:1) afforded 0.64 g (35%) of the dicarbamate *(3a)*, m.p. 168 °C.—*(3b)*, m.p. 164 °C, was prepared analogously.

Received: September 27, 1979 [Z 441a IE]
German version: Angew. Chem. 92, 324 (1980)

[1] *G. W. Gokel, H. D. Durst*, Synthesis *1976*, 168; *T. G. Back*, Tetrahedron *33*, 3041 (1977); *K. C. Nicolaou, ibid. 33*, 710 (1977); *S. Masamune, G. S. Bates, J. W. Corcoran*, Angew. Chem. *89*, 602 (1977); Angew. Chem. Int. Ed. Engl. *16*, 585 (1977).

[2] a) See, *e.g., C. Galli, L. Mandolini*, Gazz. Chim. Ital. *105*, 367 (1975); b) *E. J. Corey, K. C. Nicolaou*, J. Am. Chem. Soc. *96*, 5614 (1974); c) *S. Masamune, S. Kamata, W. Schilling, ibid. 97*, 3515 (1975); d) *A. Eschenmoser*, Pure Appl. Chem. *20*, 1 (1969).

[3] *W. J. Considine*, J. Organomet. Chem. *5*, 263 (1966).

[4] *M. F. Lappert, B. Prokai*, Adv. Organomet. Chem. *5*, 225 (1967).

[5] *K. Jones, M. F. Lappert*, J. Organomet. Chem. *3*, 295 (1966).

[6] *W. Kern, K. J. Rauterkus, W. Weber*, Macromol. Chem. *43*, 98 (1961).

[7] *D. I. Fenton*, Q. Rev. Chem. Soc. *1978*, 325.

[8] *A. J. Bloodworth, A. G. Davis*, Chem. Ind. (London) *1972*, 490; *P. J. Smith, ibid. 1978*, 1025.

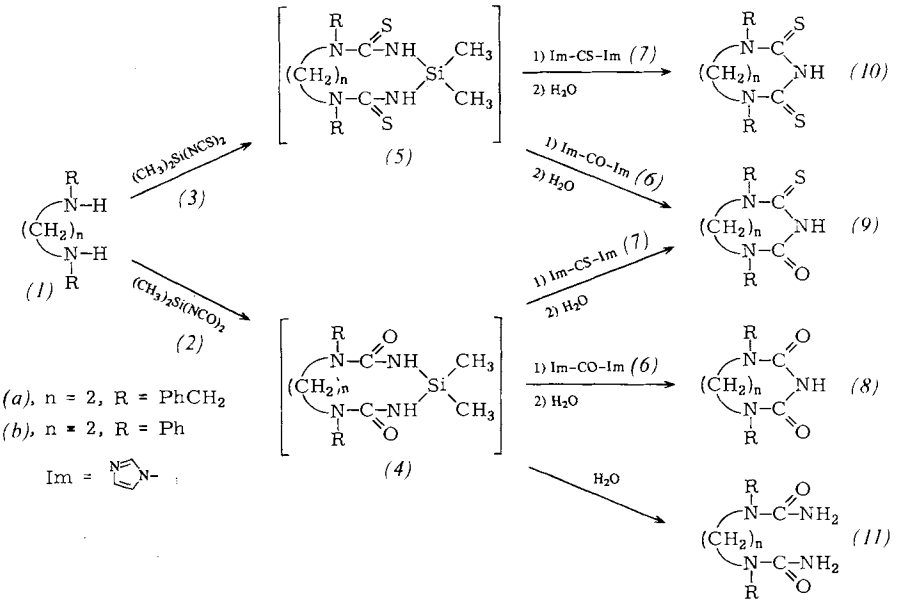
[9] Some physical data of *(3a)*: IR (KBr): ν = 3350—3300, 3080, 2980—2850, 1700, 1550, 1270, 1230, 1210, 1190, 1140, 1090, 1050, 1030 cm^{-1}; ^{1}H-NMR (DMSO): δ = 1.3 (br. s, 8H, $(CH_2)_4$), 3.0 (m, 4H, CH_2 N), 4.2 (br. s, 4H, CH_2 O), 6.7 (m, 2H, NH); MS: m/e = 230 (M^+), *etc.*

Syntheses with Metalloid Derivatives: Preparation of Heterocycles[**]

By *Abraham Shanzer*[*]

The synthesis of nitrogen heterocyclic compounds has most frequently been achieved by either intermolecular or intramolecular condensation of difunctional substrates[1,2]. While the preparation of symmetric compounds has been based on the use of symmetric precursors, the preparation of unsymmetric systems hitherto required unsymmetric substrates that are much more difficultly accessible. We have recently introduced the use of metalloid derivatives as covalent templates for the preparation of macrocyclic compounds[3]. In this communication we wish to describe the application of metalloid templates for the synthesis of non-symmetric heterocycles from symmetric precursors. The key step is the unsymmetric transannular ring closure of templated, cyclic intermediates, and its feasibility is demonstrated by the synthesis of perhydrotriazepines.

Specifically, acyclic diamines *(1)* have been added to dimethylsilicon isocyanate *(2)* or diisothiocyanate *(3)* as templates to provide cyclic, silylated diureas *(4)* and *(5)*, respectively. Condensation of the latter with carbonyl diimidazole *(6)* or thiocarbonyl diimidazole *(7)* and subsequent hydrolytic removal of the silicon template afforded the perhydrotriazepines *(8)*[4], *(9)* or *(10)*, respectively. While the diones *(8)*



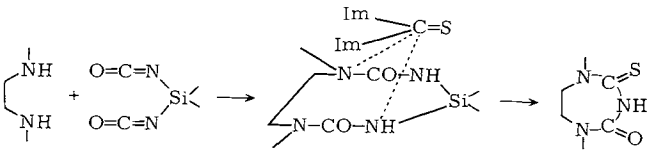
(a), n = 2, R = $PhCH_2$
(b), n = 2, R = Ph
Im =

[*] Dr. A. Shanzer
Department of Organic Chemistry, The Weizmann Institute of Science
Rehovot (Israel)

[**] This work was supported by the Israel Academy of Sciences and Humanities. The author wishes to thank Mrs. *Sara Rubinraut* for skillful technical assistance, Dr. *Z. Zaretski*, for the mass spectral analysis, and Mr. *M. Greenberg* for the measurements of the NMR spectra.

are well-known compounds[4], the thiooxoketones *(9)* and dithiones *(10)* are new compounds. Their structures have been determined by high resolution NMR and mass spectrometry; an X-ray structure analysis[5] of *(9a)* confirmed the assignments.

The first step of the synthesis—the formation of the cyclic diureas *(4)* or *(5)*—is supported by the hydrolysis of *(4)* to *(11)* in quantitative yields. The second step—the unsymmetric transannular ring closure (see Scheme 1)—might well be



Scheme 1.

accelerated by the concurrent regeneration of the isocyanate or isothiocyanate group and release of the imidazole moiety.

The above mentioned successive application of two reagents permits the synthesis of the unsymmetric product *(9)* in two ways: from *(1)* with *(2)* and *(7) via (4)* or with *(3)* and *(6) via (5)*. Moreover, this approach replaces composite reagents (carbonyl isocyanates[4] or isothiocyanates[6]) by simple ones [*(2), (3), (6), (7)*].

Experimental

A 0.5 M solution of *(1a)* in benzene is gradually mixed at room temperature with a 0.5 M solution of *(3)* in benzene (using a Sage syringe pump; Orion, Research Inc.). The resulting crystalline precipitate is dissolved in DMF and treated with 1.5 equivalents of *(6)* and heated for 30 min under reflux. The reaction mixture is then allowed to cool to room temperature and the product hydrolyzed by addition of 10 ml of 5% isopropanol and heating for 15 min under reflux. Evaporation of the solvent yields a syrup-like oil from which the azepine *(9a)* is isolated by chromatography in 70% yield.—*(8)* and *(10)* were prepared under analogous reaction conditions in comparable yields.

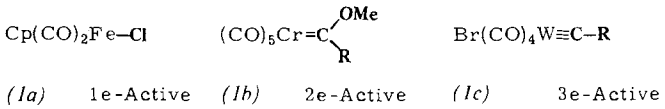
Received: November 2, 1979 [Z 441 b IE]
German version: Angew. Chem. *92*, 325 (1980)

[1] *J. A. Joule, G. F. Smith:* Heterocyclic Chemistry. Van Nostrand-Reinhold, New York 1972.
[2] *J. A. Moore, E. Mitchell* in *R. C. Elderfield:* Heterocyclic Compounds. Vol. 9. Wiley, New York 1967, p. 224.
[3] *A. Shanzer, N. Shochet, D. Rabinovich, F. Frolow*, Angew. Chem. *92*, 324 (1980); Angew. Chem. Int. Ed. Engl. *19*, 322 (1980).
[4] *H. Hagemann*, Angew. Chem. *89*, 789 (1977); Angew. Chem. Int. Ed. Engl. *16*, 743 (1977).
[5] *M. Dobler, W. Petter*, Cryst. Struct. Commun. *7*, 321 (1978).
[6] *J. Goerdeler, J. Neuffer*, Chem. Ber. *104*, 1606 (1971).

Coupling of Well-Established Organotransition Metal Chemistry Donor Groups to Multielectron Ligands[**]

By *Thomas Kauffmann, Johann Ennen, Harald Lhotak, Alfons Rensing, Fritz Steinseifer,* and *Annegret Woltermann*[*]

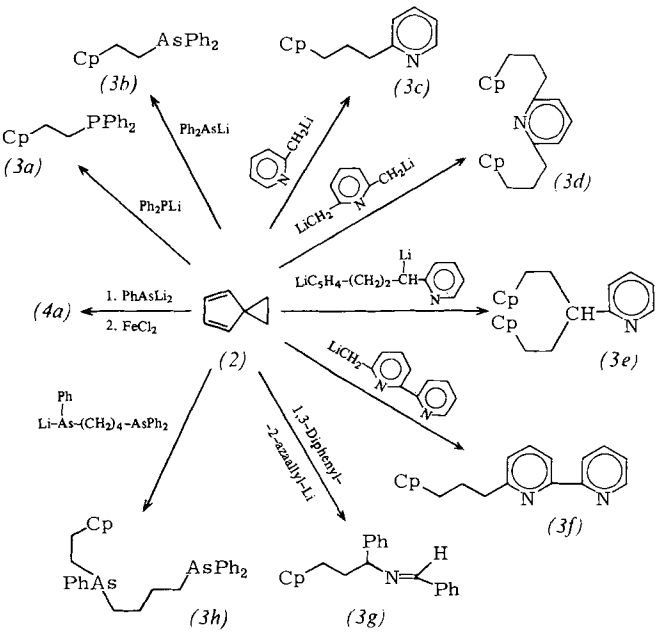
In organo-transition metal reagents and catalysts used for organic syntheses there are generally two different types of ligands: "active ligands" (bold type in examples *(1a)—(1c)*), which directly participate in the reactions, and "passive ligands" which—*cum grano salis*—have merely the task of donating electrons to the transition metal to fill its valency shell and of accepting back-bonding electrons.



(1a) 1e-Active ligand *(1b)* 2e-Active ligand *(1c)* 3e-Active ligand

The passive ligands are usually not optimal (poor thermodynamic stability of the bond to the transition metal; susceptible to nucleophilic attack, like CO or Hal; toxic, like CO). To overcome these deficiencies it is recommended that polydentate multielectron ligands, obtained by linear, branched, or cyclic[1] coupling of proven donor groups, be used as passive ligands. However, since there is a variety of metals of various electronic structures available in the d elements, a complementary variety of easily accessible multielectron passive ligands is required. As replacement for the three passive ligands in *(1a), e.g.*, a 9e-ligand would be necessary. The recently published[2] synthesis of compound *(3a)* (7e-ligand), obtained in our laboratory *via* another route, urged us to report on the coupling of the cyclopentadienyl (Cp) group with 2e- and 4e-donor groups.

Reaction of the readily accessible spirohydrocarbon *(2)*[3] with nucleophiles and subsequent treatment with water afforded the thermolabile, undistillable compounds *(3a)—(3h)*[4], which were purified by column chromatography and characterized by their ^{1}H-NMR (Table 1), IR, and mass spectra. Some of the yields might possibly be improved.



For characterization, some of the anionic ligand systems were converted with $FeCl_2$ into ferrocene derivatives without prior hydrolysis. The surprisingly high yield of the *ansa*-ferrocenes *(4a)* and *(4b)* is presumably due to the fact that—other than in earlier attempts[5] to synthesize such ferrocenes from biscyclopentadienes (max. yield 2.6%)—the biscyclopentadiene derivatives were generated directly in the stable anionic form and reacted.

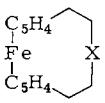
[*] Prof. Dr. Th. Kauffmann, Dipl.-Chem. J. Ennen, Dipl.-Chem. H. Lhotak, Dipl.-Chem. A. Rensing, Dipl.-Chem. F. Steinseifer, A. Woltermann
Organisch-chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] New Reagents, Part 13.—Part 12: *Th. Kauffmann, B. Altepeter, K.-J. Echsler, J. Ennen, A. Hamsen, R. Joussen*, Tetrahedron Lett. *1979*, 501.

Table 1. Yields and characteristic data of the previously undescribed compounds [4].

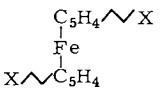
	Yield [a] [%]	M.p. (corr.) [°C]	^{1}H-NMR (δ values)		
			Phenyl/Pyridyl(ene)	Cyclopentadienyl	Alkylene
(3b)	68	oil	7.1—7.6 (m, 10H)	5.9—6.5 (m, 3H) 2.7—2.9 (m, 2H)	2.0—2.6 (m, 4H)
(3c)	43	oil	8.5—8.6 (m, 1H) 7.4—7.8 (m, 1H) 6.9—7.2 (m, 2H)	6.0—6.5 (m, 3H) 2.9—3.0 (m, 2H)	1.9—2.8 (m, 6H)
(3d)	17	oil	7.3—7.5 (m, 1H) 6.9—7.0 (m, 2H)	5.9—6.6 (m, 6H) 2.7—3.0 (m, 8H)	2.4—2.6 (m, 4H) 1.7—1.9 (m, 4H)
(3e)	43	oil	8.4—8.7 (m, 1H) 7.3—7.7 (m, 1H) 6.9—7.2 (m, 2H)	5.8—6.4 (m, 6H) 2.7—3.0 (m, 5H)	1.7—2.3 (m, 8H)
(3f)	36	oil	8.2—8.8 (m, 3H) 7.4—7.7 (m, 2H) 7.1—7.4 (m, 2H)	6.1—6.6 (m, 3H) 3.0—3.1 (m, 4H)	2.5—2.9 (m, 2H) 2.1—2.4 (m, 2H)
(3g)	87	oil	7.0—8.0 (m, 10H)	5.9—6.6 (m, 3H)	8.26 (s, 1H) 4.33 (t, 1H) 2.8—3.0 (m, 2H) 2.0—2.6 (m, 4H)
(3h)	39	oil	7.1—7.5 (m, 15H)	5.9—6.4 (m, 3H) 2.8—2.9 (m, 2H)	1.4—2.7 (m, 12H)
(4a)	28	117 [b]	7.2—7.6 (m, 5H)	4.05 (s, 8H)	2.0—2.8 (m, 8H)
(4b)	16	104 [c]	8.63 (dd, 1H) 6.9—7.8 (m, 3H)	4.08 (mc, 8H)	1.9—2.9 (m, 9H)
(5a)	37	106 [b]	7.1—7.6 (m, 20H)	3.81 (s, 8H)	2.1—2.5 (m, 8H)
(5b)	53	101 [b]	7.1—7.6 (m, 20H)	3.90 (s, 8H)	2.0—2.6 (m, 8H)
(5c)	16	35 [b]	8.4—8.6 (m, 2H) 7.4—7.7 (m, 2H) 6.9—7.2 (m, 4H)	3.98 (s, 8H)	2.7—2.9 (m, 4H) 2.3—2.5 (m, 4H) 1.8—2.1 (m, 4H)
(6b)	46	oil	7.2—8.0 (m, 10H)	5.9—6.4 (m, 3H) 2.7—2.9 (m, 2H)	1.4—2.5 (m, 8H)

[a] Referred to *(2)*; [b] from petroleum ether; [c] from diethyl ether.



(4a), X = AsPh

(4b), X = 

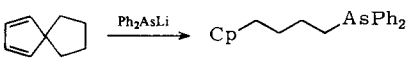


(5a), X = PPh_2

(5b), X = $AsPh_2$

(5c), X = 

As preliminary investigations (*e.g.* preparation of *(6b)*) show, the spirohydrocarbon *(6a)* is also suitable for the synthesis of multielectron ligands.



(6a) *(6b)*, 46%

Received: October 5, 1979 [Z 436 IE]
German version: Angew. Chem. *92*, 321 (1980)

[1] Biologically important passive ligand systems with cyclically coupled donor groups: porphyrin and corrin systems.

[2] *C. Charrier, F. Mathey*, J. Organomet. Chem. *170*, C41 (1979).

[3] *C. F. Wilcox Jr., R. R. Craig*, J. Am. Chem. Soc. *83*, 3866 (1961).

[4] In the case of compounds *(3a)—(3h)* and *(6b)* a mixture of isomers is formed in which the Cp is coupled to the rest of the molecule as *(7a)* or *(7b)*.

 *(7a)*  *(7b)*

[5] *A. Lüttringhaus, W. Kullick*, Makromol. Chem. *44*, 669 (1961); Angew. Chem. *70*, 438 (1958).

Multiple Electron Resonance Spectroscopy. Edited by *M. M. Dorio* and *J. H. Freed.* Plenum Press, New York 1979. xii, 512 pages, bound, $ 49.50.

As in NMR, multiple-resonance methods have recently found wide application in the study of complex spin systems in the field of ESR. In principle, what is observed is the change in the intensity or structure of an electron resonance transition caused by the simultaneous disturbance of a spin system by irradiation at one or more transition frequencies corresponding to nuclear (ENDOR and Double ENDOR or TRIPLE process) or electron resonance transitions (ELDOR process). The effects are a key to the relaxation behavior and/or, due to the higher resolution, provide structural information. Among these processes we may also rank those in which the spin concentration is varied with time and which provide essentially kinetic data. The present book deals with the whole field in 14 sometimes rather cursory articles written by experts.

After a brief historical introduction *(M. M. Dorio), D. Leniart* describes the instrumentation and the experimental procedures for ENDOR and ELDOR, several—sometimes commercial—spectrometer configurations and experimental effects being described in detail. *J. Freed* then presents the theory in his usual precise but rather telegraphic manner, with special emphasis on the connection between the observable effects and relaxation processes. The chapter by *N. M. Atherton* on ENDOR in liquid solutions stresses applications in the analysis of complex ESR spectra of radicals in solution. Zeeman modulation effects in the structure of ESR, ENDOR, and ELDOR spectra are described in detail by *L. A.* and *L. R. Dalton.* A review of ENDOR and ELDOR on radicals and solvated electrons in unordered matrices is given by *L. Kevan* and *P. A. Narayana*; *L. D. Kispert* summarizes the corresponding results on monocrystalline samples. The chapter by *C. P. Scholes* and *R. H. Sands* deals with biologically-oriented applications of electron double resonance in heme compounds and iron-sulfur proteins. *H. C. Box* writes on applications in radiation biophysics, and *M. M. Dorio* on those in the field of polymers. *M. D. Kemple* summarizes ENDOR on molecules in the optically excited triplet state, and finally *K. Moebius* and *R. Biehl* introduce the TRIPLE-resonance technique on radicals in solution, which they have developed extensively in recent years. There is also a chapter by *H. Levanon* on the principles and uses of the time variation of concentrations by means of optical irradiation, for which the author, quite superfluously, invents a new name—"Optical Perturbation EPR" (OPEPR) and which, unfortunately, is not very representative. A short subject index concludes the book.

Over-all, the book offers a splendid summary of the current state of multiple-electron resonance. It is an important source of information for specialists in electron resonance and can serve as a basis for advanced students. It is too demanding and too heterogeneous from the point of view of the presentation to be suitable as an introduction for non-specialists.

Hanns Fischer [NB 500 IE]

Liquid Crystals and Biological Structures. By *G. H. Brown* and *J. J. Wolken.* Academic Press, New York 1979. 187 pages, bound, $ 19.00.

A reader taking up a book with the above title, implying a biophysical-chemical bias, might well expect a comparison of liquid crystals and biomembranes. He will be disappointed, for the book has little to do with such subjects. The chapter on membranes—appended at the end—is all of six pages long and the main illustration in it is a cartoon of a membrane.

What, then, is the aim of this book? The main section (Chapters 5—11) describes all kinds of molecular and cellular structures such as occur in living organisms. Although the selection is somewhat arbitrary, there is a nice collection of instructive figures especially from the visual system. The text, however, is very superficial and not suitable for an introduction. At every conceivable and inconceivable opportunity the authors refer to the importance of ordered, non-crystalline formations in biology and point out that there should be consequently a close relationship to the physics of liquid crystals. These vague statements culminate on page 144 in the following sentences on the ageing—of man: "It is not known how the ageing process takes place, but the liquid crystalline state of matter must certainly be considered.", and then, after exactly 14 lines, the following is offered as a conclusion: "... ageing could be delayed or modified chemically by hydration and dehydration." Hydration of liquid crystals is the fountain of youth? The useful information contained in this chapter can also be found—and in scientifically faultless form—in textbooks on cell biology and biochemistry, and wrapping it up in simplifying pseudophysical arguments, as this book does, is fatal.

The biological part of the book is preceded by a good introduction to the field of liquid crystals (Chapters 1—4) although the liquid crystalline polymers have been overlooked. This section gives a brief outline of the physics and nomenclature of nematic and smectic metaphases. However, since other books on liquid crystals also do this, and the volume as a whole in no way lives up to its aim of demonstrating a connection between the physics of liquid crystals and biological structures, this is not a book to be recommended.

Peter Fromherz [NB 501 IE]

Air Pollution Chemistry. By *John D. Butler,* Academic Press, London—New York—San Francisco. 1st edit., viii, 408 pp., numerous figures and tables, bound, £ 25.00.

The significant efforts exerted by governments, industries and engaged individuals in keeping our environment clean have considerably increased the need for detailed knowledge concerning the chemical behavior of pollutants in the atmosphere. Not long ago, the only way to obtain such information was a laborious consultation of the technical journals specializing in these matters. In recent years, the situation has improved in that a number of monographs have appeared on the market which make the available knowledge more readily accessible and, at the same time, provide a reasonably comprehensive overview of atmospheric chemistry. The present book provides a good summary of present knowledge of atmospheric chemistry but contains in addition much detailed information germane to problems of local air pollution, thus justifying its title. The book is written from the view-point of a physical chemist and is based on second and third year undergraduate lecture courses to students of chemistry. An intermediate level of presentation is adopted. The text is well ordered and treats in seven chapters: 1. health factors; 2. sources, sinks and removal mechanisms of emissions to the atmosphere; 3. air sampling and collection; 4. analysis of pollutants by instrumental methods; 5. atmos-

pheric reactions; 6. meteorological aspects of pollutant dispersions; 7. urban atmospheres.—Under each heading a great amount of material has been assembled, mostly in tabular form, and is discussed in detail. The literature referenced at the end of each chapter originates mainly from the sixties and seventies prior to 1977. The citations are not intended to be exhaustive but provide a fairly good survey.

The on the whole positive evaluation of the book unfortunately is dampened by two shortcomings. The preface makes apparent the intent of the author to use the book for teaching purposes. In this respect, the text does not meet the didactic requirements. Since the curriculum of chemists generally does not include the fundamentals of meteorology, a short introduction into the meteorological terminology seems required. For example, the term stratosphere is mentioned first on page 51 but its meaning becomes clear from a diagram on page 272. The terms "aerosol" (p. 51) and "dry deposition" (p. 102) are similarly introduced without explanation. A second weak point is the sometimes uncritical presentation of material taken from the literature. One example concerns the sources and sinks in the budget of atmospheric nitrogen and sulfur compounds. Although the figures given agree quite well with current concepts, there is no discussion of the problem in obtaining reliable estimates, and one does not learn either how such figures are derived. Another example: the description of the spark source mass spectrometer on page 205 conveys the impression that this instrument is widely employed for the analysis of dust particulates. This, however, is not true.

With these reservations one can recommend the book to all persons who have an active interest in the problems of air chemistry and air pollution. Today, the number of readers within this circle is no longer small.

Peter Warneck [NB 502 IE]

Gel Chromatography, Theory, Methodology, Application. By *T. Kremmer* and *L. Boross.* John Wiley and Sons, Chichester, 1979.

This English translation of a book that appeared in Hungary in 1974 concentrates almost exclusively on aqueous gel chromatography on soft, swellable, stationary phases. Since the manufacturers of these gels have generously provided a detailed literature service, it is no problem to collect such data into a single coherent text. Although "the most recent" developments of the method are discussed, it is nevertheless astonishing that there is no mention of the technique of instrumental liquid chromatography, now familiar for a decade. After all, from the apparatus point of view this technique has its origins partly in gel chromatography and has given rise to a reconsideration of gel chromatography.

Part I, Principles (about 30 pages) gives a practically complete survey of the available soft gels in addition to some data on common xerogels. Surprisingly enough, the "carbon molecular sieve" of gas chromatography is included here. The "Theory" section (about 60 pages) gives models of the gel-chromatographic separation process, of band broadening, and of molecular weight determination. Sentences like "To use gels in chromatography, gel particles must be produced" and others of similar ilk must be attributed to the translation. Part II (about 70 pages) deals with the methods and techniques, including thin-layer chromatography. Finally, Part III (about 90 pages) discusses the uses of gel chromatography for the separation of proteins, nucleic acids, and carbohydrates. Separations of low molecular compounds and inorganic salts on soft gels are also described.

Newcomers to the field of aqueous gel chromatography will find many practical hints and a survey of the problems and possibilities of this classical method. The more experienced student is, however, referred to "Modern Size-Exclusion Chromatography" by *W. W. Yau, J. J. Kirkland* and *D. D. Bly,* published simultaneously by the same company.

Heinz Engelhardt [NB 505 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Advances in Chromatography, Vol. 17. Edited by *J. C. Giddings, E. Grushka, J. Cazes,* and *Ph. R. Brown.* Marcel Dekker, Basel 1979. xiv, 336 pp., bound, SFr. 75.00.—ISBN 0-8247-6902-3

Life Sciences Research Report 15. Biomedical Pattern Recognition and Image Processing. (Dahlem Conferences.) By *K. S. Fu* and *T. Pavlidis.* Verlag Chemie, Weinheim 1979. 441 pp., sewed, DM 54.00.—ISBN 3-527-12017-3

Practical NMR Spectroscopy. By *M. L. Martin, G. J. Martin,* and *J. J. Delpuech.* Heyden & Son, London 1980. xxxi, 460 pp., bound, £ 30.00.—ISBN 0-85501-462-8

Analytiker-Taschenbuch, Band 1. Edited by *H. Kienitz, R. Bock, W. Fresenius, W. Huber,* and *G. Tölg.* Springer-Verlag, Berlin 1980. 439 pp., bound, DM 78.00.—ISBN 3-540-09594-2

Topics in Current Chemistry, Vol. 87. Micelles. Edited by *F. L. Boschke, M. J. S. Dewar, K. Hafner, E. Heilbronner, S. Ito, J.-M. Lehn, K. Niedenzu, C. W. Rees, K. Schäfer,* and *G. Wittig.* Springer-Verlag, Berlin 1980. 154 pp., bound, DM 86.00.—ISBN 3-540-09639-6

Structure and Bonding, Vol. 39. Edited by *J. D. Dunitz, J. B. Goodenough, P. Hemmerich, J. A. Ibers, C. K. Jorgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Springer-Verlag, Berlin 1980. 120 pp., bound, DM 64.00.—ISBN 3-540-09787-2

Semisynthetic Proteins. By *R. E. Offord.* John Wiley & Sons, Chichester 1980. vi, 235 pp., bound, £ 17.00.—ISBN 0-471-27615-4

RKW-Handbuch Forschung, Entwicklung, Konstruktion (F+E). By *Moll/Warnecke.* Erich Schmidt Verlag, Bielefeld 1979. 8th instalment, 85 pp., loose-leaf, total work DM 76.00.

Advances in Catalysis, Vol. 28. Edited by *D. D. Eley, H. Pines,* and *P. B. Weisz.* Academic Press, New York 1979. x, 403 pp., bound, $ 42.50.—ISBN 0-12-007828-7

Biotransformation von Arzneimitteln, Band 3. By *S. Pfeifer.* Verlag Chemie, Weinheim 1979. 560 pp., bound, DM 118.00.—ISBN 3-527-25784-5

Lehrbuch der pharmazeutischen Technologie. By *R. Voigt.* Verlag Chemie, Weinheim 1979. 3rd, revised edition, 835 pp., bound, DM 84.00.—ISBN 3-527-25667-9

Die Chemische Industrie und ihre Helfer. Issued by Edition Selka, Darmstadt 1979/80. 548 pp., bound, DM 40.00.

Structure Reports for 1978. Vol. 44 A. Metals and Inorganic Sections. Edited by *J. Trotter* and *L. D. Calvert.* D. Reidel Publ., Dordrecht 1980. 387 pp., bound, *ca.* DM 110.00—ISSN 0166-6983

Molekulare Biologie der Hormone. By *F. Marks.* Gustav Fischer Verlag, Stuttgart 1979. xi, 258 pp., sewed, DM 19.80.—ISBN 3-437-10586-8

Topics in Bioelectrochemistry and Bioenergetics, Vol. 3. Edited by *G. Milazzo.* John Wiley & Sons, Chichester 1980. xiv, 359 pp., bound, £ 28.00.—ISBN 0-471-99744-7

Colorimetric Chemical Analytical Methods. By *L. C. Thomas* and *G. J. Chamberlin.* The Tintometer, Salisbury 1980. xxxvii, 625 pp., bound, £ 33.00.—ISBN 0-471276-057

Peat. Industrial Chemistry and Technology. By *C. H. Fuchsman.* Academic Press, New York 1980. xviii, 279 pp., bound, $ 28.00.—ISBN 0-12-264650-9

Molekülkristalle. By *A. I. Kitaigorodski.* Akademie-Verlag, Berlin 1979. vii, 361 pp., bound, *ca.* DM 68.00.

Physical Chemistry of Fast Reactions, Vol. 2. Reaction Dynamics. Edited by *I. W. M. Smith.* Plenum Press, New York 1980. xiii, 277 pp., bound, $ 32.50.—ISBN 0-306-40227-0

Advances in Corrosion Science and Technology, Vol. 7. Edited by *M. G. Fontana* and *R. W. Staehle.* Plenum Press, New York 1980. x, 365 pp., bound, $ 39.50.—ISBN 0-306-39507-X

Excited States, Vol. 4. Edited by *E. C. Lim.* Academic Press, New York 1979. x, 400 pp., bound, $ 42.50.—ISBN 0-12-227204-8

Preparation and Properties of Stereoregular Polymers. Edited by *R. W. Lenz* and *F. Ciardelli.* D. Reidel Publ., Dordrecht 1980. xvii, 472 pp., bound, Dfl. 85.00.—ISBN 90-277-1055-4

Symbole, Einheiten und Nomenklatur in der Physik. Physik Verlag, Weinheim 1980. x, 77 pp., sewed, DM 18.00.—ISBN 3-87664-045-8

Topics in Enzyme and Fermentation Biotechnology, Vol. 4. Edited by *A. Wiseman.* John Wiley & Sons, Chichester 1980. 242 pp., bound, £ 22.50.—ISBN 0-85312-150-8

Chemical Reactor Analysis and Design. By *G. F. Froment* and *K. B. Bischoff.* John Wiley & Sons, Chichester 1979. xxxix, 765 pp., bound, $ 35.95.—ISBN 0471-02447-3

Inorganic Reaction Chemistry: Systematic Chemical Separation. By *D. T. Burns, A. Townshend,* and *A. G. Catchpole.* Ellis Horwood, Chichester 1980. 248 pp., bound, £ 18.50.—ISBN 0-85312-118-4

Analytical Methods for Coal and Coal Products, Vol. III. Edited by *C. Karr, Jr.* Academic Press, New York 1979. xvii, 641 pp., bound, $ 55.00.—ISBN 0-12-399903-0

Anatomie und Physiologie des Menschen. Band 15. Die Haut. By *D. F. Culclasure.* Verlag Chemie, Weinheim 1980. 2nd Edit., xxv, 109 pp., sewed, DM 15.50.—ISBN 3-527-25743-8

Palladium Catalyzed Oxidation of Hydrocarbons, Vol. 2. By *P. H. Henry.* D. Reidel Publ., Dordrecht 1980. xv, 435 pp., bound, Dfl. 125.00.—ISBN 90-277-0986-6

Hohenheimer Arbeiten, Heft 104. Colchicin. Untersuchungen zur Biochemie von Colchicin-Alkaloiden. By *M. Schönharting.* Verlag Eugen Ulmer, Stuttgart 1980. 56 pp., sewed, DM 12.00.

Statistical Theory and Methodology of Trace Analysis. By *C. Liteanu* and *I. Rica.* Ellis Horwood, Chichester 1980. 446 pp., bound, £ 28.00.—ISBN 0-85312-108-7

Vinyl Cations. By *P. J. Stang, Z. Rappoport, M. Hanack,* and *L. R. Subramanian.* Academic Press, New York 1979. xi, 513 pp., bound, $ 53.00.—ISBN 0-12-663780-6

Future Sources of Organic Raw Materials, CHEMRAWN I, Toronto 1978. Pergamon Press, New York 1980. viii, 650 pp., bound, DM 113.00.—ISBN 0-08-022390-7

Polymers as Aids in Organic Chemistry. By *N. K. Mathur, C. K. Narang,* and *R. E. Williams.* Academic Press, New York 1980. xii, 258 pp., bound, $ 32.50.—ISBN 0-12-479850-0

Photochemistry, Vol. 10. Senior Reporter: *D. Bryce-Smith.* The Chemical Society, London 1979. xv, 717 pp., bound, DM 200.00.—ISBN 0-85186-590-9.—A volume in the series "Specialist Periodical Reports"

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form - by photoprint, microfilm, or any other means - nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar.* **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 5
May 1980
Pages 333–410

Computer Simulation of the Kinetics of Complicated Gas Phase Reactions

By Klaus H. Ebert, Hanns J. Ederer, and Gunther Isbarn[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Modern digital methods and powerful computers make it possible to simulate the time behavior of chemical reactions. These calculations can be performed on systems containing an almost unlimited number of elementary reactions. Generally, however, the reaction models used should contain only those elementary reactions which describe the bulk of the conversion. Such a reaction model may be obtained by reduction of the complete set of elementary reactions. Another possibility is analysis of the chemical system starting from conditions ensuring a simple chemistry, which is generally the case at low temperatures and low conversions. The reaction model may then be extended into the range of the reaction variables (temperature, time) of interest. Mathematical simulations may be helpful during the development of the reaction model, and sometimes even decisive. These methods were applied to the pyrolysis of ethylbenzene and *n*-hexane, and to CO oxidation. They yield information on the reaction paths, the importance of particular elementary reactions, and reaction stability. Furthermore, quantitative data can be obtained concerning the influence of single elementary reactions on the product distribution. The sensitivity matrix shows, *e.g.*, whether the determination of kinetic parameters of an elementary reaction from kinetic data of the overall reaction is possible in principle, and how high the accuracy of the rate constants should be for simulation of the reaction. Both results are important for modeling chemical reactions.

1. Introduction

The rapid development of modern computers has markedly advanced the possibilities and the potency of chemical kinetics. Until recently the time behavior of only those chemical reactions could be determined exactly whose rate laws could be expressed as a system of differential equations which can be integrated analytically. This is possible with elementary chemical reactions, which cannot be subdivided, and with a few simple reaction systems. It is not possible to obtain exact analytical expressions for the time dependence of most of the chemical systems of practical interest. Therefore the solution of the simultaneous differential equations requires other methods.

For reactions involving radicals—and that is the majority of all homogeneous gas phase reactions—the best known approximation method for solving such systems of differential equations is the assumption of a steady state[1]. This approxi-

[*] Prof. Dr. K. H. Ebert, Dr. H. J. Ederer, Dipl.-Chem. G. Isbarn
Institut für Angewandte Physikalische Chemie and
Sonderforschungsbereich 123 of the University
Im Neuenheimer Feld 253, D-6900 Heidelberg (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0505-0333 $ 02.50/0*

mation implies that the reactive intermediates are consumed as fast as they are produced, resulting in a zero net formation rate. This greatly simplifies the mathematical treatment (see Section 3.2).

Another method of solving complicated systems of differential equations is numerical integration, in which the time behavior is evaluated by stepwise computation. If there is a large difference in the rates of production and consumption of the various species, which is always the case in the initial period of radical reactions, very short time intervals have to be used for the calculations. In classical integration methods (*e.g.* Runge-Kutta methods[2]) this will entail considerable computational effort. Modern integration methods use variable time intervals, and are available as computer programs. Short time intervals are chosen in the area of large changes in the concentration of the species, and longer time intervals are used if these changes are smaller. Nevertheless, numerical integration of a large number of nonlinear simultaneous differential equations usually requires an enormous computational effort which can only be mastered with modern high capacity computers. Modern numerical methods tend to decrease computing time and storage size without reducing the quality of the results. Results are considered as "exact" if a reduction of the time intervals does not have any effect on the results.

Before studying the differences in the results of kinetical calculations obtained by the "exact" method and by assuming a steady state, it is useful to check how well the laws of chemical kinetics generally describe the time behavior of a chemical reaction. The classical theory of the rates of thermal reactions[3,4] is based upon two fundamental equations[*]. The time law describes the rate of homogeneous gas phase reactions in dependence upon the partial pressures:

$$\frac{dn_i}{dt} = \sum \pm k_o^1 n_m + \sum \pm k_{p,s}^2 n_p n_s \qquad (1)$$

The first term of the right side contains the components of first order reactions, and the second term those of second order reactions. The sign indicates the production (+) or the consumption (−) of the species n_i in the reaction considered. The temperature dependence of the reaction rate constant can usually be expressed by the Arrhenius equation:

$$k = A \exp(-E_a/RT) \qquad (2)$$

The number of elementary reactions participating in a chemical reaction system can vary within wide limits. Examples of reactions consisting of only few elementary reactions (*e.g.* formation of hydrogen halides from the elements) can be found in any textbook of physical chemistry. Most of the gas phase reactions of practical interest consist of many—often several hundred—elementary reactions. Of course, they will all participate to some extent in the reaction, but the question to be answered is: which reactions determine the kinetic behavior and which exert such a slight influence that they may be neglected? Reaction mechanisms with a large number of elementary reactions almost exceed the capabilities of even the most powerful computers. As a rule of thumb, the computational effort increases with the square of the number of differential equations.

It is therefore very important that complicated reaction mechanisms be reduced to a reaction model which describes the reaction with sufficient accuracy while still being suitable for kinetic calculations using either the "exact" method or the steady state assumption.

2. Reaction Models

Reaction models should be made up of elementary reactions because of their general applicability. With a knowledge of the kinetic constants, absolute values of the reaction rates can be calculated. The number of elementary reactions increases with the number of atoms present in the reactants. For the fairly simple decomposition reactions of such small molecules as butane or pentane there exist more than 500 "possible" elementary reactions, even with the limiting assumption that no products are formed with a molecular weight exceeding twice that of the parent compound[5]. On addition of other reactants, such as oxygen, water, *etc.*, the number of elementary reactions is multiplied. However, a reaction model fulfills its purpose if it describes well enough the course of the reaction within the interesting range of the reaction variables (p, T), or if it provides answers to specific questions. It may happen that the production rate of a particular by-product is of more importance than an exact description of the formation of the major products.

Of course, the lower the number of elementary reactions, the simpler becomes the mathematical treatment. However, an upper limit for this number cannot be given in general because the complexity of a reaction model also depends on the number of the participating species. However, if the number of elementary reactions approaches 50, a reduction should be considered.

It is usually not easy to decide from the kinetic constants whether a particular elementary reaction belongs to the group of those which are involved in an "important" reaction path within the conversion, and therefore cannot be neglected. Furthermore, a reaction model has to be self-consistent and to contain reactions accounting for the consumption of all radicals. A useful approach to model reduction is the combination of certain species or elementary reactions; this is called lumping. However, the "kinetic constants" of the lumped reactions rarely remain constant, and the applicability of the corresponding rate expression is consequently limited. Lumping is favored if similar species (*e.g.* radicals from unsaturated hydrocarbons) form the same major product (*e.g.* soot)[6-9].

In minimizing the number of elementary reactions for a reaction model the chemist usually adopts a different meth-

[*] Both laws are based upon the Boltzmann distribution of molecular energies, which is satisfied within the usual reaction conditions of most chemical reactions. Chemical reactions are undergone predominantly by the energy-rich molecules of the ensemble; therefore, weak interactions, which are responsible for the numerous deviations of thermodynamic properties from "ideality", are of little or no influence. In general, eqs. (1) and (2) are satisfied well. This means that reaction rates can be calculated with high accuracy in a wide range of the reaction variables if the values of the kinetic constants are known exactly. The accuracy of the calculations is usually very good relative to the experimental methods available for determining reaction rates. This is true without limitation for the elementary reactions which cannot be further subdivided and whose behavior is described by the stoichiometric equation. It should be noted that at low pressure energy transfer may influence the reaction rates, and that the assumption of the Boltzmann distribution may loose its validity in very fast reactions—at high temperatures or in reactions with a very low activation energy. Both possibilities cause deviations from eqs. (1) and (2).

od. He tries to analyze the reaction mechanism using experimental data, and in so doing he first looks for the initial reactions and then proceeds to formulate those elementary reactions describing the fate of the reactive intermediates. In this way, the construction of a reaction model is continued by considering known chemical principles and attempting to formulate the formation of the products and intermediates with a minimum set of elementary reactions. Additional investigations about particular elementary reactions[10–12] are sometimes useful. Simultaneous kinetic calculations and quantitative comparisons with the experimentally determined product distribution may also be helpful in formulating the reaction model.

It is convenient to start the development of a reaction model at low temperatures and low conversions, where the number of elementary reactions is small, and to extend it into the interesting regions of the reaction variables. This method is then always applicable if the model contains only few initial reactions, and if these form only few primary intermediates, as in the thermal decomposition of ethylbenzene (see Section 4.3). Furthermore, this method allows a clear description of reaction behavior and prediction of variations in the reaction behavior caused by variations of the reaction conditions or by the addition of various reactants.

3. Mathematical Methods

3.1. Numerical Treatment of Rate Equations

For numerical treatment, the reaction model is transformed into a system of differential equations containing one differential equation for each species taking part in the reaction. In general this is not difficult. If the number of species is greater than ten, the system should be evaluated by computer. The transformed reaction model consists of linear and quadratic terms depending on the unimolecular or bimolecular nature of the corresponding elementary reactions. (In radical recombination reactions, third order terms may occur too.)

To obtain a numerical solution of the differential equation system the values of the kinetic parameters (activation energy, pre-exponential factor) of each elementary reaction are needed. The number of elementary reactions whose kinetic constants are known with satisfactory accuracy is still small; such data have been compiled in tables[13–16]. If the kinetic constants are not known, their values should be estimated from chemical analogy or from thermodynamic considerations[16–18].

The kinetic constants of reactions of the same type often vary within close limits. These "band widths" are compiled in Table 1 for five types of reactions, which represent most of the elementary reactions occurring in the pyrolysis of hydrocarbons.

Table 1. Types of reactions in the pyrolysis of hydrocarbons and band widths of the kinetic parameters A [s^{-1}; ls^{-1} mol^{-1}] (pre-exponential factor) and E_a [kJ mol^{-1}] (activation energy); M,M′: stable molecules; R,R′: radicals.

Type no.	Elementary reaction	$\log_{10}A$	E_a
(1)	M → R+R′	15—17	200—360
(2)	M+R → R′+M′	7—11	30— 50
(3)	R → M+R′	12—15	100—180
(4)	R+R′ → M (+M′)	7—11	0
(5)	R → R′	10—12	50— 80

For these estimates, it is important to have information about the sensitivity of the reaction model to variation of the values of respective reaction constants. More detailed data on the sensitivity of a particular model and its temperature dependence can be obtained only by simultaneous computations (cf. Section 5.2). Occasionally in simple systems quantitative data are available on the sensitivity of reaction constants, *e.g.* of the activation energy of unimolecular initial reactions. In complicated systems it is mostly very difficult, if at all possible, to predict the effect of the variation of a particular kinetic constant on a model. For some elementary reactions it is evident, however, that they do not affect the reaction model noticeably, even if the rates are varied considerably.

Large differences in the sensitivities appear in all systems of differential equations in which the time constants differ by orders of magnitude; such systems are called 'stiff'.

The well-known Runge-Kutta methods[2] are not suitable for the numerical integration of stiff differential systems. Because of the huge difference in the time behavior of the individual elementary reactions the time step size has to be set extremely small in order to obtain correct results. Errors introduced by excessive step sizes in the initial period of the reactions are propagated also in regions of higher conversions. The computer time required to cover high conversions of a reaction is then extremely long.

Fast methods for the solution of stiff differential equation systems have become an important field of research in numerical mathematics. All modern "stiff solvers" contain an efficient self-adjusting optimum step size control, *i.e.* rapid variations require small step sizes, slow variations permit large step sizes[19]. A further important point is the algorithm for the numerical stability of a stiff solver. The algorithm has to prevent the accumulation of computational errors.

The program of *Gear*[20], which is very often used by chemists, is based on a "multistep predictor-corrector" algorithm which also controls the step size. The program has been very successful; until now no case of a "wrong" solution of a chemical problem is known.

Other methods for solving stiff differential equation systems are the implicit Runge-Kutta method of *Wanner*[21] and the semi-implicit algorithm of *Deuflhard*[22] which requires a considerably smaller computer storage size than the program of *Gear*.

3.2. The Steady State Assumption

The most important and most frequently applied approximative method in treating differential equation systems in chemical kinetics is based upon the quasi-steady state assumption (QSSA). In this approximation, the right-hand sides of the differential equations for the reactive intermediates are set equal to zero in order to transform these differential equations into algebraic equations. As a result, the remaining reduced system of differential equations (for the reactants and the stable products) is substantially less stiff than the original system. This may permit either an analytical solution of the differential equation system or the appli-

cation of considerably simpler numerical integration methods (*e.g.* Runge-Kutta). The QSSA does not mean, however, that the concentrations of all reactive intermediates are set constant during the reaction. According to the mathematical treatment with the singular perturbation theory[23-27], which will not be outlined in detail, there exist two types of radicals[28] depending mainly on the type of reactions in which the radical is consumed: type r_m, whose concentrations remain approximately constant, and type r_n, whose concentrations decrease according to a function similar to that governing the disappearance of the reactant in the course of the reaction.

The QSSA, as usually applied by chemists, neglects the time behavior of the initial period of the reaction in which the concentrations of all radicals increase to a limiting value corresponding to the "steady-state" value[*]. Generally, the smaller the steady-state concentrations are, the lower will be the conversion at which the steady state is attained. Therefore, the QSSA is better fulfilled at low temperatures and high pressures. The question then arises whether there exists a quantitative measure for the applicability of this approximation. The differential equations of the radicals can be transformed into a set of dimensionless differential equations. This procedure and a suitable rearrangement attributes a dimensionless constant ε_i to each dimensionless differential quotient. The ε_i-values are composed of reaction rate constants and initial concentrations of the reactants, and it can be shown that they are characteristic values for the applicability of the QSSA. Although theory supplies exact solutions for calculating the ε_i-values, in most cases more or less rough estimations are more readily available which give satisfactory information on the applicability of the QSSA.

For thermal decomposition reactions (*e.g.* the pyrolysis of ethylbenzene; cf. Table 2) the numerical values of ε_i for the two groups of radicals r_m and r_n are approximated by equations (3) and (4), respectively:

$$\varepsilon_m = \frac{\text{rate constant of initial reaction}}{(\text{rate constant of the reaction } (r_m + M)) \times M_0} \quad (3)$$

$$\varepsilon_n = \frac{\text{rate constant of initial reaction}}{\text{rate constant of the reaction of } r_n} \quad (4)$$

(M_0 = initial concentration of the educt M). In cases in which there are more than one initiation or consecutive reactions of the radicals, the sum of the rate constants of these reactions has to be used. As the number of the reactions involved in consumption of a certain radical is usually small, calculations of ε_i can be easily performed if the corresponding kinetic constants are known. The values ε_m and ε_n obtained have to be multiplied by a value η_0 which considers that part of the reactant M reacting *via* the initial reaction.

Finally, the magnitude of the product $\varepsilon_i \times \eta_0$ is the quantitative measure for the applicability of QSSA[28,29]. Comparisons of QSSA calculations with "exact" calculations show that QSSA is a good approximation if $\varepsilon_i \times \eta_0 \leq 10^{-2}$. Rough estimations can be carried out up to $\varepsilon_i \times \eta_0 = 10^{-1}$. Theoretical studies confirm the general existence of these critical values[30]. Another question is whether the $\varepsilon_i \times \eta_0$ values of all radicals participating in the reaction have to be calculated. For the model of hydrocarbon pyrolysis only the $\varepsilon_i \times \eta_0$-values of the "important" radicals have to be considered; "important" radicals are those formed in the reactions of the starting materials and those which react with the starting materials.

As an example, the comparison of QSSA data with the "exact" calculations of the ethylbenzene pyrolysis are shown in Figure 1. The conversion of the reactant and of three "important" radicals as a function of time at 950 K are shown[28]. The results show that the highest $\varepsilon_i \times \eta_0$-values are obtained for the CH_3 radical, and that the deviations are already considerable at $\varepsilon_i \times \eta_0 = 10^{-2}$. Furthermore, it is shown that disagreement is higher at low pressures.

4. Applications

4.1. Oxidation of Isobutane and Isopentane

The peroxide-initiated oxidation of isobutane and isopentane at relatively low temperatures was chosen as one of the first examples of the application of modern numerical methods of integration to complicated homogeneous gas phase reactions. The reaction models contained 20 and 32 elementary reactions, respectively[31]. The product distribution of both reactions showed good agreement with experimental data. Another result of the calculations was that the concentrations of some of the radicals remained nearly constant over a longer period of reaction time, confirming the existence of a steady state under these conditions.

4.2. Pyrolysis of Alkanes

A fundamental study of *Allara* and *Edelson* deals with the thermal decomposition of propane, *n*-butane, and *n*-pentane[5]. Very extensive reaction models were used which contain almost all the possible elementary reactions (293, 515, and 586, respectively), assuming that the products have a molecular weight not greater than twice that of the reactant. The authors adopted the philosophy "that it is far better to err on the side having too many reactions than too few". The calculations were compared with experimental data only for the pyrolysis of propane, and then only for the formation of methane. Nethertheless, interesting information was obtained by the calculations, *e.g.* on the contributions of particular reaction paths to the conversion, or on the concentration-time relation of selected radicals during the reaction, and on changes in the reaction behavior due to global variations of the reaction constants.

Froment et al.[32] studied a similar problem. A reaction scheme consisting of 133 elementary reactions was compiled, and it was assumed that this master set is applicable to the pyrolysis of saturated and unsaturated hydrocarbons generally. In order to set up a special reaction model, a suitable selection of elementary reactions (50 to 80) was taken from the master set by "trial and error" methods. The mathematical treatment of those reaction models was carried out using *Gear*'s program. Comparison of the calculated results with experimental data from a pilot reactor demonstrated that product distributions of the cracking reactions of ethane, propane, *n*-butane, and isobutane as well as of the corre-

[*] Quantitative information about the initial period can be obtained, however, by a suitable transformation of the time within the set of differential equations.

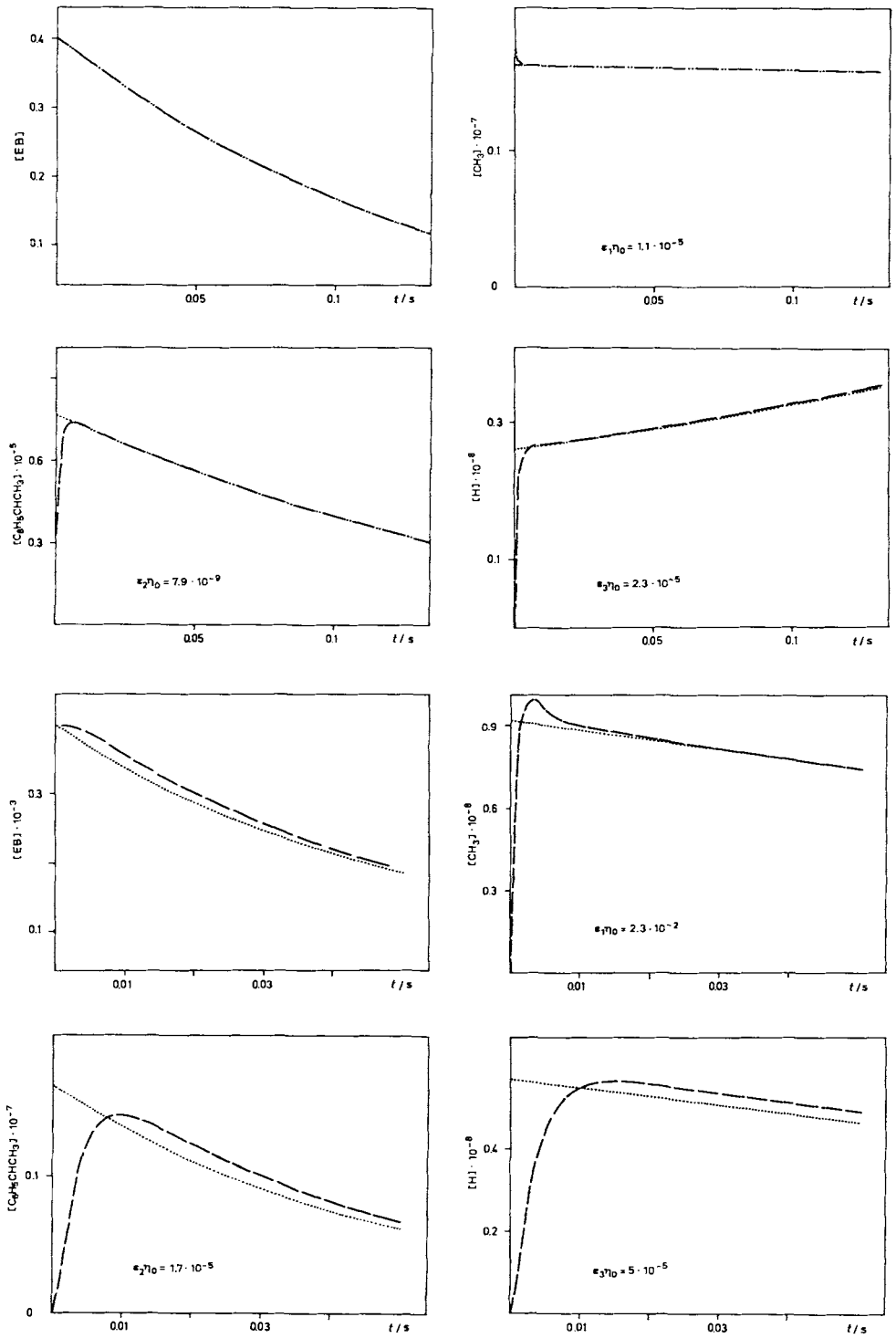


Fig. 1. Variation of concentration with time (time-conversion diagram) of ethylbenzene (EB), methyl, α-methylbenzyl, and hydrogen radicals at 950 K and 3×10^6 Nm^{-2} (30 bar) (left row) and at 3×10^3 Nm^{-2} (0.03 bar) (right row) according to QSSA (·····) and "exact" calculations (-----).

sponding olefins could be simulated satisfactorily. Distributions of the unstable products and the temperature profile along the flow reactor were further points of information obtained from the calculations. Simulation of the decomposition reactions of mixtures of the above mentioned hydrocarbons showed that the combination of reaction models by simple addition of the respective elementary reactions gave results in good agreement with experimental data. This is to be expected as long as the elementary reactions are independent and do not influence one another.

4.3. Pyrolysis of Ethylbenzene

The thermal decomposition of ethylbenzene was thoroughly investigated experimentally and computationally[33]. In order to establish the reaction model (Table 2) the stable and unstable species formed at low pressures (10^{-2} mbar) and 600—1400 K were determined by mass spectrometry[34]. Figure 2 shows the results, containing only those masses whose signal area contributed at least 1.5% to the total signal area. (Because of the different ionization propabilities of the

particular species this selection is somewhat arbitrary.) Up to 1100 K the following species were detected (the figures in parenthesis refer to the possible reaction(s) of formation in Table 2): methane (3), ethylene (8—11), benzene (4), benzyl (1), toluene (14), styrene (7), α-methylbenzyl (3—5), and bibenzyl (15), as well as undecomposed reactant.

reactions (6, 10, 11). Reactions involving a hydrogen atom attack on the aromatic ring are well known in the literature[14, 15, 35]. The experimental styrene-benzene ratio (Fig. 3) was used to adjust the competitive reactions (7) and (8), the ethylene-styrene ratio (Fig. 4) was used for the adjustment of the competitive reactions (5) and (6). With the model of Table 2 the experimental results were in good agreement up to 1150 K. At higher temperatures the formation of benzene and toluene was markedly higher than the calculated values. The model could only be adapted by adding a second initial reaction (2) and the consecutive reaction (9). With these the reaction model of the pyrolysis of ethylbenzene was increased to 15 elementary reactions.

Table 2. Reaction model of the pyrolysis of ethylbenzene (computer diagram). a: Kinetic parameters evaluated by analogy.

Reaction No.	Elementary reaction			$\log_{10}A/E_a$	Ref.
(1)	C6H5CH2CH3	→	C6H5CH2 + CH3	(15.3 /305.4)	(16)
(2)	C6H5CH2CH3	→	C6H5 + C2H5	(16.0 /347.3)	a
(3)	C6H5CH2CH3 + CH3	→	CH4 + C6H5CHCH3	(7.82/ 29.3)	(13)
(4)	C6H5CH2CH3 + C6H5	→	C6H6 + C6H5CHCH3	(11.0 / 31.4)	a
(5)	C6H5CH2CH3 + H	→	H2 + C6H5CHCH3	(10.5 / 21.0)	a
(6)	C6H5CH2CH3 + H	→	C8H11	(11.0 / 46.0)	a
(7)	C6H5CHCH3	→	C6H5CHCH2 + H	(14.85/125.5)	(16)
(8)	C6H5CHCH3	→	C2H4 + C6H5	(14.85/182.0)	a
(9)	C2H5	→	C2H4 + H	(13.0 /125.5)	(16)
(10)	C8H11	→	C2H4 + C6H7	(13.0 /105.0)	a
(11)	C6H7	→	C2H4 + C4H3	(13.0 /105.0)	a
(12)	C4H3	→	C4H2 + H	(13.0 /105.0)	a
(13)	CH3 + CH3	→	C2H6	(10.34/ 0.0)	(16)
(14)	H + C6H5CH2	→	C6H5CH3	(11.0 / 0.0)	a
(15)	C6H5CH2 + C6H5CH2	→	C6H5CH2CH2C6H5	(11.9 / 0.0)	a

Numerical integrations were performed with the most simple reaction models developed from these results (Table 2) using *Gear*'s program. The kinetic constants of the elementary reactions were taken from the literature. Values of constants not known in the literature were estimated from analogous reactions. The calculated results were compared with experimental data from a laboratory flow reactor using a gas chromatograph for analysis[33].

The mass balance showed that part of the ethylene is formed from cleavage reactions of the aromatic ring already at relatively low temperatures. This was accounted for by

Figure 5 shows that the model simulates the reaction very well at relatively short reaction times and within a wide temperature range. As Figure 6 shows, the agreement of the time-conversion plots is not as good. The simulations of the

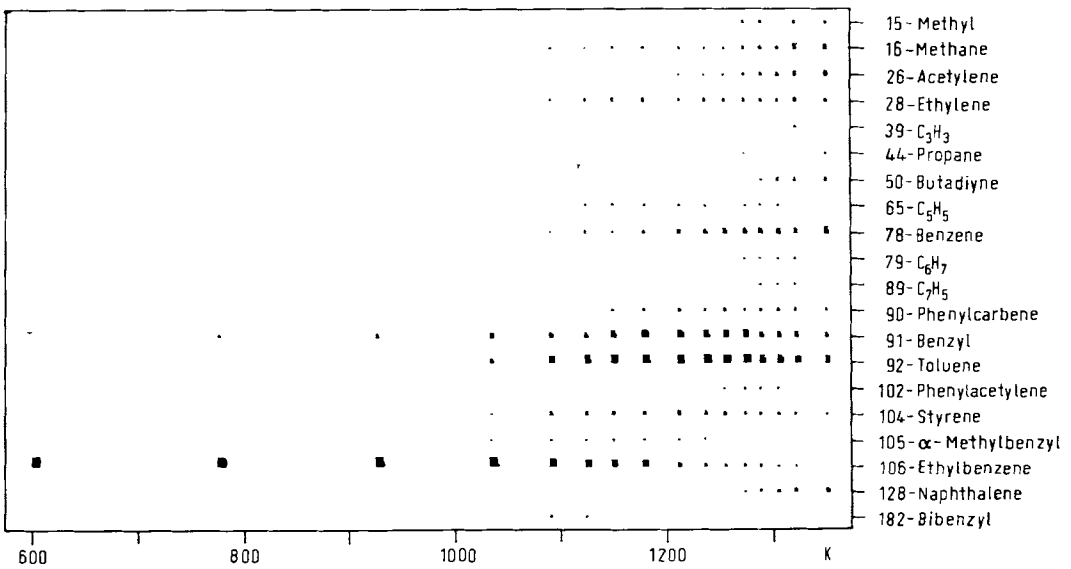


Fig. 2. Mass distribution in the pyrolysis of ethylbenzene in dependence of the temperature.

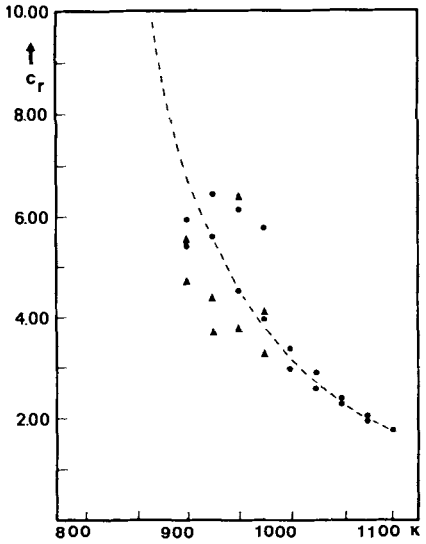


Fig. 3. Styrene/benzene ratio in dependence of the temperature (▲● experimental values, ----- calculated values).

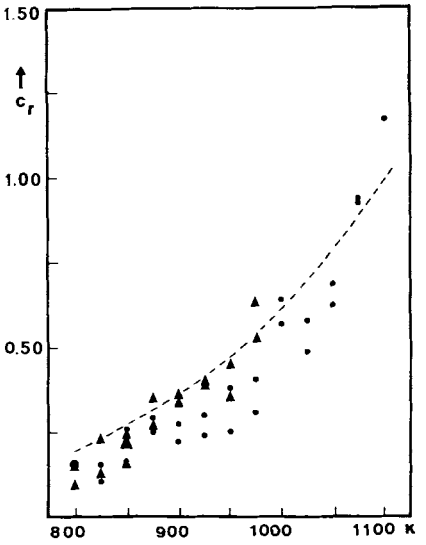


Fig. 4. Ethylene/styrene ratio in dependence of the temperature (see Fig. 3).

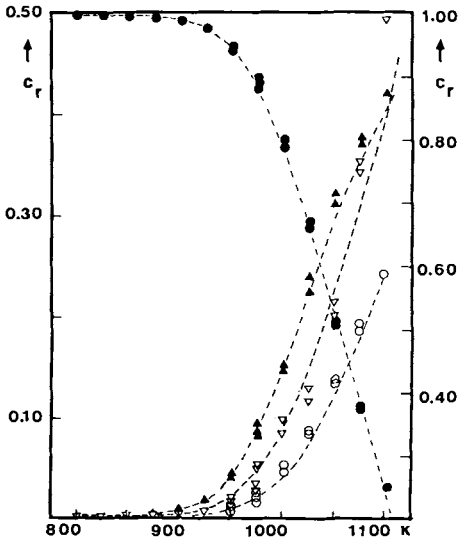


Fig. 5. Comparison of relative molar concentrations as function of temperature (● ethylbenzene; ▲ styrene; ▽ ethylene; ○ benzene; ---- calculated curves).

benzene and ethylene formation agree reasonably well, but the calculated conversion values of ethylbenzene and styrene disagree strongly with the experiments. A possible reason is the existence of reactions of styrene, decompositions, as well

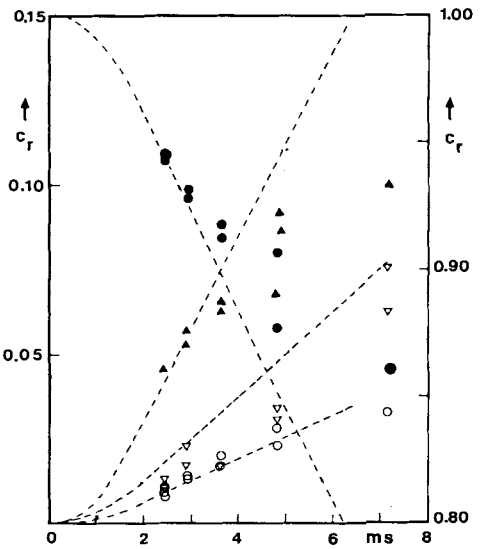


Fig. 6. Comparison of relative molar concentrations as function of time at 950 K (see Fig. 5).

as reactions with radicals. Because these reactions are very similar to those of ethylbenzene, the calculations for benzene and ethylene are not so strongly affected.

4.4. Pyrolysis of *n*-Hexane

In the last few years the pyrolysis of *n*-hexane has been investigated more intensively[36 40]. Hexane is a kind of key substance. The molecule is large enough to be considered as a model for higher paraffins, but the product distribution is not too complicated. In order to describe the reaction at relatively low temperatures and conversions a reaction model consisting of 38 elementary reactions[28] is satisfactory (Table 3). Calculations showed that the reaction rate determined in a static apparatus by the overall pressure rise can be simulated well enough (Fig. 7). Table 4 shows that experimental and calculated product distributions also agree well. At higher conversions, however, product reactions have to be considered, the reaction model then extends to about 100 elementary reactions.

The decomposition and isomerization reactions of the C_6H_{13} radicals (23—28) are of particular importance[42 48]. Calculations showed that the ratio *n*-hexyl/1-methylpentyl has a decisive influence on the ratio of the products ethylene/propene, and that in the temperature range studied the rate of the isomerization of *n*-hexyl → 1-methylpentyl is considerably higher than the rate of decomposition of the radicals. Therefore the equilibrium, which is shifted in the direction of 1-methylpentyl is established rapidly, and the most important decomposition reaction is (24). Application of the β-rule to the decomposition reactions of the C_6H_{13} radicals indicates a ratio of reactions (23—26) of about 1:14:1.5:9. This also confirms the importance of (24).

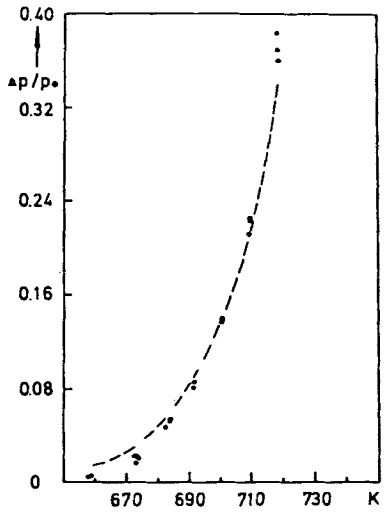


Fig. 7. Pressure rise in the pyrolysis of *n*-hexane (• experimental values; ---- calculated curve).

4.5. Oxidation of Carbon Monoxide

Pilling and *Noyes* have done some work on the oxidation of carbon monoxide by oxygen in the presence of water[49,50]. This reaction is explosive in a particular pT range. The reaction model used consists of 24 elementary reactions, selected mainly from chemical considerations. Most of the kinetic constants were taken from the literature (Table 5). For regions showing a nonexplosive behavior, computations were carried out for a flow reactor assuming a steady state and taking into account heat flow across the reactor wall. The concentrations of the radicals, the reaction rates of the elementary reactions, and the rate of heat formation inside the reactor were calculated. The heat flow was determined as a function of temperature, pressure, and the geometry of the reactor. The explosion limit was defined as the temperature at which the heat formed in the reaction cannot be completely removed.

The calculations indicate that the "critical" temperature is highly dependent on traces of water. An increase in water content from 1 to 10 to 100 ppm lowers the critical temperature from 1100 to 1000 to 900 K. Further the calculations showed that the influence of water occurs essentially *via* the reaction chains (4), (5) and (4), (12), (18) (Table 5).

4.6. Reactions in the Atmosphere

A number of publications deal with photochemically initiated reactions in the atmosphere[29,58]. Topics of interest are

Table 3. Reaction model of the pyrolysis of *n*-hexane (computer diagram). a: Kinetic parameters evaluated by analogy.

Reaction No.	Elementary reaction			$\log_{10}A/E_a$	Ref.
(1)	C6H14	→	CH3 + C5H11	(17.2/353.4)	a
(2)	C6H14	→	C2H5 + C4H9	(16.6/343.3)	a
(3)	C6H14	→	C3H7 + C3H7	(16.0/340.8)	(41)
(4)	C6H14 + H	→	H2 + 1-C6H13	(9.0/ 42.3)	a
(5)	C6H14 + H	→	H2 + 2-C6H13	(10.3/ 39.4)	a
(6)	C6H14 + H	→	H2 + 3-C6H13	(10.0/ 39.4)	a
(7)	C6H14 + CH3	→	CH4 + 1-C6H13	(8.7/ 48.1)	(13)
(8)	C6H14 + CH3	→	CH4 + 2-C6H13	(8.9/ 40.2)	(13)
(9)	C6H14 + CH3	→	CH4 + 3-C6H13	(8.6/ 40.2)	(13)
(10)	C6H14 + C2H5	→	C2H6 + 1-C6H13	(7.8/ 52.8)	a
(11)	C6H14 + C2H5	→	C2H6 + 2-C6H13	(8.0/ 43.5)	a
(12)	C6H14 + C2H5	→	C2H6 + 3-C6H13	(7.7/ 43.5)	a
(13)	C6H14 + C3H7	→	C3H8 + 1-C6H13	(7.6/ 52.8)	a
(14)	C6H14 + C3H7	→	C3H8 + 2-C6H13	(7.8/ 43.5)	a
(15)	C6H14 + C3H7	→	C3H8 + 3-C6H13	(7.5/ 43.5)	a
(16)	C2H5	→	C2H4 + H	(13.5/170.4)	(16)
(17)	C3H7	→	C3H6 + H	(13.8/159.1)	(16)
(18)	C3H7	→	C2H4 + CH3	(13.6/138.6)	(16)
(19)	C4H9	→	C3H6 + CH3	(12.1/113.5)	(16)
(20)	C4H9	→	C2H4 + C2H5	(13.6/121.4)	(16)
(21)	C5H11	→	C3H6 + C2H5	(12.5/116.8)	(5)
(22)	C5H11	→	C2H4 + C3H7	(12.6/120.2)	(5)
(23)	1-C6H13	→	C2H4 + C4H9	(12.6/120.2)	a
(24)	2-C6H13	→	C3H6 + C3H7	(13.5/108.9)	(15)
(25)	3-C6H13	→	C5H10 + CH3	(12.6/120.2)	a
(26)	3-C6H13	→	C4H8 + C2H5	(14.3/113.5)	a
(27)	1-C6H13	→	2-C6H13	(11.0/ 57.4)	(5)
(28)	2-C6H13	→	1-C6H13	(11.1/ 69.5)	(5)
(29)	CH3 + CH3	→	C2H6	(11.0/ 0.0)	a
(30)	CH3 + C2H5	→	C3H8	(10.6/ 0.0)	a
(31)	C2H5 + C2H5	→	C4H10	(10.6/ 0.0)	a
(32)	H + H	→	H2	(10.6/ 0.0)	a
(33)	C3H7 + C3H7	→	Tar	(10.6/ 0.0)	a
(34)	C4H9 + C4H9	→	Tar	(10.6/ 0.0)	a
(35)	C5H11 + C5H11	→	Tar	(10.6/ 0.0)	a
(36)	1-C6H13 + 1-C6H13	→	Tar	(10.6/ 0.0)	a
(37)	2-C6H13 + 2-C6H13	→	Tar	(10.6/ 0.0)	a
(38)	3-C6H13 + 3-C6H13	→	Tar	(10.6/ 0.0)	a

Table 4. Comparison of the product distribution (%) of the pyrolysis of *n*-hexane; 700 K, 1.3×10^4 Nm^{-2} (0.13 bar), 15% conversion.

Product	exp.	calc.
H2	-	1.42
CH4	20.83	23.51
C2H4	22.18	23.53
C2H6	13.76	11.18
C3H6	26.64	26.78
C3H8	1.39	1.59
C4H8	12.95	11.45
C5H10	2.24	0.46

by "mathematical modeling" is an important tool in chemical kinetics. In mathematics this is called the "inverse problem". A non-linear least-squares fit in dependence of the reaction parameters is performed using possibly weighted experimental data and values calculated from the model (W_i = weighting factors):

$$\sum_{i}^{n} (x_{i,\text{exp.}} - x_{i,\text{calc.}})^2 \times W_i = F(\doteq \min) \tag{5}$$

Function F should be minimized.

Table 5. Reaction model of CO oxidation (computer diagram). a: Kinetic parameters evaluated by analogy.

Reaction No.	Elementary reaction			$\log_{10}A/E_a$	Ref.
(1)	CO + O2	→	CO2 + O	(8.35 /251.2)	(51)
(2)	CO + O + M	→	CO2 + M	(8.00 / 0.0)	(52)
(3)	H2O + O	→	2OH	(10.76 / 75.4)	(53)
(4)	CO + OH	→	CO2 + H	(8.49 / 2.5)	(55)
(5)	O2 + H	→	OH + O	(11.35 / 70.3)	(54)
(6)	OH + O	→	O2 + H	(10.40 / 0.0)	(55)
(7)	H2O + H	→	H2 + OH	(10.92 / 84.2)	(53)
(8)	H2 + O	→	OH + H	(10.24 / 39.6)	(53)
(9)	H2 + OH	→	H2O + H	(10.36 / 21.8)	(55)
(10)	OH + OH	→	H2O + O	(9.76 / 3.8)	(53)
(11)	OH + H + M	→	H2O + M	(11.00 / 0.0)	(56)
(12)	O2 + H + M	→	HO2 + M	(9.51 / -4.2)	(54)
(13)	HO2 + OH	→	H2O + O2	(10.70 / 4.2)	(57)
(14)	HO2 + H	→	H2O + O	(10.70 / 4.2)	(57)
(15)	HO2 + H	→	H2 + O2	(10.40 / 2.9)	(57)
(16)	HO2 + H	→	2OH	(11.40 / 8.0)	(57)
(17)	HO2 + O	→	O2 + OH	(10.70 / 4.2)	(57)
(18)	CO + HO2	→	CO2 + OH	(8.00 / 41.9)	(57)
(19)	HO2 + HO2	→	H2O2 + O2	(10.00 / 4.2)	(57)
(20)	H2O2 + OH	→	H2O + HO2	(10.00 / 7.5)	(54)
(21)	H2O2 + H	→	H2 + HO2	(10.37 / 38.5)	(54)
(22)	H2O2 + H	→	H2O + OH	(11.50 / 37.7)	(54)
(23)	H2O2 + O	→	HO2 + OH	(10.70 / 5.0)	a
(24)	H2O2 + M	→	2OH + M	(14.07 /190.5)	(54)

the influence of particular substances emitted from the earth's surface on the ozone layer in the upper atmosphere, and the formation of smog. One of the most interesting examples was the formation of the Los Angeles smog, which was studied using a model of 92 elementary reactions[29]. In this work, the main problem is the formulation of suitable reaction models. The calculated time dependence of the reaction systems agreed relatively well with the experimental data obtained in a smog chamber. The computations are rather complex because of fluctuations in the radiation density and because of the need to include diffusion processes and convective transport phenomena in the calculations, which are difficult to describe exactly.

Though experimental results can be only partly explained by model computations, important information has been attained on the participation of particular substances in smog formation, and there is no doubt that these methods will help to increase our understanding of chemical reactions in the atmosphere and their further consequences.

5. The "Inverse Problem"

5.1. Evaluation of Kinetic Constants

Besides the "simulation" of chemical reactions, the evaluation of kinetic constants of particular elementary reactions

The usual mathematical methods for the solution of such optimization problems can be divided into two groups:

1) Direct search methods: For each experimental value a corresponding value has to be calculated according to a model. The set of optimal parameters is obtained by a systematic search of certain parameter sets, frequently expressed as lattice points in higher dimensions.

2) Descent methods: These methods require in addition to the function F also the partial derivatives of F with respect to the parameters. These derivatives are used to find the steepest descent to the minimum of F.

Bremermann and *Milstein* tested a number of different methods from each group[59]. A direct search method with random vectors proved to be most effective and robust. The direction indicating the variation of the parameter vector is chosen by a random number generator. The "best" parameter set in this direction is determined by a special iteration method. This new parameter set is the starting point for the next random vector, and the calculation is continued until the new random vectors do not result in further improvements of the parameter sets. This method was applied to experimental data from the Calvin photosynthesis cycle[61]. The reaction model consisted of 22 reactions with 18 species. Optimal reaction constants were calculated for all reactions. The model calculation agreed very well with the experimental time behavior of the 18 species within the course of the reaction.

Another method, which is often more effective although more cumbersome, is the frequently used "trial-and-error" approach. The "improvement step", *i.e.* the selection of the new parameter set, is executed "manually" taking into account all the previous results.

In the numerical optimization procedure it is the "stiff solver" subroutine which demands the greatest proportion of computer time. Therefore, the greatest potential for improving the method lies in this area. The steady-state assumption decreases the computational effort considerably. Various parameters or relations between parameters can then often be evaluated and described by simple linear regression. Thus it is hardly surprising that nearly all parameter fittings in complex reaction systems assume QSSA conditions.

It may happen that in such a parameter optimization procedure the minimum of the function F can be determined, but no satisfactory consistency between the experimental and the calculated values is obtained. This is a clear indication that the chemistry of the reaction model is incorrect.

5.2. Sensitivities of Kinetic Parameters

If for a reaction mechanism one of the optimization methods yields a set of parameter values which fits the experimental results well, an often heard objection is that almost any conceivable set of data can be simulated by so many parameters (even the shape of an elephant!), and that all these sets of parameters will describe the measurements more or less correctly. This objection is fundamentally wrong, as can be clearly demonstrated by an error analysis of the individual parameters. This is best done by evaluating a sensitivity matrix, which contains the variations of the concentrations of the different chemical species in dependence of the variations of the parameters of the individual elementary reactions. Such sensitivity matrices also depend on temperature, initial conditions, and reaction time. Table 6 shows the sensitivity matrix of the model for hexane pyrolysis (Table 3) at 718 K and initial concentrations of 0.0023 mol/l within the steady-state region.

The columns contain the stable compounds, and the rows contain the elementary reactions. The elements of the matrix represents the percentage change in concentration of a particular species if the reaction constant of the corresponding elementary reaction is increased by a factor of 2. (In fact, however, the coefficients were calculated with the assumption of a differential variation of the system.) Negative values indicate that the concentrations decrease. The matrix of Table 6 was calculated assuming a steady state, which remarkably reduced the computational effort. A comparison shows that in this case the agreement of the QSSA values with the "exact" values is better than 0.1% under the conditions chosen.

The matrix demonstrates that there are only a few reaction constants which significantly influence the concentrations of most of the products. Most rate constants are "insensitive" and their absolute values have little influence on the product

Table 6. Sensitivity matrix of the reaction model of the pyrolysis of *n*-hexane (see Table 3) (computer diagram).

Product / Reaction	C6H14	H2	CH4	C2H4	C2H6	C3H6	C3H8	C4H8	C4H10	C5H10	Tar
1	18	18	18	18	17	18	18	18	35	18	35
2	24	23	23	24	24	23	24	23	47	23	47
3	9	9	9	9	9	9	9	9	18	9	18
4	0	0	0	0	-0	0	0	-0	-0	0	0
5	3	3	4	4	-1	4	4	-1	-1	4	8
6	-3	-3	-4	-4	1	-4	-4	1	1	-4	-8
7	6	6	9	9	-0	9	9	-0	-0	9	18
8	37	36	53	52	-0	53	53	-1	-1	53	107
9	-32	-31	-51	-50	12	-51	-51	12	23	-51	-102
10	9	6	10	10	7	10	10	6	-3	10	20
11	65	46	73	71	50	73	73	47	-22	73	145
12	9	-0	-0	-0	31	-0	-0	29	-0	-0	0
13	0	-0	-0	-0	0	0	8	-0	0	0	-0
14	2	-0	-0	-0	0	2	61	-0	0	3	-0
15	-2	-2	-4	-4	1	-3	27	1	1	-2	-8
16	4	34	4	6	-1	4	4	4	-1	4	8
17	0	66	-4	-4	1	5	-4	1	1	0	-9
18	1	-61	10	10	1	-3	-89	1	2	1	-179
19	0	0	0	0	-0	0	0	0	-0	0	0
20	-0	-0	-0	-0	0	-0	-0	-0	0	-0	-0
21	-0	-0	-0	-0	0	-0	-0	-0	0	-0	-0
22	0	0	0	0	-0	0	0	0	-0	0	0
23	-1	-1	-1	-0	0	-1	-1	-1	0	-1	-2
24	0	2	1	2	-0	3	3	0	-0	-97	5
25	0	-1	0	-2	0	-2	-2	0	0	98	-4
26	0	0	0	0	0	0	0	0	0	0	-0
27	1	1	1	0	-0	1	1	1	-0	1	2
28	-1	-1	-1	-0	0	-1	-1	-1	0	-1	-2
29	-2	-2	-2	-2	-2	-2	-2	-2	-5	-2	-5
30	-6	-6	-6	-6	-6	-6	-6	-6	-12	-6	-12
31	-40	-40	-40	-40	-40	-40	-40	-40	19	-40	-80
32	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	0	0
33	-1	-1	-1	-1	-1	-1	-1	-1	-2	-1	98
34	-0	-0	-0	-0	-0	-0	-0	-0	-0	-0	0
35	0	0	0	0	0	0	0	0	0	0	0
36	-0	-0	-0	-0	-0	-0	-0	-0	-0	-0	0
37	-0	-0	-0	-0	-0	-0	-0	-0	-0	-0	0
38	0	0	0	0	0	0	0	0	0	0	0

distribution. From different sensitivity matrices evaluated on the basis of different experimental parameters a new matrix can be calculated containing the variances (standard deviations) and covariances of the reaction parameters[60]. These variances depend again on the experimental conditions (number of measurements, initial conditions, temperature, *etc.*) and on the accuracy of the experimental data. Thus, if a given kinetic parameter is to be evaluated with greater accuracy from experimental data, the experimental conditions must be such that the variance becomes as small as possible. This can also be done by selecting special initial conditions, *e.g.* by the addition of reactants which increase the sensitivity of the elementary reaction in question. Another possibility is the selection of another reaction system in which this particular elementary reaction has *a priori* a high sensitivity.

6. Outlook

Work on the kinetics of complicated chemical reactions with the aim of solving all the details of a given mechanism and its dynamics were considered to be more or less hopeless until recently, because no methods were available for evaluating more general quantitative conclusions from the experimental materials. Today the very opposite seems to apply.

Computational methods for kinetic treatment of even complicated chemical systems have been developed to a high standard, and they will surely be further improved. As computer capacity becomes much more readily available in the future, these methods will become more generally applicable. The quality of the reaction model will then be the limiting factor. The quality of models, however, largely depends on the accuracy with which the kinetic constants of the particular elementary reactions are known. Therefore methods of experimental determination and evaluation of kinetic constants will become more important.

The application of such methods will initially be focused upon more special problems such as the effect of additional substances on reaction rates and product distributions. Within this kind of work the "inverse problem" and sensitivity analysis play an important part in obtaining quantitative information. The scope of these methods will be enhanced if they can be extended to the computation of heterogeneous reactions too. For this type of reaction, absorption, desorption, and diffusion processes have to be included in the reaction scheme. This does not mean that the reaction models become more complicated. On the contrary, in catalytic processes the number of "important" elementary reactions is comparatively small.

Although the methods outlined above may be viewed with skepsis, perhaps due to the complicated mathematics involved, they nevertheless supply detailed information about the mechanism and time dependence of complicated reactions and permit a fast and reliable simulation of the influences of different parameters on chemical reactions. This is a significant progress in chemical kinetics.

Received: October 31, 1979 [A 315 IE]
German version: Angew. Chem. *92*, 331 (1980)

[1] *M. Bodenstein*, Z. Phys. Chem. *85*, 329 (1913).
[2] *E. Stieffel:* Einführung in die numerische Mathematik. Teubner, Stuttgart 1970.
[3] *S. W. Benson:* The Foundations of Chemical Kinetics. McGraw-Hill, New York 1960.
[4] *V. N. Kondratiev:* Chemical Kinetics of Gas Reactions. Pergamon Press, Oxford 1964.
[5] *D. L. Allara, D. Edelson*, Int. J. Chem. Kinet. *7*, 479 (1975).
[6] *J. Wei, C. W. Kuo*, Ind. Eng. Chem. Fundam. *8*, 114, 124 (1969).
[7] *Y. Ozawa*, Ind. Eng. Chem. Fundam. *12*, 191 (1973).
[8] *S. V. Golikeri, D. Luss*, Chem. Eng. Sci. *29*, 845 (1974).
[9] *S. M. Jacob, B. Gross, S. E. Voltz, V. W. Weekman, Jr.*, AIChE J. *22*, 701 (1976).
[10] *G. L. Pratt:* Gas Kinetics. Wiley, London 1969.
[11] *M. R. Mulcahy:* Gas Kinetics. Nelson, London 1973.
[12] *L. H. Bamford, C. F. H. Tipper:* Comprehensive Chemical Kinetics. Vol. 1. Elsevier, Amsterdam 1969.
[13] *J. A. Kerr, M. J. Parsonage:* Evaluated Kinetic Data on Gas Phase Hydrogen Transfer Reactions of Methyl Radicals. Butterworth, London 1976.
[14] *J. A. Kerr, M. J. Parsonage:* Reactions of Atoms and Radicals with Alkenes, Alkynes, and Aromatic Compounds. Butterworth, London 1972.
[15] *V. N. Kondratiev:* Rate Constants of Gas Phase Reactions. NSRDS-NBS, Washington 1972.
[16] *S. W. Benson, H. E. O'Neal:* Kinetic Data on Gas Phase Monomolecular Reactions. NSRDS-NBS 21, Washington 1970.
[17] *S. W. Benson:* Thermochemical Kinetics. Wiley, New York 1976.
[18] *S. W. Benson*, Int. J. Chem. Kinet. Symp. *1*, 359 (1975).
[19] *Y. N. I. Chan, I. Birnbaum, L. Lapidus*, Ind. Eng. Chem. Fundam. *17*, 133 (1978).
[20] *W. C. Gear:* Numerical Initial Value Problems in Ordinary Differential Equations. Prentice-Hall, New York 1972.
[21] *B. A. Gottwald:* Preprints Discussion Meeting: Kinetics of Physicochemical Oscillations. Aachen 1979.
[22] *P. Deuflhard*, personal communication.
[23] *R. E. O'Malley:* Introduction to Singular Perturbation Theory. Academic Press, New York 1974.
[24] *A. H. Nayfeh:* Perturbation Methods. Wiley, New York 1973.
[25] *C. di Prima Richard:* Modern Modeling of Continuum Phenomena. Vol. 16. American Mathematical Society, Providence, Rhode Island 1977.
[26] *W. Schneider:* Mathematische Methoden der Störungsmechanik. Vieweg, Braunschweig 1978.
[27] *C. E. Pearson:* Handbook of Applied Mathematics. Van Nostrand Reinhold, New York 1974, Chap. 14.
[28] *K. H. Ebert, H. J. Ederer, G. Isbarn*, Preprint No. 31, SFB 123, Universität Heidelberg 1979.
[29] *E. Hesstvedt, Ö. Hov, I. S. A. Isaksen*, Int. J. Chem. Kinet. *10*, 971 (1978).
[30] *F. C. Hoppenstedt*, personal communication.
[31] *D. L. Allara, D. Edelson, K. C. Irwin*, Int. J. Chem. Kinet. *4*, 345 (1972).
[32] *K. M. Sundaram, G. F. Froment*, Ind. Eng. Chem. Fundam. *17*, 174 (1978).
[33] *K. H. Ebert, H. J. Ederer, P. S. Schmidt*, ACS Symp. Ser. *65*, 313 (1978).
[34] *H. J. Ederer*, Dissertation, Universität Heidelberg 1975.
[35] *K. Hoyermann, A. W. Preuss, H. Gg. Wagner*, Ber. Bunsenges. Phys. Chem. *79*, 156 (1975).
[36] *F. E. Frey, H. J. Hepp*, Ind. Eng. Chem. *25*, 441 (1933).
[37] *J. Chrysochoos, W. A. Bryce*, Can. J. Chem. *43*, 2092 (1965).
[38] *L. Szepesy, V. Illes, K. Welther, J. Simon*, Acta Chim. Acad. Sci. Hung. *78*, 341 (1973).
[39] *V. Illes, K. Welther, I. Pleszkats*, Acta Chim. Acad. Sci. Hung. *78*, 357 (1973).
[40] *V. Illes, I. Pleszkats, L. Szepesy*, Acta Chim. Acad. Sci. Hung. *79*, 259 (1973).
[41] *W. Tsang*, J. Phys. Chem. *76*, 143 (1972).
[42] *A. Kossiakoff, F. O. Rice*, J. Am. Chem. Soc. *65*, 590 (1943).
[43] *A. S. Gordon, J. R. McNesby*, J. Chem. Phys. *31*, 853 (1959).
[44] *M. J. Pearson, B. S. Rabinovitch*, J. Chem. Phys. *42*, 1624 (1965).
[45] *F. Doue, G. Guiochon*, J. Phys. Chem. *73*, 2804 (1969).
[46] *D. C. Tardy, B. S. Rabinovitch, C. W. Larson*, J. Chem. Phys. *45*, 1163 (1966).
[47] *V. M. Rybin, Yu. P. Yampolskii*, Pet. Chem. USSR *16*, 167 (1976).
[48] *D. A. Leathard, J. H. Purnell*, Annu. Rev. Phys. Chem. *21*, 197 (1970).
[49] *M. J. Pilling, R. M. Noyes*, Int. J. Chem. Kinet. *11*, 821 (1979).
[50] *D. Edelson*, Int. J. Chem. Kinet. *11*, 687 (1979).
[51] *C. H. Yang, A. L. Berlad*, J. Chem. Soc. Faraday Trans. I *70*, 1661 (1974).
[52] *D. L. Baulch, D. D. Drysdale, A. C. Lloyd:* High Temperature Reaction Rate Data, No. 1. Leeds University 1968.
[53] *D. L. Baulch, D. D. Drysdale, A. C. Lloyd:* High Temperature Reaction Rate Data, No. 2. Leeds University 1968.
[54] *D. L. Baulch, D. D. Drysdale, A. C. Lloyd:* High Temperature Reaction Rate Data, No. 3. Leeds University 1969.
[55] *W. E. Wilson*, J. Phys. Chem. Ref. Data *1*, 535 (1972).
[56] *W. A. Trush*, Prog. React. Kinet. *3*, 63 (1972).
[57] *A. C. Lloyd*, Int. J. Chem. Kinet. *6*, 169 (1974).
[58] *S. W. Benson*, Int. J. Chem. Kinet. Symp. *1* (1975).
[59] *J. Milstein, H. J. Bremermann*, J. Math. Biol. *7*, 99 (1979).
[60] *J. Milstein*, J. Appl. Math. *35*, 479 (1978).
[61] *J. A. Bassham, M. Calvin:* The Path of Carbon in Photosynthesis. Prentice Hall, Englewood Cliffs 1957.

Cyclodextrin Inclusion Compounds in Research and Industry

By Wolfram Saenger[*]

α-, β-, and γ-Cyclodextrins are cyclic oligosaccharides consisting of six, seven, or eight glucose units, which can be obtained on a large scale from starch. They form inclusion compounds with smaller molecules which fit into their 5—8 Å cavity. These (crystalline) complexes are of interest for scientific research as, contrary to the classical clathrates, they exist in aqueous solution and can be used to study the hydrophobic interactions which are so important in biological systems. Cyclodextrins also serve as models both for polymeric starch and, in the form of their polyiodide complexes, for "blue iodine-starch". As cyclodextrins catalyze several chemical reactions they and their functionalized derivatives provide useful enzyme models. Cyclodextrins can be used to advantage in the production of pharmaceuticals, pesticides, foodstuffs, and toilet articles—the (micro-encapsulated) active and aromatic substances enclosed within them are protected from the effects of light and atmosphere and can be easily handled and stored in powder form. Substances which are not very soluble in water become more soluble in the presence of cyclodextrins—creams and emulsions can be stabilized, and the growth and yield of grain harvests can be increased. Cyclodextrins can be chemically modified for many different purposes; polymerized cyclodextrin or cyclodextrin bound to a polymer carrier have already been employed in gel inclusion and affinity chromatography.

1. Introduction

The increasing number of publications and patents dealing with inclusion compounds shows that general interest in their physical and chemical properties has grown considerably over the past twenty years. This is due, on the one hand, to the fact that the study of inclusion compounds in fundamental research furnishes information about non-covalent, intermolecular forces and that they also serve as models for studying topochemical problems and the mode of action of enzymes. On the other hand, inclusion compounds are also utilized in laboratories, industry, and the home as ion exchangers, as catalysts in chemical reactions, or for the microencapsulation of sensitive, active, and aromatic substances.

The most important property of inclusion compounds is that a "host" component can admit "guest" components into its cavity without any covalent bonds being formed. Montmorillonites, kaolinites, zeolites, tobernite, transition metal chalcogenides, graphite, and clathrates formed with water[1-6] are all known inorganic host components; urea, deoxycholic acid, tri-*o*-thymotide, *Dianin*'s compound, hydroquinone, crown ethers, and cyclodextrins are organic host components[1,7-18]; biological macromolecules such as ionophoric antibiotics, starch, and enzymes[1,8,19-21] can also take up guest (substrate) components. This article will only deal with the inclusion compounds of cyclodextrins as these substances best demonstrate the possibilities that this class of compounds offers to the research or industrial chemist.

Cyclodextrins were first isolated in 1891 by *Villiers* as degradation products of starch[22] and they were characterized as cyclic oligosaccharides in 1904 by *Schardinger*[23,24]. It is for this reason that cyclodextrins (cycloamyloses) are described by some authors, especially in the older literature, as Schardinger dextrins. In 1938 *Freudenberg et al.* reported that cyclodextrins are constructed from α(1→4)-linked glucose units[25]; the molecular weights of the most common α-, β-, and γ-cyclodextrins were, however, determined much later[26-28] (Figs. 1 and 2, Table 1). *Freudenberg et al.* recognized that cyclodextrins could form inclusion compounds[28] and, like *French et al.*[25,29], worked out procedures for synthesizing pure cyclodextrins. The formation of the cyclodextrin guest complexes was studied systematically by *Cramer et al.*[8,13,30]; *Cramer* also discovered that cyclodextrins have a catalytic action in some reactions[31] and described racemate resolution with cyclodextrins[32]. These experiments laid the foundations for the chemistry discussed in this review.

The present article can only concentrate on some features of general interest as the number of publications dealing with cyclodextrin inclusion compounds alone amounts to more than 600. In the last 25 years several review articles and books on this subject[1,8-17,33-36] have appeared; one book[37],

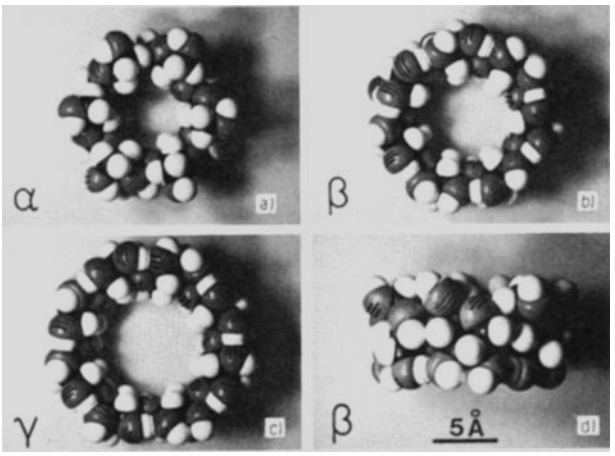


Fig. 1. a) α-Cyclodextrin from the O(6) side, b) and c) β- and γ-cyclodextrins respectively as seen from the O(2), O(3) side with a closed ring of O(3)...O(2) hydrogen bonds between adjacent glucose units; d) side view of β-cyclodextrin (CPK model). All of the cyclodextrins have a ring height of approximately 8 Å (cf. Fig. 2).

[*] Prof. Dr.-Ing. W. Saenger
Abteilung Chemie, Max-Planck-Institut für Experimentelle Medizin
Hermann-Rein-Strasse 3, D-3400 Göttingen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0505-0344 $ 02.50/0

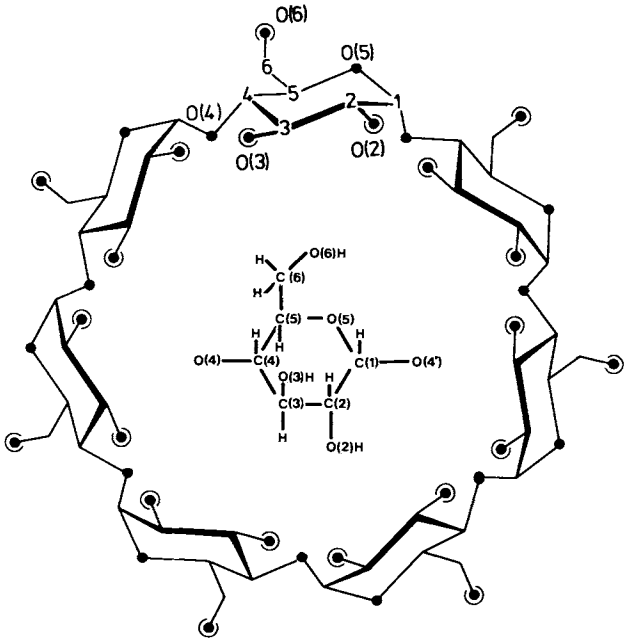


Fig. 2. Chemical structure and numbering of the atoms shown for β-cyclodextrin; ● oxygen atoms, ⊙ hydroxy groups.

and can therefore be utilized for synthesizing interesting new oligo- and polysaccharides[45,46] (G = glucose unit).

As the enzymes never detach entirely specific lengths, the resulting cyclodextrins contain 6—12 glucose units per ring[47]. A five-membered cyclodextrin is unlikely due to ring strain[48] and has not been observed. The main fractions contain α-, β-, and γ-cyclodextrins (with 6, 7, or 8 glucose units respectively); the relative quantities of these three groups depend on the type of enzyme employed and can be influenced by the addition of organic compounds[10,34].

The glycosyl transferase from Bacillus No. 38-2 has proved to be a highly suitable enzyme for the industrial production of β-cyclodextrin. It is still active at 80 °C and at pH 6—10, *i.e.* under conditions which prevent damage by other microorganisms[34]. 80% of the starch is converted to β-cyclodextrin with only small amounts of the other cyclodextrins being produced in the medium[40]. This method has the advantage that there is no need to add an organic compound (which is often toxic) in order to obtain good yields of β-cyclodextrin.

Table 1. Some physical properties of the cyclodextrins. Height of the cyclodextrin ring: 7.9—8 Å (measured with the aid of CPK models).

Cyclodextrin	No. of glucose units	Mol. wt.	Water solubility [a]	$[\alpha]_D^{25}$ (after [29])	Cavity diameter [Å] [b]	External
α	6	972	14.5	150.5 ± 0.5	4.7—5.2	14.6 ± 0.4
β	7	1135	1.85	162.5 ± 0.5	6.0—6.4	15.4 ± 0.4
γ	8	1297	23.2	177.4 ± 0.5	7.5—8.3	17.5 ± 0.4

T	Solubility [c] in					
	water	ethanol	*n*-propanol	glycerol	dimethyl formamide	dimethyl sulfoxide
25 °C	1.79	0.1	0.1	4.3	excellent	
45 °C	3.1	0.1	0.1	0.8		

[a] g/100 ml solution at room temperature (according to [29]). [b] As measured on CPK models (see Fig. 1); the smaller value is for the ring of H atoms bonded to C(5) and the larger value for the ring of H atoms bonded to C(3). [c] g β-cyclodextrin/100 ml solution (according to [36]).

which only describes the chemistry of the cyclodextrins and their use as enzyme models, contains over 300 references.

2. Synthesis of Cyclodextrins

Cyclodextrins can be obtained by enzymatic degradation of starch[23-25,29], a linear polysaccharide consisting of α(1→4)-linked glucose units arranged into a left-threaded screw with six glucose units per turn (V-amylose[38,39,20]). Cyclodextrin glycosyl transferases, a type of amylase, can detach a turn from the starch helix and link the two ends of this fragment to give a cyclic molecule. There are certainly many organisms which contain glycosyl transferases[40], but only those enzymes from *Bacillus macerans*[10,24], *Bacillus megaterium*[41], an alkaline bacillus[42], *Krebsiella pneumoniae M 5 al*[43], and *Bacillus stereothermophilus*[44] have been examined in more detail. All of these glycosyl transferases act according to the scheme

$$G_n \underset{\text{Coupling}}{\overset{\text{Cyclization}}{\rightleftharpoons}} G_{(n-x)} + \text{Cyclodextrin } (= \textit{cyclo}\text{-}G_x)$$

3. Biochemical Properties and Toxicity

The utilization of the sweet tasting cyclodextrins in the pharmaceutical and food industries depends to a large extent on the effects they have on living organisms. The toxicity of β-cyclodextrin (*Thomas* and *French*; cited in [10]) determined with rats is probably accounted for by the fact that the β-cyclodextrin used was not quite pure. In 1963 it was discovered that in rats ^{14}C-labeled α- and β-cyclodextrins, similarly to ^{14}C-starch, are incorporated into tissues and organs[49]. It is remarkable that on feeding ^{14}C-starch the ^{14}C-level of the $^{14}CO_2$ expired reached a maximum after about 1 h whereas, in the case of ^{14}C-β-cyclodextrin, the maximum appeared after approximately 9 h; the total quantity of expired $^{14}CO_2$ when related to the carbohydrate consumed was about equal in both experiments (Fig. 3). The cyclodextrins are not metabolized as rapidly as starch; this is because they are cleaved more slowly by α-1,4-glucanohydrase than linear dextrins[10] and are not hydrolyzed by enzymes which attack terminal groups. The metabolism of degraded cyclodextrins and starch is, however, comparable.

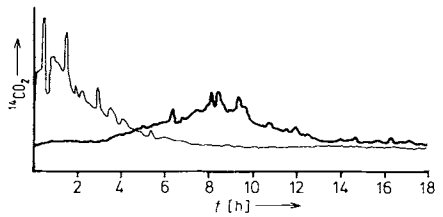


Fig. 3. $^{14}CO_2$ expired by rats after being fed with ^{14}C-labeled starch (—) and ^{14}C-labeled β-cyclodextrin (—) (according to [49]).

Tests for determining the acute toxicity of β-cyclodextrin on mice and rats gave such high LD_{50} values (Table 2[50]) that these compounds can scarcely be considered as having a toxic action. Long term tests carried out over a period of 6—9 months on rats, rabbits, and beagles led to similar conclusions[51 53]. No anatomical or histopathological changes

Table 2. Acute toxicity of β-cyclodextrin (according to [50]).

	LD_{50} [g/kg]	
	Mouse (♂ and ♀)	Rat (♂ and ♀)
Oral	>12.5	>12
Subcutaneous	> 0.9	> 1.5
Intraperitoneal	> 0.9	> 1.2

could be detected after feeding 0.2, 0.4, and 0.6 g β-cyclodextrin/kg body weight for 6 months to rats and dogs; neither embryotoxic nor teratogenic effects nor mutations were observed in rats[53]. Other studies on rats showed that renal necrosis occurred after daily subcutaneous, intraperitoneal, or intravenous injection of 0.45 g β-cyclodextrin/kg body weight. No ill effects could be demonstrated after giving doses of 0.1 g/kg 1, 2, 4, or 7 times daily, whereas daily doses of 0.9 g/kg resulted in death within 4 d[54].

All toxicity tests have shown that orally administered cyclodextrin is harmless. According to reports of the FAO, enzymatically modified starch—this includes cyclodextrins—is also toxicologically harmless[55].

The biochemical properties of cyclodextrins can be defined in more detail if they are allowed to act as substrates for purified enzymes. Cyclodextrins are metabolized by glucanotransferase from *Klebsiella pneumoniae*[56], cyclodextrinases in Taka diastase[57], and by amylases from *Aspergillus niger* and *oryzae* and *Bacillus polymyxa*[34]. They are largely resistant to the action of amylases from *Bacillus subtilis* and human saliva[34] and in general to the action of amylases which degrade linear polysaccharides from their terminus. Cyclodextrins also act as competitive inhibitors for phosphorylase[34,58] and β-amylase[34,59] from potatoes, for pancreatic amylase (which can simultaneously bind three β-cyclodextrin molecules in its active center[60-62]), and for pullulanase from *Aerobacter aerogenes*[63].

4. Synthesis of Cyclodextrin Inclusion Compounds

The most remarkable property of the cyclodextrins is their ability to form inclusion compounds with a variety of molecules which apparently only have to satisfy one condition—they must fit entirely or at least partially into the cyclodextrin cavity. The method used for the synthesis of the cyclodextrin·guest complexes depends on the properties of the guest components[8,30,34].

1) Equimolar quantities or a ten-fold excess of water-soluble substances are dissolved directly in concentrated hot or cold aqueous solutions of the cyclodextrins. The inclusion compounds crystallize out immediately or on slow cooling or evaporation.

2) Substances which are not water-soluble are dissolved in ether, chloroform, benzene, *etc.* and are then shaken with or layered over or underneath a concentrated aqueous cyclodextrin solution. In the case of layering, crystals are formed at the interface or as a precipitate. The inclusion compounds must be washed with an organic solvent to remove any adhering substances.

3) The first two procedures are suitable for the laboratory preparation of cyclodextrin inclusion compounds. For their industrial synthesis, the kneading procedure is more suited. Here the liquid or dissolved guest components are added to a slurry of the cyclodextrin and 2 to 5 times as much water. On stirring in a mixer, the viscosity of the mixture usually increases, giving a paste which can then be dried, powdered, and washed. If the inclusion compounds are readily soluble in water or decompose on drying, it is advisable to lyophilize them. They then retain their finely dispersed form which is of advantage, especially in the pharmaceutical industry, as it has a high solubility.

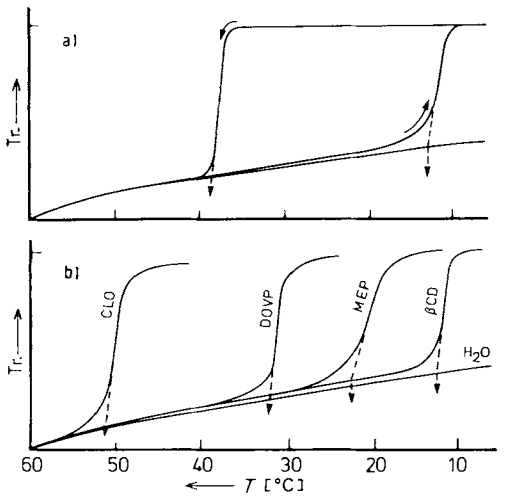


Fig. 4. Turbidity curves a) for 3 per cent. aqueous β-cyclodextrin solutions and b) for these solutions with additives. β: β-cyclodextrin alone; MEP: +0.45% 3-methyl-1-pentyn-3-ol; DDVP: +0.582% *O*-(2,2-dichlorovinyl)-*O*,*O*-dimethylphosphate + 25% ethanol; CLO: +0.57% clofibrinic acid (according to [64]). The turbidity (Tr.) is plotted against temperature. H_2O indicates the zero line (pure water); the hysteresis in a) shows that supersaturation (supercooling) occurs on crystallization of β-cyclodextrin.

The crystallization of β-cyclodextrin and β-cyclodextrin inclusion compounds from aqueous solutions has been studied by monitoring the turbidity which appears on cooling[64,65] (Fig. 4). Solutions of up to 2% β-cyclodextrin show a single phase in the temperature range examined (2—60 °C), whilst at a concentration of 3% crystals separate out at temperatures of below 13 °C. This process is reversible, but there is considerable hysteresis (Fig. 4a). Similar experiments with β-cyclodextrin and guest molecules demonstrate that, in general, the onset of turbidity depends strongly on the concentration of the guest molecule (cf. Fig. 4b).

5. Characterization of Inclusion Compounds

5.1. Inclusion Compounds in the Solid State

During the synthesis of cyclodextrin inclusion compounds the guest components could be enclosed within the cavity, thus forming a true complex, or merely aggregate to the outside of the cyclodextrin molecule.

The first systematic study of 54 guest components within α-, β-, and γ-cyclodextrins[30] showed that the law of constant proportions applies to the inclusion. Complexes with a constant guest/cyclodextrin ratio always crystallized out regardless of the molar ratio guest/cyclodextrin in aqueous solution (or in a mixture with ether). The ratio was 1:1 in only a few cases and sometimes varied within the series α-, β-, γ-cyclodextrin. The ratios were, however, always constant and indicated a real inclusion phenomenon.

Inclusion complexes can be detected quickly and directly by physical methods. In the case of crystalline substances, X-ray powder diagrams can be made. If the diffraction pattern does not correspond to those of the pure components, a true inclusion complex may exist (Fig. 5)[66-68].

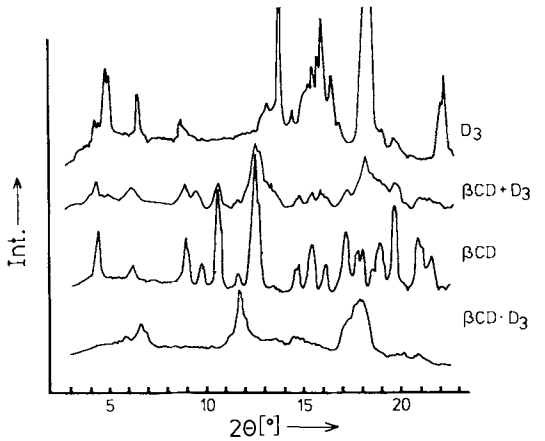


Fig. 5. X-Ray diffraction diagram of crystalline β-cyclodextrin (βCD), vitamin D_3 (cholecalciferol, D_3), a mixture (βCD + D_3), and the complex (βCD·D_3). The intensity maxima of βCD + D_3 correspond with those of βCD and D_3, whereas the maxima of the complex βCD·D_3 are different and indicate a true inclusion complex as opposed to a mixture (according to [257]).

TAS (Thermomikro-Abtrenn-Transfer- und Auftragsverfahren von Substanzen, thermomicro-separation-transfer and application of substances) provides another method for detecting inclusion complexes[65,69]. Several mg of the complex are put into a sample tube together with wet silica gel or starch which are able to release water vapor; the open end of the tube is drawn out into a capillary. The tube is slowly heated, a thin layer chromatography plate is held in front of the capillary opening and as the temperature increases the plate is moved. The escaping water vapor carries volatile substances which are adsorbed onto the TLC plate. In the case of inclusion compounds, the guest components are driven off at considerably higher temperatures. The behavior of marjoram oil is typical. In its pure form or in admixture with β-cyclodextrin it escapes at 100 °C but when complexed with β-cyclodextrin it can first be detected chromatographically at temperatures above 160 °C.

Thin layer chromatography can be similarly employed if a solvent can be found in which the complex is sufficiently stable[65]. The free guest component or a guest/cyclodextrin mixture exhibits a higher R_f value than the inclusion complex. As an equilibrium always exists between the associated and dissociated components, the guest component can migrate somewhat but is on the whole retarded.

In the case of sublimable guest molecules, vacuum sublimation can be utilized to monitor complex formation[65]. Salicylic acid vaporizes at 150 °C/5 torr, whereas its complex with β-cyclodextrin does not sublime.

IR spectroscopic techniques are not generally suitable for detecting the inclusion of compounds. On the one hand, the cyclodextrin bands change only slightly on complex formation; on the other hand, the fraction of the guest molecule contained in the complex is less than 25% and bands which could be assigned to the guest molecule are easily masked by the bands due to cyclodextrin and the ever-present water of crystallization.

Single crystal X-ray structure analysis is the best method for detecting complex formation. The precise geometrical relationships between the guest and host molecules can be established and interactions can be identified. This technique is, however, too complicated for routine use. Several results of X-ray structure analysis will be considered in more detail in Section 6.1.2.

5.2. Inclusion Compounds in Solution

Whereas clathrates generally only form inclusion compounds in the solid state (this is due to the special crystal lattice of the host component), cyclodextrin complexes exist in aqueous solution. They can therefore be elegantly studied by spectroscopic or calorimetric methods.

If a guest component absorbs light in the visible or UV range[70-77], if it fluoresces[78-81] or is a free radical[82-85], then formation of an inclusion complex can be followed by titrating with cyclodextrin (Fig. 6). Changes in the circular dichroism (CD) of the guest component on addition of cyclodextrin can be similarly exploited. It is interesting that even achiral molecules which do not exhibit any CD bands become CD-active due to the chirality of the cyclodextrin[74,77,86,97]. Recently, NMR methods have contributed

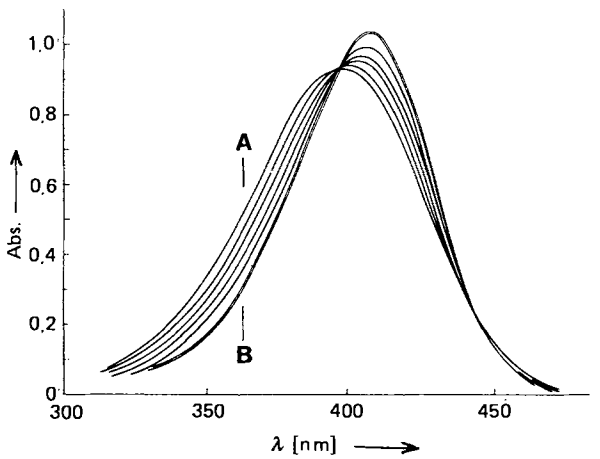


Fig. 6. Spectrum of the *p*-nitrophenolate anion (5×10^{-5} mol/l, pH = 11, 20 °C) on addition of increasing concentrations of α-cyclodextrin; from A to B: 0, 10^{-4}, 2.5×10^{-4}, 5×10^{-4}, 10^{-3}, 5×10^{-3}, 10^{-2} mol/l (according to [73]).

greatly to the understanding of guest/cyclodextrin interactions. As a result of the development of the high resolution spectrometers the original qualitative data[97,98] were so improved that it became possible to make quantitative statements about the thermodynamic and kinetic parameters of complex formation[99 102,74,76]. Atomic interactions between the guest and host can be identified and geometrical relationships can thus be established. Whereas X-ray structure analysis reflects the atomic details of the static complex in the solid state, NMR spectroscopy allows its dynamic properties in solution to be studied[100-102] (Fig. 7).

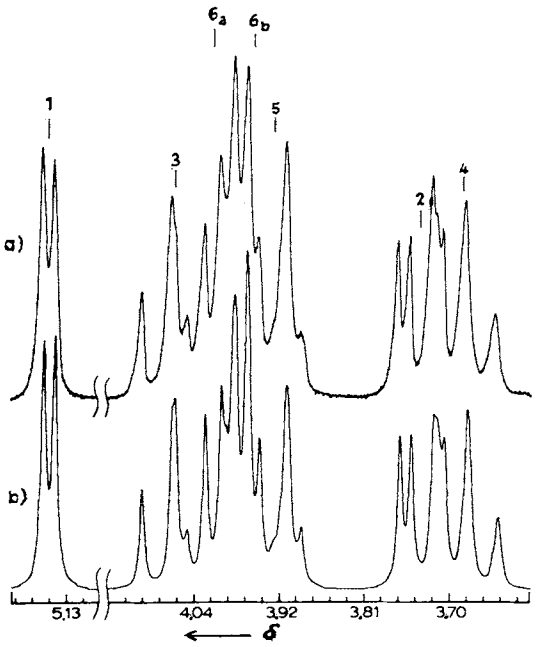


Fig. 7. a) 220 MHz-^{1}H-NMR spectrum of 0.1 M α-cyclodextrin in D_2O (68 °C, pD = 7.5) and b) computer-simulated spectrum (according to [101]). The numbers denote the H atoms (see Fig. 2).

Inclusion of a guest molecule can also be followed by monitoring changes in its conductivity[67-94,103,106-108] and polarographic properties[109,110], apparent changes in its basicity[76,77], increases or decreases in its solubility in the presence of cyclodextrin[111,112], or by measurement of supersonic relaxation[113]. Microcalorimetry is an important method for directly measuring the thermodynamic properties of complex formation[114-116].

6. Cyclodextrins as Model Compounds

6.1. The Inclusion Process and the Structure of the Cyclodextrin Complex

Complex formation between cyclodextrins and their guest molecules is the subject of a comprehensive literature[8,10-14,73-116]. A great deal of interest has been shown in this phenomenon due to the fact that two components associate with each other without any specific interactions taking place and because parallels can be drawn with many biochemical processes.

6.1.1. Thermodynamics and Kinetics of the Inclusion Process

Complex (CS) formation between the cyclodextrin (C) and guest (substrate, S) components according to

$$C + S \rightleftarrows C \cdot S \qquad K_D = [C] \cdot [S]/[C \cdot S] \quad [mol/l]$$

can be quantitatively described by the dissociation constant K_D. Depending on the nature of the substrate, K_D can be determined by the methods mentioned previously[73-116] or by employing competition of a substrate in cyclodextrin-catalyzed ester hydrolysis[117-121]. The most common studies are those which exploit light absorption (Fig. 6); K_D is obtained by plotting the absorption change of the substrate (at a constant wavelength) against the cyclodextrin concentration according to *Benesi* and *Hildebrand*[122]. Isosbestic points signify a 1:1 equilibrium. In the case of a 2:1 inclusion according to the scheme

$$2C + S \underset{}{\overset{K_{D1}}{\rightleftharpoons}} C \cdot S + C \overset{K_{D2}}{\rightleftharpoons} C_2 \cdot S$$

(as has been established for methyl orange in aqueous solution[73], and later in the crystalline state[123]), one isosbestic point for K_{D1} is found at low cyclodextrin concentrations.

On further addition of cyclodextrin a new isosbestic point for K_{D2} appears because the elongated methyl orange molecule is able to accommodate two cyclodextrin rings.

If two different substrate molecules S^1 and S^2 are simultaneously offered to the cyclodextrin, they can compete for the cyclodextrin molecule:

$$\begin{array}{ccc} & C + S^1 + S^2 & \\ {\scriptstyle K_{D1}}\swarrow & & \searrow{\scriptstyle K_{D3}} \\ C \cdot S^1 + S^2 & \overset{K_{D2}}{\rightleftharpoons} & C \cdot S^2 + S^1 \end{array}$$

This scheme can be utilized to obtain K_D for equilibria which cannot be measured directly[73,124]. The cyclodextrins behave like enzymes which can competitively bind substrates and inhibitors in their active centers. Preferential binding of one of the components is determined in both cases by the dissociation constants K_D.

The K_D values for several cyclodextrin inclusion compounds are compiled in Table 3. Generally speaking, the values all lie close to 10^{-3} mol/l and are characteristic of weak intermolecular interactions. It is remarkable that there is no obvious correlation between the chemical properties (functional groups) of the guest molecules and the dissociation constants. Inclusion thus does not seem to depend primarily on the character of the guest.

The thermodynamic parameters enthalpy (ΔH) and entropy (ΔS) can be obtained from the temperature dependence of the dissociation constant. ΔH is always negative, *i.e.* the complex dissociates when the temperature is increased. ΔS can be positive or negative—this indicates that, depending on the guest molecule, several forces are involved in complex formation. Very exact ΔH and ΔS values can be derived from calorimetric measurements[114-116]. If ΔH is plotted against ΔS (according to [125]) for different guest molecules, a linear relationship (compensation) is seen; an "isoequili-

Table 3. Thermodynamic parameters of some cyclodextrin inclusion compounds at 25 °C (for further K_D and ΔH values see Tables 4 and 5).

Substrate	Cyclo-dextrin	K_D [mol/l]	ΔH [kcal/mol]	ΔS [cal·mol^{-1}·K^{-1}]	Method [a]	Ref.
p-Nitrophenol	α	2.6×10^{-3} [b]	− 4.2	− 2.8	Sp	[73]
p-Nitrophenolate	α	0.27×10^{-3} [b]	− 7.2	− 8.7	Sp	[73]
	α		− 9.04	−14.97	Ca	[314]
	α	8×10^{-3}	− 7.3	−15	Ca	[115]
Perchloric acid	α	2.5×10^{-2}	− 7.5	−17	Ca	[115]
Sodium perchlorate	α	5×10^{-2}	− 9.7	−23	Ca	[115]
Anilinium perchlorate	α	3×10^{-2}	−12.3	−35	Ca	[115]
Benzoic acid	α	10^{-3}	− 9.6	−18	Ca	[115]
4-Aminobenzoic acid	α	1.6×10^{-1}	−11.6	−26	Ca	[115]
2-Aminobenzoic acid	α	10^{-5}	− 0.3	21	Ca	[115]
Diisopropyl phosphorofluoridate	α	2.1×10^{-1}	− 7.3	−21	Ki	[315]
m-Chlorophenyl acetate	β	3.5×10^{-3}	− 1	8	Ki	[118]
m-Ethylphenyl acetate	β	2.2×10^{-3}	− 4.6	− 3	Ki	[118]
Benzoylacetic acid	β	9.8×10^{-3} [c]	− 5.7	− 8.6	Ki	[121]

[a] Sp, Ca, Ki signify spectroscopic, calorimetric and kinetic methods respectively. [b] At 14 °C. [c] At 50.3 °C.

brium" temperature can be determined from the slope of the resulting straight line (Fig. 8)[75, 115, 126]. As compensation is generally correlated with the participation of water molecules in complex formation[125], it must be assumed that the guest molecule loses its hydration sphere on entering the cyclodextrin cavity, and that water molecules are expelled from the "empty" cyclodextrin cavity.

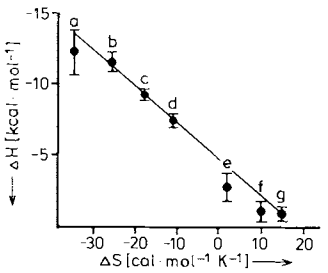


Fig. 8. $\Delta H/\Delta S$ compensation for some of the substrates listed in Table 3 (according to [115]). a) to g) signify anilinium perchlorate, 4-aminobenzoic acid, benzoic acid, hydrocinnamic acid, pyridine, L-tyrosine, L-phenylalanine, The linear relationship reveals that water participates in complex formation; an "isoequilibrium temperature" of 265 K is obtained from the slope of the straight line.

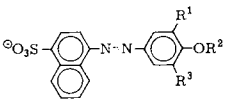
The thermodynamic parameters give a macroscopic picture of the inclusion process which can be described in detail by means of kinetic data. The rate constants k_D for dissociation and k_R for recombination of the cyclodextrin · substrate complex C·S

$$C + S \underset{k_R}{\overset{k_R}{\rightleftharpoons}} C \cdot S \qquad K_D = k_D/k_R$$

can be obtained by relaxation[73, 113] and mixing techniques[73]; they are compiled in Tables 4 and 5.

The dyes of the type 4-(4-hydroxyphenylazo)-1-naphthalenesulfonate listed in Table 4 form 1:1 complexes with α-cyclodextrin as only the phenyl group can penetrate the cavity. The thermodynamic parameters (K_D) do not reveal any significant differences between the azo dyes as regards complex formation and thus indicate that the intermolecular guest/host interactions are similar; the kinetic parameters, however, demonstrate that as the volume of the substituent (H, CH_3, C_2H_5) which is *ortho* to the hydroxy group increases, the inclusion and dissociation processes slow down by a factor of 10^5. This can be accounted for by the fact that the hydroxyphenyl group must thread in and out of the α-cyclodextrin ring; furthermore, the hydrophobic methyl and ethyl groups could stabilize the hydration sphere surrounding the hydroxy group and thus increase steric hindrance. Complex formation can be subdivided into several steps[73]: 1) Approach of the substrate and α-cyclodextrin. 2) Elimination of water molecules from the α-cyclodextrin cavity and the im-

Table 4. Thermodynamic and kinetic parameters for the formation of complexes between α-cyclodextrin and *p*-nitrophenol, *p*-nitrophenolate, or azo dyes of 4-(4-hydroxyphenylazo)-1-naphthalenesulfonate type (according to [73]).



Substrate			K_D [mol/l]	ΔH [kcal/mol]	k_R [mol^{-1} s^{-1}]	k_D [s^{-1}]
O_2N C_6H_4OH			2.6×10^{-3}	−4.2	$\geqq 4 \times 10^7$	$\geqq 10^5$
O_2N $C_6H_4O^{\ominus}$			0.27×10^{-3}	−7.2	1.4×10^8	3.1×10^4
R¹	**R²**	**R³**				
H	H	H	3.7×10^{-3}	−7.0	1.3×10^7	5.5×10^4
H	⊖	H	1.55×10^{-3}	−6.3	1.7×10^5	2.6×10^2
CH_3	⊖	H	2.1×10^{-3}	−5.8	1.5×10^2	2.8×10^{-1}
C_2H_5	⊖	H	3.5×10^{-3}	−7.7	2.8	1×10^{-2}
CH_3	⊖	CH_3	no inclusion			

mediate vicinity of the hydroxyphenyl group. 3) Assimilation of these water molecules by the surrounding water (gain in entropy). 4) Interaction of α-cyclodextrin and the substrate as a result of van der Waals forces and possibly formation of hydrogen bonds. 5) Reconstitution of the hydrated structure around the finished complex.

The parameters for the formation of inclusion compounds from β-cyclodextrin and salts are compiled in Table 5[113].

Table 5. Thermodynamic and kinetic parameters for the formation of complexes between β-cyclodextrin and several anions (according to [113]).

Substrate	K_D [mol/l]	k_R [mol^{-1} s^{-1}]	k_D [s^{-1}]
$Cl^{\ominus}$	0.39	5.4×10^7	2.1×10^7
$Br^{\ominus}$	0.15	4.5×10^7	6.9×10^6
$I^{\ominus}$	0.055	6.5×10^7	3.6×10^6
$SCN^{\ominus}$	0.10	4.4×10^7	4.4×10^6
$NO_3^{\ominus}$	0.18	4.5×10^7	8.2×10^6
$ClO_4^{\ominus}$	0.037	2.0×10^9	7.4×10^7

The substrate molecules are so small that there is no steric hindrance, the complexes are therefore formed more quickly than those of the azo dyes; the reactions are not, however, diffusion controlled. As the stripping off of the hydration sphere surrounding the anions cannot be rate determining, a (slower) conformational change of β-cyclodextrin on inclusion was inferred. One such change, due to rotation of a glucose unit, could be directly monitored kinetically[113], spectroscopically[127], and crystallographically[128-131] for α-cyclodextrin but not for the more rigid β-cyclodextrin. As will be described in Section 6.1.2, rotation of the O(6)H groups about the C(5) C(6) bonds may be considered as a conformational change.

6.1.2. Structure of the Cyclodextrin Inclusion Compounds

The cyclodextrins and their adducts can be crystallized from water and examined by X-ray crystallography as "empty" molecules or as inclusion complexes. Depending on the size and ionic or molecular character of the substrate, "chan-

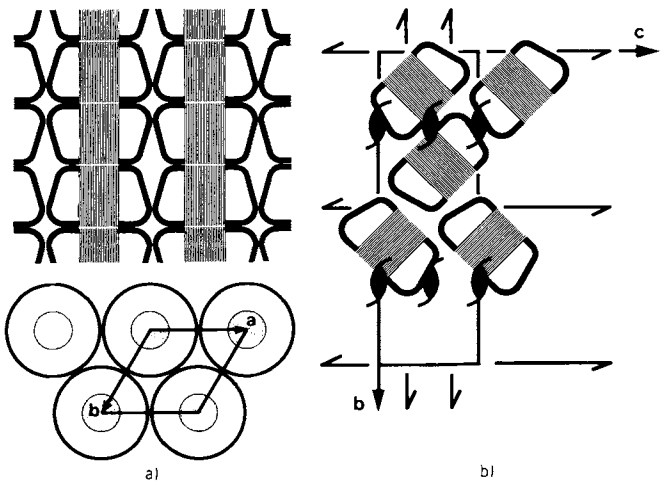


Fig. 9. Schematic representation of the arrangement of cyclodextrins in crystals. The cavities are hatched. a) Channel structure as seen from above and from the side (hexagonal packing of the stacks); b) cage structure (space group $P2_12_12_1$). The lens-shaped structures and arrows represent crystallographic screw dyads. The size and nature (ionic or molecular) of the guest molecule determines which of the two structures is adopted (according to [132]).

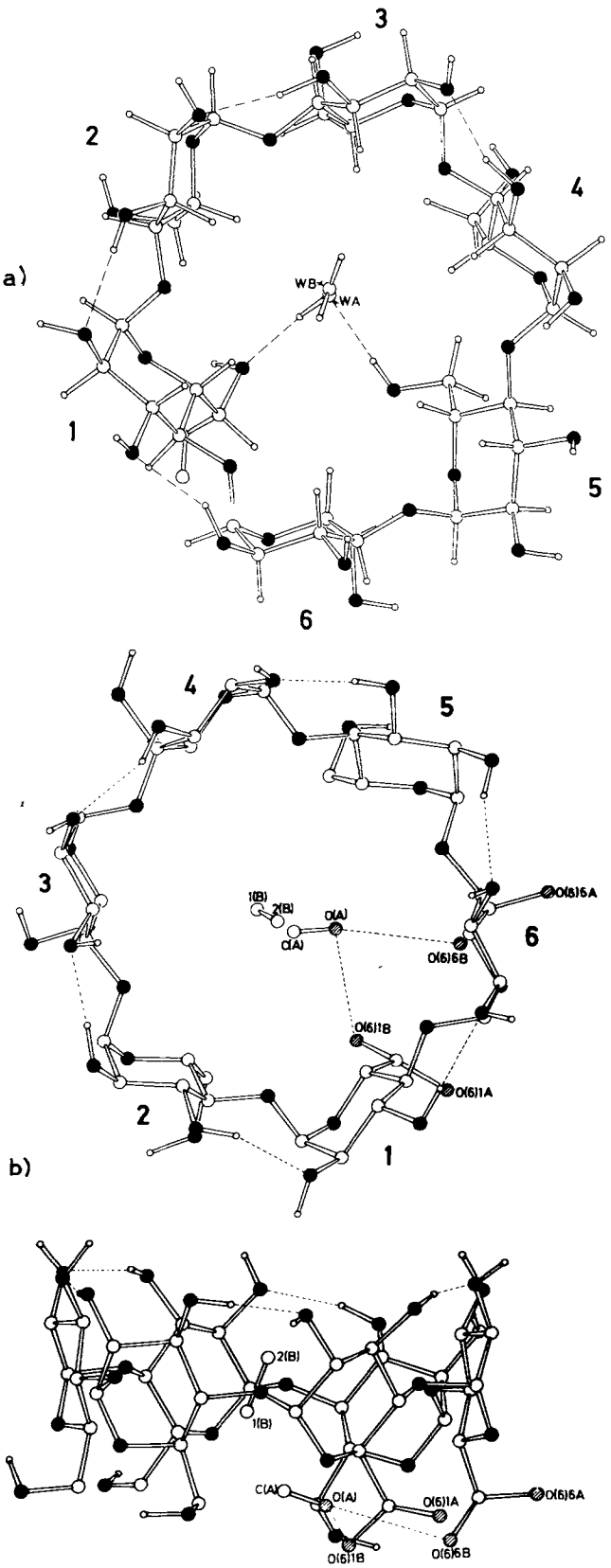


Fig. 10. Results from X-ray structure analyses of cage structures of a) α-cyclodextrin·6H_2O (according to [128]) and b) α-cyclodextrin·CH_3OH·4H_2O (according to [129]). ○ = H, ○ = C, ● = O; ◎ in (b) denotes disordered OH groups at C(6) and in the methanol molecule, the H atoms bonded to C are not shown in (b). O H...O hydrogens bonds in (b) form a ring between the O(2)H and O(3)H groups of adjacent glucose units; in (a) this ring is interrupted at the "inwardly" rotated glucose (numbered 5). (a) Contains two molecules of water (WA, WB), (b) contains one methanol molecule in two statistically occupied positions [O(A) C(A); 1(B) 2(B)]; in each case one of these molecules is hydrogen bonded to O(6)H groups ((+)-*gauche* conformation). The four molecules of water which lie "outside" the cyclodextrin molecule are not shown.

nel" or "cage" structures are formed in which the cyclodextrin molecules are stacked like coins in a roll or arranged in a herring-bone pattern[132] (Fig. 9).

In addition to the α-cyclodextrin complexes formed with water[128], methanol[129], and polyiodide[133] shown in Figures 10 and 11, complexes with iodine[134], krypton[135], *n*-propanol[136], *p*-iodoaniline[137,138], dimethyl sulfoxide and methanol[139], *m*-nitrophenol[140], methyl orange[123], and potassium acetate[141] have also been analyzed. In the case of β-cyclodextrin, the crystal structures of its complexes with water[142], *n*-propanol[143], *p*-iodophenol[143], 2,5-diiodobenzoic acid[144], and *p*-nitroacetanilide[145] have been determined; the structures of γ-cyclodextrin complexes with propanol/water[146] and water[147] have recently been described.

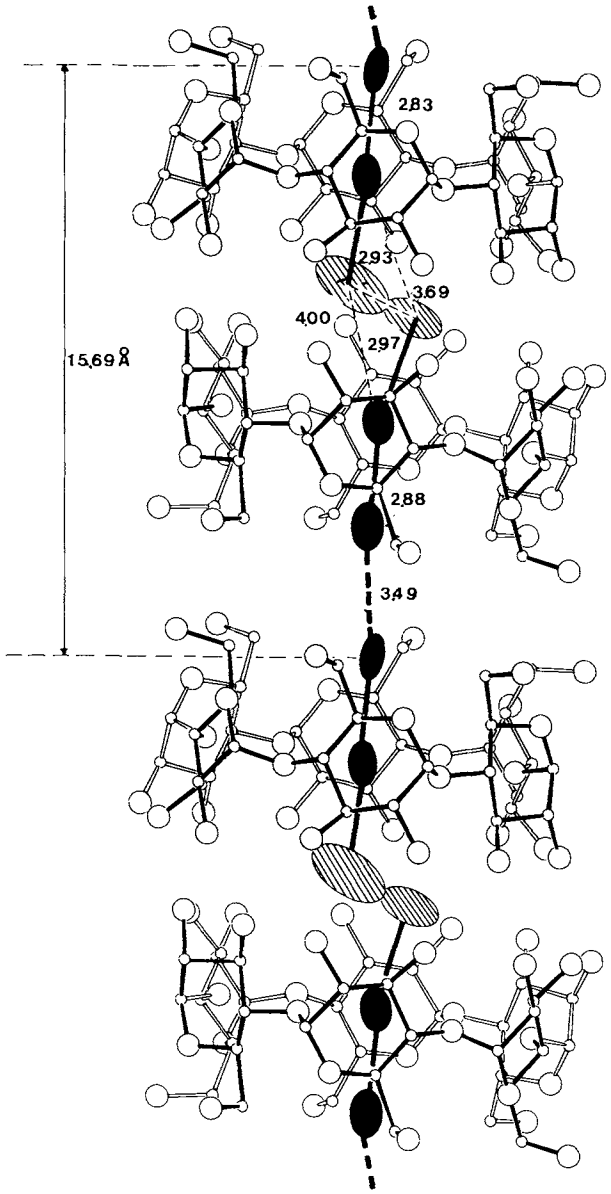


Fig. 11. Greatly simplified side view of the channel structure of the complex (α-cyclodextrin)$_2$·LiI_3·I_2·8H_2O. ○ = C, ○ = O, ● = I, ⊗ = disordered iodine, the iodine atoms are represented as thermal ellipsoids. Water molecules, cations, hydrogen atoms and hydrogen bonds between O(2)H, O(3)H and O(6)H groups have been omitted for the sake of clarity (according to [133]). I...I^- distances and the translation period along the channel axis are given (in Å). The mean I...I distance, 3.14 Å agrees with the values of ≈3.1 Å obtained for the iodine-starch complex [166] and other α-cyclodextrin-polyiodide complexes [316].

Comparison of the crystal structure analyses of the α-, β-, and γ-cyclodextrin complexes reveals that the cyclodextrins always have a "round", slightly conical form whose narrower opening contains the O(6)H groups whereas the wider opening is occupied by the O(2)H and O(3)H groups. The glucose units always have a C1-chair conformation, the C(6)—O(6) bonds are preferentially directed away from the center of the ring (torsion angle O(5)—C(5)—C(6)—O(6) is (−)-*gauche*); these bonds can, however, turn "inwards" (torsion angle O(5)—C(5)—C(6)—O(6) (+)-*gauche*) after formation of hydrogen bonds between the O(6)H group and the guest molecule.

Intramolecular hydrogen bonds O(3)—H...O(2) and O(3)...H—O(2) exist between the secondary hydroxy groups of adjacent glucose units. These interactions stabilize the cyclodextrin macrocycle (Figs. 2 and 10) and cause a significant broadening of the γ_{OH} bands in the IR spectrum as compared with normal alcoholic OH bands[97,148]. Deuterium exchange as followed by means of ^{1}H-NMR spectroscopy showed that these hydrogen bonds are very stable even in dimethyl sulfoxide solutions[148,149]. The values of the equilibrium constants for the equation

$$2\ \text{Cyclodextrin-OH} + D_2O \rightleftharpoons 2\ \text{Cyclodextrin-OD} + H_2O$$

are 0.75 and 0.65 for α- and β-cyclodextrin respectively; these values are smaller than that for amylose (0.85) and indicate that the interactions in amylose (polymer) and α-cyclodextrin are weaker than those in β-cyclodextrin. The X-ray data show that the mean O(2)...O(3) distances are clearly different in α-, β-, and γ-cyclodextrins (3.00, 2.86, and 2.81 Å respectively); the interactions in α-cyclodextrin are weaker and its flexibility is thus greater than is the case for β- and γ-cyclodextrins—a statement which is in agreement with deuterium exchange studies as well as with theoretical[48] and spectroscopic data[127].

The interactions between the guest molecule and the surrounding cyclodextrin are generally weak and are largely due to van der Waals and dispersion forces. It is for this reason that small molecules are often statistically disordered within the cyclodextrin cavity[129,135,136,142–144,146,147], even if hydrogen bonds are formed with the O(6)H groups. The guest molecule apparently strives to fill up the cyclodextrin cavity and if this is not possible for spatial reasons, it begins to "rattle".

The structure of α-cyclodextrin·6H_2O (Fig. 10a) is unusual. When α-cyclodextrin is complexed with included methanol, krypton and *n*-propanol, the guest molecules are statistically disordered and occupy several positions; (empty) α-cyclodextrin has a "round" structure with a ring of hydrogen bonds between the O(2)H and O(3)H groups. When water is the guest molecule, however, α-cyclodextrin is somewhat collapsed; two of the O(3)—H...O(2) bridges are opened and one glucose unit is rotated inwards to allow formation of a O(6)...H_2O hydrogen bond. This rotation causes steric strain within the macrocycle[128]; the α-cyclodextrin in this complex has a higher energy than in all other complexes.

NMR studies have revealed that, in aqueous solution, aromatic guest molecules such as *p*-iodoaniline and *p*-nitrophenol interact with the H atoms at C(3) and C(5) inside the cy-

clodextrins[101,149,150] to form a complex which has a structure similar to that found in the crystalline state[137,138,140]. Nitrophenol enters the cavity from the O(2), O(3) side with its nitro group, it can penetrate further into β-cyclodextrin than α-cyclodextrin and is more strongly bonded by α-cyclodextrin. It has been deduced from ^{2}H- and ^{13}C-NMR data obtained with deuterated cinnamic acid derivatives that the mobility of the substrate within the complex is greater than that of the cyclodextrin and that the interaction between guest and host is only weak[100].

6.1.3. The Driving Force for Complex Formation

As long as the cyclodextrin inclusion compounds have been known, the intermolecular interactions responsible for complex formation have been discussed[8,10,37,73,130,151]. It has been shown that several forces act simultaneously. The extent to which each of them is involved is related to the substrate concerned.

The dependence of the binding constants on substrate polarizability[118,152] indicates that, in general, van der Waals forces predominate; the formation of hydrogen bonds between the guest and (preferentially) the O(6)H groups of the substrate has been demonstrated crystallographically. Hydrophobic interactions[153,73,154] are also involved—on inclusion within the cyclodextrin cavity the guest molecule must expel the water molecules already present and strip off its own hydration sphere. The liberated water molecules are taken up by the bulk water; they gain degrees of freedom and contribute to the stability of the complex owing to the resulting increase in entropy.

As inclusion is largely independent of the chemical properties of the guest molecule, it has also been suggested that forces inherent in the cyclodextrin contribute to association. The water enclosed within the "empty" cyclodextrin cavity could exert such a force; this water is in an unfavorable, hydrophobic environment, it cannot satiate its (tetrahedral) hydrogen bond potential and is thus "activated"[154,142]. On expulsion, complex formation is favored by a gain in entropy as well as by a gain in potential energy[118,119].

As α-cyclodextrin in its "empty" state is strained (Fig. 10a)[128], energy is also gained if this strain is relieved on complex formation and if the ring of hydrogen bonds is formed between the O(2)H and O(3)H groups of adjacent glucose units[130]. This gain in energy can only occur with α-cyclodextrin; "empty" β- and γ-cyclodextrins are not strained[142,147].

Although more recent experiments[152,154-156] and theoretical considerations[157,158] have shown that van der Waals forces and hydrophobic interactions probably dominate in complex formation, the other forces discussed above inherent in the "empty" cyclodextrin·water complex may also be involved; the extent to which these forces contribute depends on the nature of the enclosed guest molecule. The inherent ring structure of the cyclodextrins is, however, decisive as inclusion complexes are only formed if there is a good spatial fit between the guest and host components.

6.2. Cyclodextrins as Starch Models

As cyclodextrins represent closed turns detached from the starch helix, it seemed obvious that they could be used as models for starch. IR spectroscopy studies showed that starch and cyclodextrins exhibit similar C1-glucose conformation[159]; information about the possible helical forms of the starch molecule was obtained from potential energy calculation[159]; information about the possible helical forms of the from crystallographic data[160]. Detailed investigations assumed that two-, four-, six-, seven-, and eightfold helices were constructed from a flexible glucose unit in order to explain the observed polymorphism of starch[161]; the recently determined crystal structures of β- and γ-cyclodextrins have provided a firm basis for these studies. It should finally be mentioned that it would hardly be possible to interpret starch X-ray diagrams if the structures of the cyclodextrins were not known[38,39,161,162].

6.3. Cyclodextrin·Polyiodide Inclusion Compounds as Models for the Blue Iodine-Starch Complex

The blue iodine-starch complex has been known since 1814[163] and was studied in detail on account of its unusual color properties for both practical and theoretical reasons[20,164,165]. X-ray diffraction studies on fibers of the iodine-starch complex only gave the dimensions of the starch helix and showed that polyiodide chains were located in the channel-like cavities within the helix with a mean I...I distance of 3.1 Å[166]; the nature of the iodine-starch interactions was, however, still unknown and became the subject of controversial discussions[20,166].

A solution of α-cyclodextrin, iodine and iodide produces almost black, metallic crystals. In these, α-cyclodextrin molecules are piled up in stacks. The cavities form channels in which, analogous to the starch-iodine complex[166], polyiodide is enclosed (Fig. 11). The arrangement of the α-cyclodextrin-polyiodide stacks within the crystal depends on the countercation[167] as the latter can interact with hydroxy groups or water molecules and thus influence the packing of neighboring stacks[133]. The α-cyclodextrin·polyiodide complexes with Li^+ and Cd^{2+} as counterions have been examined in detail. The polyiodide chains have differing structures and in the case of the Li^+ complex they can be considered as alternating $I_2...I_3^-...I_2...I_3^-$ whereas in the Cd^{2+} complex $I_5^-...I_5^-...I_5^-$ is found. The I_2, I_3^-, or I_5^- units interact strongly with one another as the longest I...I distances ≈ 3.5 Å are about 0.8 Å shorter than the sum of the van der Waals radii for iodine. It was concluded that the deep color of these complexes is a result of charge transfer within the iodine chains and that the dominant interactions between the iodine and the surrounding α-cyclodextrin are merely H...I van der Waals contacts with the inwardly directed H atoms at C(3) and C(5). The I...O charge transfer interactions[168,169] previously proposed on the basis of spectroscopic data can be ruled out.

The α-cyclodextrin-polyiodide complexes with Li^+ and Cd^{2+} counterions have been compared with the iodine-starch complex by means of resonance-Raman[170,171] and Mössbauer[171] spectroscopy. It was demonstrated that iodine starch does not contain detectable quantities of unperturbed I_2 or I_3^- but has instead I_2, I_3^-, or I_5^- units which interact with one another, and which are similar to the units found in the model α-cyclodextrin·polyiodide complexes.

6.4. Cyclodextrins as Enzyme Models

Racemic mandelic acid esters are hydrolyzed 1.38 times more rapidly in the presence of cyclodextrin than in its absence. In this process, partial optical activation occurs[172]; the cyclodextrins thus possess, like enzymes, specific catalytic properties. This finding led to an intensive study of cyclodextrins as enzyme models. The results have been recently summarized in a monograph[37] (see also [12]).

Table 6. Reactions catalyzed by cyclodextrins (according to [37]). f_{max} = maximum acceleration factor related to the uncatalyzed reaction. K, N, U respectively denote that the catalysis proceeds *via* a covalently bound intermediate, does not involve such an intermediate, or proceeds *via* an as yet unknown mechanism.

Reactions	Substrate	f_{max}	Nature of catalysis
Ester hydrolysis (asymmetric induction)	Phenyl esters	300	K
	Mandelic esters	1.4	U
Amide hydrolysis	Penicillins	89	K
	N-Acylimidazoles	50	K
	Acetanilides	16	K
Cleavage of phosphoric and phosphonic esters	Pyrophosphates	>200	K
	Diaryl methylphosphonates	66	K
Cleavage of carbonates	Aryl carbonates	19	N
Intramolecular acyl migration	2-Hydroxymethyl-4-nitrophenyl pivalate	6	N
Decarboxylation	Glyoxylate ion	4	N
	Cyanoacetate ion	44	N
Oxidation	α-Hydroxyketones	3	N

Table 6 shows several of the chemical reactions which are catalyzed by cyclodextrins. The catalyses can be divided into two groups depending on whether or not the cyclodextrin forms a covalently bonded intermediate. The former case can be formulated in general as[118,119]:

$$\begin{array}{l} S + C \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C\cdot S \xrightarrow{k_2} P^1\text{—}C + P^2 \xrightarrow{k_3} P^1 + C + P^2 \\ \quad\downarrow k_{un} \\ P^1 + P^2 \end{array}$$

k_{un} is the rate constant for the uncatalyzed reaction without cyclodextrin (C), whilst k_1 reflects the rate of "enzyme-substrate" complex formation (C·S). k_2 describes the formation of the covalent intermediate P¹—C which is hydrolyzed according to k_3 to give cyclodextrin and the end product. In the second case, catalysis is a result of a "microsolvent" effect of the "microheterogeneous" cavity[8] within the cyclodextrin; there is no intermediate P¹—C but all other reaction steps are analogous. Since the substrate reacts in the form of an inclusion complex (C·S), the reaction rates must asymptotically approach a limiting value with increasing cyclodextrin concentration (analogous to Michaelis-Menten kinetics[173]) [118,174-182]; furthermore, inhibition must occur if an inert molecule is added which can compete with the substrate for the binding site of the cyclodextrin[118,167,173,175]. Both phenomena have been studied in many cyclodextrin-catalyzed reactions and indicate that, as cyclodextrins show the behavior typical of enzymatic reactions, they serve as good enzyme models.

The hydrolysis of phenyl esters in the presence of cyclodextrins has been investigated in particular detail[118,119,177] as a great deal is known about the analogous biochemical system—ester cleavage by chymotrypsin[173]. Phenyl acetates are best hydrolyzed in the presence of cyclodextrins at pH ≈ 11[119,37]; this indicates that the cyclodextrin attacks the carboxy group of the substrate nucleophilically with its deprotonated secondary hydroxy groups acting as the active species (Fig. 12). The unexpectedly low pK_a value of these hydroxy groups (≈ 12.2) has been confirmed by independent measurements[119,183] and is probably due to stabilization of the negative charge by inductive effects and hydrogen bonding between the neighboring O(2)H and O(3)H groups. It has been shown that the primary O(6)H group is not involved by using β-cyclodextrin permesylated in this position[184,119].

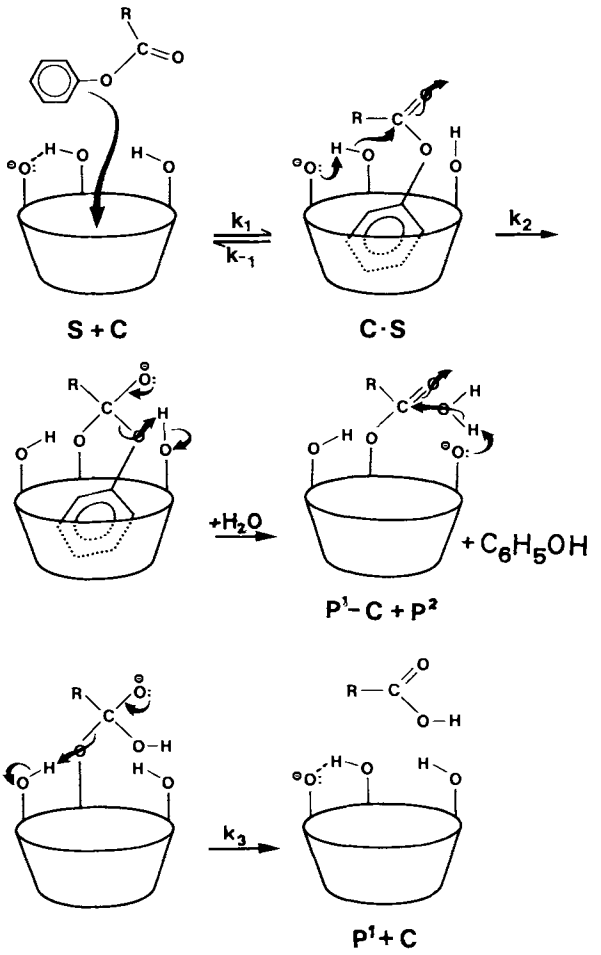


Fig. 12. Schematic representation of the hydrolysis of phenyl acetate (S) to acetic acid (P¹) and phenol (P²) as catalyzed by cyclodextrin (C).

Experiments with *meta*- and *para*-substituted phenyl acetates revealed that the catalysis as expressed by the ratio k_2/k_{un} depends very strongly on the geometry of the substrate[118]. k_2/k_{un} values of 3.3 and 95 (at pH = 10.6 and 25 °C) were obtained for *para*- and *meta*-toluyl acetate respectively, the corresponding values under the same conditions for *para*- and *meta-tert*-butylphenyl acetate (their substituents are much larger) were 1.1 and 260 respectively. These data can be explained by assuming that the substituent penetrates the cyclodextrin cavity axially and that, in the case of *para* substitution, the orientation of the acetate group is largely axial. When, however, the substituent is in the *meta* position, the acetate group is brought in the vicinity of the

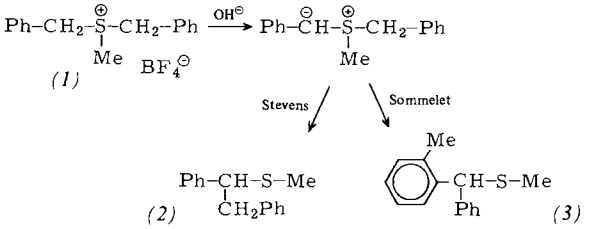
ring formed from hydrogen bonds between O(2)H and O(3)H so that a sterically favorable interaction can take place.

Attack of the O(2) or O(3) substituents produces the P¹—C intermediate which has been isolated in several cases[119,185,186]. Depending on the substrate, liberation of cyclodextrin from P¹—C by hydrolysis (step k_3) can be several 100 fold slower[119,185] than the formation (k_2) of P¹—C; the cyclodextrins are therefore not ideal enzymes. The first catalytic step is comparable both for chymotrypsin and cyclodextrin; it must, however, be remembered that cyclodextrin shows its optimal activity in the strongly alkaline range whereas chymotrypsin is optimally active in the neutral range (pH ≈ 8), and that step k_3 is very rapid for the enzyme but slow for cyclodextrin. During the course of a long evolution the enzyme chymotrypsin was specialized in the hydrolysis of esters and amides (peptide bonds) whereas cyclodextrins can moderately accelerate many reactions (Table 6).

Attempts have been made to facilitate cleavage of the intermediate P¹—C by substituting the O(2) or O(3) of the cyclodextrin with various groups, thus simulating the active center of chymotrypsin in which serine and histidine chains are situated opposite one another and form part of a "charge relay" system[173,187]. Substitution (probably at C(6)) of cyclodextrin with imidazolyl had little effect[188] but incorporation of a histamine residue at C(3) gave a cyclodextrin derivative which (at pH = 8.37 and 25 °C) was more effective in hydrolyzing *p*-nitrophenylacetate than unsubstituted cyclodextrin[189]. Other substitutions with basic groups accelerated the hydrolysis considerably[189-191]. Like ester hydrolyses, amide hydrolyses are catalyzed by cyclodextrins; examples are penicillin derivatives[181], acetanilide[182] and *N*-acylimidazole[185]. The cleavage of diarylpyrophosphate proceeds with participation of Ca^{2+} *via* a P¹—C type intermediate (phosphorylated cyclodextrin[175]); this substance has been synthesized and used as an enzyme model for the hydrolysis of *p*-nitrophenyl tetrahydropyranyl ether and for tritium exchange in the methylene group of *p-tert*-butylphenacyl alcohol[192]. Covalent P¹—C intermediates are also formed in the hydrolysis of diarylmethylphosphonates, diarylcarbonates[193], organophosphorus compounds, and thiophosphates[194].

If the cyclodextrin catalysis does not involve an intermediate P¹—C, the "microsolvent" effect[8,37] and the steric properties of the inclusion complex on which the chemical reaction is carried out play important roles. The decarboxylation of activated carboxylic acids such as 2-cyano-2-phenylpropionic acid[195-197], substituted acetoacetic acids[196], and trihaloacetic acids[196] are typical examples of the "microsolvent" effect. Other examples are the oxidation of α-hydroxyketones to α-diketones[198], the hydrolysis of 2,4-dinitrophenylsulfonate[199] and the elimination of HCl from the insecticide trichlorophone (*O*-(2,2,2-trichloro-1-hydroxyethyl)-*O,O*-dimethylphosphate)[200]. Inhibition of reactions (negative catalysis) is observed in the decomposition of hydroperoxide in water[201], of alkyl esters such as methyl and ethyl benzoates, and the ethyl ester of *trans*-cinnamic acid[119,176,183]. This effect will be encountered again when the utilization of cyclodextrins for the micro-encapsulation of chemically unstable compounds is discussed (Section 9.1).

Rearrangements are also influenced by cyclodextrins as the three-dimensional structure of the complexed substrate is different from that of the free substrate. The benzidine rearrangement of hydrazobenzene requires a sandwich-like transition state and is slowed down by α- and β-cyclodextrins by a factor of approximately 10[202]. The rearrangement of dibenzylmethylsulfonium tetrafluoroborate *(1)* in an alkaline medium is of interest. In the absence of cyclodextrin the products *(2)* and *(3)* are formed by Sommelet and Stevens reactions in the ratio 0.38:1 *via* an ylide. In the presence of cyclodextrin, however, the ratio *(2)/(3)* is shifted to 1.5:1[203].

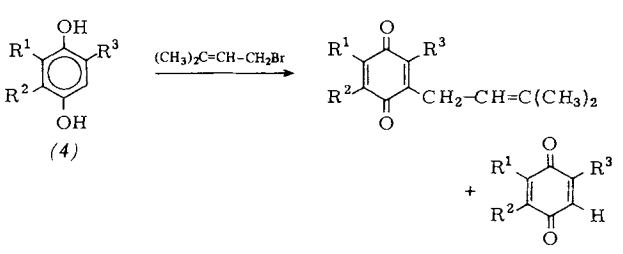


(1) *(2)* *(3)*

A still greater effect is found when anisole is chlorinated by HOCl in the presence of α-cyclodextrin[204,205]. If cyclodextrin is not added, *para*- and *ortho*-isomeric chloroanisoles are produced in the ratio 1.48:1. This ratio increases to 21.6:1 as the α-cyclodextrin concentration is raised. The formation of *ortho*-chloroanisole is reduced to less than 1% if the free cyclodextrin is replaced by a polymer synthesized from α-cyclodextrin and (chloromethyl)oxirane (epichlorohydrin) under basic conditions[205]. The HOCl chlorination is probably the result of formation of a cyclodextrin hypochlorinated at C(3) which attacks the enclosed anisole. The reaction is of the second order without cyclodextrin but of the first order if cyclodextrin is added. The course of the Reimer-Tiemann reaction, in which *para*- and *ortho*-formylated phenol is produced from phenol and chloroform under alkaline conditions, can be similarly controlled[206]; increasing quantities of β-cyclodextrin shift the *para/ortho* ratio which is 0.95:1 in the absence of cyclodextrin, to 19:1.

The Fries rearrangement of phenyl acetate is also affected by cyclodextrin[207]. On irradiating the substrate, *para*- and *ortho*-hydroxyacetophenones are formed in the ratio 1:1 together with the hydrolysis product, *viz.* phenol. Addition of β-cyclodextrin alters the *para/ortho* ratio to 6.2:1, increases the rate of rearrangement by a factor of 3.5, and suppresses phenol production.

Substitution of cyclodextrins with 1,4-diaminoethane[208], polyamines[209], or pyridinecarbaldehyde oxime[210] furnishes derivatives which can complex metal ions and which can be considered as models for metalloenzymes. The cyclodextrins can also be modified by bridging one side so that the interior of the molecule becomes more hydrophobic and complex formation with the substrate is favored[211,80].



(4)

The importance of the cyclodextrins in preparative chemistry has been underlined in several recent publications. The allylation-oxidation reaction of hydroquinone derivatives *(4)* proceeds with yields of between 71 and 86% depending on the substituents R^1, R^2, and R^3 in the presence of β-cyclodextrin; if cyclodextrin is omitted the yields amount to 12—35%[212]. This reaction has been employed for synthesizing vitamin K_1 and K_2 derivatives in one step with yields of 40–60% (without cyclodextrin 12–22%)[213]. The conversion of prostaglandin A_1 to its B_1 isomer is also of interest; this reaction is accelerated by α- and β-cyclodextrin[214,215].

7. Chemical Modification of Cyclodextrins

As has already been described in Section 6 and [216], many cyclodextrin derivatives have been synthesized which contain functional groups derived from imidazole, polyamines, histamine, hydroxamic acid, *etc.* in place of their primary or secondary hydroxy groups. The starting material for these compounds is often monosubstituted 6-*O*-*p*-toluenesulfonylcyclodextrin which can be synthesized according to [217]; this compound can be converted to 6-azido- or 6-halogeno-6-deoxycyclodextrin and other products.

All primary hydroxy groups react with *p*-toluenesulfonyl chloride[184,218,219] or better still with mesitylenesulfonyl chloride[220]; the products can undergo further reactions. In a recent study, perbenzoylated α- or β-cyclodextrin was used[221] to introduce 6-amino-, 6-azido-, 6-methoxy-, 6-amino-2,3-dimethoxy- or 6-azido-2,3-dimethoxy substituents and also to synthesize the corresponding 2,3-dibenzoyl derivatives with 6-azido, 6-amino, or 6-methoxy substituents which can be employed for the synthesis of further derivatives. Tritylation of the O(6)H groups permits the synthesis of symmetrical triamino-α-cyclodextrin[222]. Methylation of heptakis(6-bromo-6-deoxy)-β-cyclodextrin with dimethylsulfate/$Ba(OH)_2$ furnishes the 2-*O*-methyl derivative which, after replacing the 6-bromine atom with benzoate and hydrolysis, can be converted to 2-*O*-methyl-β-cyclodextrin[223]. Alkylation of β-cyclodextrin with 3-bromopropene gives heptakis(2,6-*O*-diallyl)-β-cyclodextrin whose seven glucose units can all be 3-*O*-alkylated[224].

The following quantitative and non-quantitative substitutions of the cyclodextrins will be mentioned: the aminations [cyclodextrin-$(OC_2H_4NH_2)_n$, -$(NH_2)_n$, -$(NCH_3(CHO))_n$], esterifications [cyclodextrin-$(ONO_2)_n$, -$(OSO_3H)_n$, -$(OPO_3H_2)_n$, -$(OCOC_6H_5)_n$, -$(OCOR)_n$, -$(OCO(CH_2)_x$-COOH$)_n$], etherifications [cyclodextrin-$(OCH_3)_n$, -$(OCH_2CO_2Na)_n$, -$(O(CH_2)_xR)_n$, -$(OCH_2CHOHCH_2OH)_n$, -$(O(CH_2CH_2O)_mR)_n$, -$(O(CH_2)_mSO_3H)_n$] tabulated in [34] and the cross-linkages resulting in cyclodextrin polymers discussed in Section 8.

Cyclodextrins are very stable in an alkaline medium but are hydrolytically cleaved by strong acids. The opening up of the macrocycle proceeds 3–5 times more slowly than the degradation of the resulting linear oligosaccharides[225–229]. The oligosaccharides have been characterized[227] and the thermodynamic parameters of the reaction, which depends very strongly on temperature and acid concentration, have been determined[229]. If β-cyclodextrin solutions are cooled in the presence of HCl, HBr, or HI, a stable complex crystallizes out which contains roughly two bound equivalents of acid per β-cyclodextrin[230]. The HI complex can be formulated as (β-cyclodextrin·HI·H_2O)·HI·$7H_2O$; only one HI is enclosed, the other one being located "outside" the cyclodextrin[142].

The γ-radiolysis of β-cyclodextrin in oxygen-free solutions involves free radicals and is probably initiated by loss of a hydrogen atom from C(5)[231]. The glucose radical formed opens up the C(1)—O(5) bond; the C(1)—O(4) bond with the adjacent glucose is broken and a linear heptasaccharide is produced in which the opened glucose unit is its reducing terminal. This unit is cleaved hydrolytically to give a hexasaccharide and, in a subsequent reaction, shorter oligosaccharides. The γ-radiolysis of β-cyclodextrin in the solid state is described in [232].

Cyclodextrins can be threaded like beads onto a linear polymer, without forming any covalent bonds with it; two such preparations have been reported. If vinyl derivatives are reacted in dimethylformamide[233] or chlorides of dibasic acids in water[234] at high temperatures in the presence of β-cyclodextrin, the free reagents and those enclosed within the β-cyclodextrin polymerize to give linear structures, some of which are enclosed by the cyclodextrin. In the case of vinyl polymerization, the maximal proportion of cyclodextrin on a weight basis was 72%.

8. Cyclodextrin Polymers

The special properties of cyclodextrins are largely retained when they are linked together to form polymers. If the degree of polymerization is sufficiently high, the cyclodextrins bound within the matrix become insoluble[235,236]. In initial studies the cross-linkage of heptamino-β-cyclodextrin by hexamethylene diisocyanate was reported[237]; later, direct block polymerization of α-, β- and γ-cyclodextrins by di- or polyfunctional reagents[238–240] and bead polymerization were described[241]. If cyclodextrins are linked to polyethers, water-soluble polymers are produced[242–245]; the polymerization of β-cyclodextrin acrylate (obtained by acylation of cyclodextrin with included *m*-nitrophenylacrylate) yielded a macromolecule (molecular weight 10^4—10^5) which is water-soluble and, as it only has one linkage site per cyclodextrin, exhibits almost the same properties as the free cyclodextrin[246,247]. The cyclodextrins can also be bound to polymeric resins such as Sepharose 6B[248].

The characteristic physical data for the swelling capacity of these polymers can be determined[235,240,246,247] and an "apparent void concentration" obtained which expresses the cyclodextrin concentration (mol cyclodextrin/g resin)[249]. Polymerized cyclodextrins are preferentially used for chromatography ("gel inclusion chromatography")[249]. A HETP optimum (HETP = "height equivalents of a theoretical plate") of 0.7—0.8 was found at room temperature for aromatic amino acids run on a β-cyclodextrin polymer with a flow rate of 10—20 ml/h[235]. Several applications of gel inclusion chromatography are described in Section 9.

The complexation behaviors of monomeric and polymer-fixed cyclodextrin can be different. Small gas molecules which form 1:1 complexes are not bound by the polymer as strongly as by the monomer. In the case of larger guest molecules which can react with two cyclodextrins, the polymer complexes were shown to be more stable than those formed

with free cyclodextrin; this is due to the fact that the high local concentration of the cyclodextrin within the polymer allows cooperativity between adjacent molecules[250].

9. Applications of Cyclodextrins

The practical application of cyclodextrins has gained in importance over the past few years. This is reflected especially by the increasing number of patents. As inclusion represents a micro-encapsulation, this phenomenon contributes in particular to the stabilization of sensitive toxic substances and improves their handling and dosage. Cyclodextrins bound to polymers are also highly suited for column chromatography; a remarkable agricultural application has recently been reported.

9.1. Micro-encapsulation

Each guest molecule within an inclusion complex is individually surrounded by cyclodextrin and is thus, from the microscopical point of view, encapsulated. As this can lead to advantageous changes in the chemical and physical properties of the guest molecule, experiments have been performed with the aim of introducing micro-encapsulation by cyclodextrins into industries which manufacture drugs, foodstuffs, plant protective agents, and toilet articles. The use of cyclodextrin complexes in industry brings about the following improvements[15-17,34-36]:

I) Stabilization of light- or oxygen-sensitive substances

II) Modification of the chemical activity of guest molecules
   a) Reactive substances are protected by inclusion and can be mixed with other substances without any risk.
   b) Reactions can be made selective by inclusion of functional groups.
   c) Reactions can be promoted or suppressed (see I).

III) Fixation of very volatile substances
   a) Storage and handling are improved, especially in the case of toxic substances.
   b) The quantity of the volatile substance required can be reduced since little or no vaporization takes place.
   c) The quantities of aromatic and physiologically active substances can be better measured out.

IV) Modification of the physicochemical properties of guest molecules
   a) Substances which are sparingly soluble in water are made more soluble by the addition of cyclodextrins or they can be more easily emulsified.
   b) Powdered, freeze-dried cyclodextrin complexes are finely dispersed and more soluble than uncomplexed guest molecules which are only sparingly soluble in water.
   c) Pigments can be masked or the color of substances can be altered as inclusion generally produces changes in the spectrum of the molecule.
   d) Unpleasant tastes can be suppressed.

Several examples will be mentioned in order to illustrate these applications.

I: The most active components of "Dalmatian insect powder" from *flores pyrethri* are pyrethrins, *i.e.* derivatives of chrysanthemummonocarboxylic acid ester and their synthetic analogues[251]. They are very toxic towards insects but are harmless for warm-blooded animals. Pyrethrins are yellowish, light-sensitive oils and their use is therefore limited. Inclusion in β-cyclodextrin gives a powder which is easy to handle, very stable, and toxic for insects long after its application (Fig. 13a, Table 7[34,252]). The insecticide DDVP (*O*-(2,2-dichlorovinyl)-*O*,*O*-dimethylphosphate) is also unstable in its pure form but can be used to advantage after inclusion within β-cyclodextrin[253].

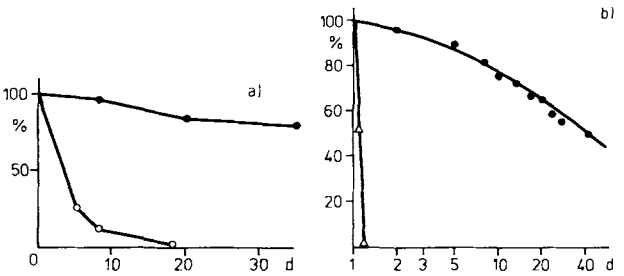


Fig. 13. Stabilization of active substances by β-cyclodextrin. a) Decomposition of allethrin (a pyrethrin) in a talc mixture (○) and when complexed with β-cyclodextrin (●). The samples were sprayed onto glass plates and exposed to sunlight (according to [252]); b) decomposition of vitamin D_3 (cholecalciferol) in its free form or in a mixture with β-cyclodextrin (△) and when complexed with β-cyclodextrin (•) at 80 °C (according to [257]).

Table 7. Decline in the activities of resmethrin and pyrethrins (in their free forms and when complexed with β-cyclodextrin) against the pine caterpillar *Dendrolinus spectabilis* Butler. Pine branches were immersed in aqueous solutions containing the doses indicated (according to [252]).

Active cpd.	Formulation	Dose [%]	Caterpillars killed [%] after 0	1 weeks	2
Resmethrin	Emulsifiable concentrate	0.1	100	0	0
		0.05	100	0	0
	Inclusion complex	0.1	100	90	90
		0.05	100	100	40
Pyrethrins	Emulsifiable concentrate	0.1	90	10	0
		0.05	50	0	0
	Inclusion complex	0.1	90	100	90
		0.05	100	100	40

Other unsaturated substances which are unstable when exposed to air and light can, like these insecticides, be stored after micro-encapsulation. The extremely labile vitamin D_3 (cholecalciferol) should be mentioned here; the chemical, physical, and pharmacological properties of its β-cyclodextrin complex[254-256] have been studied in detail[257]. The thermal stability of this complex is considerably higher than that of pure vitamin D_3 (Fig. 13b); after complexation the oxygen uptake measured in a Warburg apparatus is very low even after 20 days and the light sensitivity is much lower than that of uncomplexed vitamin D_3. The cyclodextrin complexes of prostaglandins I_2 (prostacyclin)[258], F_{2a}[259], E_2 (dinoprostone)[35,260], and E_1 have been shown to have similar advantageous properties. Prostaglandin E_1 is now commercially available in the form of its α-cyclodextrin complex [Ono Pharmaceuticals Co. Ltd. (Japan)][261-265] and has been clinically tested[266].

β-Cyclodextrin has also been shown to have a stabilizing influence on benzocaine[267], procaine, atropine, aspirin, phe-

nylbutazone[268], salicylic acid, ascaridole, the ethyl ester of chaulmoogric acid[269], and linoleic acid[269,270]. Indomethazine is stabilized by β- but not by α-cyclodextrin[271]. Azapropazone[271] and the insecticide trichlorophone[34,200,272] are, however, deactivated more rapidly by β-cyclodextrin. Similarly, β-cyclodextrin promotes the isomerization of prostaglandin A_1 to prostaglandin B_1[215] and the dechlorination of chlorpromazine[273]. Cyclodextrin inclusion also affects the stability of phenothiazines[274].

The stabilization of aromatic substances by cyclodextrins is of importance for the foodstuff and toilet article industries[34,36,275-277]. Anethole which is normally sensitive to oxidation, becomes largely resistant after inclusion within β-cyclodextrin; the oily aromatic substances contained in camomile, onions, dill, garlic, caraway, horseradish, and mustard can be stabilized in the form of easy-to-handle, powdered substances by inclusion within β-cyclodextrin. Interestingly the principal and subsidiary components are complexed to the same extent; the full taste and smell are thus retained[34,36]. The conservation of aromatic substances is also utilized in toilet articles such as bath additives[278] and toothpaste (neohesperidine dihydrochalcone)[279].

II: Particular mention should be made of the stabilization of nitroglycerin by inclusion within β-cyclodextrin[280]. The crystalline adduct can easily be made into tablets and is no longer explosive. Further applications have already been described (see I).

III: Inclusion of ethylene in cyclodextrin furnishes an easy-to-handle powder which can be used to control plant growth[281]. The bitter taste of protein hydrolyzates can be suppressed by cyclodextrin[282]; the previously mentioned, volatile, aromatic substances (see I) are fixed by inclusion. Allicin, the antibacterial, antifungicidal, evil-smelling, unstable active substance of garlic can be largely "neutralized" by inclusion in β-cyclodextrin[283]; the volatile insecticide DDVP (see I) can be stabilized against the influences of light and the atmosphere and is retained within the cyclodextrin cavity.

IV: Admixture of 1—3% cyclodextrin stabilizes emulsions. This has been demonstrated with mayonnaise made from edible oil which can be beaten without egg on addition of β-cyclodextrin; margarine or butter creams can be stabilized by β-cyclodextrin[284]. The yield of meringue from egg white (cm^3 foam per g egg white) is improved on addition of β-cyclodextrin; this beaten egg white is more stable for a period of months (at −15 °C) than egg white without cyclodextrin[285].

There are many examples to demonstrate the effect of cyclodextrins on the solubility of substances which are sparingly soluble in water. The solubility of the guest component increases linearly with the amount of cyclodextrin added, in some cases the solubility passes through a maximum (Fig. 14). The most important of such studies concern the water solubility of fatty acids[111,270,286], of amines such as procaine, lidocaine, meperdine, adipherine, the steroids cortisone acetate and testosterone[287], hydroxybenzoic acids[112], an anthranilic acid derivative[288], benzocaine, aspirin, *p*-aminobenzoic acid, tetracycline, sulfadiazine, morphine, vanillin, ephedrine, sorbic acid[289], several phenyl-substituted carbonic acids[290], ketoprofene and other antipyretic agents[291,292,106], vitamin D_3[36], coumarin anticoagulants[293], sulfonamides[294] and barbiturates[295]. Cyclodextrin com-

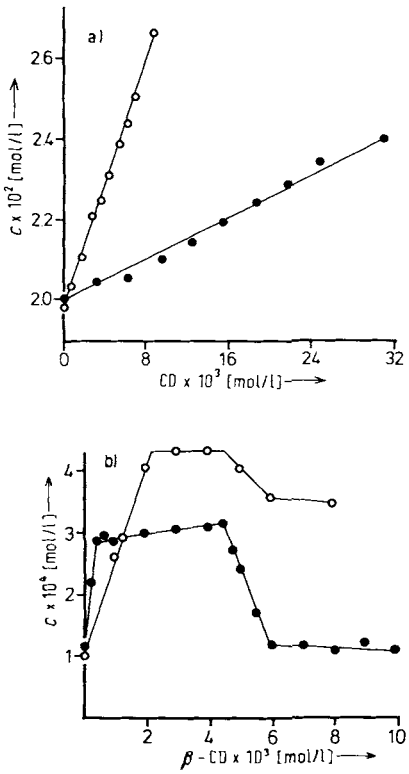


Fig. 14. Increase in the solubility of substances sparingly soluble in water brought about by addition of cyclodextrins. a) Aspirin with α- (●) and β-cyclodextrin (○) at 30 °C (according to [289]); b) cortisone acetate (○) and testosterone (●) with β-cyclodextrin at 30 °C (according to [287]).

plexes in powder form often dissolve not only more easily but also more rapidly than the guest components[296] (Fig. 15). Even if the complexes do not dissolve, they are absorbed

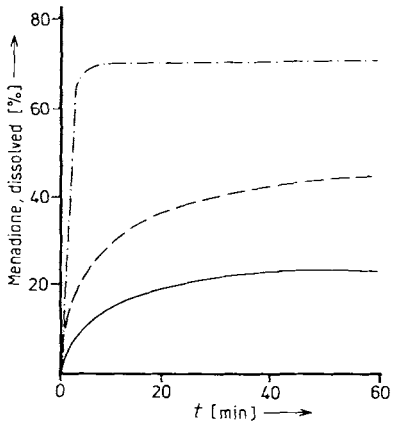


Fig. 15. Rate of solution of menadione (—), of a menadione/β-cyclodextrin mixture (---) and the menadione·β-cyclodextrin complex (·····) in water, pH = 7.5, 37 °C (according to [296]).

by living organisms very well due to the fact that they are finely dispersed. This leads to a more rapid and, in many cases, more potent action. Tests on rabbits and dogs showed that the antipyretic substances flufenamic acid, ibuprofene, and ketoprofene were detected much sooner in blood and urine when they were administered orally as their β-cyclodextrin complexes than when they were given in their free forms[297] (Fig. 16). Inclusion of the anti-rheumatic agent indomethazine in β-cyclodextrin improved but did not acceler-

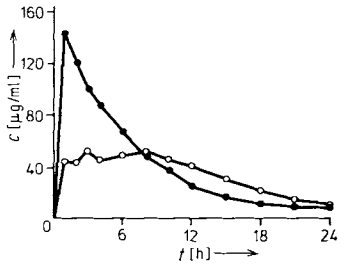


Fig. 16. Ketoprofene concentration in the blood of rabbits after oral administration of 100 mg lyophilized ketoprofene. β-cyclodextrin complex (•), lyophilized ketoprofene (○) (according to [297]).

ate its action; its ulcerogenic properties were almost totally suppressed[36,298]. T-labeled stearic acid and ^{14}C-labeled icosatrienic acid were fed to rats in their free forms and as their β-cyclodextrin complexes. The distribution of the radioactivity in urine, blood, and lymph was then monitored. Here too the cyclodextrin complexes were taken up more quickly and efficiently than the uncomplexed compounds[35].

It is known that an overdose of drugs, including barbiturates, can be partly removed by peritoneal dialysis. Rats were injected intraperitoneally with a physiological saline solution corresponding to 15% of the body weight with and without 1.5% β-cyclodextrin; a phenobarbital solution (100 mg/kg body weight) was simultaneously injected into a sublingual artery. Samples taken from the peritoneum at intervals of 15 min showed that the cyclodextrin solutions took up three times as much barbiturate as the control solutions.

Utilization of cyclodextrins also permits the chromatographic separation of prostaglandins A, B, and E[300] and allows vitamin K_1 and K_2 derivatives to be synthesized in one step[214].

Another application for cyclodextrins was discovered after it had been observed that they dramatically increase the fluorescence intensity of dansyl derivatives[301]. As these derivatives play an important part in peptide analysis, the detection limit can be improved considerably.

9.2. Cyclodextrin Polymers in Gel Inclusion Chromatography

The cyclodextrin polymers described in Section 8 are preferred as filling materials for column chromatography (gel inclusion chromatography[249,302]). When compared with customary Sephadex, it is apparent that cyclodextrin polymers have the advantage that they strongly retard molecules of an appropriate size and molecules with similar molecular weights or even isomers can be separated. *o*- and *p*-nitrophenol[239], benzoic and *o*-chlorobenzoic acid[249] are examples; these substances can be well separated on cyclodextrin polymers but not on Sephadex. Similar separations have been achieved with amino acids—particularly those with aromatic side groups[235,239]. Chromatography of nucleosides and nucleotides on cyclodextrin polymers also produced successful results; the polymers select, subject to the pH value, according to the position of the phosphate group in the sugar residue[303,304]. Diastereomers of the Cr-ATP complex have been separated on a cyclodextrin polymer[305]. Oligonucleotides, RNA fragments, and intact tRNA are not suitable for chromatography on these polymers but good results are obtained if diethylaminoethyl groups are incorporated because these groups serve additionally as anion exchangers[306]. Phenols are also bound well by cyclodextrin polymers[236] and can thus be filtered out from cigarette smoke. The different affinities of non-branched and branched paraffins for soluble cyclodextrin resins cross-linked to epichlorohydrin[307,308,236] could be exploited in oil refineries; a similar effect was demonstrated for urea adducts about fourty years ago.

The polymer-linked cyclodextrins can be used to advantage for affinity chromatography of amylases which bind cyclodextrins as inhibitors but do not act upon them enzymatically. β-Amylase from potatoes, for example, is retarded by a column filled with α-cyclodextrin-Sepharose whilst the closely related α-amylase passes through the column without hindrance. After the separation the β-amylase was eluted with α-cyclodextrin[248].

The cyclodextrins can also act catalytically in the polymer complex. As has already been described for the chlorination of anisole[205] (see Section 6.4), polymerized β-cyclodextrin controls the *o/p* ratio more effectively than the monomer; the *p*-nitrophenyl esters of fatty acids are likewise hydrolyzed up to three times more rapidly in the presence of a β-cyclodextrin polymer than in the presence of free β-cyclodextrin[246].

9.3. Racemate Resolution with Cyclodextrins

One application of the cyclodextrins, particularly of cyclodextrin polymers, which seems to be of promise is the resolution of racemates by means of complex formation—this was already described in 1959[32]. As cyclodextrins themselves are optically active molecules they form a diastereomeric pair with each included racemate; the two components of the pair exhibit different physical properties:

$$\left.\begin{array}{l}\text{D}(+)\text{-Cyclodextrin}\cdot(+)\text{-antipode}\\ \text{D}(+)\text{-Cyclodextrin}\cdot(-)\text{-antipode}\end{array}\right\}\ \text{Diastereomers}$$

If a 5—10 fold excess of a cyclodextrin solution is mixed with a racemate, one of the cyclodextrin·antipode complexes precipitates out preferentially resulting in partial racemate resolution. This phenomenon was first demonstrated with the esters of mandelic, phenylchloroacetic, and atrolactic acids, with 2,2′- and 4,4′-dichlorobenzoin, cinnamic acid dibromide (2,3-dibromo-3-phenylpropionic acid), and dibromosuccinic acid[32]. In these cases, 3—10% enantiomeric purity was achieved. Much better yields, with up to 84% enantiomeric purity of the included antipode, were obtained when separating racemic isopropyl methylphosphinates and their ethyl analogues with α- and β-cyclodextrins[309]. Racemates of chiral sulfinyl compounds such as sulfoxides, sulfinates, and thiosulfinate *S*-esters could be resolved into their antipodes after inclusion in β-cyclodextrin; an enantiomeric purity of 15% (in the case of isopropyl methanesulfinate up to 68%) was usually achieved in one separation step[310].

The catalytic action of α-cyclodextrin on a racemate has been investigated using (*S*)-(+)- and (*R*)-(−)-sarin (isopropyl methylphosphonofluoridate)[311]. Here too partial racemate resolution occurs as a result of preferential hydrolysis of an antipode. Whereas the dissociation constants show that (*S*)-(+)-sarin is bound 7 times more strongly by α-cyclodextrin than (*R*)-(−)-sarin, the rate constants (which reflect the

nucleophilic attack by the secondary hydroxy groups (O(2)H or O(3)H) of α-cyclodextrin on the sarin phosphorus atom) demonstrate that (*R*)-(−)-sarin reacts 36 times faster than (*S*)-(+)-sarin. It is evident that a higher affinity is not synonymous with a quicker reaction. The same conclusion was also drawn in the cyclodextrin-catalyzed hydrolysis of substituted phenyl acetates[118].

9.4. Cyclodextrins in Agriculture

As already mentioned in Section 9.1, cyclodextrins can be employed for the molecular encapsulation and thus stabilization of unstable or very volatile insecticides and herbicides.

Surprisingly, cyclodextrins can also be used to improve the yields of grain harvests[312]. If the grain is treated with an aqueous β-cyclodextrin solution before being sown, germination is delayed by about ten days; this is because some of the amylases which degrade the starch depot of the seeds are at least partially inhibited. The young plants are at first smaller than plants from untreated seeds but soon grow more quickly and vigorously finally giving a 20—45% larger harvest. Cyclodextrins also have a beneficial effect on the customary treatment of the seed with herbicides as these substances suppress not only the growth of weeds but also that of the grain. The delay in germination and the subsequent improved plant growth largely compensate for the adverse effects of the herbicide.

10. Outlook

Cyclodextrins can be employed in a large variety of ways owing to the fact that they can form complexes with almost all small molecules having a diameter of 5—8 Å. In the next few years the processes reponsible for the formation of cyclodextrins from starch, their modification, complex formation, and catalytic properties will still be interesting topics for the research worker; as far as the applied use of cyclodextrins is concerned, attention will be concentrated on the micro-encapsulation of sensitive aromatic substances, pharmaceuticals, herbicides, and insecticides and on chromatography with cyclodextrin polymers. The current price of α- and β-cyclodextrins (36 and 25 DM/5 g[313] respectively) is much too high for industrial purposes, but with production of at least 200 t per year the price of the cyclodextrins may well become reasonable enough for technical purposes[317]. It is to be hoped that the chemical spirit of invention will soon discover so many other fields of applications for the cyclodextrins that it will be profitable to manufacture them on an industrial scale.

I would like to thank Professor Friedrich Cramer, one of the pioneers of cyclodextrin research, for his generous support and interest shown while I carried out the studies cited in this article. These studies were helped by the enthusiastic assistance of K. Beyer, Dr. B. Hingerty, K. Lindner, Dr. P. C. Manor and Dr. M. Noltemeyer who were generously supported by grants from the Max-Planck-Gesellschaft, the Deutsche Forschungsgemeinschaft, the Alexander-von-Humboldt-Stiftung, and NATO. I thank Dr. Takaji Fujiwara, Osaka University, for translation of the Japanese publication[34], Dr. Mifune, Teijin Co. (Tokyo), and Dr. Szejtli, Chinoin (Budapest) for their frank exchange of information. I am also grateful to the Yamada Science Foundation for a four-week stay in Osaka which made a very great contribution to the writing of this article.

Received: January 23, 1980 [A 316 IE]
German version: Angew. Chem. *92*, 343 (1980)
Translated by Dr. *Gail Schulz*, Weiterstadt (Germany)

[1] *L. Mandelcorn:* Non-Stoichiometric Compounds. Academic Press, New York 1964.
[2] *A. Weiss, K. Hartl, U. Hofmann*, Z. Naturforsch. *B 12*, 351 (1957).
[3] *G. A. Jeffrey, R. K. McMullan*, Prog. Inorg. Chem. *8*, 43 (1967).
[4] *W. Eitel:* Silicate Science. 5 Volumes. Academic Press, New York 1964—1966.
[5] *N. V. Belov:* Crystal Chemistry of Large Cation Silicates. Consultants Bureau, New York 1963.
[6] *D. W. Breck*, J. Chem. Educ. *41*, 678 (1964).
[7] *W. Schlenk jr.*, Fortschr. Chem. Forsch. *2*, 92 (1951); Chem. Unserer Zeit *3*, 120 (1969); Justus Liebigs Ann. Chem. *1973*, 1145.
[8] *F. Cramer:* Einschlussverbindungen. Springer, Heidelberg 1954.
[9] *W. Saenger*, Umschau *74*, 635 (1974).
[10] *D. French*, Adv. Carbohydr. Chem. *12*, 189 (1957).
[11] *J. A. Thoma, L. Stewart* in *R. L. Whistler, E. F. Paschall:* Starch. Chemistry and Technology. Academic Press, New York 1965, pp. 209ff.
[12] *D. W. Griffiths, M. L. Bender*, Adv. Catal. *23*, 209 (1973).
[13] *F. Cramer, H. Hettler*, Naturwissenschaften *54*, 625 (1967).
[14] *R. J. Bergeron*, J. Chem. Educ. *54*, 204 (1977).
[15] *K. H. Frömming*, Pharm. Unserer Zeit *2*, 109 (1973).
[16] *S. G. Frank*, J. Pharm. Sci. *64*, 1585 (1975).
[17] *J. Szejtli*, Stärke *30*, 427 (1978).
[18] *F. Vögtle, E. Weber*, Angew. Chem. *91*, 813 (1979); Angew. Chem. Int. Ed. Engl. *18*, 753 (1979); *F. Vögtle*, Chimia *33*, 239 (1979).
[19] *Yu. A. Ovchinnikov, V. T. Ivanov, A. M. Shkrob:* Membrane-Active Complexones. B. B. A. Library, Vol. 12. Elsevier, Amsterdam 1974.
[20] *W. Banks, C. T. Greenwood:* Starch and its Compounds. University Press, Edinburgh 1975.
[21] *R. E. Dickerson, I. Geis:* The Structure and Action of Proteins. Harper & Row, New York 1969; Struktur und Funktion der Proteine. Verlag Chemie, Weinheim 1971.
[22] *A. Villiers*, C. R. Acad. Sci. *112*, 536 (1891).
[23] *F. Schardinger*, Wien. Klin. Wochenschr. *17*, 207 (1904).
[24] *F. Schardinger*, Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. II *29*, 188 (1911).
[25] *K. Freudenberg, M. Meyer-Delius*, Ber. Dtsch. Chem. Ges. *71*, 1596 (1938); *K. Freudenberg, E. Plankenhorn, H. Knauber*, Chem. Ind. (London) *1947*, 731; Justus Liebigs Ann. Chem. *558*, 1 (1947).
[26] *D. French, M. Levine, J. Pazur*, J. Am. Chem. Soc. *71*, 356 (1949).
[27] *D. French, R. E. Rundle*, J. Am. Chem. Soc. *64*, 1651 (1942).
[28] *K. Freudenberg, F. Cramer*, Z. Naturforsch. *B 3*, 464 (1948).
[29] *D. French, M. L. Levine, J. H. Pazur, E. Norberg*, J. Am. Chem. Soc. *71*, 353 (1949).
[30] *F. Cramer, F. M. Henglein*, Chem. Ber. *90*, 2561 (1957).
[31] *F. Cramer*, Chem. Ber. *86*, 1576 (1953).
[32] *F. Cramer, W. Dietsche*, Chem. Ber. *92*, 378 (1959).
[33] *W. Saenger* in *B. Pullman:* Environmental Effects on Molecular Structure and Properties. D. Reidel, Dordrecht 1976, pp. 265ff.
[34] *A. Mifune, A. Shima*, J. Synth. Org. Chem. Jap. *35*, 116 (1977).
[35] *J. Szejtli*, Stärke *29*, 26 (1976).
[36] Company publication: β-Cyclodextrin. Chinoin Pharmaceutical and Chemical Factories Ltd., Laboratory for Biochemical Research, Budapest 1979.
[37] *M. L. Bender, M. Komiyama:* Cyclodextrin Chemistry. Springer, Berlin 1978.
[38] *W. T. Winter, A. Sarko*, Biopolymers *13*, 1447, 1461 (1974).
[39] *V. G. Murphy, B. Zaslow, A. D. French*, Biopolymers *14*, 1487 (1975).
[40] *K. Horikoshi*, Process Biochem. *1979*, 26.
[41] *S. Kitahata, N. Tsuyama, S. Okada*, Agric. Biol. Chem. *39*, 387 (1974); *S. Kitahata, S. Okada*, J. Biochem. *79*, 641 (1976).
[42] *N. Nakamura, K. Horikoshi*, Agric. Biol. Chem. *40*, 753 (1976).
[43] *H. Bender*, Arch. Microbiol. *111*, 271 (1977); *113*, 49 (1977).
[44] *M. Shirosaka, H. Fumiya*, Amylase Symp. Proc. *8*, 43 (1973).
[45] *S. Chiba, S. Okada, S. Kitahata, T. Shimomura*, Agric. Biol. Chem. *39*, 2353 (1975).
[46] *H. Bender*, Carbohydr. Res. *65*, 85 (1978).
[47] *A. O. Pulley, D. French*, Biochem. Biophys. Res. Commun. *5*, 11 (1961).
[48] *P. R. Sundarajan, V. S. R. Rao*, Carbohydr. Res. *13*, 351 (1970).
[49] *G. H. Andersen, F. J. Robbins, F. J. Domingues, R. G. Moores, C. L. Long*, Toxicol. Appl. Pharmacol. *5*, 257 (1963).

[50] *A. Mifune*, J. Synth. Org. Chem. Jap. *32*, 889 (1974); Company publication: β-Cyclodextrin catalog, Teijin Co. (Japan).
[51] Company publication: Industrial Bio-Test Laboratories, personal communication 1968, cited in [34].
[52] *T. Makita, N. Koshima, Y. Hashimoto, H. Ide, M. Tsuji, Y. Hujisaki*, Pharmacometrics *10*, 499 (1975).
[53] *J. Szejtli, G. Sebestyén*, Stärke *31*, 385 (1979); Company publication: Chinoin Internal Toxicology Report, Budapest 1978.
[54] *D. W. Frank, J. E. Gray, R. N. Weaver*, Am. J. Pathol. *83*, 367 (1976).
[55] FAO Nutrition Meetings, Series No. 46, A. WHO/Food AAD/70.36.
[56] *H. Bender*, Arch. Microbiol. *113*, 49 (1977).
[57] *E. Ben-Gershom*, Nature *175*, 593 (1955).
[58] *B. Pfannemüller*, Stärke *20*, 351 (1968).
[59] *J. A. Thoma, D. E. Koshland, jr.*, J. Am. Chem. Soc. *82*, 3329 (1960).
[60] *M. Ohnishi*, J. Biochem. (Tokyo) *69*, 181 (1971).
[61] *S. Mora, I. Simon, P. Elodi*, Mol. Cell. Biochem. *4*, 205 (1974).
[62] *I. Simon, S. Mora, P. Elodi*, Mol. Cell. Biochem. *4*, 211 (1974).
[63] *J. J. Marshall*, FEBS Lett. *37*, 269 (1973).
[64] *J. Szejtli, Zs. Budai*, Acta Chim. Acad. Sci. Hung. *99*, 433 (1979).
[65] *J. Szejtli*, Stärke *30*, 427 (1978).
[66] *K. Takeo, T. Kuge*, Agric. Biol. Chem. *33*, 1174 (1969); *34*, 568 (1970).
[67] *J. Szejtli, E. Bánky-Elöd, A. Stadler, P. Tétényi, I. Héthelyi, L. Kernóczy*, Acta Chim. Acad. Sci. Hung. *99*, 447 (1979).
[68] *J. Szejtli, Zs. Budai*, Acta Chim. Acad. Sci. Hung. *94*, 383 (1977).
[69] *L. Kernóczy, P. Tétényi, E. Mincsovics, J. Szejtli*, Q. J. Crude Drug Res. *16*, 153 (1978).
[70] *W. Broser, W. Lautsch*, Z. Naturforsch. *B 8*, 711 (1953).
[71] *W. Lautsch, W. Broser, W. Biedermann, H. Gnichtel*, Angew. Chem. *66*, 123 (1954).
[72] *J. A. Thoma, D. French*, J. Am. Chem. Soc. *80*, 6142 (1958).
[73] *F. Cramer, W. Saenger, H.-Ch. Spatz*, J. Am. Chem. Soc. *89*, 14 (1967).
[74] *K. Uekama, M. Otagiri, Y. Kanie, S. Tanaka, K. Ikeda*, Chem. Pharm. Bull. *23*, 1421 (1975).
[75] *M. Otagiri, T. Miyaji, K. Uekama, K. Ikeda*, Chem. Pharm. Bull. *24*, 1146 (1976).
[76] *T. Miyaji, Y. Kurono, K. Uekama, K. Ikeda*, Chem. Pharm. Bull. *24*, 1155 (1976).
[77] *K. A. Connors, J. M. Lipari*, J. Pharm. Sci. *65*, 379 (1976).
[78] *R. J. Bergeron, P. McPhie*, Bioorg. Chem. *6*, 465 (1977).
[79] *C. L. Seliskar, L. Brand*, Science *171*, 799 (1971).
[80] *I. Tabushi, K. Fujita, L. C. Yuan*, Tetrahedron Lett. *1977*, 2503.
[81] *H. Kondo, H. Nakatani, K. Hiromi*, Carbohydr. Res. *52*, 1 (1976).
[82] *H. E. Edwards, J. K. Thomas*, Carbohydr. Res. *65*, 173 (1978).
[83] *R. M. Paton, E. T. Kaiser*, J. Am. Chem. Soc. *92*, 4723 (1970).
[84] *J. Martinie, J. Michon, A. Rassat*, J. Am. Chem. Soc. *97*, 1818 (1975).
[85] *J. Michon, A. Rassat*, J. Am. Chem. Soc. *101*, 995 (1979).
[86] *K. Flohr, R. M. Paton, E. T. Kaiser*, J. Am. Chem. Soc. *97*, 1209 (1975).
[87] *R. J. Bergeron, D. M. Pillor, G. Gibeily, W. P. Roberts*, J. Am. Chem. Soc. *7*, 263 (1978).
[88] *K. Harata*, Bull. Chem. Soc. Jpn. *51*, 2737 (1978).
[89] *K. Nishida, S. Ishida, H. Watanabe*, Colloid Polym. Sci. *254*, 481 (1976).
[90] *K. Harata, H. Uedaira*, Bull. Chem. Soc. Jpn. *48*, 375 (1975).
[91] *H. Yamaguchi, N. Ikeda, F. Hirayama, K. Uekama*, Chem. Phys. Lett. *55*, 75 (1978).
[92] *N. Ikeda, H. Yamaguchi*, Chem. Phys. Lett. *56*, 167 (1978).
[93] *H. Yamaguchi, N. Ikeda, K. Uekama, F. Hirayama*, Z. Phys. Chem. (Frankfurt am Main) *109*, 173 (1978).
[94] *N. Matsuura, S. Takenaka, N. Tokura*, J. Chem. Soc. Perkin Trans. II *1977*, 1419.
[95] *C. Formoso*, Biochem. Biophys. Res. Commun. *50*, 999 (1973); Biopolymers *13*, 909 (1974).
[96] *K. Uekama, F. Hirayama, S. Yamasaki, M. Otagiri, K. Ikeda*, Chem. Lett. *1977*, 1389.
[97] *B. Casu, M. Reggiani, G. G. Gallo, A. Vigevani*, Tetrahedron *22*, 3061 (1966); Carbohydr. Res. *12*, 157 (1970).
[98] *P. V. Demarco, A. L. Thakkar*, Chem. Commun. *1970*, 2.
[99] *K. Uekama, F. Hirayama, N. Matsuo, H. Koinuma*, Chem. Lett. *1978*, 703.
[100] *J. P. Behr, J. M. Lehn*, J. Am. Chem. Soc. *98*, 1743 (1976).
[101] *D. J. Wood, F. E. Hruska, W. Saenger*, J. Am. Chem. Soc. *99*, 1735 (1977).
[102] *R. I. Gelb, L. M. Schwartz, R. F. Johnson, D. A. Laufer*, J. Am. Chem. Soc. *101*, 1869 (1979).
[103] *R. I. Gelb, L. M. Schwartz, C. T. Murray, D. A. Laufer*, J. Am. Chem. Soc. *100*, 3553 (1978).
[104] *K. Takeo, K. Hirose, T. Kuge*, Chem. Lett. *1973*, 1233.
[105] *R. J. Bergeron, M. A. Channing, K. A. McGovern*, J. Am. Chem. Soc. *100*, 2878 (1978).
[106] *J. F. Wojcik, R. P. Rohrbach*, J. Phys. Chem. *79*, 2251 (1975).
[107] *T. Okubo, H. Kitano, N. Ise*, J. Phys. Chem. *80*, 2661 (1976).
[108] *B. Siegel, D. Eberlein, D. Rifkin, K. A. Davis*, J. Am. Chem. Soc. *101*, 775 (1979).
[109] *S. Yamaguchi, T. Tsukamoto*, Nippon Kagaku Kaishi *1976*, 1856.
[110] *T. Ota, T. Matsue, M. Fujihara*, Heterocycles *6*, 1833 (1977).
[111] *H. Schlenk, D. M. Sand*, J. Am. Chem. Soc. *83*, 2312 (1961).
[112] *J. Cohen, J. L. Lach*, J. Pharm. Sci. *52*, 132 (1963).
[113] *R. P. Rohrbach, L. J. Rodriguez, E. M. Eyring, J. F. Wojcik*, J. Phys. Chem. *81*, 944 (1977).
[114] *H. Kondo, H. Nakatani, K. Hiromi*, J. Biochem. *79*, 393 (1976); Carbohydr. Res. *52*, 1 (1976).
[115] *E. A. Lewis, L. D. Hansen*, J. Chem. Soc. Perkin Trans. II *1973*, 2081.
[116] *G. E. Hardee, M. Otagiri, J. H. Perrin*, Acta Pharm. Succ. *15*, 188 (1978).
[117] *M. Komiyama, M. L. Bender*, J. Am. Chem. Soc. *100*, 2259 (1978).
[118] *R. L. Van Etten, J. F. Sebastian, G. A. Clowes, M. L. Bender*, J. Am. Chem. Soc. *89*, 3242 (1967).
[119] *R. L. Van Etten, G. A. Clowes, J. F. Sebastian, M. L. Bender*, J. Am. Chem. Soc. *89*, 3253 (1967).
[120] *D. L. Van der Jagt, F. L. Killian, M. L. Bender*, J. Am. Chem. Soc. *92*, 1016 (1970).
[121] *T. S. Straub, M. L. Bender*, J. Am. Chem. Soc. *94*, 8881 (1972).
[122] *H. A. Benesi, J. H. Hildebrand*, J. Chem. Soc. *71*, 2703 (1949).
[123] *K. Harata*, Bull. Chem. Soc. Jpn. *49*, 1493 (1976).
[124] *K. Mochida, A. Kagita, Y. Matsui, Y. Date*, Bull. Chem. Soc. Jpn. *46*, 3703 (1973).
[125] *R. Lumry, S. Rajender*, Biopolymers *9*, 1125 (1970).
[126] *K. Ikeda, K. Uekama, M. Otagiri*, Chem. Pharm. Bull. *23*, 201 (1975).
[127] *D. A. Rees*, J. Chem. Soc. *B 1970*, 877.
[128] *P. C. Manor, W. Saenger*, J. Am. Chem. Soc. *96*, 3630 (1974).
[129] *B. Hingerty, W. Saenger*, J. Am. Chem. Soc. *98*, 3357 (1976); Nature *255*, 396 (1975).
[130] *W. Saenger, M. Noltemeyer, P. C. Manor, B. Hingerty, B. Klar*, Bioorg. Chem. *5*, 187 (1976).
[131] *B. Klar, B. Hingerty, W. Saenger*, Acta Crystallogr., in press.
[132] *R. K. McMullan, W. Saenger, J. Fayos, D. Mootz*, Carbohydr. Res. *31*, 37 (1973).
[133] *M. Noltemeyer, W. Saenger*, Nature *259*, 629 (1976); J. Am. Chem. Soc. *102*, 2710 (1980).
[134] *R. K. McMullan, W. Saenger, J. Fayos, D. Mootz*, Carbohydr. Res. *31*, 211 (1973).
[135] *W. Saenger, M. Noltemeyer*, Chem. Ber. *109*, 503 (1976); Angew. Chem. *86*, 594 (1974); Angew. Chem. Int. Ed. Engl. *13*, 552 (1974).
[136] *W. Saenger, R. K. McMullan, J. Fayos, D. Mootz*, Acta Crystallogr. *B 30*, 2019 (1974).
[137] *W. Saenger, K. Beyer, P. C. Manor*, Acta Crystallogr. *B 32*, 120 (1976).
[138] *K. Harata, H. Uedaira*, Nature *253*, 190 (1975).
[139] *K. Harata*, Bull. Chem. Soc. Jpn. *51*, 1644 (1978).
[140] *K. Harata, H. Uedaira, J. Tanaka*, Bull. Chem. Soc. Jpn. *51*, 1627 (1978).
[141] *A. Hybl, R. E. Rundle, D. E. Williams*, J. Am. Chem. Soc. *87*, 2779 (1965).
[142] *K. Lindner, W. Saenger*, Angew. Chem. *90*, 738 (1978); Angew. Chem. Int. Ed. Engl. *17*, 694 (1978).
[143] *J. J. Stezowski, K. H. Jogun, E. Eckle, K. Bartels*, Nature *274*, 617 (1978).
[144] *J. A. Hamilton, M. N. Sabesan, L. K. Steinrauf, A. Geddes*, Biochem. Biophys. Res. Commun. *73*, 659 (1976).
[145] *M. M. Harding, J. M. McLennan, R. M. Paton*, Nature *274*, 621 (1978).
[146] *K. Lindner, W. Saenger*, Biochem. Biophys. Res. Commun. *92*, 933 (1980).
[147] *J. M. MacLennan, J. J. Stezowski*, Biochem. Biophys. Res. Commun. *92*, 926 (1980).
[148] *B. Casu, M. Reggiani, G. G. Gallo, A. Vigevani*, Chem. Soc. Spec. Publ. *23*, 217 (1968).
[149] *R. J. Bergeron, M. A. Channing*, Bioorg. Chem. *5*, 437 (1976).
[150] *R. J. Bergeron, R. Rowan III*, Biorg. Chem. *5*, 425 (1976).
[151] *W. Broser*, Z. Naturforsch. *B 8*, 722 (1953).
[152] *R. J. Bergeron, M. A. Channing, G. J. Gibeily, D. M. Pillor*, J. Am. Chem. Soc. *99*, 5146 (1977).
[153] *G. Nemethy, H. A. Scheraga*, J. Chem. Phys. *36*, 3401 (1962).
[154] *M. Komiyama, M. L. Bender*, J. Chem. Phys. *100*, 2259 (1978).
[155] *E. S. Hall, H. J. Ache*, J. Phys. Chem. *83*, 1805 (1979).
[156] *R. J. Bergeron, D. M. Pillor, G. Gibeily, W. P. Roberts*, Bioorg. Chem. *7*, 263 (1978).
[157] *K. Harata*, Bull. Chem. Soc. Jpn. *49*, 2066 (1976).
[158] *I. Tabushi, Y.-I. Kiyosuke, T. Sugimoto, K. Yamamura*, J. Am. Chem. Soc. *100*, 916 (1978).
[159] *B. Casu, M. Reggiani*, J. Polym. Sci. *C 7*, 171 (1964).
[160] *V. S. R. Rao, P. R. Sundarajan, C. Ramakrishnan, G. N. Ramachandran* in *G. N. Ramachandran:* Conformation of Biopolymers. Academic Press, London 1967, pp. 721 ff.
[161] *A. D. French, V. G. Murphy*, Polymer *18*, 489 (1977); Cereal Foods World *22*, 61 (1977); Carbohydr. Res. *27*, 391 (1973).
[162] *P. Zugenmaier, A. Sarko*, Biopolymers *12*, 435 (1973); *15*, 2121 (1976).
[163] *C. de Claubry*, Ann. Chim. Paris *90*, 87 (1814).
[164] *J. F. Kennedy*, Adv. Carbohydr. Chem. Biochem. *29*, 398 (1974).
[165] *J. Holló, J. Szejtli* in: Starch and its Derivatives. 4th Edit. Chaucer Press, London 1968, pp. 203 ff.

[166] *R. E. Rundle, R. R. Baldwin,* J. Am. Chem. Soc. *65*, 554 (1943); *R. E. Rundle, D. French, ibid. 65*, 558, 1707 (1943); *R. E. Rundle, F. C. Edwards, ibid. 65*, 2200 (1943).
[167] *F. Cramer, U. Bergmann, P. C. Manor, M. Noltemeyer, W. Saenger,* Justus Liebigs Ann. Chem. *1976*, 1169.
[168] *B. Pfannemüller, H. Meyerhöffer, R. C. Schulz,* Makromol. Chem. *121*, 147 (1969).
[169] *C. T. Greenwood, H. Rossotti,* J. Polym. Sci. *27*, 481 (1958).
[170] *M. Mizuno, J. Tanaka,* Nagoya University, personal communication; ACS/CSJ Chemical Congress, Symposium on Low Dimensional Solids, Hawaii 1979.
[171] *R. C. Teitelbaum, S. L. Ruby, T. J. Marks,* J. Am. Chem. Soc. *100*, 3215 (1978).
[172] *F. Cramer, W. Dietsche,* Chem. Ber. *92*, 1739 (1959); Chem. Ind. (London) *1958*, 892.
[173] *A. L. Lehninger:* Biochemistry. 2nd Edit. Worth Publ., New York 1975; Biochemie. 2nd Edit. Verlag Chemie, Weinheim 1977.
[174] *F. Cramer,* Angew. Chem. *73*, 49 (1961).
[175] *N. Hennrich, F. Cramer,* J. Am. Chem. Soc. *87*, 1121 (1965).
[176] *J. L. Lach, T.-F. Chin,* J. Pharm. Sci. *53*, 924 (1964).
[177] *M. L. Bender,* Trans. N. Y. Acad. Sci. *29*, 301 (1967).
[178] *C. Van Hooidonk, C. C. Groos,* Recl. Trav. Chim. Pays-Bas *89*, 845 (1970).
[179] *C. Van Hooidonk, J. C. A. E. Breebaart-Hansen,* Recl. Trav. Chim. Pays-Bas *89*, 289 (1970).
[180] *K. Flohr, R. M. Paton, E. T. Kaiser,* Chem. Commun. *1971*, 1621.
[181] *D. E. Tutt, M. A. Schwartz,* Chem. Commun. *1970*, 113; J. Am. Chem. Soc. *93*, 767 (1971).
[182] *M. Komiyama, M. L. Bender,* J. Am. Chem. Soc. *99*, 8021 (1977).
[183] *T.-F. Chin, P.-H. Chung, J. L. Lach,* J. Pharm. Sci. *57*, 44 (1968).
[184] *W. Lautsch, R. Wiechert, H. Lehmann,* Kolloid-Z. *135*, 134 (1954).
[185] *M. Komiyama, M. L. Bender,* Bioorg. Chem. *6*, 323 (1977).
[186] *Y. Kuromo, V. Stamoudis, M. L. Bender,* Bioorg. Chem. *5*, 393 (1976).
[187] *M. Komiyama, E. J. Breaux, M. L. Bender,* Bioorg. Chem. *6*, 127 (1977).
[188] *F. Cramer, G. Mackensen,* Angew. Chem. *78*, 641 (1966); Angew. Chem. Int. Ed. Engl. *5*, 601 (1966); Chem. Ber. *103*, 2138 (1970).
[189] *Y. Iwakura, K. Uno, F. Toda, S. Onozuka, K. Hattori, M. L. Bender,* J. Am. Chem. Soc. *97*, 4432 (1975).
[190] *W. B. Gruhn, M. L. Bender,* Bioorg. Chem. *3*, 324 (1974).
[191] *C. Van Hooidonk, D. C. de Korte, M. A. C. Reuland-Meereboer,* Recl. J. R. Neth. Chem. Soc. *96*, 25 (1977).
[192] *B. Siegel, A. Pinter, R. Breslow,* J. Am. Chem. Soc. *99*, 2309 (1977).
[193] *H. J. Brass, M. L. Bender,* J. Am. Chem. Soc. *95*, 5391 (1973).
[194] *K. Mochida, Y. Matsui, Y. Ota, K. Arakawa, Y. Date,* Bull. Chem. Soc. Jpn. *49*, 3119 (1976).
[195] *T. S. Straub, M. L. Bender,* J. Am. Chem. Soc. *94*, 8875 (1972).
[196] *F. Cramer, W. Kampe,* J. Am. Chem. Soc. *87*, 1115 (1965).
[197] The mechanism proposed in [196]—participation of a hydrogen bond between cyclodextrin and oxo- or cyano group of the substrate—is considered unlikely in [37] (p. 53) because the reaction is insensitive to the geometry of the substrate and pH value and to the absence of buffer catalysis [195]; a nonspecific microsolvent effect is proposed instead.
[198] *F. Cramer,* Chem. Ber. *86*, 1576 (1953).
[199] *W. I. Congdon, M. L. Bender,* Bioorg. Chem. *1*, 424 (1971).
[200] *J. Szejtli, E. Bánky-Elöd,* Acta Chim. Acad. Sci. Hung. *91*, 67 (1976).
[201] *Y. Matsui, H. Naruse, K. Mochida, Y. Date,* Bull. Chem. Soc. Jpn. *43*, 1910 (1970).
[202] *Y. Matsui, K. Mochida, O. Fukumoto, Y. Date,* Bull. Chem. Soc. Jpn. *48*, 3645 (1975).
[203] *M. Mitani, T. Tsuchida, K. Koyama,* J. Chem. Soc. Chem. Commun. *1974*, 869.
[204] *R. Breslow, P. Campbell,* Bioorg. Chem. *1*, 140 (1971).
[205] *R. Breslow, H. Kohn, B. Siegel,* Tetrahedron Lett. *1976*, 1645.
[206] *M. Ohara, J. Fukuda,* Pharmazie *33*, 467 (1978).
[207] *M. Ohara, K. Watanabe,* Angew. Chem. *87*, 880 (1975); Angew. Chem. Int. Ed. Engl. *14*, 820 (1975).
[208] *R. Breslow, L. E. Overman,* J. Am. Chem. Soc. *92*, 1075 (1970).
[209] *I. Tabushi, N. Shimizu, T. Sugimoto, M. Shiozuka, K. Yamamura,* J. Am. Chem. Soc. *99*, 7100 (1977).
[210] *Y. Matsui, T. Yokoi, K. Mochida,* Chem. Lett. *1976*, 1037.
[211] *I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, K. Fujita,* J. Am. Chem. Soc. *98*, 7855 (1976).
[212] *I. Tabushi, Y. Kuroda, K. Fujita, H. Kawabuko,* Tetrahedron Lett. *1978*, 2083.
[213] *I. Tabushi, K. Yamamura, K. Fujita, H. Kawabuko,* J. Am. Chem. Soc. *101*, 1019 (1979).
[214] *F. Hirayama, K. Uekama,* Chem. Pharm. Bull. *27*, 435 (1979).
[215] *K. Uekama, F. Hirayama, M. Daiguji,* Chem. Lett. *1978*, 327.
[216] *T. Kuge, K. Takeo,* J. Jap. Soc. Starch Sci. *21*, 151 (1974).
[217] *L. D. Melton, K. N. Slessor,* Carbohydr. Res. *18*, 29 (1971).
[218] *F. Cramer, G. Mackensen, K. Sensse,* Chem. Ber. *102*, 494 (1969).
[219] *S. Umezawa, K. Tatsuta,* Bull. Chem. Soc. Jpn. *41*, 464 (1968).
[220] *K. Tsujihara, H. Kurita, M. Kawazu,* Bull. Chem. Soc. Jpn. *50*, 1567 (1977).
[221] *J. Boger, R. J. Corcoran, J.-M. Lehn,* Helv. Chim. Acta *61*, 2190 (1978).
[222] *J. Boger, J. R. Knowles,* Ciba Found. Symp. 1968 (new series). Excerpta Medica, New York 1968.
[223] *K. Takeo, T. Kuge,* Stärke *28*, 226 (1976).
[224] *R. J. Bergeron, M. P. Melley,* Bioorg. Chem. *5*, 121 (1976).
[225] *M. A. Swanson, C. F. Cori,* J. Biol. Chem. *172*, 797 (1972).
[226] *K. Myrbäck, T. Järneström,* Ark. Kemi *1*, 129 (1949); *K. Myrbäck, ibid. 1*, 161 (1949).
[227] *D. French, M. L. Levine, J. H. Pazur,* J. Am. Chem. Soc. *71*, 356 (1949).
[228] *S. Veibel, S. Hjorth,* Acta Chem. Scand. *6*, 1355 (1952).
[229] *J. Szejtli, Zs. Budai,* Acta Chim. Acad. Sci. Hung. *91*, 73 (1976).
[230] *J. Szejtli,* Stärke *29*, 410 (1977).
[231] *T. Komiya, T. Yamada, S. Nara,* Agric. Biol. Chem. *40*, 1917, 2095 (1976).
[232] *G. O. Phillips, M. Young,* J. Chem. Soc. *A 1966*, 383.
[233] *M. Maciejewski, A. Gwizdowski, P. Peczak, A. Pietrzak,* J. Macromol. Sci. Chem. *A 13*, 87 (1979).
[234] *N. Ogata,* 815. Japanese Kogiren Lecture (1975), cited in [34].
[235] *B. Zsadon, M. Szilasi, K. H. Otta, F. Tüdös, E. Fenyvesi, J. Szejtli,* Acta Chim. Acad. Sci. Hung. *100*, 265 (1979).
[236] *J. Szejtli, E. Fenyvesi, B. Zsadon,* Stärke *30*, 127 (1978).
[237] *W. Lautsch, R. Wiechert,* Kolloid Z. *153*, 103 (1957).
[238] *S. A. Buckler, R. F. M. Stamford, R. I. Moshi,* US-Pat. 344248 (1964).
[239] Société des Produits Nestlé S. A., Neth. Pat. Appl. 6505361 (1964).
[240] *J. Solms, R. H. Egli,* Helv. Chim. Acta *48*, 1125 (1965).
[241] *N. Wiedenhof, C. L. van Panthaleon van Eck, J. N. J. J. Lammers,* Brit. Pat. 1244990 (1968); *N. Wiedenhof, J. N. J. J. Lammers, C. L. van Panthaleon van Eck,* Stärke *21*, 119 (1969).
[242] *R. E. Gramera, R. J. Caimi,* French Pat. 1548917 (1966).
[243] *L. C. Case, L. K. Case,* US-Pat. 3502601 (1962); US-Pat. 3501471 (1967).
[244] *C. K. Johnson,* US-Pat. 3654261 (1968).
[245] *S. M. Parmerter, E. E. Allen, Jr., D. H. Le Roy,* US-Pat. 3453259 (1967).
[246] *M. Furue, A. Harada, S.-I. Nozakura,* J. Polym. Sci. Polym. Lett. Ed. *13*, 357 (1975).
[247] *A. Harada, M. Furue, S.-I. Nozakura,* Macromolecules *9*, 701 (1976).
[248] *P. Vretblad,* FEBS Lett. *47*, 86 (1974).
[249] *N. Wiedenhof,* Stärke *21*, 163 (1969).
[250] *A. Harada, M. Furue, S.-I. Nozakura,* Macromolecules *9*, 705 (1976); *10*, 676 (1977).
[251] *R. P. Miskus, R. L. Lyon* in *J. E. Casida:* Pyrethrum, the Natural Insecticide. Academic Press, New York 1973, pp. 281 ff.
[252] *I. Yamamoto, T. Unai, Y. Suzuki, Y. Katsuda,* J. Pesticide Sci. *1*, 41 (1976).
[253] Teijin Co., Esuesu Seiyaku, Jap. Kokai 74 134,844 (1974).
[254] *H. Ikura, K. Takeuchi, S. Nakabachi,* Jap. Kokai 76 128,417 (1976).
[255] *A. Shima, H. Ikura,* Jap. Kokai 77 130,901 (1977).
[256] *J. Szejtli, É. Bolla, G. Nagy, Gy. Körmöczy, Zs. Nagy,* Ung. Pat. CI-1878 (1978).
[257] *J. Szejtli, É. Bolla, P. Szabó, T. Ferenczy,* Pharmazie, in press.
[258] *J. Szejtli, M. Szejtli, Gy. Cseh, I. Stadler,* DOS 2840142 (1979); Ung. Pat. Appl. 1770 (1977).
[259] *K. Uekama, F. Hirayama,* Chem. Pharm. Bull. *26*, 1195 (1978).
[260] *S. G. Frank, M. J. Cho,* J. Pharm. Sci. *67*, 1665 (1978).
[261] Ono Pharmaceuticals Co., Jap. Pat. 4739057 (1972); Jap. Kokoku 50-3362 (1975); Jap. Kokai 47-39057 (1972); 50-35319 (1975); 50-35324 (1975).
[262] *M. Hayashi, A. Ishihara,* Jap. Pat. 50 119/70 (1971).
[263] *Y. Hitachi, K. Inaba,* Jap. Kokai 74 26,416 (1974), Ono Pharmaceuticals Co.
[264] *N. Hayasaki, T. Tsutomu, T. Matsumoto, K. Inaba,* DOS 2353797 (1974), Ono Pharmaceuticals Co.
[265] Sterling Drug Inc., US-Pat. 2170954 (1975).
[266] *S. Sakaguchi, A. Kusaba, Y. Mishima, K. Kamiya, A. Nishimura, K. Furukawa, S. Shionoya, M. Kawashima, T. Katsumura, A. Sakuma,* VASA *7*, 263 (1978).
[267] *J. L. Lach, T.-F. Chin,* J. Pharm. Sci. *53*, 924 (1964).
[268] *K. Koizumi, J. Tatsumi, M. Ohae, H. Kumagai, T. Hayata,* Yakugaku Zasshi *89*, 1594 (1969); *K. Koizumi, K. Fujimura, ibid. 92*, 32 (1972).
[269] *K. H. Frömming, R. Sandman, I. Weyermann,* Dtsch. Apoth.-Ztg. *112*, 707 (1972).
[270] *H. Schlenk, D. M. Sand, J. A. Tillotson,* J. Am. Chem. Soc. *77*, 3587 (1955); US-Pat. 2827452 (1958).
[271] *Y. Hamada, N. Nambu, T. Nagai,* Chem. Pharm. Bull. *23*, 1205 (1975).
[272] *K. Noda, K. Furuya, S. Miyata, S. Tosu, T. Yonecia,* DOS 2356098 (1974).
[273] *K. Uekama, T. Irie, F. Hirayama,* Chem. Lett. *1978*, 1109.
[274] *M. Otagiri, K. Uekama, K. Ikeda,* Chem. Pharm. Bull. *23*, 188 (1975).
[275] *J. Szejtli, L. Szente, Gy. Körmöczy, P. Tétényi, Á. Dávid, T. Zilahi, A. Kelemen, J. Harshegyi,* Ung. Pat. Appl. (1978).
[276] Teijin Co., Takasagokoryo, Jap. Kokai 75 82,262 (1975).
[277] Hausu Syokuhin, Jap. Kokai 75 101,564 (1975).
[278] Teijin Co., Tsumurajuntendo, Jap. Kokai 75 64,418 (1975); Teijin Co., Tsumurajuntendo, Takasagokoryo, Jap. Kokai 74 63,126 (1974).
[279] Sanstar Hamigaki, Jap. Kokai 75 35,349 (1975).

[280] *E. Akito, Y. Nakajima, M. Horioka*, Jap. Kokai 75 129,520 (1975).
[281] Teijin Co., Jap. Kokai 75 58,226 (1975).
[282] *Y. Suzuki*, Jap. Kokai 75 69,100 (1975).
[283] *J. Szejtli, L. Szente, G. Kulcsár, Gy. Körmöczy*, Ung. Pat. Appl. (1978).
[284] Teijin Co., Ribon Syokuhin; Teijin, Kyupi, patents applied for, cited in [34].
[285] Teijin Co., Kyupi, Jap. Kokai 74 102,870 (1974).
[286] *J. Szejtli, E. Banky-Elöd*, Stärke *27*, 368 (1975).
[287] *J. L. Lach, W. A. Pauli*, J. Pharm. Sci. *55*, 32 (1966).
[288] *S. Kawamura, M. Murakami, H. Kawata, J. Terao*, Jap. Kokai 75 94,108 (1975); Chem. Abstr. *83*, 197823p (1975).
[289] *J. L. Lach, J. Cohen*, J. Pharm. Sci. *52*, 137 (1963).
[290] *W. A. Pauli, J. L. Lach*, J. Pharm. Sci. *54*, 1745 (1965).
[291] *M. Kurozumi, N. Nambu, T. Nagai*, Chem. Pharm. Bull. *23*, 3062 (1975).
[292] *K. Ikeda, K. Uekama, M. Otagiri, M. Hatano*, J. Pharm. Sci. *63*, 1186 (1974).
[293] *M. Otagiri, J. G. Fokkens, G. E. Hardee, J. H. Perrin*, Pharm. Acta Helv. *53*, 241 (1978).
[294] *K. Uekama, F. Hirayama, M. Otagiri, Y. Otagiri, K. Ikeda*, Chem. Pharm. Bull. *26*, 1162 (1978).
[295] *A. L. Thakkar, P. B. Kuehn, J. H. Perrin, W. L. Wilham*, J. Pharm. Sci. *61*, 1841 (1972).
[296] *K. H. Frömming, I. Weyermann*, Arch. Pharm. (Weinheim) *305*, 290 (1972).
[297] *N. Nambu, M. Shimoda, Y. Takahashi, H. Ueda, T. Nagai*, Chem. Pharm. Bull. *26*, 2952 (1978).
[298] *J. Szejtli, L. Szente, Á. Dávid, S. Virág, Gy. Sebestyén, A. Mándi*, Ung. Pat. Appl. CI-1679 (1976).
[299] *J. H. Perrin, F. P. Field, D. A. Hansen, R. A. Mufson, G. Torosian*, Res. Commun. Chem. Pathol. Pharmacol. *19*, 373 (1978).
[300] *K. Uekama, F. Hirayama, K. Ikeda, K. Inaba*, J. Pharm. Sci. *66*, 706 (1977).
[301] *T. Kinoshita, F. Iinuma, A. Tsuji*, Biochem. Biophys. Res. Commun. *51*, 666 (1973); Chem. Pharm. Bull. *22*, 2413, 2421, 2735 (1974).
[302] *N. Wiedenhof, R. G. Trieling*, Stärke *23*, 129 (1971).
[303] *J. L. Hoffman, R. M. Bock*, Fed. Proc. Fed. Am. Soc. Exp. Biol. *26*, 501 (1967).
[304] *J. L. Hoffman*, Anal. Chem. *33*, 209 (1970).
[305] *R. D. Cornelius, W. W. Cleland*, Abstr. Am. Chem. Soc. Meeting, Biol. Chem. *13*, Sept. 1977.
[306] *J. L. Hoffman*, J. Macromol. Sci. Chem. *7*, 1147 (1973).
[307] *J. N. J. J. Lammers, J. L. Koole, A. J. G. van Diemen*, Recl. Trav. Chim. Pays-Bas *91*, 483 (1972).
[308] *J. N. J. J. Lammers, A. J. G. van Diemen*, Recl. Trav. Chim. Pays-Bas *91*, 733 (1972).
[309] *H. P. Benschop, G. R. Van den Berg*, Chem. Commun. *1970*, 1431.
[310] *M. Mikolajczyk, J. Drabowicz*, J. Am. Chem. Soc. *100*, 2510 (1978).
[311] *C. Van Hooidonk, J. C. A. E. Breebart-Hansen*, Recl. Trav. Chim. Pays-Bas *89*, 289 (1970).
[312] *J. Szejtli, M. Tétényi*, to be published.
[313] SERVA-Feinbiochemica, Heidelberg (1978).
[314] *K. Takeo, T. Kuge*, Stärke *24*, 331 (1972).
[315] *C. Van Hooidonk, J. C. A. E. Breebart-Hansen*, Recl. Trav. Chim. Pays-Bas *90*, 680 (1971).
[316] *H. von Dietrich, F. Cramer*, Chem. Ber. *87*, 806 (1954).
[317] *J. Szejtli*, personal communication.

Trimethylphosphane Complexes of Nickel, Cobalt, and Iron—Model Compounds for Homogeneous Catalysis

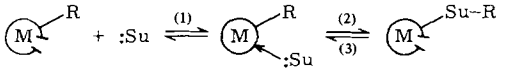
By Hans-Friedrich Klein[*]

One of the greatest achievements of organometallic chemistry in the last ten years has been the experimental proof that transition metal-to-carbon bonds are thermodynamically about as stable as those between main group elements and carbon. The present contribution demonstrates how simply constituted alkylnickel, -cobalt, and -iron complexes are obtained by means of a kinetic stabilization using suitable neutral ligands and what information these model compounds can provide with respect to the course of processes in homogeneous catalyses.

1. Introduction

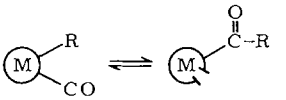
1.1. Key Reactions at the MC Bond

The crucial steps of a large group of practically important catalytic processes in homogeneous phase[1-3] may be described by the following scheme:



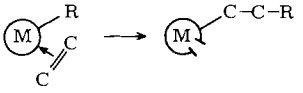
A transition metal center M, protected in solution by a number of ligands or by solvent molecules (circle), is substituted by a functional group R. In the cases of interest, R is a hydrogen or an alkyl group. Substrate molecules are induced to react as they occupy a vacant coordination site at the metal (open circle) and subsequently react with R in the first coordination sphere. Formally we consider:

Reversible coordination of unsaturated substrate molecules [reaction (1)];
insertion reactions [reaction (2)],
reversible: *e. g.*



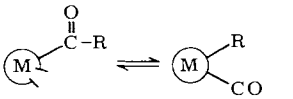
R = H, Alkyl

("Oxo synthesis", Fischer-Tropsch synthesis)
irreversible: *e. g.*



R = Alkyl

(olefin oligomerizations, Ziegler-Natta polymerizations)
elimination reactions [reaction (3)] reversible:
e. g. decarbonylation

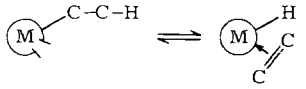


R = H, Alkyl

[*] Prof. Dr. H.-F. Klein
Anorganisch-chemisches Institut der Technischen Universität München
D-8046 Garching, Lichtenbergstrasse 4 (Germany)

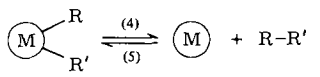
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0505-0362 $ 02.50/0

and β-elimination



(detachment of a polymer chain from a metal center)

Two σ-bonded groups R can depart from a metal after a coupling reaction (4). As the formal oxidation number of the metal decreases by two units this step is conventionally termed "reductive elimination".



R = R′ = H: *e.g.* hydrogenation of olefins;
R = H, R′ = alkyl: reversible C—H scission in hydrocarbons;
R = R′ = alkyl: reversible C—C scission in hydrocarbons.

As a necessary requirement, R and R′ have to occupy *cis* positions.

The two last-mentioned processes presently rate among the greatest challenges of organometallic chemistry. In particular, the activation of aliphatic hydrocarbons at transition metal centers [eq. (5)] is on the verge of a development which is raising great expectations.

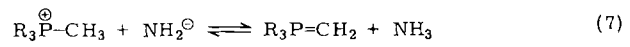
As is evident from these examples, a central problem is the labile and reactive metal-to-carbon σ-bond, particularly with regard to the most probable decomposition pathways, for preliminary data concerning bond-dissociation energies[3,4] have meanwhile demonstrated that metal-to-carbon σ-bonds in the transition groups are no less stable than those involving main group elements. We therefore turn our attention to the question, under which conditions alkyl metal compounds become kinetically unstable.

1.2. σ-Methylmetal Compounds

In order to circumvent β-elimination as the dominant decomposition mode of alkylmetal complexes, we employ organic groups CH_2—X (X = H, C_6H_5, $C(CH_3)_3$, $Si(CH_3)_3$, *etc.*)[5,6]. However, in the simplest case of the methylmetal complexes there are still further decomposition pathways accessible; a methyl group attached to a basic metal center providing an empty coordination site can rearrange *via* proton migration to give a hydride-carbene function.

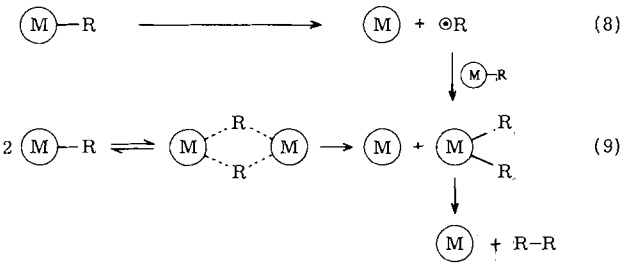


(6)



(7)

This *α-elimination* was established comparatively recently[6] while the reverse reaction (6) has been known longer[7]. The double bond formulation of the carbene fragment illustrates that the equilibrium (6) essentially differs from the acid-base equilibrium (7) only in that the base in (7) approaches from the outside while the deprotonation is intramolecular with the metal base in (6).



(8)

(9)

Further possibilities are a radical process (8) or a dismutation reaction (9) involving transfer of alkyl groups. Unlike (9), reaction (8) does not initially require a vacant coordination site; the reaction essentially depends on the appearance potential of the radical ⊙R. In this sense benzylmetal compounds are more labile than the corresponding methyl compounds.

The approach chosen here for the stabilization of methyl complexes of nickel, cobalt, and iron is based upon the assumption that it is possible to block all coordination sites of these metals in all their common oxidation states by using small ligands which can occupy all sites given by the inert gas rule (18-electron rule) without encountering steric problems.

Furthermore in complexes of catalytically active metals, the lowest possible reactivity of the coordinated ligand is desirable.

1.3. Trimethylphosphane

The principle of permethylated primary compounds has a long tradition in organometallic chemistry[8]. It is profitably applied to the phosphanes which proved to be good ligands for transition metals: Trimethylphosphane is the sterically least demanding of the triorganophosphanes. It forms stable metal complexes, reactions of the coordinated ligand are essentially unknown, and its high symmetry in complexes (local C_{3v}) facilitates spectroscopic investigations (IR, NMR).

Tolman[9] has defined the steric requirements of phosphane ligands by the vertex angle θ of a cone with its vertex at the metal which encloses the van der Waals boundaries of the substituents at the phosphorus atom. The value given for trimethylphosphane in nickel(0) complexes, $\theta = 118°$ for $d(NiP) = 228$ pm[9], is much smaller than for other trialkylphosphanes: $P(C_2H_5)_3$, $\theta = 132°$; $P(C_6H_5)_3$, $\theta = 145°$. In cobalt and iron complexes [$d(CoP) = 218$ pm[10], $d(FeP) = 224$ pm[11]] larger values of θ have to be taken into account. Nevertheless, salts of a stable cation $FeCH_3L_5^{\oplus}$ ($L = PMe_3$)[12] can be obtained. However, it is difficult to estimate the minimum spatial requirements of a phosphane ligand which are important to the preparative chemist.

Trimethylphosphane is a base ($pK_a = 8.65$; for comparison: Me_3N 9.80, pyridine 5.25). As a σ-donor, it is a good ligand in complexes of metals in high oxidation states, while from its position in the series of π-acids

$$CO \approx PF_3 > PCl_3 > AsCl_3 \approx SbCl_3 > P(OR)_3 > PPh_3 > PMe_3 > SMe_2 > RCN > NR_3 \approx ROH > H_2NCOR$$

no affinity for low valent metal centers is expected[13]. However, these insights which have emerged from investigations

of metal carbonyl complexes should not be applied directly to carbonyl-free systems because a change of central metal has to be considered as well as the sum of all ligand effects in a complex[14]. The σ-donor/π-acceptor properties of a ligand are not constant.

Reactions of trimethylphosphane with electrophiles are well known:

$$(CH_3)_3P \xrightleftharpoons{HX} [(CH_3)_3PH]^{\oplus}X^{\ominus} \quad (10)$$

$$(CH_3)_3P \xrightarrow{RX} [(CH_3)_3PR]^{\oplus}X^{\ominus} \rightleftharpoons R(CH_3)_2P{\cdot\cdot}CH_2 + HX \quad (11)$$

X = Halogen, *etc.*

The reversible protonation (10) corresponds to the quarternization (11) which upon action of base is not reversed but leads to alkylidenephosphoranes. Both reactions are more difficult at the coordinated ligand because of its phosphonium character.

Nucleophiles in general fail to react with trimethylphosphane. Only the strongest organometallic bases, *e.g. tert*-butyllithium, are able to abstract protons[15,16]. This reaction should be facilitated in the coordinated ligand. However, since the competing attack at the metal is usually faster, no report of a clear-cut proton abstraction from a trialkylphosphane ligand has yet appeared.

The oxidation of trimethylphosphane by oxygen to give trimethylphosphane oxide is a slow reaction under ambient conditions but is accelerated in metal complexes by oxidation-reduction catalysis. From some of these reactions peroxo complexes have been isolated[17], *e.g.* a triphenylphosphane complex in a reaction sequence according to eq. (12)[18].

$$Ni(PPh_3)_4 \xrightarrow[-2\,PPh_3]{O_2} (PPh_3)_2Ni\begin{smallmatrix}O\\O\end{smallmatrix} \quad (12)$$

$$\xrightarrow{4\,PPh_3} Ni(PPh_3)_4 + 2\,PPh_3O$$

These reactions explain the air sensitivity of many phosphane complexes.

1.4. Preparation of Methyl Metal Compounds

A methylmetal function can be generated in two fundamentally different ways: (A) by an anionic alkylation, *e.g.* substitution of halide ligands by methyllithium or methylmagnesium bromide. Its counterpart is a cationic methylation (B) using reagents such as methyl iodide or tosylate. If both synthetic routes are to give identical products, route (B) requires a complex anion $M^{\ominus}$ in an oxidation state which is lower by two units (d^{n+2}) because in a formal heterolytic cleavage the bonding electron pair is transferred to the *C*-bonded ligand. For this reason reaction (B) is called an oxidative addition.

Substitution

$$d^n: (M)\text{—}X \xrightarrow[-X^{\ominus}]{+CH_3^{\ominus}} (M)\text{—}CH_3 \quad (A)$$

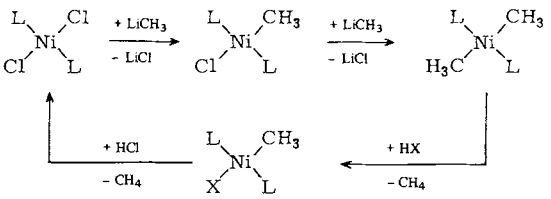
$$d^{n+2}: (M)^{\ominus} \xrightarrow{+CH_3^{\oplus}} (M)\text{—}CH_3 \quad (B)$$

Oxidative addition

2. Square Planar Complexes

2.1. Mononuclear Complexes

The anionic alkylation of bis(phosphane)nickel dihalides by organoalkali metal, Grignard, or organoaluminum compounds is the usual method for the preparation of alkylnickel phosphane complexes[23]. Methyllithium affords methyl and dimethylnickel complexes according to eq. (13) in high yields of both steps[21].

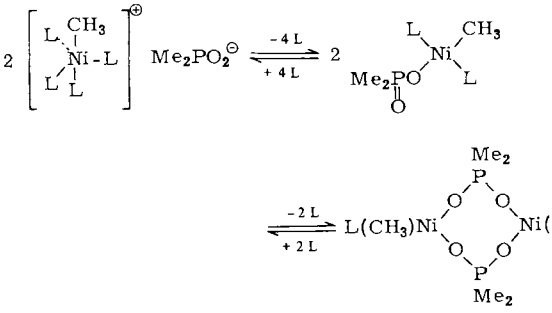


(13)

L = PMe_3
X = OH, OCH_3, OC_6H_5, $OSiMe_3$, SMe, O_2CCH_3, F, etc.

The stepwise alkylation corresponds to a two-step protolytic cleavage of the $NiCH_3$ functions. Alcohols or water cleave only one of the NiC bonds, while the other reacts only with strong mineral acids, liberating methane[21]. The high reactivity of a *trans* dialkyl arrangement indicates the *trans* influence of alkyl ligands. The stability of monomethylnickel compounds in (oxygen-free) aqueous solution can be compared with methylmercury compounds[24]. Square-planar Ni^{II} compounds are 16-electron complexes and can add a further ligand, adopting a trigonal-bipyramidal geometry (see Section 3). However, according to eq. (14) they can also release phosphane ligands. Both reactions are responsible for a fast ligand exchange which is conveniently observed by dynamic spectroscopic methods[19,22].

The mononuclear neutral methylnickel dimethylphosphinate can only be detected in a solution from which the ligand-rich and the dinuclear complex are actually isolated [eq. (14)].



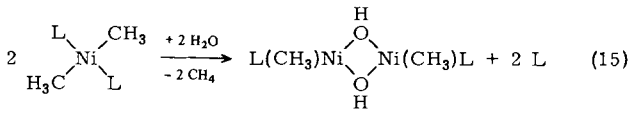
(14)

The dinuclear dimethylphosphinate complex is cleaved by phosphane in nonpolar medium to give the mononuclear complex; in a polar medium providing efficient anion solvation the pentacoordinate cation is formed.

2.2. Dinuclear Complexes in *cis* and *trans* Forms

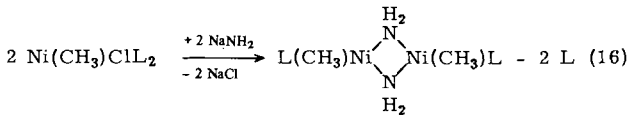
Three types of reaction can be used for a synthesis of dinuclear methylnickel compounds[25,26]:

a) Protolytic fission of dimethylnickel compounds, *e.g.*



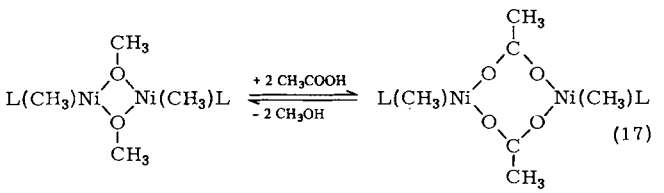
(15)

b) Exchange of halide in methylnickel halides, *e. g.*



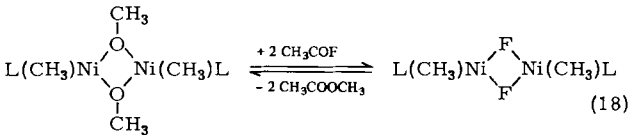
(16)

c) Exchange of anion bridges in equilibria, *e. g.*



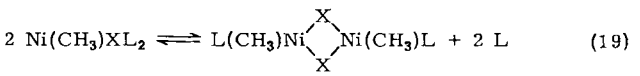
(17)

d) Transesterification, *e. g.*



(18)

An investigation of a large number of methylnickel compounds[25-28] participating in equilibrium (19)

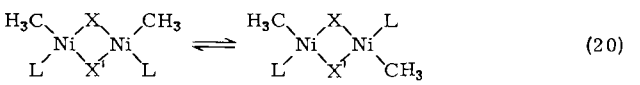


(19)

has resulted in a sequence of anions which show an increasing tendency to form anion-bridged complexes.

$X^{\ominus} = Cl^{\ominus} < O_2CCH_3^{\ominus}$, $O_2PMe_2^{\ominus} < OPh^{\ominus}$, $SPh^{\ominus} < OR^{\ominus}$, $SR^{\ominus}$, $OSiMe_3^{\ominus} < F^{\ominus} < OH^{\ominus} < NH_2^{\ominus} < NMe_2^{\ominus}$

The square-planar coordination of the nickel centers allows for *cis* and *trans* isomers. In particular the dinuclear compounds containing a four-membered ring system are found to occur as *cis* and *trans* forms in equilibria[29].

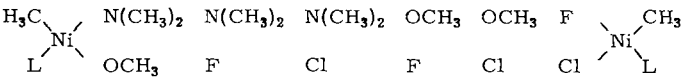


(20)

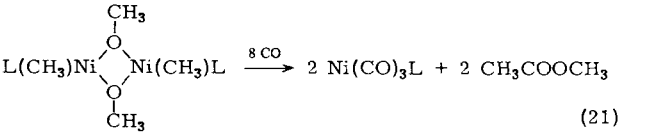
cis-(X = X', X ≠ X) *trans*-(X = X')

Methyl(trimethylphosphane)nickel amide dimer crystallizes in the *trans*-form. Upon dissolution in pyridine ($\varepsilon = 12.3$) at 30 °C it isomerizes within a few hours to give an equilibrium concentration of the *cis*-isomer (36%). In toluene this equilibrium reaches only 20% of the *cis*-isomer. In a number of solvents the molar fraction of the polar *cis*-form in equilibria is roughly proportional to the dielectric constants suggesting a kind of linear free energy relation[30].

Dinuclear methylnickel compounds containing different bridging ligands (X ≠ X') are only known as *cis*-isomers. Moreover, the bridging ligand with the lowest tendency towards bridge formation occupies the position opposite to both methyl groups:



Simple olefins like ethene or propene have little influence on the position of equilibria (19). In spite of numerous possibilities of coordination at the nickel no olefin insertion into Ni—CH_3 bonds is observed. In contrast all dinuclear methylnickel compounds react with carbon monoxide already at low temperatures[31]. One finds products of reductive elimination reactions according to eq. (21) rather than methyl or acetylnickel compounds.

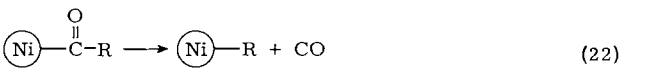


(21)

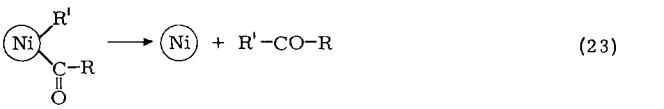
On the other hand the insertion reaction of CO into Ni—C bonds could be conveniently investigated in mononuclear methylnickel halides.

2.3. Acetylnickel Compounds

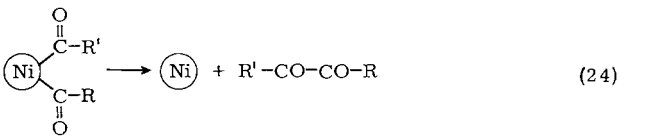
Equilibria involving carbonylation and decarbonylation reactions of organoplatinum and palladium complexes have been known for a long time through the work of *Chatt et al.*[32]. Until a few years ago, stable acylnickel complexes had only been isolated in a few exceptional cases[33]. More success had usually been prevented by either a dominant decarbonylation (22) or by C—C coupling reactions, (23) and (24), at the nickel center[34].



(22)

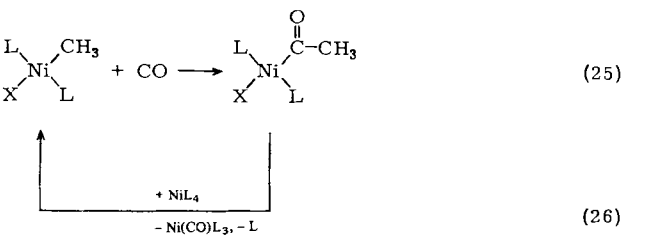


(23)



(24)

Carbonylation of trimethylphosphane methylnickel halides at normal pressure according to eq. (25) yields stable acetylnickel complexes[35].



(25)

(26)

Acetylnickel halides adopt a *trans*-configuration and display intermolecular exchange of ligands in solution, and thus closely resemble the corresponding methylnickel halides. The *trans* square-planar structure of acetylbis(trimethylphosphane)nickel chloride has been confirmed by a single crystal X-ray structural analysis (Fig. 1)[36].

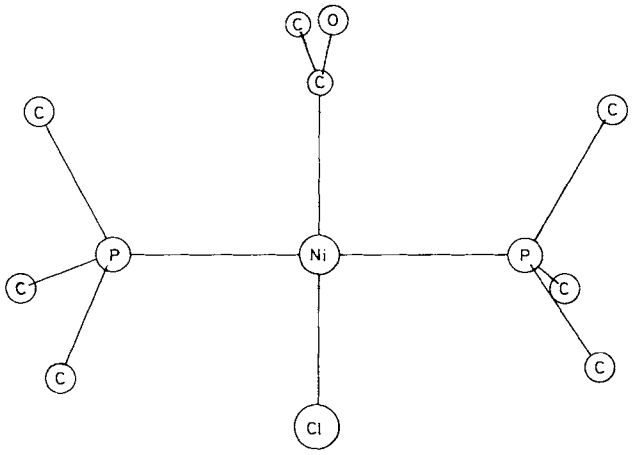


Fig. 1. Structure of *trans*-$Ni(COCH_3)Cl(PMe_3)_2$ (cf. [36]).

The ketone type carbonyl group points out of the nickel coordination plane at right angles. The Ni—C distance is 10 pm shorter than in methylnickel complexes of similar structures[37] and reflects some strengthening by π-interaction. The C—C bond is longer than in ketones, indicating an easy mobilization of the CO fragment. The preparative decarbonylation is achieved using CO-acceptor complexes like tetrakis(trimethylphosphane)nickel(0) according to eq. (26).

Acylnickel compounds are particularly interesting because of their crucial position in catalytic cycles of the following kind: a) oxidative addition to the nickel(0) complex; b) CO insertion into the Ni—C bond; c) reductive elimination leading back to the nickel(0) state. In this connection, the reaction of acyl halides with Ni^0 complexes has been repeatedly investigated. In most cases decarbonylation products had been obtained[38]. These results are now understood as there is always a competing reaction according to eq. (26) which is relatively fast. A cationic acylation of nickel(0) complexes can only succeed if oxidative addition according to eq. (27) is faster than both competing reactions: decarbonylation according to eq. (26) and the quarternization of the trialkylphosphane according to eq. (28) giving acylphosphonium salts[35].

$$NiL_4 + RCOX \rightarrow Ni(COR)XL_2 + 2L \quad (27)$$

$$RCOX + PMe_3 \rightarrow [RCOPMe_3]^{\oplus}X^{\ominus} \quad (28)$$

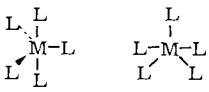
Although there is some additional acylation of the nickel(0) complex by the acylphosphonium salt, this reaction is so slow that the overall processes is dominated by the decarbonylation reaction according to eq. (26). Yet another competing reaction is C—C linkage *via* attack of acyl halide at the acylnickel function with its changed polarity. This reaction according to eq. (29) will start only at elevated temperatures.

$$Ni(COCH_3)ClL_2 + CH_3COCl \rightarrow NiCl_2L_2 + CH_3COCOCH_3 \quad (29)$$

Meanwhile, further syntheses of acylnickel compounds have been reported[39], the conditions being such as to allow for an undisturbed reaction according to eq. (27). This route includes a successful synthesis of benzoyl and phenylnickel halides[40].

3. Trigonal-Bipyramidal Complexes

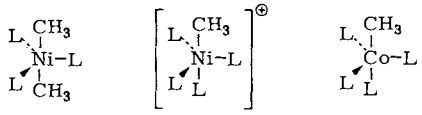
Pentacoordinate molecules or complexes in their ground states adopt either a trigonal-bipyramidal or a square-pyramidal geometry, the differences in energy being small[41] particularly in complexes with five identical ligands.



$M(d^8) = Ni^{II}, CO^{I}, Fe^{0}$

A typical feature of these molecules is a dynamic behavior involving an intramolecular change of positions of substituents or ligands, respectively, by a pseudorotation process (Berry mechanism, turnstile mechanism)[42].

18-electron species of methylnickel compounds can be reversibly obtained by addition of trimethylphosphane to coordinatively unsaturated complexes [see eq. (14), reverse reaction]. In contrast, there exists only one methylcobalt(I) complex, $CoCH_3L_4$ (18 electrons), out of a number of isoelectronic species.



In the ground state the methyl groups of dimethyltris(trimethylphosphane)nickel occupy axial positions; intermolecular ligand exchange is activated more easily than pseudorotation[21]. The pseudorotation process can be observed by spectroscopy with the methylnickel cation; only at the

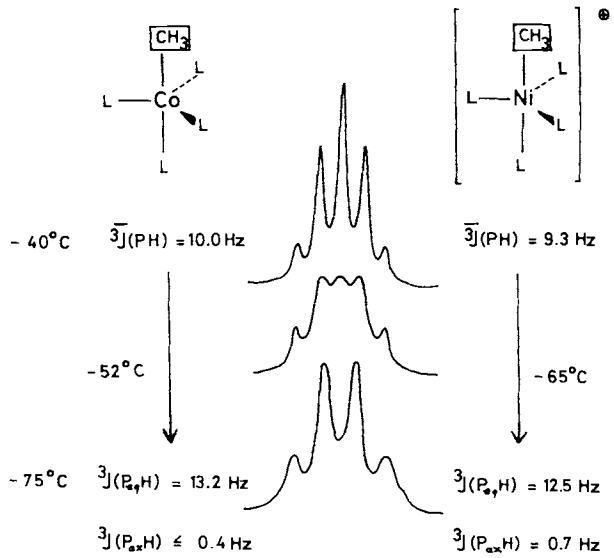
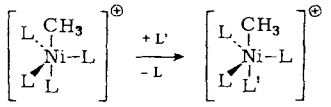
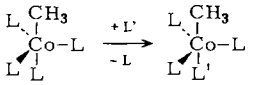


Fig. 2. Temperature dependent ^{1}H-NMR spectra of isosteric methyl compounds $CoCH_3L_4$ (in toluene) and $[NiCH_3L_4]^{\oplus}$ (in CH_2Cl_2), L = PMe_3, due to pseudorotation.

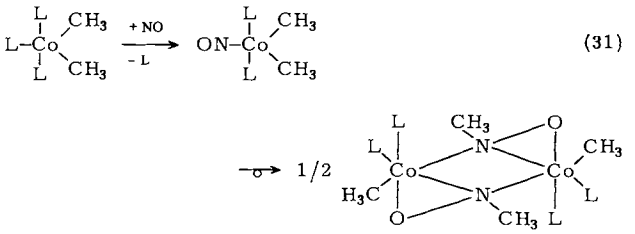
stage of rapid motion is this superimposed by intermolecular exchange[43]. The neutral isoelectronic species, $CoCH_3L_4$, finally shows only pseudorotation in the temperature range recorded[44]. In spite of differing charge on the complexes[45], both intramolecular movements have the same activation energy (50—55 kJ/mol) which proves the validity of the concept of isosteric species for this type of complex.

The *trans* influence of the axial methyl group causes all entering ligands [L′ = CO or $P(OCH_3)_3$] to regioselectively occupy the second axial position; a second substitution reaction becomes significantly more difficult for $L' = P(OCH_3)_3$.


(30a)


(30b)

In contrast to the 18-electron complex $Ni(CH_3)_2L_3$ the 17-electron compound $Co(CH_3)_2L_3$[46] adopts a *cis* configuration. The equatorial positions of the two methyl groups are suggested by the reactions with acids which unspecifically remove one or both methyl groups and also by the equatorial position of the NO ligand in a diamagnetic nitrosyl derivative.

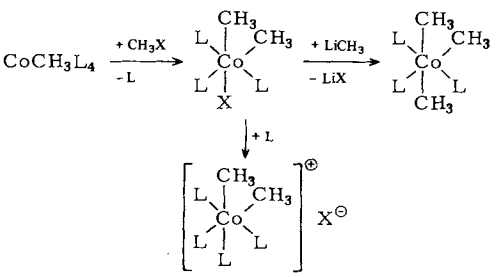

(31)

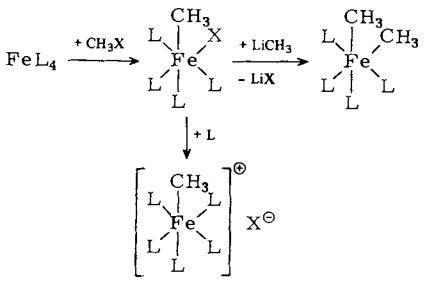
Subsequent rearrangement *via* insertion of NO into one of the Co—C bonds followed by dimerization leads to an octahedral Co^{III} complex containing bridging nitrosomethane ligands [eq. (31)].

4. Octahedral Complexes

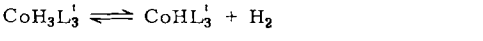
While octahedral nickel(IV) complexes containing phosphane ligands remain unknown to date, a large number of examples have been described for cobalt(III) and iron(II). If these complexes only contain unidentate ligands, the preferred arrangement of neutral and anionic ligands of the metal(d^6) center is recognized.

Oxidative addition of methyl halide to metal(d^8) systems proceeds analogously for cobalt(I)[44,47,48] and iron(0)[49].

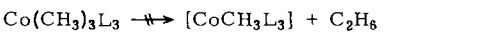

(32a)


(32b)

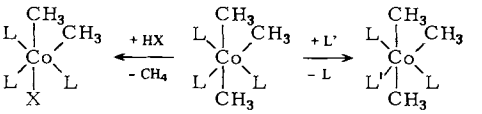
Neutral methylcobalt(III) complexes have a meridianal configuration. Unlike *mer*-hydridocobalt(III) complexes [eq. (33)], a reductive elimination of *cis*-fixed methyl groups according to eq. (34) does not occur.


(33)

L′ = PPh_3

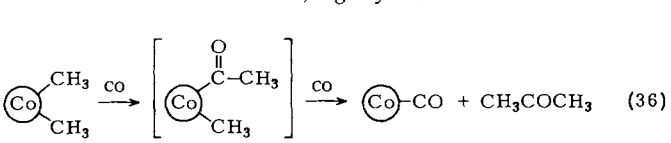

(34)

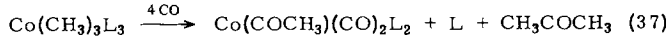
L = PMe_3


(35)

X = Cl, Br; L′ = $P(OMe)_3$

The reactions of trimethylcobalt complexes according to eq. (35) are similarly regiospecific like those of dimethylnickel [eq. (13)] and of the isosteric complexes $[Ni(CH_3)L_4]^{\oplus}$ and $Co(CH_3)L_4$ [eq. (30a, b)]. The cleavage by protic acids proceeds in the C—C axis of the molecule, the substituting neutral ligand enters a position *trans* to the unique methyl group. In isosteric complexes $[Co(CH_3)_2L_4]^{\oplus}$ and $Fe(CH_3)_2L_4$ disubstitution with neutral ligands is again found[12] to occur in both positions *trans* to the methyl groups. In this case both methyl groups experience *trans* influences of equal neutral ligands prior to, as well as after, the disubstitution, while in all methylcobalt complexes of eq. (35) there are methyl groups with a different degree of polarization of the Co—C bonds. This should favor an elimination on ethane. However, in all methylcobalt complexes containing more than one methylcobalt function[46,48] a spontaneous reductive elimination only occurs after transformation, *e.g.* by CO insertion.


(36)


(37)

As soon as a CO insertion into one of the Co—C bonds has occurred, acetone is formed according to eq. (36)—presumably from an acetyl(methyl)cobalt species. No such intermediates can be trapped in a normal pressure carbonylation reaction according to eq. (37).

5. Hydridophosphane Complexes

The first phosphane-substituted analogues of the familiar carbonyl hydrides, $FeH_2(CO)_4$, $CoH(CO)_4$, and of the iso-

electronic $Ni(CO)_4$, were the phosphorus trihalide complexes[50]. The low oxidation states of the three metals formally arising from strongly acidic M—H functions (-II, -I, 0) led to the assumption that σ-donating ligands like the trialkylphosphanes would not prove satisfactory by themselves. This is not so, however, as has been shown by the preparation of trimethylphosphane complexes NiL_4[51], $CoHL_4$[47,51], and FeH_2L_4[51-54] ($L = PMe_3$) which are more stable thermally than their carbonyl and trifluorophosphane counterparts.

Unlike NiL_4, which has a tetrahedral NiP_4 skeleton, the isoelectronic hydride complexes are called pseudotetrahedral, because the hydrogen residing on the metal needs little space and moves around a slightly distorted tetrahedral MP_4 skeleton (tetrahedral-edge-traverse mechanism[55-59]).

This concept can be extended to cationic complexes $[NiHL_4]^{\oplus}$ (18 electrons)[60] and $[CoHL_4]^{\oplus}$ (17 electrons)[44] ($L = PMe_3$). The IR spectra of all hydride complexes display broad ν(MH) bands with a bathochromic shift when compared with complexes of strongly π-accepting ligands.

In parallel fashion, the acidity of the metal hydride function decreases: $CoH[P(OMe)_3]_4$ can still be deprotonated using potassium hydride[55], while the trimethylphosphane complexes $CoHL_4$ and FeH_2L_4 resist attack by strong base[51].

6. Tetrahedral Complexes ML_4

Metal(d^8) configuration: Depending upon the nature of the monodentate ligands, bis(phosphane)nickel(II) halides adopt a square-planar (diamagnetic) or a tetrahedral (paramagnetic) configuration. For some compounds transitions between the two classes are induced by simply varying the environment (solvation, crystal lattice)[61]. The interesting question of the magnetic properties of a tetrakis(trimethylphosphane)nickel dication is still open, because in equilibria with the preferred $[NiL_5]^{2\oplus}$ ($L = PMe_3$)[62] it could not be fully characterized. On the other hand, the isoelectronic cation $[CoL_4]^{\oplus}$ is likely to be tetrahedral because of its magnetic moment, while a diamagnetic cation $[CoL_5]^{\oplus}$ cannot be prepared with trimethylphosphane ligands only[63]. (For a survey see Table 1.)

There is some evidence for the paramagnetic nature of the neutral molecule in this series, FeL_4[53,64], which has been proved to exist in an equilibrium of an intramolecular oxidative addition (see Section 8) by an indirect method. The 18-electron compound FeL_5 also could not be obtained, while phosphite complexes of an analogous composition are known[52,54,65].

Metal(d^9) configuration: Solutions of methyltetrakis(trimethylphosphane)nickel(II) tetraphenylborate evolve ethane and methane on exposure to diffuse daylight. According to eq. (38), a salt of the tetrakis(trimethylphosphane)nickel(I) cation[66] is formed.

$$[NiCH_3L_4]^{\oplus}[BPh_4]^{\ominus} \xrightarrow{h\nu} [NiL_4]^{\oplus}[BPh_4]^{\ominus} + C_2H_6 + CH_4 + \cdots \quad (38)$$

$$NiL_4 + NiCl_2L_2 + 2L + 2NaX \rightleftharpoons 2[NiL_4]^{\oplus}X^{\ominus} + 2NaCl \quad (39)$$

$L = PMe_3$, $X = BPh_4$, BF_4, PF_6

In contrast to the known nickel(I) complexes $NiXL'_3$ [$L' = P(C_6H_5)_3$, X = halide][67], a trimethylphosphane complex of this stoichiometry cannot be obtained. Only after precipitating the halide ligands is a cationic nickel(I) complex formed in an oxidation reduction equilibrium (39).

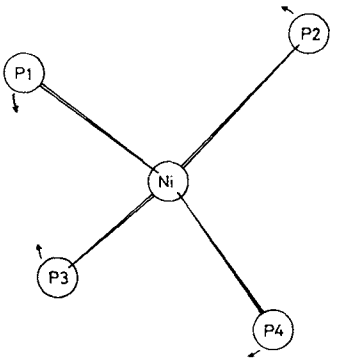


Fig. 3. Distortion of the NiP_4 tetrahedron in the cation $Ni(PMe_3)_4^{\oplus}$ (P1NiP3 104.6(1)°, P2NiP4 119.9(1)°).

In the crystal lattice (Fig. 3) the PNiP angles of the cation $[Ni(PMe_3)_4]^{\oplus}$ differ only slightly from the ideal tetrahedral geometry of the NiP_4 skeleton and do not give any indication of a Jahn-Teller distortion which can be expected in a d^9 configuration of metal valence electrons. The ESR spectrum (77 K) consists of only one isotropic line ($g = 2.12$).

More favorable conditions for relaxation in the isosteric $Co(PMe_3)_4$ result in a well-resolved hyperfine structure of the ESR spectrum (4 K, toluene glass)[68] containing two sets of eight lines ($I_{Co} = 7/2$).

Table 1. Range of existence of tetrahedral trimethylphosphane complexes ($L = PMe_3$). [Species in brackets have not yet been isolated.]

Electrons	16	17	18	16	17	18	16	17	18
M(d^8)	FeL_4		$[FeL_5]$	$CoL_4^{\oplus}$		$[CoL_5^{\oplus}]$	$NiL_4^{2\oplus}$		$NiL_5^{2\oplus}$
M(d^9)		$[FeL_4^{\oplus}]$			CoL_4			$NiL_4^{\oplus}$	
M(d^{10})	$[FeL_3^{2\ominus}]$		$[FeL_4^{2\ominus}]$	$[CoL_5^{\oplus}]$		$CoL_4^{\ominus}$	$[NiL_3]$		NiL_4

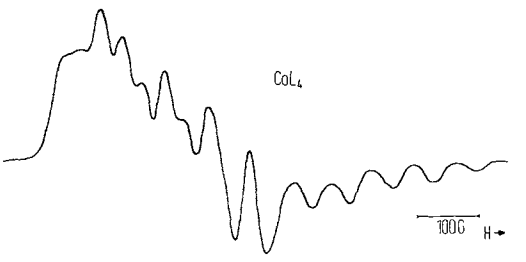


Fig. 4. ESR spectrum of $Co(PMe_3)_4$ (toluene glass, 4 K).

In the ground state $Co(PMe_3)_4$ therefore adopts an axial symmetry, as has been elucidated for $Co(CO)_4$ in low temperature matrices[69].

Reduction of the system $CoCl_2$/4 Me_3P/THF with magnesium in a sort of Grignard reaction under argon (not under nitrogen, see Section 10) affords tetrakis(trimethylphosphane)cobalt(0) in high yield[44].

$$CoCl_2 \xrightarrow[-MgCl_2]{+4\,L,\,Mg} CoL_4$$

$$CoL_4 \xrightarrow{PhN=NPh} Co(PhN{=}NPh)L_2 \quad (40)$$

$$CoL_4 \xrightarrow{CO} [L_2Co(CO)_2]_2 \quad (41)$$

$$CoL_4 \xrightarrow{3/2\,I_2} CoIL_3 + Me_3PI_2 \quad (42)$$

$$CoL_4 \xrightarrow{NO} Co(NO)L_3 \quad (43)$$

In substitution reactions, the paramagnetic valence state of $Co(PMe_3)_4$ can be preserved [eq. (40)] or lost by dimerization [eq. (41)] or through an incoming three-electron ligand such as NO [eq. (43)]. Under carefully adjusted reaction conditions halogen oxidizes the metal complex and the liberated phosphane ligand (42). The magnetic properties of cobalt(I) halides[63] ($\mu_{eff}/\mu_B = 3.0$—3.2) suggest a C_{3v} symmetry in the $CoXP_3$ skeleton, which is also favored with other phosphane ligands[70].



L = PMe_3
X = Cl, Br, I, O_2CCH_3

Surprisingly a methylcobalt compound of comparable composition does not exist[44].

$$CoClL_3 \xrightarrow[-LiCl]{+LiCH_3} 3/4\,CoCH_3L_4 + 1/4\,Co + \cdots \quad (44)$$

In an attempted synthesis according to eq. (44) cobalt metal is deposited until enough phosphane ligands become available for the formation of the 18-electron compound $CoCH_3L_4$.

In a sequence of tetrahedral trimethylphosphane complexes ML_4, the influence of increasing electron density is recognized by means of infrared spectroscopy from the bands of the coordinated trimethylphosphane.

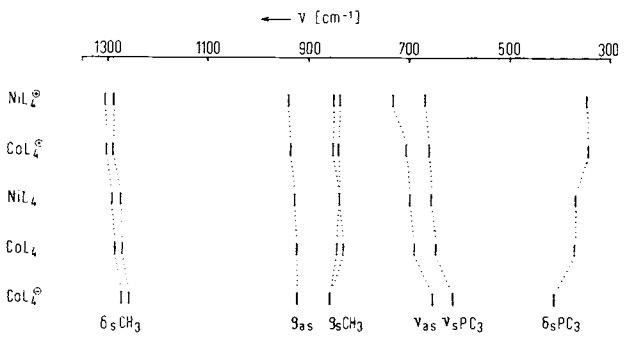


Fig. 5. Sequence of increasing electron density in tetrahedral complexes $M(PMe_3)_4$ derived from given IR bands.

In Figure 5 all bands are listed which have been observed within the given limits except for the low intensity metal phosphorus stretching modes (ν(M—P) = 300—250 cm^{-1}). According to *Goubeau et al.*[71] at least the PC_3 stretching mode is regarded as a reliable indicator of electronic changes in the trimethylphosphane ligand. Furthermore all other bands in the sequence (as we go from top to bottom in Fig. 5) are shifted in a characteristic way as a consequence of increasing induction of negative charge from the complex center into the P—C—H bonding system. We cannot decide whether only the skeleton of σ-bonds is affected or whether there are additional π-components between metal and phosphorus atoms, which could well be larger than estimates obtained from phosphane-carbonyl complexes[72]. Unexpectedly the properties of the complexes listed in Figure 5 did not result in a parallel sequence of increasing dissociation of trimethylphosphane ligands.

Metal(d^{10}) configuration: The neutral molecules NiL_4[51,60] and CoL_4[44] can be sublimed *in vacuo*[73], and even the alkali metal cobaltates $MCoL_4$ (M = Li, Na, K) under the same conditions (80 °C, 0.1 torr) do not release more phosphane ligands than the other compounds in Figure 5. The thermal stability of anionic complexes is worth mentioning because at the cobaltate stage a clear limit of loading charge on tetrahedral trimethylphosphane complexes is reached[47] [eq. (45)].

$$CoL_4 + M + x\,OR_2 \rightleftharpoons M^{\oplus}CoL_4^{\ominus} \cdot x\,OR_2 \quad (45)$$

L = PMe_3, M = Li, Na, K OR_2 = THF; $x = 0.5$
$OR_2 = OEt_2$; $x = 1$

According to eq. (45) yellow to orange solids are obtained which display interesting thermochromic and solvatochromic effects: In the low temperature limit, the ethereal solutions become orange and diamagnetic. At 20 °C and with poor solvation of cations, *e.g.* in pentane, brown coloration by CoL_4 and turbidity of the solution is seen to arise from finely dispersed alkali metal. Upon chilling, these solutions display the ESR signal of CoL_4 (Fig. 4).

Three variables favor the formation of alkali metal cobaltates:

a) Lowering the temperature;

b) increasing concentrations of diethyl ether or—more efficiently—THF;

c) an increasing reduction potential of alkali metals: Li < Na < K.

Thus the anion $CoL_4^{\ominus}$ rates among the strongest known soluble reducing agents. Benzophenone or naphthalene are readily transformed into radical anions at −30 °C. Butadiene and isoprene are efficiently polymerized. However, there is no clear distinction as to which is the active species: the cobaltate anion or the finely dispersed alkali metal.

Alkali metal cobaltates are strong bases and very reactive nucleophiles. Reactions with organic or inorganic electrophiles and even simple protonation reactions proceed according to the scheme of an oxidative addition[47].

7. Oxidative Addition Reactions

Metal(d^{10}) configuration: Oxidative additions to tetrakis(trimethylphosphane)nickel(0) are successfully carried out according to eq. (46) in polar medium only.

Under the conditions of oxidative substitution reactions according to eq. (47), the methylnickel intermediate is attacked faster by the electrophile than it is generated[60].

The stronger nucleophile cobaltate attacks methyl halides even at −70 °C. The first product of the reaction according

$$NiL_4 + CH_3I \xrightarrow[CH_3CN,\ 20\,^\circ C]{} NiCH_3L_4^{\oplus}I^{\ominus} \quad (46)$$

$$NiL_4 + CH_3I \xrightarrow[OEt_2,\ 20\,^\circ C]{} [Ni(CH_3)IL_2] + 2\ L \quad (47)$$

$$[Ni(CH_3)IL_2] \xrightarrow{L,\ CH_3I} NiI_2L_3 + C_2H_6$$

to eq. (48), $CoCH_3L_4$, undergoes a subsequent oxidative substitution reaction at slightly higher temperatures. Both steps can be conducted separately; chloromethane is best suited for the preparation of $CoCH_3L_4$.

$$CoL_4^{\ominus} \xrightarrow[-X^{\ominus}]{+CH_3X} CoCH_3L_4 \xrightarrow[-L]{+CH_3X} Co(CH_3)_2XL_3 \quad (48)$$

X = Cl, Br, I X = Br, I

$$CoL_4^{\ominus} + CH_3X \longrightarrow \{CoL_4 + CH_3X^{\ominus}_{\bullet}\} \xrightarrow[-X^{\ominus}]{} CoCH_3L_4 \quad (48a)$$

$$CH_3X^{\ominus}_{\bullet} \longrightarrow {}^{\bullet}CH_3 + X^{\ominus}$$

$$^{\bullet}CH_3 \xrightarrow{CoL_4} CH_4 + L_3Co\overset{CH_2}{\underset{PMe_2}{|}} \quad (48b)$$

The high reduction potential of the cobaltate (2.6—3 V[47]) suggests a radical chain mechanism according to eq. (48a, b). Furthermore, the products in the first step strongly depend on temperature and solvent: In the more stable solvent cage of ether molecules at low temperatures a methyl radical is trapped by CoL_4 as soon as it is formed [eq. (48a)]. For pentane at 20 °C, eq. (48b) designates the reaction mode: the "hot" methyl radical abstracts hydrogen from a trimethylphosphane ligand, yielding a three-membered metallacycle of cobalt(I)[75].

With aromatic halides such as chlorobenzene hydrogen abstraction dominates. In an analogous reaction and even under favorable conditions phenyltetrakis(trimethylphosphane)cobalt is formed only in minor quantities.

Metal(d^9) configuration: We find one of the few examples of oxidative addition reactions at paramagnetic complex centers[76] in the chemistry of tetrakis(trimethylphosphane)cobalt(0) which is also a strong nucleophile.

$$CoL_4 \xrightarrow{CH_3I} [CoCH_3L_4^{\oplus}I^{\ominus}] \xrightarrow{CoL_4} CoCH_3L_4 + CoIL_3 + L \quad (49)$$

$$CoL_4 \xrightarrow{HCl} CoHL_4^{\oplus}Cl^{\ominus} \xrightarrow{CoL_4} CoHL_4 + CoClL_3 + L \quad (50)$$

Reacting iodomethane even at low temperatures in ether gives a green solid, presumably $CoCH_3L_4^{\oplus}I^{\ominus}$, which is rapidly reduced by further Co^0 complex yielding Co^I products in an overall 2:1 stoichiometry. The steps of reaction (49) cannot be clearly separated, as the activation energy of this alkylation must be high. However, after protonation according to eq. (50) the corresponding hydridocobalt(II) salt is isolated and can be separately reduced by CoL_4.

8. Reactions at the Coordinated Ligand

When applied to 1,1-dihalides like CH_2Cl_2, the 2:1 stoichiometry of oxidative additions to Co^0 complexes formally results in a (chloromethyl)cobalt compound according to eq. (52a). This species appears to be less stable than the analogous (methoxymethyl)cobalt compound which is obtained according to eq. (51)[47].

$$CoL_4^{\ominus} + CH_3OCH_2Cl \xrightarrow[-Cl^{\ominus}]{} \begin{matrix} L & CH_2OCH_3 \\ & | \\ & Co-L \\ L & | \\ & L \end{matrix} \quad (51)$$

$$2\ CoL_4 + CH_2Cl_2 \longrightarrow \left[\begin{matrix} L & CH_2Cl \\ & | \\ & Co-L \\ L & | \\ & L \end{matrix}\right] + CoClL_3 + L \quad (52a)$$

$$[Co(CH_2Cl)L_4] \longrightarrow [Co(CH_2PMe_3)ClL_3] \quad (52b)$$

$$CoClL_3 + Me_3P{=}CH_2 \longrightarrow \quad (52c)$$

$$\longrightarrow 1/2\ Co(CH_2PMe_3)_2Cl_2 + 1/2\ CoL_4 + L$$

$$3\ CoL_4 + 2\ CH_2Cl_2 \longrightarrow Co(CH_2PMe_3)_2Cl_2 + 2\ CoClL_3 + 4\ L \quad (52)$$

By attack of a phosphane according to eq. (52a, b) the carbenoid moiety is converted into a coordinated phosphorane[77]. In a similar reaction, Fischer-type carbene complexes take up phosphane to form phosphorane complexes[78].

Phosphoranecobalt(I) complexes undergo a dismutation reaction according to eq. (52b, c), which is also observed in an attempted direct synthesis according to eq. (52c). Finally, this reaction gives a bisphosphoranecobalt(II) complex together with CoL_4, thereby explaining the remarkable 3:2 stoichiometry of the overall reaction which is observed exactly by all the 1,1-dihalides investigated[77].

$$Co(CH_2PMe_3)_2Cl_2 + 4\ L \xrightarrow{Na} Me_3P{=}CH_2 + L_3Co\overset{CH_2}{\underset{PMe_2}{|}} + \cdots \quad (53)$$

Phosphoranes are liberated by reductive disintegration of their cobalt complexes, but reasonable yields are only achieved by supplying phosphane ligands for the low-valent cobalt at the same time [eq. (53)]. In the absence of this addition, the phosphorane is converted into a phosphane ligand. This type of conversion is exemplified by reaction of nickel, which is significant because of the mild conditions in a low temperature matrix[79].

$$Ni\ atoms + 4Me_3P \quad CH_2 \rightarrow Ni(PMe_3)_4 + \cdots \quad (54)$$

It has not been possible to elucidate the formation of the three-membered metallacycle according to eq. (53) which could either occur by decomposition of a phosphorane ligand or by proton abstraction from a trimethylphosphane ligand. There is only one rational synthesis for this compound which proceeds by deprotonation of free phosphane according to *Peterson*[15], followed by reaction with Co^I halide according to eq. (55)[16].

$$Me_2PCH_2Li + CoClL_3 \xrightarrow[-LiCl]{} L_3Co\overset{CH_2}{\underset{PMe_2}{|}} \quad (55)$$

A proton abstraction from the coordinated phosphane has been attempted according to eq. (56); however, it was found unable to compete with the reaction at the cobalt center.

$$Me_3CLi + CoClL_3 \xrightarrow[-LiCl]{} L_4CoH + Me_2C{-}CH_2 + Co + \cdots \quad (56)$$

Thus it was all the more surprising that trimethylphosphane at the iron(0) center undergoes smooth and reversible C—H cleavage.

$$FeL_4 \rightleftharpoons \begin{array}{c} L \quad H \quad CH_2 \\ \diagdown \; | \; \diagup \\ Fe \\ \diagup \; | \; \diagdown \\ L \quad L \quad PMe_2 \end{array} \quad (57)$$

Equilibrium (57) is essentially shifted to the side of the hydridoiron(II) complex. However, derivatives of the iron(0) isomer can be obtained directly under suitable conditions[80,81]. C—H cleavage is exclusively intramolecular. In a mixture with perdeuterated complex H/D exchange fails to occur, thus excluding any dinuclear species containing hydride or CH_2PMe_2 bridges.

Equilibrium (57) is a key reaction for the C—H cleavage of activated aliphatic hydrocarbons at metal centers[82-84]. Unfortunately we still do not know the decisive factor promoting this reaction[85]. Steric considerations and the structure of $Fe(CO)_4$[64] support a paramagnetic and slightly distorted molecule FeL_4. The high electron density facilitates oxidative addition type reactions, to which class equilibrium (57) belongs. On the other hand, there are electron-rich compounds like NiL_4 and $CoL_4^{\ominus}$(d^{10}) which have the same composition but do not show any tendency to undergo a similar addition of the coordinated ligand. Even the paramagnetic valence state of CoL_4 does not give rise to a reaction which could yield the known diamagnetic products[51,75] of eq. (58). Likewise, a reverse reaction according to eq. (58) could not be enforced so far.

$$2\ CoL_4 \not\rightleftharpoons CoHL_4 + L_3Co\begin{array}{c} CH_2 \\ | \\ PMe_2 \end{array} \quad (58)$$

$$CoL_4^{\oplus} \not\rightleftharpoons \left[\begin{array}{c} H \quad CH_2 \\ \diagdown \; | \; \diagup \\ L_3Co \\ \diagup \; | \; \diagdown \\ \quad PMe_2 \end{array}\right]^{\oplus} \quad (59)$$

The cation $CoL_4^{\ominus}$ which is isoelectronic with FeL_4 does not exist in an equilibrium with a hydridocobalt(III) complex in the sense of eq. (59).

So far there is only one example of a C—H fission reaction at a cobalt center, *i.e.* of dinitrogen cobaltates (see Section 10).

9. Monoolefincobalt Complexes

Simple olefins like ethene or propene do not form stable complexes of cobalt in its usual oxidation states[86]. Only on stepwise increase of electron density does the cobalt center become attractive for these π-accepting ligands[87,88].

In the cobalt(I) state coordination of ethene is still feeble and is detected only at low temperatures. On slightly increasing the electron density, *e.g.* on going to the methylcobalt(I) compound according to eq. (60), stable olefin complexes are formed. Reduction to the cobalt(0) state has the same effect.

$$\begin{array}{lllll} d^7 & CoCl_2L_2 \overset{C_2H_4}{\rightleftharpoons\!\!\!/} & CoCl_2(C_2H_4)L_2 & & \\ & \downarrow 1/2\ Mg,\ L & & & \\ d^8 & CoClL_3 \overset{C_2H_4}{\rightleftharpoons} & CoCl(C_2H_4)L_3 & \xrightarrow[-LiCl]{+LiCH_3} & CoCH_3(C_2H_4)L_3 \quad (60) \\ & \downarrow 1/2\ Mg & & & CoH(C_2H_4)L_3 \\ d^9 & [CoL_3] \xrightarrow{C_2H_4} & Co(C_2H_4)L_3 & & \quad (61) \\ & & \downarrow K & \nearrow H^{\oplus} & \\ d^{10} & & Co(C_2H_4)L_3^{\ominus}\ K^{\oplus} & & \quad (62) \end{array}$$

Tris(trimethylphosphane)olefincobalt(0) complexes are monomeric and paramagnetic ($\mu_{eff}/\mu_B = 1.85$); they can be sublimed *in vacuo* with some decomposition. Like CoL_4 they give well structured ESR spectra (toluene glass) which as a rule contain three sets of eight lines (Fig. 6) due to a low molecular symmetry[87].

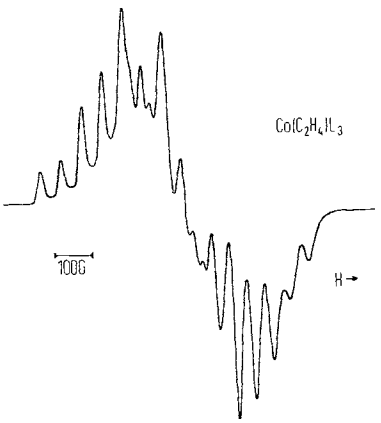


Fig. 6. ESR spectrum of $Co(C_2H_4)(PMe_3)_3$ (toluene glass, 77 K).

Reduction of olefincobalt(0) complexes on the surface of alkali metals in ether solvents proceeds to completion (as distinct from pentane[89]) according to eq. (63).

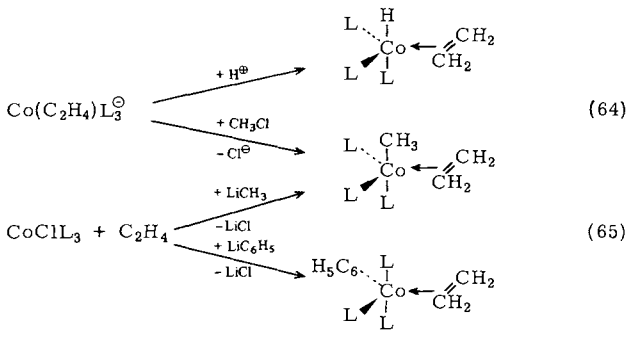
$$Co(C{-}C)L_3 + M \xrightarrow{OR_2} M^{\oplus}Co(C\quad C)L_3^{\ominus} \cdot x\,OR_2 \quad (63)$$

C–C = C_2H_4, C_3H_6, cyclopentene
M = Na, K, Rb, Cs; $OR_2 = O(C_2H_5)_2$, THF; $x = 0.5$—1

The olefincobaltates are orange solids which contain the usual small number of ether molecules for the solvation of alkali metal ions. The thermochromic and solvatochromic effects are less spectacular than with the tetrakis(trimethylphosphane)cobaltates.

Again reactions with electrophiles are of the oxidative addition type. According to eq. (64) they yield a new type of olefincobalt(I) complexes[90] which are also obtained in complementary fashion by anionic alkylation or arylation according to eq. (65)[91].

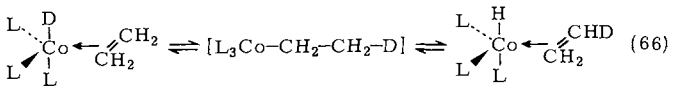
Spectroscopic investigations of these diamagnetic and readily soluble compounds demonstrate a trigonal-bipyramidal ground state configuration in which the σ-bonded ligand and the freely rotating olefin occupy adjacent positions: axial/equatorial and equatorial/equatorial, respectively. The



(64)

(65)

complexes synthesized according to eq. (64) are model compounds for investigations of the insertion step of homogeneous catalysis. The complexes possess all postulated[92] prerequisites: a σ-bound and a π-bound ligand at angles of 90° and 120°, respectively, at the cobalt atom. Furthermore the propeller type rotation of the olefin and the motions of all ligands in the sense of a pseudorotation provide virtually any orientation suitable for the insertion process. Actually this has been verified solely for the hydrido(olefin)cobalt complexes.



(66)

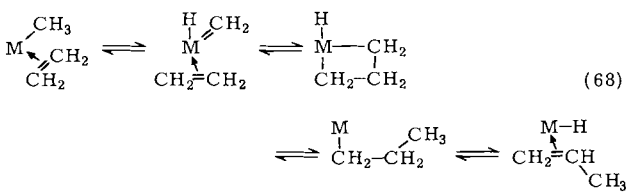
Reaction of the ethenecobaltate with $D^{\oplus}$ according to eq. (64) through equilibrium (66) causes the deuterium to be distributed approximately statistically over five positions: one at the cobalt and four in the ethene. Moreover, this result demonstrates that catalytic reaction of an 18-electron compound is not impaired by the stabilizing effect of the trimethylphosphane ligands[93].

In contrast, the homologous methylcobalt complexes exhibit surprising thermal stability. We would expect insertion into the Co—C bond to be essentially nonreversible because the reverse reaction, which requires *ca.* 75 kJ/mol for the C—C cleavage, cannot compete with the β-elimination needing only about 14 kJ/mol[94]. We therefore expect a reaction sequence according to eq. (67), leading to the hydrido(propene)cobalt complex.

$$CoCH_3(C_2H_4)L_3 \not\rightleftharpoons Co(C_3H_7)L_3 \rightleftharpoons CoH(CH_2{=}CHCH_3)L_3 \qquad (67)$$

This complex can be obtained by a protonation corresponding to eq. (64), but is not formed in reaction (67); nor can it be detected under the conditions necessary for thermolysis of the methylcobalt compound[95].

An olefin insertion into $Co(d^6)$—CH_3 bonds has recently been demonstrated[96]. In view of the high activation energy for this step we still have to consider alternative models, for instance the Green-Rooney mechanism[97] involving metallacycles:



(68)

Numerous examples of olefin insertions into metal-carbene functions have been described[98-100]. Hence an sp^2-carbon attached to a metal could be more prone to insertion than the sp^3-carbon of the methylmetal function.

This idea is contradicted by the properties of a complex $CoC_6H_5(C_2H_4)(PMe_3)_3$ (Fig. 7) which has been recently prepared[91].

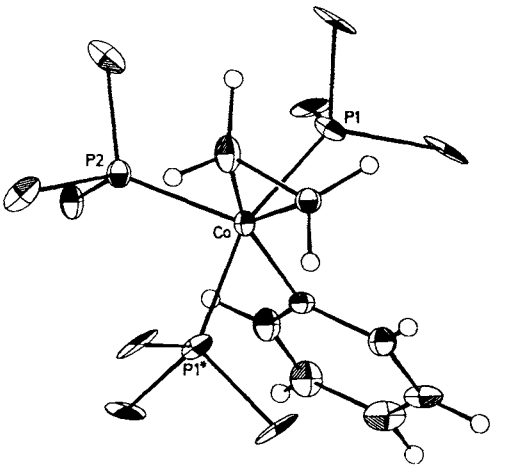


Fig. 7. Structure of $Co(C_6H_5)(C_2H_4)(PMe_3)_3$. Co atom, phenyl group, and C atoms of ethene lie in the equatorial plane.

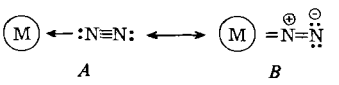
Although in the crystal the cobalt atom and all carbon atoms which are required for the insertion lie in one plane, no insertion product (styrene) can be found in the smooth high yield decomposition reaction in solution according to eq. (69).

$$CoC_6H_5(C_2H_4)L_3 \xrightarrow[\text{Toluene}]{40\,^{\circ}C} Co(C_2H_4)L_3 + 1/2\,C_6H_5{-}C_6H_5 \qquad (69)$$

Further investigations are needed in order to establish all the requirements for this important reaction step in homogeneous catalysis. Last but not least, this includes syntheses of further model compounds and investigations of their reactivity.

10. Dinitrogen Complexes

The high reduction potential of the trimethylphosphane cobaltates should suffice to reduce the dinitrogen molecule, provided a reduced moiety can be stabilized as a product. Today dinitrogen complexes of transition metals are known for almost all Group III to VIII elements[101]. Compared with the dinitrogen molecule (d(NN) = 110 pm), their bond lengths are generally only slightly elongated (d(NN) = 110—113 pm), and only in exceptional cases is there a considerable increase (d(NN) = 135 pm[102]) which may be correlated with the degree of reduction of the N_2 unit. Electron-rich metal centers provide just one of several conditions for stable dinitrogen complexes *A*. Polarization of the N_2 ligand by the metal in the sense of a limiting formula *B*, which is recognized by a strong IR absorption (ν_{NN}), can be enhanced by placing an electron-rich metal center at one end and a polarizing cation at the opposite end of the NN axis.



A *B*

As has been known for ten years[103] the ν_{NN} frequency falls drastically on going from the Co^{I} state over to dinitrogencobaltates.

$CoH(N_2)L_3$ $\quad \nu_{NN} = 2060\ cm^{-1}$ (benzene)

$[CoN_2L_3]^{\ominus}Na^{\oplus}$ $\quad \nu_{NN} = 1875\ cm^{-1}$ (tetrahydrofuran)

$L' = P(C_2H_5)_2C_6H_5$

This observation remained unexplained until recently.

The preparation and structural characterization (Fig. 8) of dinitrogentris(trimethylphosphane)cobaltates containing electropositive main group elements as counterions ($K^{\oplus}$, $Mg(THF)_4^{2\oplus}$)[104-106] have provided a better understanding of the role of the cations: While four tetrahydrofuran donors surround the counterion in the magnesium cobaltate, the potassium cobaltate with its remarkable association of a $(KN_2)_6$ cluster core (Fig. 8) interacts with ether donors only in the

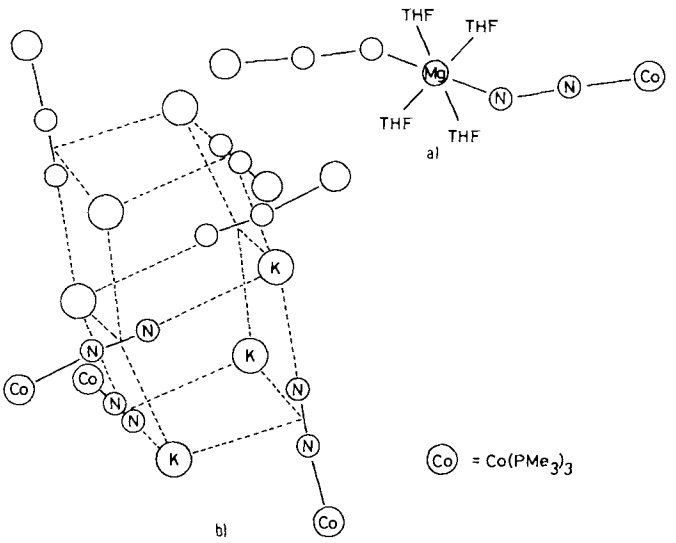
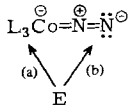


Fig. 8. Structures of dinitrogen cobaltates: a) $L_3Co(N_2)Mg(THF)_4(N_2)CoL_3$ and b) $[K.Co(N_2)L_3]_6$ ($L = PMe_3$).

second coordination sphere even in solution[106], because the interactions between potassium and coordinated dinitrogen dominate along the NN axis as well as perpendicular thereto. In both structures the NN bond lengths (116–118 pm) in the cobaltate ion suggest the following representative limiting formula of an ambidentate anion:



Electrophiles E may attack at two points: (a) at the cobaltate center and (b) at the terminal nitrogen. Both reactions have been accomplished. As an oxidative addition of ethyl iodide or benzyl bromide route (a) leads to complete loss of dinitrogen, yielding organocobalt(I) complexes[106] according to eq. (70 a, b).

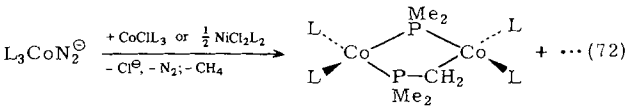
$$L_3CoN_2^{\ominus} + C_2H_5I \xrightarrow[-I^{\ominus}]{} CoH(C_2H_4)L_3 \qquad (70a)$$

$$L_3CoN_2^{\ominus} + C_6H_5CH_2Br \xrightarrow[-Br^{\ominus}]{} Co(\eta^3\text{-}CH_2C_6H_5)L_3 \qquad (70b)$$

$$L_3CoN_2^{\ominus} + ClSnMe_3 \xrightarrow[-Cl^{\ominus}]{} L_3Co{-}N{\equiv}N{-}SnMe_3 \qquad (71)$$

Route (b) is more interesting because it affords substituted cobalt diazenides (N in a formal oxidation state −I) with reagents such as trimethylchlorosilane or trimethyltin chloride according to eq. (71). However, an extensive reduction of the N_2 unit has not been achieved so far[40].

Oxidations of dinitrogen cobaltates by cobalt(I) or nickel(II) halide complexes according to eq. (72) take an unexpected turn.



Loss of dinitrogen and (formally) methane affords a remarkably stable and weakly paramagnetic dinuclear compound containing a μ-dimethylphosphide and a μ-dimethylphosphanemethanide moiety[107]. As demonstrated by X-ray diffraction (Fig. 9) the last-mentioned ligand contains a PC double bond (171 pm), and an sp^2-CH_2 function is bound to one of the cobalt atoms at a PCCo angle of 88°. The structural subunit $CoPMe_2CH_2Co$ may therefore be described as a *P*-metalated methylenephosphorane which, upon coordination and in contrast to all known phosphorane-metal complexes[108], does not change its ylide function into an sp^3-C atom. In accord with the normal behavior of phosphorane complexes, there is no CO insertion into this particular Co—C bond as became evident from the synthesis of a carbonyl derivative, $L(CO)_2Co(PMe_2)(PMe_2CH_2)Co(CO)_2L$. CO usually undergoes fast insertion into all Co—C-σ bonds[107].

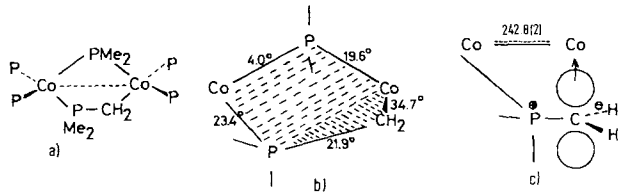


Fig. 9. Structure of $L_2Co(PMe_2)(CH_2PMe_2)CoL_2$ ($L = PMe_3$). a) Geometry around the C atoms; b) dihedral angles of the heterocycle; c) interpretation of bonding in the $Co(CH_2PMe_2)Co$ subunit.

Reaction according to eq. (72) illustrates the role of C—H and P—C bond cleavage under the influence of electron-rich metal centers. In homogeneous catalysis it provides a model for the deactivation of catalysts containing alkylphosphanes.

11. Outlook

The elementary steps of many important processes in homogeneous catalysis have still not been elucidated. Syntheses of simple model compounds therefore provide valuable insights, especially if they simulate complex entities which are thought to serve as switching points in catalytic cycles. In spite of a strongly stabilizing effect of monodentate alkylphosphane ligands, which is largely independent of the electron density at the metal center, the model character of the compounds is not lost: Even 18-electron complexes undergo elementary steps such as the formal insertion of an olefin

into a metal-hydride function unassisted by a cocatalyst. Further model reactions can be easily designed on the basis of the concept of isosteric compounds. However, the real challenge always lies in the synthesis of the model compounds.

Particular interest attaches to the trialkylphosphane cobaltates because their reduction potential equals that of the most electropositive elements. Their pronounced readiness to undergo oxidative additions suggests an approach to C—H and C—C bond cleavage reactions. Furthermore, the synthetic potential of these compounds is not in the least exhausted.

Extensive reduction of dinitrogen in the metalate-counterion matrix may be regarded as a first step in the synthesis of organonitrogen compounds which might possibly be brought about catalytically.

The organometallic and coordination chemistry of the three "foundry metals", nickel, cobalt, and iron, will continue to command a lively interest, both academic and practical.

A sincere word of acknowledgment is directed firstly to my co-workers, Dr. H. H. Karsch, Dr. R. Hammer, J. Wenninger, and J. Gross, who have advanced the present work through their enthusiasm, perseverance, and skill, to my colleagues in the laboratory, and to the Deutsche Forschungsgemeinschaft (Schwerpunktprogramm "Homogenkatalyse") and the Fonds der Chemischen Industrie for generous financial support.

Received: December 11, 1979 [A 318 IE]
German version: Angew. Chem. *92*, 362 (1980)

[1] *G. Henrici-Olivé, S. Olivé:* Coordination and Catalysis, Verlag Chemie, Weinheim 1977, p. 122.
[2] *J. L. Davidson*, Inorg. React. Mech. *5*, 346 (1977).
[3] *F. Calderazzo*, Angew. Chem. *89*, 305 (1977); Angew. Chem. Int. Ed. Engl. *16*, 299 (1977).
[4] *H. A. Skinner*, J. Chem. Thermodyn. *10*, 309 (1978).
[5] *P. L. Davidson, M. F. Lappert, R. Pearce*, Acc. Chem. Res. *7*, 209 (1974).
[6] *M. L. H. Green*, Pure Appl. Chem. *50*, 27 (1978), and references cited therein.
[7] *M. F. Lappert, J. S. Poland*, Adv. Organomet. Chem. *9*, 397 (1970).
[8] *E. G. Rochow:* Einführung in die Chemie der Silicone, Verlag Chemie, Weinheim 1952, p. 86; *H. Schmidbaur*, Angew. Chem. *77*, 206 (1965); Angew. Chem. Int. Ed. Engl. *4*, 201 (1965).
[9] *C. A. Tolman*, Chem. Rev. *77*, 313 (1977).
[10] *D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, Chem. Ber. *107*, 3706 (1974).
[11] *C. Krüger, B. L. Barnett, D. Brauer* in *E. A. Körner von Gustorf, F. W. Grevels, I. Fischler:* The Organic Chemistry of Iron. Vol. 1. Academic Press, New York 1978, p. 70.
[12] *H. H. Karsch*, Chem. Ber. *110*, 2712 (1977).
[13] *F. A. Cotton, G. Wilkinson:* Advanced Inorganic Chemistry. 3rd Ed., Wiley, New York 1972. Chap. 22.
[14] *M. Bigorgne*, J. Organomet. Chem. *2*, 68 (1964).
[15] *D. J. Peterson, H. R. Hays*, J. Org. Chem. *30*, 1939 (1965); *D. J. Peterson*, J. Organomet. Chem. *8*, 199 (1967).
[16] *H. H. Karsch, H. Schmidbaur*, Z. Naturforsch. *B 32*, 762 (1977).
[17] *J. S. Valentine*, Chem. Rev. *73*, 235 (1973).
[18] *G. Wilke, H. Schott, P. Heimbach, Angew. Chem. 79*, 62 (1967); Angew. Chem. Int. Ed. Engl. *6*, 92 (1967).
[19] *J. P. Fackler, Jr., J. A. Fetchin, J. Mayhew, W. C. Seidel, T. J. Swift, M. Weeks*, J. Am. Chem. Soc. *91*, 1941 (1969).
[20] *H. Elser, H. Dreeskamp*, Ber. Bunsenges. Phys. Chem. *73*, 619 (1969).
[21] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *105*, 2628 (1972).
[22] *G. Mavel*, Prog. Nucl. Magn. Reson. Spectrosc. *1*, 251 (1969).
[23] *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Vol. 1. Academic Press, New York 1974, p. 168.
[24] Very little is known about the physiological effects of organonickel compounds. Regardless of their fast oxidation they could be toxic under anaerobic conditions.
[25] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *106*, 1433 (1973).
[26] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *106*, 2438 (1973).
[27] *H. H. Karsch*, Thesis, University of Würzburg 1974.
[28] *Y. Toshikatsu, T. Okano, S. Otsuka*, J. Chem. Soc. Dalton Trans. *1976*, 993.
[29] *J. Chatt, J. H. Davidson*, J. Chem. Soc. *1964*, 2433.
[30] *Ch. Reichardt*, Angew. Chem. *91*, 119 (1979); Angew. Chem. Int. Ed. Engl. *18*, 98 (1979).
[31] *H.-F. Klein*, unpublished.
[32] *G. Booth, J. Chatt*, J. Chem. Soc. *A 1966*, 634.
[33] *H.-F. Klein*, Angew. Chem. *85*, 403 (1975); Angew. Chem. Int. Ed. Engl. *12*, 402 (1975).
[34] See [23], p. 166.
[35] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *109*, 2524 (1976).
[36] *G. Huttner, O. Orama, V. Bejenke*, Chem. Ber. *109*, 2533 (1976).
[37] See [23], p. 197.
[38] See [23], p. 170.
[39] *D. R. Fahey, J. E. Mahan*, J. Am. Chem. Soc. *99*, 2501 (1977).
[40] *H.-F. Klein, J. Wenninger*, unpublished.
[41] *E. L. Muetterties*, Acc. Chem. Res. *3*, 266 (1970).
[42] *J. R. Shapley, J. A. Osborn*, Acc. Chem. Res. *6*, 305 (1973); *I. Ugi, D. Marquarding, H. Klusacek, P. Gillespie, F. Ramirez*, Acc. Chem. Res. *4*, 288 (1971).
[43] *H.-F. Klein, H. H. Karsch, W. Buchner*, Chem. Ber. *107*, 537 (1974).
[44] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *108*, 944 (1975).
[45] $[NiCH_3L_4][B(C_6H_5)_4]$ in dichloromethane, $CoCH_3L_4$ in toluene solution; $L = P(CH_3)_3$.
[46] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *109*, 1453 (1976).
[47] *R. Hammer, H.-F. Klein*, Z. Naturforsch. *B 32*, 138 (1977).
[48] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *108*, 956 (1975).
[49] *H. H. Karsch*, Chem. Ber. *110*, 2699 (1977).
[50] *Th. Kruck*, Angew. Chem. *79*, 27 (1967); Angew. Chem. Int. Ed. Engl. *6*, 53 (1967).
[51] *H.-F. Klein, H. Schmidbaur*, Angew. Chem. *82*, 885 (1970); Angew. Chem. Int. Ed. Engl. *9*, 903 (1970); *H.-F. Klein, ibid. 82*, 885 (1970), and *9*, 903 (1970), resp.
[52] *H. H. Karsch, H.-F. Klein, H. Schmidbaur*, Chem. Ber. *110*, 2200 (1977).
[53] *J. W. Rathke, E. L. Muetterties*, J. Am. Chem. Soc. *97*, 3272 (1975).
[54] *S. D. Ittel, C. A. Tolman, A. D. English, J. P. Jesson*, J. Am. Chem. Soc. *98*, 6073 (1976).
[55] *E. L. Muetterties, F. J. Hirsekorn*, J. Am. Chem. Soc. *95*, 5419 (1973).
[56] *P. Meakin, E. L. Muetterties, J. P. Jesson*, J. Am. Chem. Soc. *94*, 5271 (1972).
[57] *P. Meakin, J. P. Jesson, F. N. Tebbe, E. L. Muetterties*, J. Am. Chem. Soc. *93*, 1797 (1971).
[58] *F. N. Tebbe, P. Meakin, J. P. Jesson, E. L. Muetterties*, J. Am. Chem. Soc. *92*, 1068 (1970).
[59] *P. Meakin, J. P. Jesson, D. H. Gerlach, F. N. Tebbe, L. J. Guggenberger, W. G. Peet, E. L. Muetterties*, J. Am. Chem. Soc. *92*, 3482 (1970).
[60] *H.-F. Klein, H. H. Karsch*, Chem. Ber. *109*, 2515 (1976).
[61] *M. C. Browning, J. R. Mellor, D. J. Morgan, S. A. J. Pratt, L. E. Sutton, L. M. Venanzi*, J. Chem. Soc. *1962*, 693.
[62] *P. F. Meier, A. E. Merbach, M. Dartiguenave, Y. Dartiguenave*, Inorg. Chem. *18*, 610 (1979).
[63] *H.-F. Klein, H. H. Karsch*, Inorg. Chem. *14*, 473 (1975).
[64] M. Poliakoff, Chem. Soc. Rev. *53*, 257 (1978).
[65] *T. V. Harris, J. W. Rathke, E. L. Muetterties*, J. Am. Chem. Soc. *100*, 6966 (1978).
[66] *A. Gleizes, M. Dartiguenave, Y. Dartiguenave, J. Galy, H.-F. Klein*, J. Am. Chem. Soc. *99*, 5187 (1977).
[67] *P. Heimbach*, Angew. Chem. *76*, 586 (1964); Angew. Chem. Int. Ed. Engl. *3*, 648 (1964).
[68] The author thanks Prof. Dr. *E. Lüscher* and Dipl.-Phys. *G. Stetter*, Physics Department E 13, Technical University München, for the facilities offered and for recording some ESR spectra.
[69] *L. A. Hanlan, H. Huber, E. P. Kündig, B. R. McGarvey, G. A. Ozin*, J. Am. Chem. Soc. *97*, 7054 (1975), and references cited therein.
[70] *M. Aresta, M. Rossi, A. Sacco*, Inorg. Chim. Acta *3*, 227 (1969); *A. Yamamoto, S. Kitazume, C. S. Pu, S. Ikeda*, J. Am. Chem. Soc. *93*, 371 (1971); *L. W. Gosser, G. W. Parshall*, Inorg. Chem. *13*, 1947 (1974); *M. C. Rakowski, E. L. Muetterties*, J. Am. Chem. Soc. *99*, 739 (1977).
[71] *J. Goubeau, D. Köttgen*, Z. Anorg. Allg. Chem. *360*, 182 (1968).
[72] *L. M. Haines, M. H. B. Stiddard*, Adv. Inorg. Chem. Radiochem. *12*, 53 (1969).
[73] Gas phase photoelectron spectra could not be obtained because of extensive dissociation of both compounds at higher temperatures [74].
[74] *J. Green*, personal communication.
[75] *H. H. Karsch, H.-F. Klein, H. Schmidbaur*, Angew. Chem. *87*, 630 (1975); Angew. Chem. Int. Ed. Engl. *14*, 637 (1975).
[76] *P. W. Schneider, P. F. Phelan, J. Halpern*, J. Am. Chem. Soc. *91*, 77 (1969), and references cited therein.
[77] *H.-F. Klein, R. Hammer*, Angew. Chem. *88*, 61 (1976); Angew. Chem. Int. Ed. Engl. *15*, 42 (1976).

[78] *F. R. Kreissl, C. G. Kreiter, E. O. Fischer*, Angew. Chem. *84*, 679 (1972); Angew. Chem. Int. Ed. Engl. *11*, 643 (1972).
[79] *P. S. Skell*, personal communication.
[80] *H. H. Karsch*, Chem. Ber. *110*, 2213 (1977).
[81] *H. H. Karsch*, Chem. Ber. *110*, 2222 (1977).
[82] *G. W. Parshall*, Acc. Chem. Res. *8*, 113 (1975).
[83] *A. E. Shilov, A. A. Shtheinman*, Coord. Chem. Rev. *24*, 97 (1977).
[84] *D. E. Webster*, Adv. Organomet. Chem. *15*, 147 (1977).
[85] *C. A. Tolman, S. D. Ittel, A. D. English, J. P. Jesson*, J. Am. Chem. Soc. *101*, 1742 (1979).
[86] Gmelin: Handbook of Inorganic Chemistry. Supplement of 6th Ed. Vol. 5, part 1. Cobaltorganic Compounds, p. 205.
[87] *R. Hammer*, Thesis, Technical University München 1977.
[88] *K. Jonas, L. Schieferstein, C. Krüger, Y.-H. Tsay*, Angew. Chem. *91*, 590 (1979); Angew. Chem. Int. Ed. Engl. *18*, 550 (1979).
[89] *H.-F. Klein, J. Gross, J. M. Basset, U. Schubert*, Z. Naturforsch., in press.
[90] *H.-F. Klein, R. Hammer, J. Wenninger, J. Gross* in *B. Pullman:* Catalysis in Chemistry and Biochemistry. Vol. 12. Reidel, Dordrecht 1979, p. 285.
[91] *H.-F. Klein, R. Hammer, J. Gross, U. Schubert*, Angew. Chem., in press.
[92] *D. L. Thorn, R. Hoffmann*, J. Am. Chem. Soc. *100*, 2079 (1978).
[93] All synthesized hydrido(olefin)cobalt complexes isomerize 1-pentene in bulk [87].
[94] *H. Kollmar*, J. Am. Chem. Soc. *100*, 2665 (1978).
[95] Thermolysis of $CoCH_3(C_2H_4)L_3$ yields CH_4, C_2H_4, and a mixture of cobalt(I) complexes which proved difficult to separate, including $L_2Co(PMe_2)(CH_2PMe_2)CoL_2$ ($L = PMe_3$), see Section 10 and Fig. 9.
[96] *E. R. Evitt, R. G. Bergman*, J. Am. Chem. Soc. *101*, 3973 (1979).
[97] *M. L. H. Green, R. Mahtab*, J. Chem. Soc. Chem. Commun. *1978*, 604.
[98] *F. N. Tebbe, G. W. Parshall, G. S. Reddy*, J. Am. Chem. Soc. *100*, 3611 (1978).
[99] *R. R. Schrock*, Acc. Chem. Res. *12*, 98 (1979).
[100] *A. E. Stevens, J. L. Beauchamp*, J. Am. Chem. Soc. *101*, 6449 (1979).
[101] *J. Chatt, J. R. Dilworth, R. L. Richards*, Chem. Rev. *78*, 589 (1978).
[102] *K. Jonas*, Angew. Chem. *85*, 1051 (1973); Angew. Chem. Int. Ed. Engl. *12*, 997 (1973); *C. Krüger, Y.-H. Tsay, ibid. 85*, 1051 (1973) and *12*, 998 (1973), respectively.
[103] *A. Sacco, M. Rossi*, Chem. Commun. *1979*, 471; *M. Aresta, C. F. Nobile, M. Rossi, A. Sacco*, Chem. Commun. *1971*, 781.
[104] *R. Hammer, H.-F. Klein, U. Schubert, A. Frank, G. Huttner*, Angew. Chem. *88*, 648 (1976); Angew. Chem. Int. Ed. Engl. *15*, 612 (1976).
[105] *R. Hammer, H.-F. Klein, P. Friedrich, G. Huttner*, Angew. Chem. *89*, 499 (1977); Angew. Chem. Int. Ed. Engl. *16*, 485 (1977).
[106] *H.-F. Klein, R. Hammer, J. Wenninger, P. Friedrich, G. Huttner*, Z. Naturforsch. *B 33*, 1267 (1978).
[107] *H.-F. Klein, J. Wenninger, U. Schubert*, Z. Naturforsch. *B 34*, 1391 (1979).
[108] *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1975).

Thermal Degradation of Polymers to Polymeric Carbon—An Approach to the Synthesis of New Materials[**]

By Erich Fitzer[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

One hundred years ago, *Edison* succeeded in preparing carbon fibers for his incandescent lamp bulb by thermal decomposition of natural polymeric fibers. Ten years ago, progress reports about "Novel Forms of Carbon" predicted outstanding properties and promising new applications for the carbonization products of synthetic polymers. Research and development in this field have been promoted by the problems of conventional technology (shortages of raw material and energy, pollution problems). Polymeric carbon materials—prepared by thermal degradation of synthetic polymers—exhibit a special ribbon-like microstructure. They will provide the chemist with many challenges.

1. Introduction

The thermal degradation of polymeric, organic natural substances, which is one of the oldest technologies of mankind, results in residues with high carbon content. They have a porous structure and low strength, because the cellular structure of the natural precursor material is preserved after carbonization. Moreover, the fibrilous structure of fibrous natural precursor materials is also found in the carbon residues. The mass loss due to elimination of volatile by-products during pyrolysis causes additional porosity and, above all, isotropic shrinkage. Only low carbon yields (<30%) are obtained if no special chemical pretreatment of the precursor is performed before the carbonization.

An essential condition for making carbon fibers from polymers is carbonization as a solid without softening or melting. This was realized in case of the carbon fiber in *Edison*'s incandescent light bulbs and also in case of the first high strength carbon fibers produced from rayon in the 1960's[1,2]. The revolutionary increase of strength and stiffness of the carbon fibers in the last ten years has not been accomplished merely by chemical means, *i.e.* by using fully synthetic polymer fibers, but by way of morphological changes in the initially formed porous carbon material. These morphological changes can be induced by hot stretching or hot working, at temperatures above 2600 °C (cf.[3]), as in the hot working of glasses or metals.

The hot working of carbon requires similar techniques to the hot formation of metals, the drawing of molten glass, or methods of shaping for thermoplastics, but at much higher temperatures. In the wake of this success of hot-stretched carbon fibers not only were prospects for the applications of carbon fibers discussed, but chemical research was also started on the pyrolysis mechanism of polymers[4]. It was expected that the properties important for the technical appli-

[*] Prof. Dr. Erich Fitzer
Institut für Chemische Technik der Universität Karlsruhe
Kaiserstrasse 12, D-7500 Karlsruhe 1 (Germany)

[**] Based on a lecture presented at the GDCh General Meeting at Berlin on September 12, 1979.

cation can be improved by using suitable synthetic polymers instead of rayon as precursor material.

The chemist may be surprised that a material with improved properties should result on decomposition and destruction of the polymeric structure. It is therefore appropriate to consider the outstanding properties of carbon. Pure carbon is resistant to attack by weather, water, fungicides, and bacteria. It is also resistant to almost all organic solvents and compounds, to salt solutions, alkalis, and acids. Furthermore, it is not inflammable and oxidizes only slowly in air above 500 °C. Combustion can be accomplished in very hot flames. Carbon resists deformation at temperatures up to more than 2000 °C, it shows an outstanding creeping strength, it is not susceptible to aging, is non-polluting, and above all it is absolutely biocompatible, *i.e.* suitable for implantation in human medicine.

However, of decisive importance for the usefulness of carbon as material are its mechanical properties, and above all its strength. It was therefore appropriate to check which structural prerequisites of the polymer must be fulfilled in order to achieve by pyrolysis a carbon residue with maximum possible strength combined with tolerable fracture behavior despite the absence of plastic deformability. Table 1 provides a survey.

after thermal degradation. This product became known as "glassy carbon" or "vitreous carbon". The difficult process of thermal degradation, and the impossibility of producing objects with a thickness of more than 5 mm, limit the applicability of glassy carbon.

During the last ten years we have also discovered how to modify thermoplastic polymers in respect to the shape-retaining thermal degradation after the shaping into thermosetting polymers by a "stabilization" treatment. It is possible to produce in a simplified process carbon fibers with an anisotropic tensile strength up to 4000 MN/m^2 (400 kg/mm^2) (type II) and a Young's modulus of about 400 GN/m^2 (40×10^3 kg/mm^2) (type I) from synthetic fibers, and above all from polacrylonitrile (PAN). The resulting fibers are suitable as reinforcing material for organic polymers. The prices of such high quality products are not only one tenth of those of other reinforcing fibers[6], but also of the first carbon fibers[7-9].

A promising recent development are the all-carbon composites, where carbon fibers are embedded in a carbon matrix. One example of an application is the surgical replacement of damaged joints. This underlines the fact that these special carbon materials have numerous, rather than just a few potential applications[10].

Table 1. Tensile strength of polymeric carbon, depending on starting material, stabilization, and annealing. PAN = polyacrylonitrile; MA = methyl acrylate.

Starting material	Stabilization treatment	Annealing	Carbon yield [%]	Tensile strength [MN/mm^2]	Ref.
Polyvinyl alcohol	Air oxidation 200 °C	up to 2500 °C	*ca.* 20	500	[48]
Poly(2,6-diphenyl-*p*-phenylene oxide)	N_2 or Cl_2, 370–500 °C	up to 1300 °C	*ca.* 50	1200	[49]
Acenaphtylene	Oxidation in O_2	up to 800 °C	*ca.* 50	700	[50]
Phenolic resin		up to 900 °C	*ca.* 65	2000	[51]
Rayon	HCl or O_2	up to 1300 °C	30	700	[3]
		up to 2900 °C	25	700	
		Stretch graphitization up to 2900 °C	25	3500	
PAN copolymer with *ca.* 6% MA, industrial production, wet spun	Oxidation 220–250 °C	up to *ca.* 1100 °C	≈60	2000–2500	[52]
		up to *ca.* 1500 °C		3000–4000	
		up to *ca.* 2500 °C		2000–2500	
PAN lab. sample					
Homopolymer	Air oxidation 240 °C/4 h	1400 °C	≈50	1060	[53]
1% MA				1200	
5% MA				900	
Spun in clean room	Air oxidation 220 °C/8 h	1000 °C	*ca.* 50	2200	[54]
		1400 °C		2400	
		2500 °C		2700	
Control under non-clean room conditions		1000 °C		1950	
		1400 °C		1300	
		2500 °C		1500	

There exists one special type of carbon material which is formed by the pyrolysis of polymers and which is superior in its mechanical properties on account of its special ribbon-like structure (cf. Fig. 1a and 2). This form of carbon is therefore called "polymeric carbon". Glassy carbon, which is mentioned in the following, and the high strength carbon fibers number among the polymeric carbons.

Since about 1960 it has been known that some synthetic thermosetting polymers, *e.g.* polyfurfuryl alcohol[5], can result in extremely hard and impermeable carbon residues with an isotropic bending strength up to 150 MN/m^2 (15 kg/mm^2)

2. The Microstructure of "Polymeric Carbon"

Figure 1 shows the well-known modifications of carbon: On the upper left we see graphite, a modification stable under normal conditions; the high pressure modification diamond is seen on the bottom left. The pyrolysis residue suitable for technical applications shows none of these lattice orders. It has been known since the 1930's from X-ray diffraction measurements that coke and other carbon residues, formerly called amorphous carbon, actually exhibit a two-dimensional order similar to that in graphite layers. From the

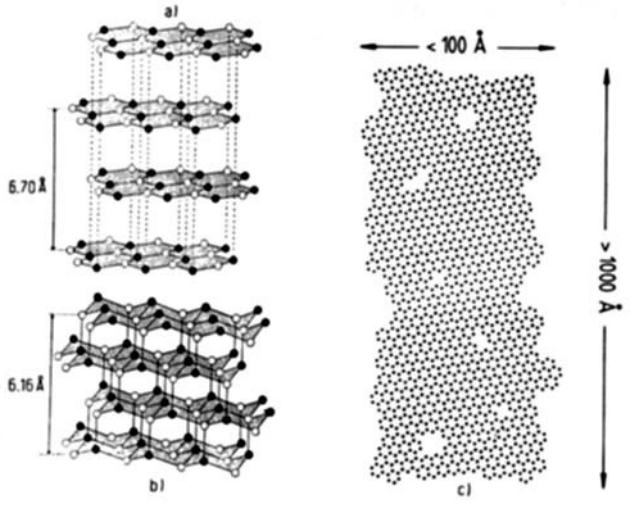


Fig. 1. Structures of elemental carbon: a) Graphite (C/C distance 1.41 Å, C/C bond energy 430 kJ/mol); b) diamond (C/C distance 1.54 Å, C/C bond energy 350 kJ/mol); c) polymeric carbon (especially glassy carbon, C/C distance about 1.42 Å).

broadening of the diffraction profile areas of only a few nm^2 could be concluded. *Braun*[11] showed in 1978 by careful structural analysis of glassy carbon produced from polyfurfuryl alcohol, that bigger average areas of coherent dispersion (apparent $\bar{L}_a$ data) up to 10 nm can be proved by extensive correction of the (10)-interferences with respect to distortion effects.

Today it is known from adsorption measurements (see *e.g.*[12]), and above all from high-resolution transmission electron microscopy (compare [13]), that glassy carbon shows a ribbon- or plate-like structure indicated on the right-hand side of Figure 1. Some of these ribbons can be stacked one upon the other to form plate-like structures which are distinct from a graphitic structure. Figure 2[14] shows the cross-linking between the layers, which corresponds almost to the coiling of chain polymers.



Fig. 2. a) Structural model, b) transmission electron micrograph of glassy carbon produced from polyfurfuryl alcohol as a typical example for isotropic polymeric carbon (see [14]).

No concept has yet been developed for an exact description of this special arrangement of the carbon atoms. Comparison with the structure of polymers seems to be the most suitable, except that polymeric carbon does not consist of chain- or ladder polymers but of planar macromolecules. These polyaromatic layers can be arranged differently and can be cross-linked. Therefore the term "polymeric carbon" is suggested for this carbon with plate- or ribbon-like structure, which is obtained after the pyrolysis of polymers. *Jenkins*[15] introduced the term "polymeric carbon" for the same products, but only in view of the nature of the precursor materials and not of the structure of the pyrolysis residue.

Attempts to establish the presence of tetrahedral structural units, expected for sp^3-hybridization, in polymeric carbon by X-ray methods have remained unsuccessful. *Braun*[16] observed an accumulation in the distribution of the radial interatomic distances at 1.42 Å for the products obtained at all stages of the thermal degradation of polyfurfuryl alcohol, but not at 1.54 Å. This result does not rule out the existence of a partial sp^3-hybridization, for example in interlamellar bonds, at the edges of the layers, or at defects.

The formation and the growth of ribbons of polymeric carbon during thermal degradation has been studied thoroughly for polyfurfuryl alcohol (Fig. 3).

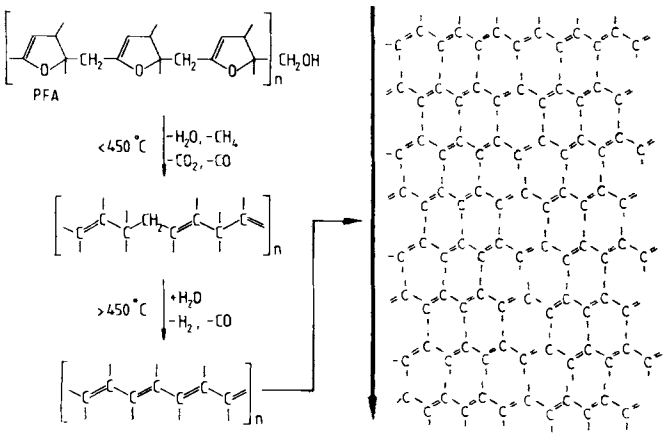


Fig. 3. Intermediate products formed during thermal degradation of polyfurfuryl alcohol (PFA) [17] and direction of growth (thick arrow) of the polymeric carbon ribbons formed by the fixed C/C chains [14].

The furan ring is cleaved at temperatures above 350 °C with concomitant loss of H_2O, CH_4, CO, and CO_2. The methylene linkages are dehydrogenated and fixed contiguous C/C chains with conjugated double bonds result. They are able to cross-link to give two-dimensional polymeric plates (Fig. 3 right) at temperatures above 500 °C[17].

X-ray studies[14] seem to show that the longitudinal growth of the ribbons is controlled by the longitudinal growth of the fixed chains. This shows that the structure of polymeric carbon can be influenced by the chemical composition and the structure of the primary polymer as well as by the process control during the thermal degradation.

The accessibility of the slot-shaped micropores between the layer packings was established by *Kalka*[12] in adsorption measurements with gases. The typical precursor materials for glassy carbon, such as phenolic resins and polyfurfuryl alcohol, give similar results regarding pore sizes, with a maximum at degradation temperatures of about 700 °C, as shown in Figure 4[18] for *p*-polyphenylenes. The pores are clearly seen to shrink with increasing degradation temperature. Contraction perpendicular to the ribbons of polymeric carbon thus can be delayed by a chemical modification of the polymer. For instance, Figure 4b demonstrates the effect of

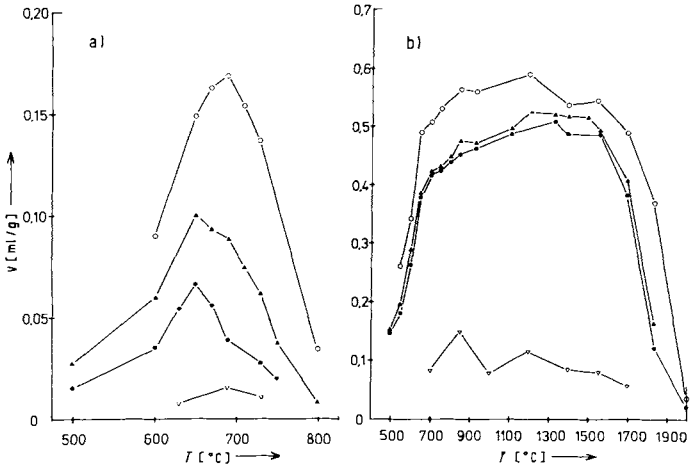


Fig. 4. Volume of micropores V of polymeric carbon produced from: a) p-polyphenylene and b) chlorinated p-polyphenylene as a function of the heat treatment temperature T, measured with: ○, nitrogen; ▲, isobutane; ●, neopentane; ▽, α-pinene. p_{rel} (partial pressure of gas used/total pressure) = 0.25.

chlorination of the polymer prior to pyrolysis. The thermal loss of hydrogen is assisted by dehydrohalogenation occurring in a temperature range insufficient for the growth of carbon ribbons with only few defects. Oxygen (introduced *via* the monomer or *via* the polymer by oxidation) acts similarly. The change in density with degradation temperature clearly reveals the influence of oxygen on the structure of carbon[19]. Stabilization of the slot-shaped pores is of importance for the application of polymeric carbons as catalyst supports or as molecular sieves.

Taking the structure of glassy carbon as a basis and considering that the mass loss of 40 to 50% during thermal degradation causes a linear shrinkage of up to 25%, it can be estimated what internal stresses are set up in this pyrolysis residue. This is the reason for the hardness of glassy carbon, not the tetrahedral structural units as was previously assumed. However, the numerous internal slots limit its ultimate strength: glassy carbon is extremely brittle; nevertheless its bending strength can equal that of the best ultrafine grained types of polygranular graphites (Fig. 5).

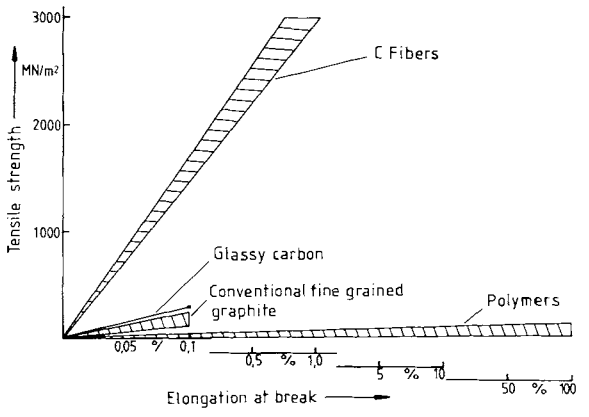


Fig. 5. Deformation behavior up to breaking of isotropic polymeric carbon (glassy carbon) and anisotropic polymeric carbon (carbon fibers), of the primary polymers, and of high quality fine grained graphite.

The stress and fracture properties are greatly improved if the polymeric carbon sheets can be given a preferred orientation. This has been achieved for the high tensile strength carbon fibers, to which a preferred orientation parallel to the fiber axis has been imparted (Fig. 5).

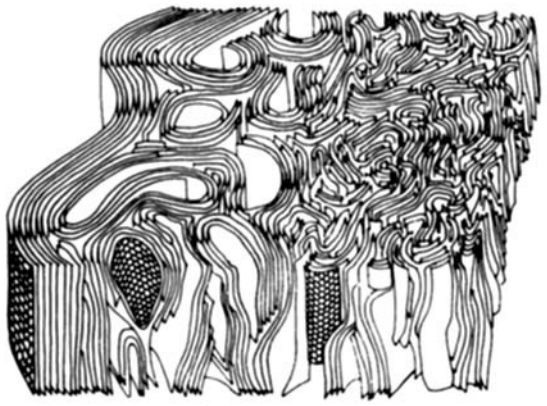


Fig. 6. Structural model of high strength carbon fibers from polyacrylonitrile, designed on the basis of transmission electron microscope studies [13].

Figure 6 shows a structural model of high tensile carbon fibers, designed by *Bennett* and *Johnson*[13] on the basis of transmission electron microscopy studies. Unlike the first high modulus fibers, which were produced by stretch graphitization, present-day efforts are focused—despite maximal orientation of the polymeric backbones parallel to the fiber axis—on maintaining cross-linking perpendicular to the fiber axis in order to ensure transversal, compressive, and torsional strength[9].

3. Pyrolysis of Thermosetting Polymers to Give Polymeric Carbon

The special structure of the carbon layers is achieved largely by chemical modification of the primary polymer. The first structural prerequisite for the formation of polymeric carbon is the non-meltability of the primary polymer; this means that no intermediate liquid phase may occur during thermal degradation. Moreover, it should be possible to impart the final shape desired for the polymeric carbon to the primary polymers.

Chemically, it is essential that the molecular structure should result in a high carbon yield; hence polymers containing aromatic or polyaromatic compounds are the best starting materials[20]. The liberation of volatile low-molecular carbon compounds should be prevented by appropriate chemical composition and cross-linking of the primary polymer. Only ligands should be released, and under ideal circumstances only hydrogen in case of polyannelated hydrocarbons.

Phenolic resins are suitable primary substances because they contain benzene rings joined by methylene groups and the degree of cross-linking can be controlled over a wide range by way of the formaldehyde content and the amount of catalyst. The coke residue is about 60 to 65%, corresponding to a carbon yield of about 85%[17].

Figure 7 shows the mass loss of two polymers during thermal degradation and the amount and the nature of the volatile by-products, from which the mechanism of degradation

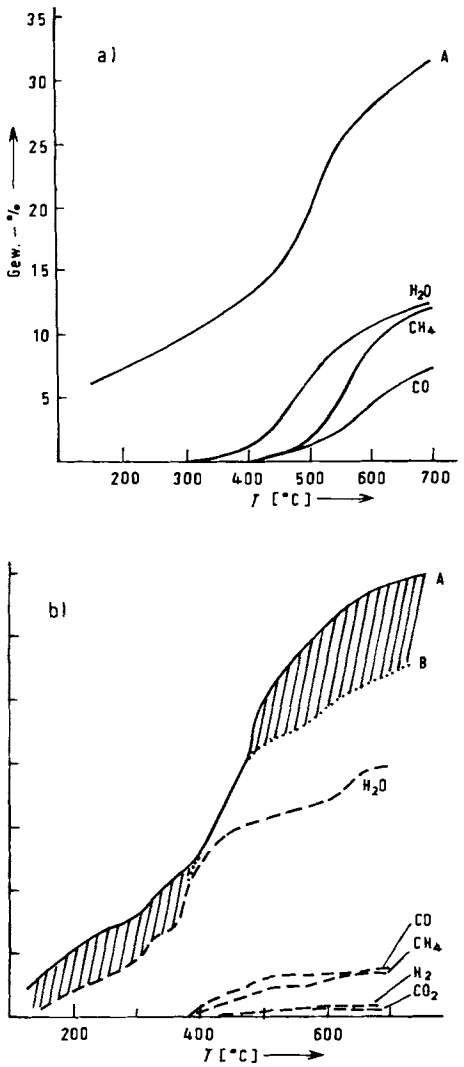


Fig. 7. Thermal degradation of phenolic resins: a) sufficiently cross-linked resin with a phenol : formaldehyde ratio of 2:3; b) insufficiently cross-linked commercial phenolic resin with greater proportion of formaldehyde. A, total mass loss; B, summary of the volatile products; hatched: low molecular substances.

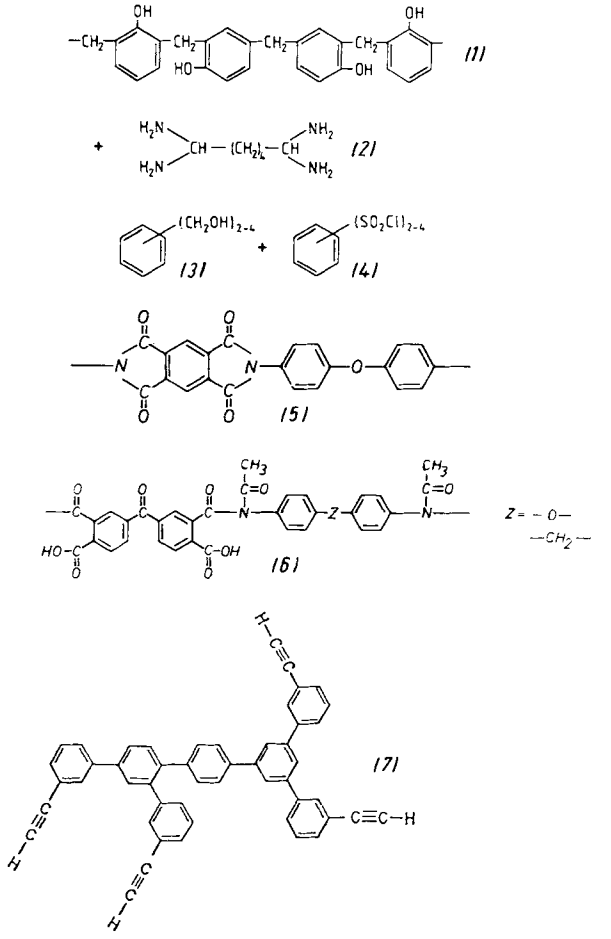


Fig. 8. Phenolic resins, polyimides, and polyphenylenes as thermosetting polymers suitable for the production of polymeric carbon [21, 22].

can be concluded. Figure 7a shows the behavior of a resin with a phenol : formaldehyde ratio of 2:3. The behavior of a resin with a higher proportion of formaldehyde is shown in Figure 7b. The additional mass loss resulting from insufficient cross-linking is seen. The transport of the volatile byproducts is strongly hindered by the microporous structure of the residue. That is why the speed of the condensation and cleavage reactions are of such great importance. With regard to the absence of cracks in the polymeric carbon product the novolacs with 1,1,6,6-hexanetetramine *(2)* as hardener and sulfonyl chlorides *(4)* as catalysts have proved of value (Fig. 8)[21].

Typical ladder polymers such as the polyimides are also very suitable precursors for polymeric carbon. They combine the advantage of high carbon residues resulting from their preformed aromatic rings and their relatively large monomeric units with a degree of prior three-dimensional order over relatively large molecular regions with respect to the formation of the ribbons of polymeric carbon. Therefore preformed ladder polymers show a smaller shrinkage than other polymers. Since the isotropy of shrinkage is also weakened, it becomes possible to produce *e.g.* impermeable polymeric carbon foils from the condensation product of pyromellitic anhydride and 4,4-oxydianiline (H-foil, Dupont) [*(5)* in Fig. 8][22].

p-Polyphenylene is a precursor polymer with ideal chemical and structural groups; it consists solely of benzene rings and is one of the few linear polymers with a complete orientation of the macromolecules. Figure 9 shows its degradation mechanism[23]. Carbon yields up to more than 90% are achieved. The defects in the polymeric carbon sheets, detected by IR-spectroscopic analysis of the C—H bond content, anneal completely at temperatures above 700 °C. Sterically hindering aromatic groups are eliminated simultaneously. The measurements provide an indication of the kind of orientation mechanism operating during the formation of the polymeric carbon ribbons. Additional information is gained from ESR measurements[24], which reveal a second temperature range between 1000 and 1400 °C, where sterically hindering C—C bonds are ruptured. The only disadvantage of *p*-polyphenylene is the difficulty encountered in its shaping by pressing and sintering. The chemist can adopt one of two approaches to avoid this problem: one starts from a thermosetting resin consisting of polyphenylene units with lateral chains of acetylene [see *(7)* in Fig. 8, HA 43 resin, a test product of Hercules Inc.]. This resin proved to be very good as a precursor for polymeric carbon, and particu-

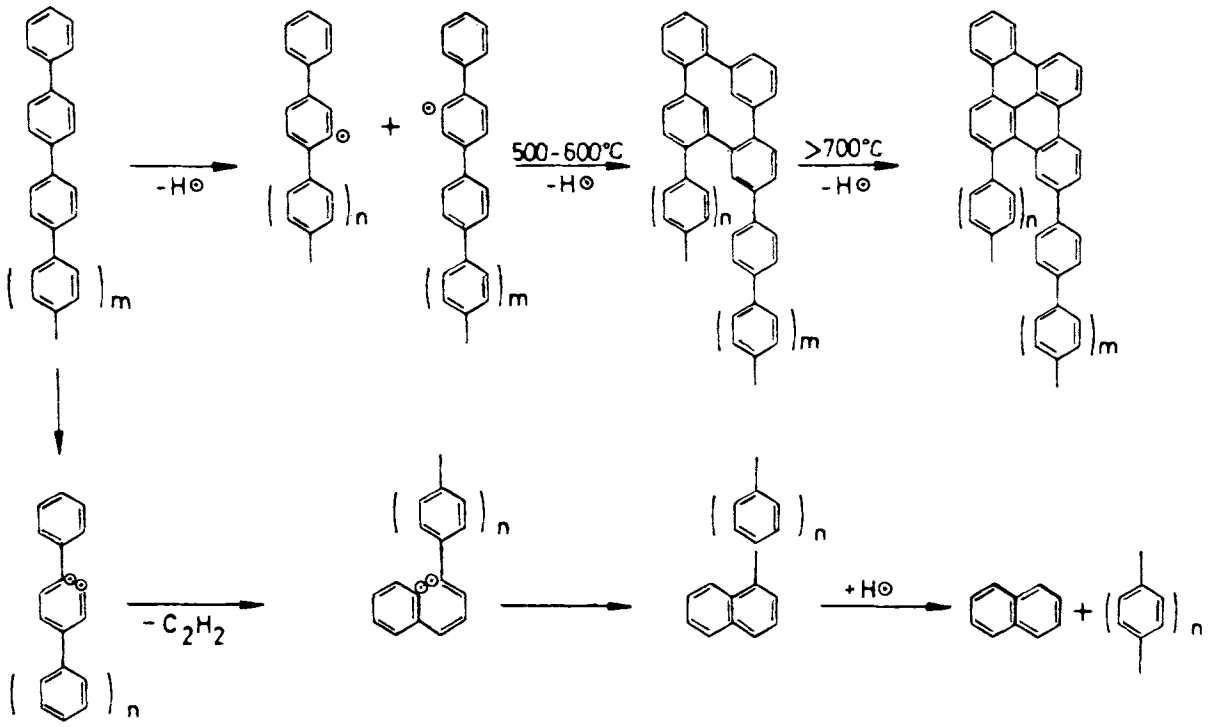


Fig. 9. Thermal degradation of *p*-polyphenylene [23].

larly as matrix precursor in C/C composites. However, production of the resin is difficult and it is not commercially available. The second possibility is to use isomeric polyphenylenes, which are accessible by anionic polymerization of biphenyl. These isomeric mixtures are meltable and can be considered as synthetic pitches. Figure 10 shows structural

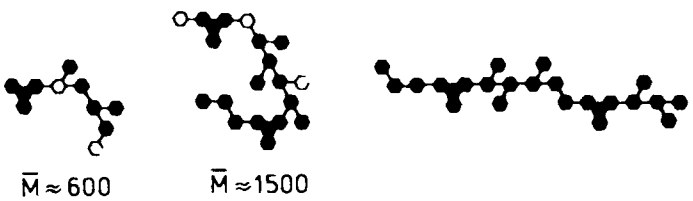


Fig. 10. Structural models of fractions from isomeric polyphenylenes [25]. From left to right: soluble in petroleum ether; soluble in quinoline; insoluble in quinoline. Solid rings, arenes; open rings and chains: aliphatics.

models of some fractions[25]. The solubility or meltability is mainly caused by the aliphatic structural parts. Meltable primary polymers require stabilization before pyrolysis (see Section 4) and have a lower carbon yield.

4. Stabilization of Thermoplastic Polymers for Production of Polymeric Carbon

Meltable primary polymers are unsuitable for the production of polymeric carbon for two reasons: the shape of the polymer is lost and pyrolysis leads to graphitizable residues rather than the metastable, but thermally and chemically stable polymeric carbon (cf. [26]).

Nevertheless, such meltable polymers can be transformed into suitable precursor polymers by a stabilization treatment, involving, *e.g.*, dehydrogenation, cross-linking, cyclization, and aromatization.

A well-studied example is stabilization of polyacenaphthylene *(9)* by hydrogenation and cross-linking with sulfur[27].

Acenaphthylene *(8)*, a component of coal tar pitch, polymerizes thermally at temperatures above 200 °C to polyacenaphthylene *(9)*. Thermal degradation (Fig. 11) *via* the dimer

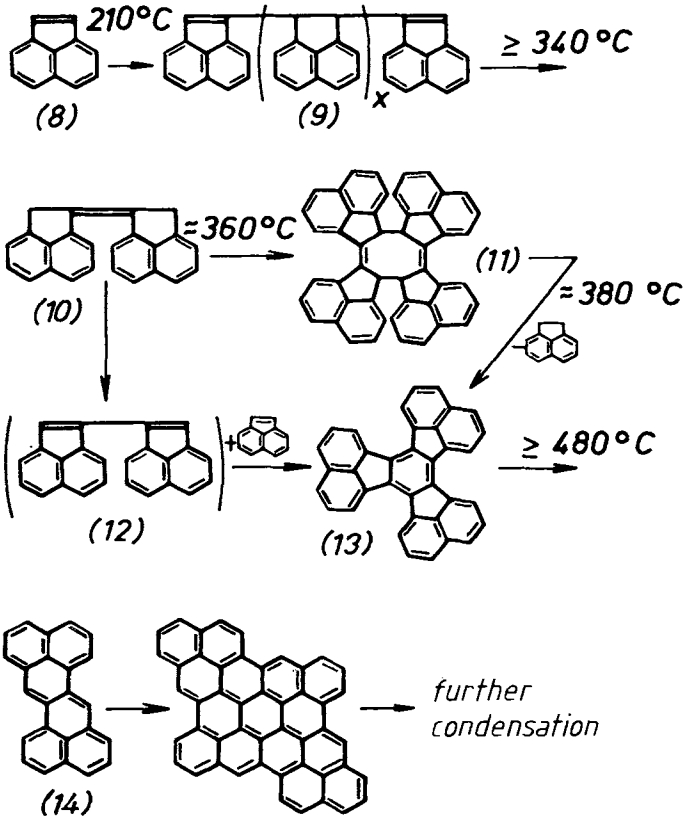


Fig. 11. Formation and degradation of polyacenaphthylene *(9) via* fluorocyclene *(11)*, decacyclene *(13)*, and zethrene *(14)* [27].

(10) leads to polyarenes such as the fluorocyclenes *(11)* and above all to the stable planar decacyclene *(13)*. Tar-like substances which act as a matrix for the formation of a mesophase are formed.

Addition of up to 10% of sulfur relative to the hydrogen content of the monomers leads to a dehydrogenation with formation of H_2S. This increases the carbon yield, but leaves the formation of the mesophase and hence the graphitizibility unaffected. Further addition of sulfur, however, leads to primary cross-linking by formation of polysulfide bonds, as seen from dehydrogenation and formation of H_2S at high temperatures. These residues do not melt, the carbon yield increases to 50%, and the product is a completely isotropic glass-like carbon.

The stabilization process used for the production of anisotropic polymeric carbon plays a key role in the manufacture of fibers from polyacrylonitrile (PAN). On the one hand, cyclization of the polymer with a continuous C/C chain to a ladder polymer takes place, and on the other hand a dehydrogenation to arenes is achieved. There are hundreds of literature references to the cyclization mechanism because of its connection with thermal yellowing of textile PAN fibers. "Black orlon" fiber, a preliminary stage in the production of carbon fibers from PAN, is subjected to mechanical stretching or at least mechanical maintenance of the textile stretching in addition to the oxidizing cyclization in order to keep the preferred orientation of the PAN macromolecules parallel with the fiber axis, also in the case of the ladder polymers which cannot be changed in their steric position thermally or mechanically.

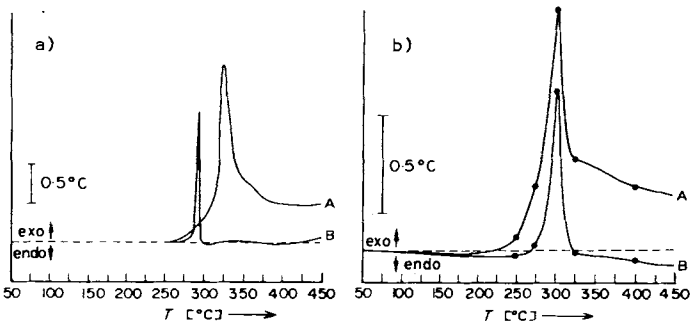


Fig. 12. Differential thermal analysis curves of commercial PAN fibers in air (A) and nitrogen (B) (heating rate 10 °C/min). a) Dry spun homopolymeric acrylonitrile (DRALON T); b) wet spun copolymeric acrylonitrile (DOLAN, 6% methyl acrylate).

First of all we studied the mechanism of the cyclization in an oxidizing atmosphere and the interpretation of the shrinkage during the stabilization treatment. A comparison of the results of differential thermal analysis (DTA) for homopolymeric acrylonitrile in Figure 12a shows an oxidation to precede the exothermic cyclization reaction and another one to follow. Moreover, the cyclization is slowed down by oxygen. This delay is eliminated in copolymeric acrylonitrile, but the sequence of reactions is the same as above[28].

A careful analytical study of the volatile products eliminated during cyclization[29] permits calculation of the stoichiometry and thus provides information about the overall reaction. Figure 13 shows that in the case of homopolymeric acrylonitrile dehydrogenations of the contiguous C/C chains

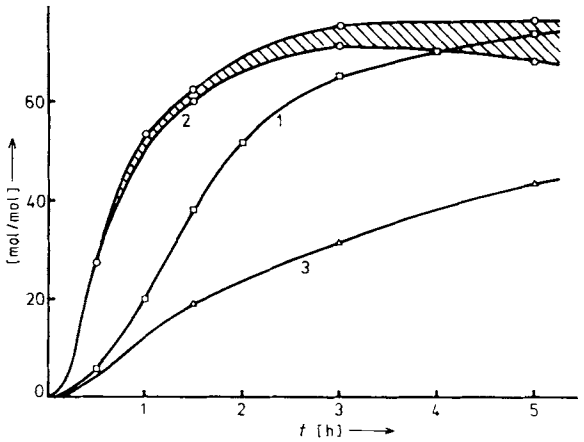


Fig. 13. Course of stabilization of homopolymeric acrylonitrile depending upon the oxidation temperature (t). 1, Cyclization (formation of heterocyclic compounds from nitrile groups); 2, dehydrogenation, based on the monomer units; 3, oxygen taken up by the ladder polymer per monomer unit [29].

(curve 1) precede the cyclization reaction (curve 2). Subsequent oxidation (curve 3) is undesirable, for it lowers the carbon yield and increases the number of defects.

A hypothetical mechanism describing shrinkage during stabilization could be derived from these analytic studies. Furthermore, the chemical effects of mechanical treatment undertaken to prevent cyclization shrinkage can be explained by these studies.

Contrary to the view often expressed in the literature that the stabilization shrinkage is merely an entropy effect, the analytical results mentioned above indicate that chemical effects must also play a part in shrinkage. Dehydrogenation of the carbon chain leads to conjugated double bonds and thus to planar molecular structures. If the tacticity of the chain changes, a kink appears on formation of the bonding angle of 120°; however, if the fiber is stretched during this dehydrogenation reaction, the chain rotates around the single bond at the location of the change in tacticity and no shortening occurs. The previously atactically oriented nitrile groups adopt the same orientation (as a consequence of the formation of the bonding angle of 120°). A molecular struc-

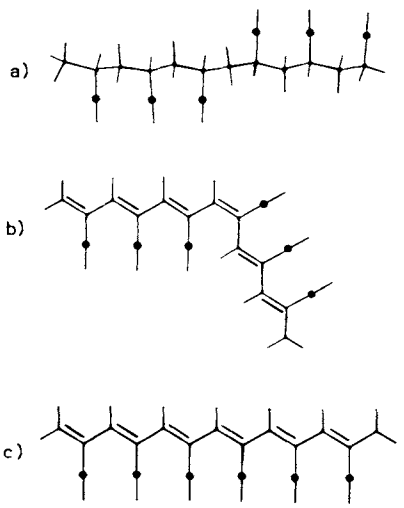


Fig. 14. Structural model a) of atactic polyacrylonitrile; b) of the bending of the molecule chain after the formation of a planar structure with conjugated double bonds; c) of the turning of the atactic lateral groups into a continuous *cis* configuration during stretching [30].

ture with continuous *cis*-configuration thus results, as shown in Figure 14. The subsequent cyclization which can take place only with isotactic sequences is facilitated by the stretching[30].

There has been no lack of attempts to accelerate the cyclization; the diffusion of oxygen through the ladder polymer layer determines the rate of oxidation. An increase in temperature above 250 °C is ruled out by the danger of overheating the fiber during the exothermal reaction and hence thermal decomposition prior to completion of stabilization. Lewis acids in combination with nitrobenzene as oxidizing agent proved to be the best catalysts; a mixture of nitrobenzene and *p*-nitrophenol accelerates stabilization similarly to Lewis acids. The fibers must be swollen in dimethylformamide (DMF) in order to effectively introduce the stabilization catalysts into the fiber. This swelling effect appears to promote the preferred orientation in the polymer in a similar way to mechanical methods, *e.g.* stretching[31]. The copolymer and dyeing additives always present in PAN fibers may also have a catalyzing influence (cf.[32]).

The general trend in the production of high quality carbon fibers seems to be directed less to the development of special polymers particularly suitable for a technically facile stabilization process than to the adaptation of the technical stabilization conditions to cheap polymer fibers on the market as mass produced textile articles.

A knowledge of the stabilization and degradation mechanism also permits continuous production of hollow fibers of polymeric carbon on a laboratory scale (Fig. 15)[33]. Technical and medical applications are expected for these fibers.

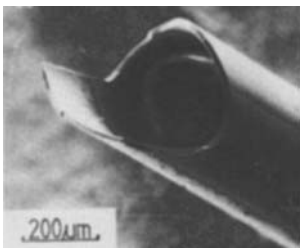


Fig. 15. Hollow fiber of polymeric carbon, produced continuously on a laboratory scale from wet spun hollow PAN fibers containing 6% of methyl acrylate [33].

5. Biocompatibility of Polymeric Carbon

The biocompatibility of smooth carbon surfaces with blood, muscle, and bone tissue has been known for many years. Isotropic polymeric carbon competes as solid material with pyrocarbon as coating material for prosthetic applications in human medicine. Pyrocarbon is deposited on substrates by chemical vapor deposition (CVD).

Figure 16[34] summarizes routine and experimental applications of polymeric carbon in human medicine. Particular mention should be made of the well-established use of glassy carbon in aorta valves.

Anisotropic polymeric carbon is unbeatable as a replacement of tendons and ligaments. The first experiments were carried out at Cardiff[35]. In animal experiments, *e.g.*, knee ligaments were removed and replaced by tows of carbon fibers (Fig. 17a)[36]. Three months later a new, functioning ligament tissue had been formed around the implanted carbon fibers (Fig. 17b). The new ligament including the implant has a greater strength than the original ligament. The elasticity can be increased by stranding the carbon fibers to form tapes. A histological section (Fig. 17c) shows that the new tissue around the carbon fibers contains only few giant cells; this means only slight scarring. The carbon fibers are not chemically decomposed. It appears that residues from mechanically degraded fibers are deposited in the lymphatic nodes.

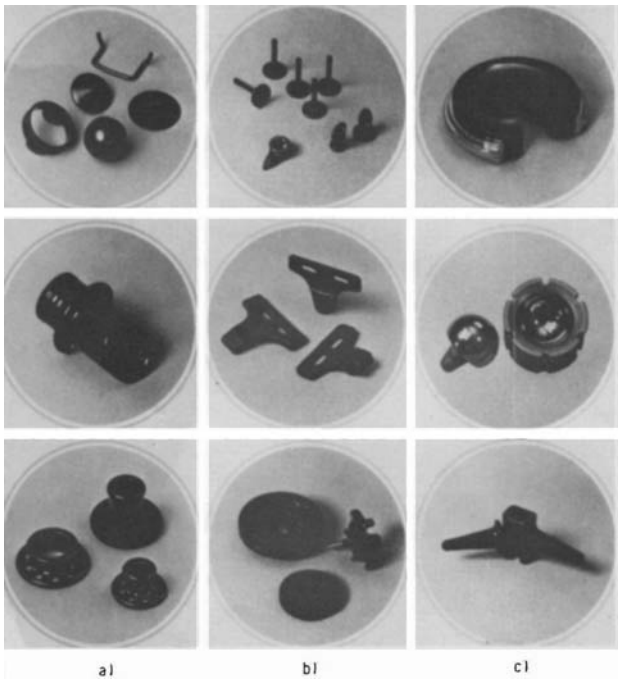


Fig. 16. Present applications of carbon in human medicine. a) Parts made of pyrocarbon/glassy carbon (from top to bottom): Heart valve components, left ventricular apex outlet, percutaneous leads. b) Parts made of pyrocarbon/glassy carbon (from top to bottom): otological prostheses, dental implants, blood pump components. c) Parts made of pyrocarbon (from top to bottom): replacement parts for knee, hip, and finger joints [34].

A recent publication in the Indian press states that such ligament replacing operations have been carried out successfully on about 50 racehorses[37].

Fibers of polymeric carbon can be woven like textile fibers, also with glass fibers to form a hybrid fabric or with organic high modulus fibers. Such fabrics are used mainly in industry, but experiments are being carried out to test their medical potential. Animal experiments performed at Ulm have concentrated on the replacement of abdominal walls by carbon fiber fabrics. A new abdominal wall was found to grow into the implant or around the fabric[38].

6. Chemical Adhesion of Carbon Fibers in a Polymer Matrix

The main and surely revolutionary application of polymeric carbon is its use as reinforcing fiber in composites. The preferred orientation of the carbon ribbons in the marginal zones of the fiber parallel with the surface is the reason

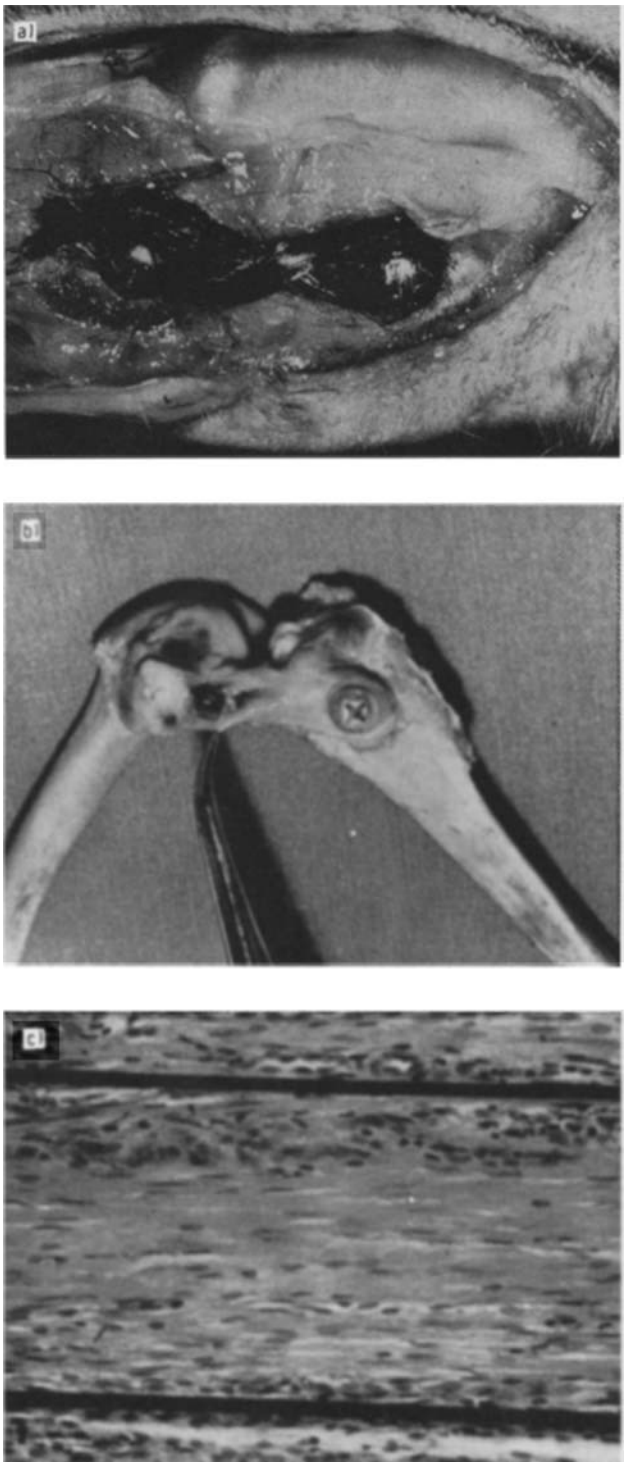


Fig. 17. a) Replacement of a knee ligament by carbon fibers in an animal experiment. b) Reformation of ligament around the implant three months later. c) Histological section through the tissue of the grown ligaments [36].

for the strength of the fiber, and also for chemical inertness of the surface and poor adhesion to the matrix. This precludes the desired transfer of stress between the two components of the composite, resulting in poor shear strength which in turn can cause failures by delamination.

Empirical work aimed at achieving mechanical linking by coating of the fibers with whiskers or by roughening of the fiber surfaces was unsuccessful. Only an oxidizing after-treatment of the fiber surface improves the adhesion behavior.

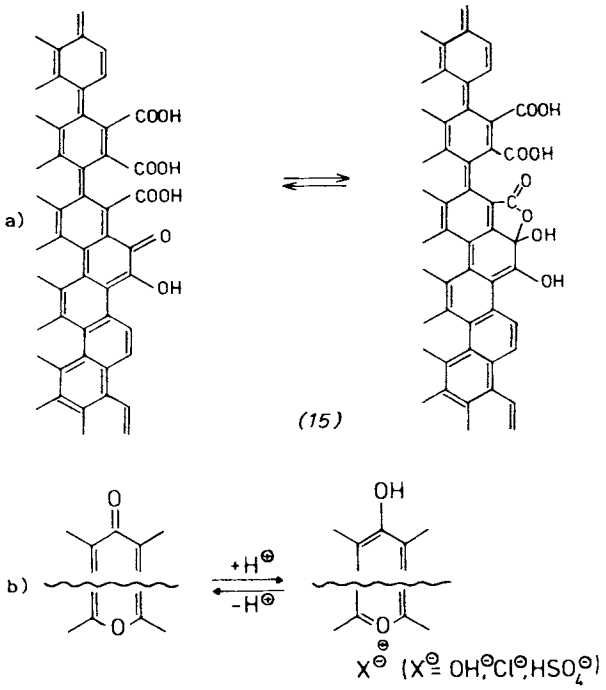


Fig. 18. Presumed structure of a) acidic and b) basic surface groups on carbon (activated carbon fibers) [39, 39a].

The surface groups on the fibers formed by anodic or by wet oxidation react with the matrix components; they can be of an acidic or a basic nature (Fig. 18)[39]. Wet oxidation in boiling nitric acid led to a controlled increase of acid groups; the reinforcing effect in composites with a phenolic resin matrix, measured by the utilization of the fiber strength in the composite, is directly proportional to the concentration of the acid surface groups. Ether groups and ester groups are formed between the phenolic resin matrix and the surface groups[40]. The adhesion aspects are perhaps even more important if epoxy resins are used as matrix. It was shown in an extensive study[41] that prolonged wet oxidation not only improves the adhesion after curing but the reactivity of the carbon fibers can already be measured by wetting experiments. The prepolymer without hardener shows poor wetting, while a diamine hardener wets very well. Therefore the hardener initiates wetting in a mixture of prepolymer and hardener, and acts as an adhesion promotor between the fibers and the prepolymer (Fig. 19).

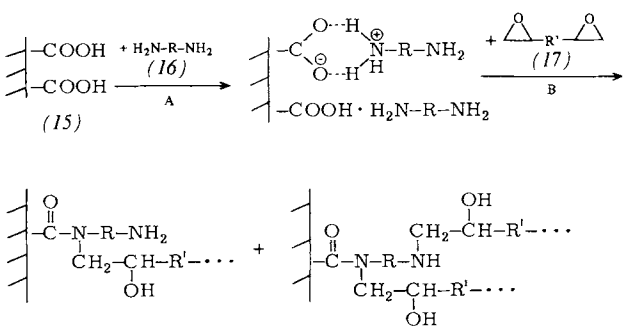


Fig. 19. Reaction steps for the adhesion of hardener *(16)* and prepolymer *(17)* to the surfaces of carbon fibers activated by wet oxidation with nitric acid [compare *(15)* in Fig. 18] [41]. Step A, linkage between fiber and hardener; step B: linkage between hardener and prepolymer at the fiber surface.

7. Applications of Carbon Fiber Reinforced Polymers and of All-Carbon Composites

Now that the adhesion problem between fibers and the polymer has been solved, reinforcement of conventional curable polymers by polymeric carbon fibers can be expected to become the commonest application, *e.g.* the reinforcement of epoxy, polyester, or phenolic resins, and ultimately perhaps the reinforcement of thermoplastic polymers too. The volume fraction and the geometrical arrangement of the carbon fibers will then determine the properties of the composite materials. As a rule, a two-dimensional reinforcement with up to 60 vol % of endless carbon fibers is used.

Expectedly, these materials are widely used in the aerospace industry. Today there is no supersonic aircraft containing less than 15% of such structural materials, and their utilization in other aircraft is already being tested[42].

The American automotive industry is presently considering the possibility of incorporating 50 to 100 kg carbon materials per car[43]. A large-scale technical application of polymeric carbon depends on the costs; the original costs of up to 1000 DM per kg carbon fibers were prohibitive. Today the prices are about 100 DM/kg. A further reduction of 50% seems likely in the near future. This will be of the same order of magnitude as the cost of high quality reinforcing glass fibers; the carbon fibers are superior, however, because of their much higher Young's modulus and their far lower density.

Finally, an application of polymeric carbon without organic polymers may be mentioned, *viz.* all-carbon composites. Such materials contain at least 50 vol% of carbon fibers in a matrix of pure carbon. The matrix may also consist of polymeric carbon formed by thermal degradation of, *e.g.*, a polyphenylene or a phenolic resin or a polyimide. We have also succeeded in producing a carbon matrix oriented parallel to the fiber starting from cheap meltable arene mixtures. They contribute to the mechanical properties of the composite in a similar way as the fibers (Fig. 20)[45].

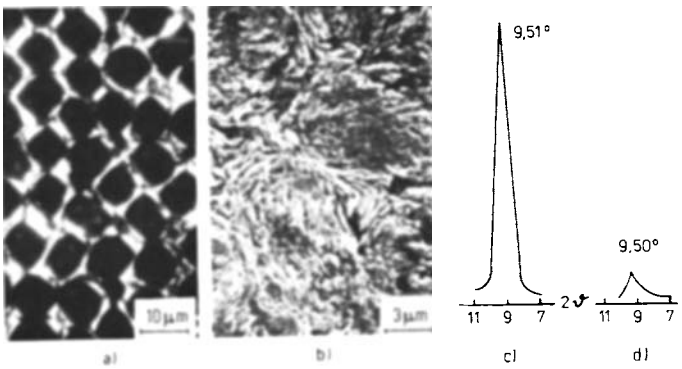


Fig. 20. Orientation of the carbon matrix in all-carbon composites: a) Cross-section, photographed with polarized light; b) cross-section scanning electron micrograph; c) X-ray diffraction, parallel and d) perpendicular to the fiber direction [45].

Carbon fiber reinforced composites are interesting also in medicine as bone plates. The healing of bone fractures can be facilitated by a direct fixing of the broken bone parts using bone plates. However, the metal plates usually employed can induce degeneration of the bone. The detrimental alteration or catabolism of the bone is caused by the difference in the Young's modulus of the bone and the plate, by which a stress gradient across the bone is built up. The disadvantages of metal plates can be avoided by use of carbon fiber reinforced composites. Figure 21 shows bone plates of carbon fiber reinforced epoxy resin, whose surfaces have been sputtered with carbon, and plates of all-carbon composites[44].

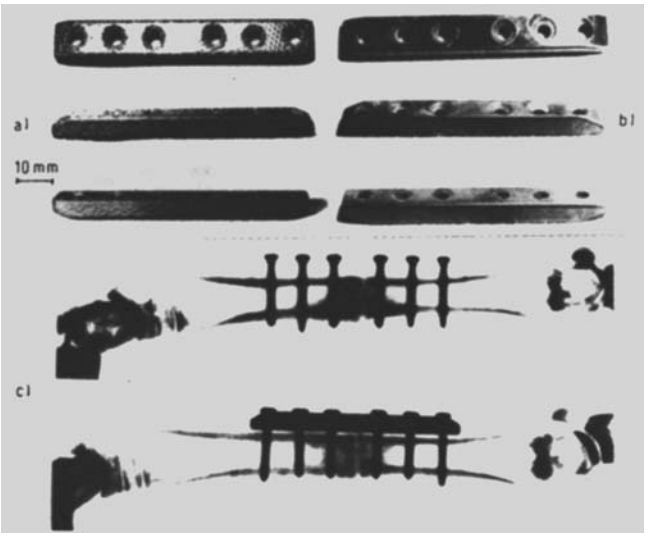


Fig. 21. a) Bone plates made of all-carbon composites; b) bone plates of carbon fiber reinforced epoxy resin with a carbon surface produced by sputtering; c) X-ray photograph of animal bones broken and fixed with bone plates after a healing time of eight weeks [44].

The plates have been tested in preliminary animal experiments and an improvement in the healing process over that with steel plates was found. This success justifies further work on this application.

All-carbon composites have also found technical application in the two-dimensional reinforcement of aircraft brakes, and in the three-dimensional reinforcement of ablation shields, mainly in rocketry. The greatest reinforcing effect in the fiber direction is naturally reached for unidirectionally reinforced composites [material strengths more than 1000 MN/m^2, high temperature strengths up to more than 2000 °C (Fig. 22)]; but three-dimensionally reinforced, *i.e.*,

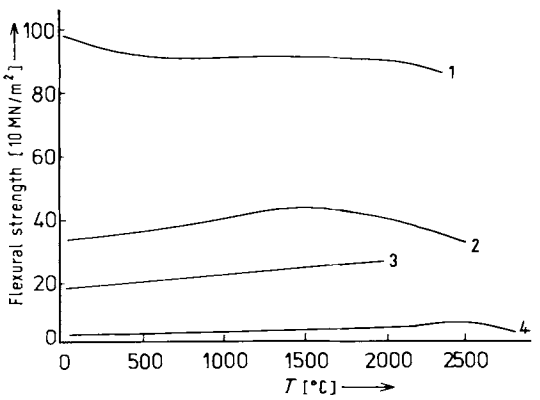


Fig. 22. Short-time flexural strengths at temperatures up to 2500 °C of: 1) uni-directionally and 2) three-dimensionally reinforced all-carbon composites compared with 3) pyrolitic graphite and 4) fine grained graphite ATJ [46].

practically isotropic, all-carbon composites achieve strengths of about 350 MN/m^2 in all directions up to more than 2000 °C. The strength of these composites exceeds not only that of conventional fine grained graphite and of glassy carbon but also that of light metals, ceramics, and glasses. A three-dimensionally reinforced all-carbon composite does not exhibit a real brittle fracture behavior at room temperature, but behaves like a pseudoplastic material. Stress maxima on initial loading are absorbed by microcracks within the macrostructure[46].

The new materials are not only suitable for modern high temperature applications in the aerospace industry. In the Federal Republic of Germany some research programs have been sponsored in order to develop hip joint replacements of all-carbon material. They are superior to the conventional steel replacements (which corrode and work loose) on account of their excellent biocompatibility, the possibility of cement-free implantation, and above all the controllability of the mechanical properties. It is possible with composites to effectively imitate the stress behavior of bone (Fig. 23)[44,46,47]. However, routine application to human medicine is still a long way off. The present medical experiments have been carried out mainly with dogs.

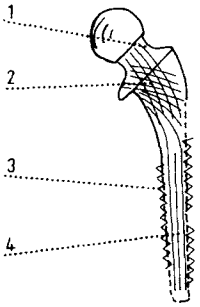


Fig. 23. Suggested approaches to imitation of the femur structure with all-carbon composites; 1-D, 2-D, 3-D stand for uni-, two-, and three-dimensional reinforcement [46].

The possibility of optimum tailoring of the polymeric carbon, depending on the application conditions, will ensure a promising future for these materials.

Received: September 14, 1979 [A 317 IE]
German version: Angew. Chem. *92*, 375 (1980)

[1] *H. Böder, E. Fitzer,* Naturwissenschaften *57*, 29 (1970).
[2] *O. Vohler, P. L. Reiser, R. Martina, D. Overhoff,* Angew. Chem. *82*, 401 (1970); Angew. Chem. Int. Ed. Engl. *9*, 414 (1970).
[3] *R. Bacon,* Chem. Phys. Carbon *9*, 1 (1973).
[4] *E. Fitzer, K. Müller, W. Schäfer,* Chem. Phys. Carbon *7*, 237 (1971).
[5] *E. Fitzer, W. Schäfer, S. Yamada,* Carbon *7*, 643 (1969).
[6] *E. Fitzer, J. Schlichtung,* Vortrag Chemiefasertagung Dornbirn (1979).
[7] *E. Fitzer, A. K. Fiedler, D. J. Müller,* Chem.-Ing.-Tech. *43*, 923 (1971).
[8] *E. Fitzer, A. K. Fiedler, D. J. Müller,* Chem.-Ing.-Tech. *43*, 1022 (1971).
[9] *R. J. Diefendorf, E. Fitzer, M. Heym,* Chem.-Ing.-Tech. *48*, 765 (1976).
[10] *E. Dönges, O. Vohler,* Chem.-Ing.-Tech. *42*, 1197 (1970).
[11] *W. Braun, E. Fitzer,* Carbon *16*, 81 (1978).
[12] *E. Fitzer, J. Kalka,* Carbon *10*, 173 (1972).
[13] *S. C. Bennett, D. J. Johnson,* Proc. Fifth London Int. Carbon and Graphite Conf. 1978, Vol. I, p. 377.
[14] *F. Rousseaux, D. Tschoubar,* Carbon *15*, 63 (1977).
[15] *G. M. Jenkins, K. Kawamura:* Polymeric Carbon. Cambridge University Press, London 1976.
[16] *W. Braun, E. Fitzer,* Carbon 72. Baden-Baden, June 1972, Paper 18.
[17] *E. Fitzer, W. Schäfer,* Carbon *8*, 353 (1970).
[18] *E. Fitzer, P. Laudenklos,* 12th Conf. on Carbon, Pittsburgh 1975. Preprints, Paper No. AI-1, p. 21.
[19] *E. Fitzer, J. Kalka,* High Temp. – High Pressures *3*, 53 (1971).
[20] *D. W. van Krevelen,* Chem.-Ing.-Tech. *47*, 793 (1975).
[21] *E. Fitzer, K. H. Geigl, W. Hüttner,* Proc. Fifth London Int. Carbon and Graphite Conf. 1978, Vol. I, p. 493.
[22] *A. Bürger, E. Fitzer, M. Heym, B. Terwiesch,* Polym. Chem. Polym. Preprints *14*, 430 (1973).
[23] *E. Fitzer, J. Kalka,* High Temp. – High Pressures *3*, 53 (1971).
[24] *A. K. Fiedler, E. Fitzer, F. Rozploch,* Carbon *11*, 426 (1973).
[25] *E. Fitzer, F. Grieser,* Proc. Fifth London Int. Carbon and Graphite Conf. 1978, Vol. I, p. 266.
[26] *J. L. White,* Aerospace Report (1974); No. TR 0074 (4250-40), 1.
[27] *E. Fitzer, K. Müller,* Ber. Dtsch. Keram. Ges. *48*, 269 (1971); *H. Marsh, E. Mochida et al.,* Fuel *52*, 243 (1973).
[28] *E. Fitzer, D. J. Müller,* Carbon *13*, 63 (1975).
[29] *A. K. Fiedler, E. Fitzer,* Prep. 1. Int. Kohlenstofftagung Carbon 72 Baden-Baden 1972, p. 299.
[30] *D. J. Müller,* Dissertation, Universität Karlsruhe 1973.
[31] *E. Fitzer, M. Heym,* Chem. Ind. (London) *1976*, 663.
[32] *W. Watt, W. Johnson,* Abstracts, Strength and Structure in Carbons and Graphite (1979), in press; cf. Nature *257*, 210 (1975).
[33] *K.-H. Geigl,* Dissertation, Universität Karlsruhe 1979.
[34] *E. Fitzer, W. Hüttner, D. Wolter,* Man-Made Text. India *21*, No. 8, p. 389 (1978).
[35] *D. H. R. Jenkins, J. W. Forster, B. McKibbin, Z. A. Ralis,* J. Bone Jt. Surg. *59/B*, No. 1, p. 53 (1977).
[36] *E. Fitzer, W. Hüttner, D. Wolter,* Abstracts 13. Bienn. Conf. of Carbon, Irvine 1977, p. 180.
[37] Hindu *16*, Sept. 15, 1979.
[38] *R. Neugeber, L. Claes, G. Helbing, D. Wolter,* 11. Int. Biomat. Symp. 5. Annual Meet. Soc. Biomat., Clemson S.C. (USA) 1979, Vol. 3, p. 135.
[39] *H. P. Boehm, E. Diehl, W. Heck,* Proc. 2nd Int. Conf. on Carbon and Graphite, London 1966, p. 369; *M. Voll, H. P. Boehm,* Carbon *9*, 473, 741 (1971).
[40] *E. Fitzer, K.-H. Geigl, L. M. Manocha,* Proc. Fifth London Int. Carbon and Graphite Conf. 1978, Vol. I, p. 405.
[41] *R. Weiss,* Diplomarbeit, Universität Karlsruhe 1978.
[42] *G. C. Deutsch,* 23. Nat. SAMPE Symp. and Exhib., Anaheim (Calif.) 1978, p. 34.
[43] News Release, Ford Motor Company, October 1977.
[44] *E. Fitzer, W. Hüttner, L. M. Manocha, D. Wolter,* Proc. Fifth London Int. Carbon and Graphite Conf. 1978, Vol. I, p. 454.
[45] *E. Fitzer,* Post Symp. of Int. Symp. of Densification Sintering of Oxides, Tokyo 1978.
[46] *J. Jortner,* Abstracts 13. Bienn. Conf. of Carbon, Irvine 1977, p. 443.
[47] *H. Brückmann,* Dissertation, Universität Karlsruhe 1979.
[48] *A. Shindo, Y. Nakanishi, J. Soma* in *J. Preston:* High Temperature Resistant Fibres From Organic Polymers. Interscience, New York 1969, p. 271.
[49] DBP 2021328 (1970), Azko N. V.
[50] DBP 2315144 (1973), Union Carbide.
[51] *K. Kawamura, G. M. Jenkins,* J. Mater. Sci. *5*, 262 (1970).
[52] *E. Fitzer, E. Fritz, M. Heym, W. Hüttner,* Kernforschungsanlage Jülich, JRW, I-B-16/78 (1978).
[53] *J. Simitzis,* Dissertation, Universität Karlsruhe 1975.
[54] *R. Moreton, W. Watt,* Carbon *12*, 543 (1974).

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Amorphous Silver Silicates, Storage Elements with Low Switching Field Strength[**]

By *Martin Jansen* and *Hans Herbert Käs*[*]

Like many other silver-rich oxides, the silver silicates $Ag_6Si_2O_7(I)$[1a], $Ag_6Si_2O_7(II)$[1b], and $Ag_{10}Si_4O_{19}$[1c] studied thus far also have characteristic silver substructures[2]. In spite of the valence shell of Ag^{1+} generally being regarded as closed, apparently there are attractive interactions between such particles which lead, in part, to shorter Ag···Ag distances than in metallic silver; as a rule, the silver arrays correspond to sections from the face-centered cubic structure of elemental silver. To check whether these particular structural features are associated also with particular physical properties, we have investigated the electrical behavior of—in the first instance amorphous (glassy)—silver(I) silicates.

After an electrical forming process, silver(I) silicate glasses exhibit a bistable switching behavior and are thus suitable for digital information storage. Besides having the well-known advantages of amorphous storage systems, silver silicate storage elements are distinguished by having a very low external switching field strength of the order of 10 V/mm. This property makes them of particular interest regarding their practical applications.

The switching behavior is produced by a forming process. The sample is subjected to a burst of alternating current ($f = 50$ Hz), whose amplitude is determined by the forming resistance R_F and whose duration t_F is controlled with an electronic time switch[3]. To illustrate the switching behavior a typical current-voltage curve is reproduced in Figure 1. After the forming process the material has a high resistance. On increasing the voltage, one initially observes ohmic and subsequently voltage-dependent resistance (VDR) behavior until, at Point A on the characteristic curve, a jump occurs into the low-resistance ("ON") part of the curve (Point B). If the voltage is now reduced, the material remains low-resistant. Reversible re-switching to Point D of the high-resistance ("OFF") state follows as soon as Point C in the low-resistance part of the curve is reached.

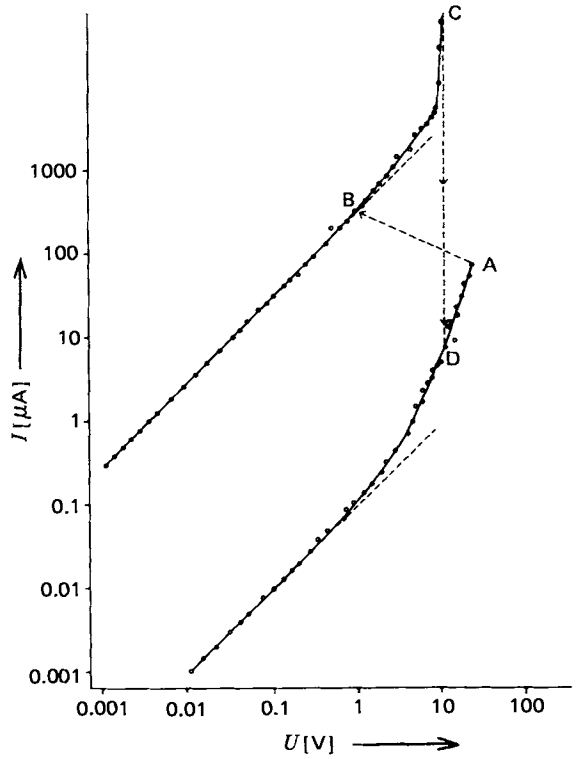


Fig. 1. Current-voltage curve of a formed silver silicate storage element (sample thickness 0.4 mm, Ag/Si = 4, $R_F = 1$ MΩ, $t_F = 0.5$ s).

To investigate the switching behavior the samples were switched with single square-wave pulses of duration t_R and amplitude U_s at a protective resistance R_s and the current and voltage logged on a storage oscilloscope. The switching characteristics depend on the composition of the glasses (Ag/Si ratio), the forming conditions (R_F, t_F) and the switching parameters (t_s, U_s, R_s). Samples with an Ag/Si ratio of 4 formed with $R_F = 1$ MΩ and $t_F = 0.5$ s proved to have the best switching characteristics.

The mechanism of the switching processes is still unclear in detail. Presumably "silver clusters" are of importance, as have been detected in crystalline silver(I) silicates by X-ray diffraction methods[1a,2], and which very likely are also present in the glasses investigated. Such silver-rich zones along with silver-deficient regions were also discussed in explaining the comparable switching behavior of silver metaphosphate glasses[4]. Since the storage state set at any given time remains the same without holding current, structural changes must take place during the switching process. Therefore a comparison of the structures of the material in the two switching states (ON/OFF) would appear to prove especially informative; a relevant series of investigations are presently under way.

Experimental

For preparation of the glasses very finely ground (agate ball mill) mixtures of Ag_2O (Merck) and SiO_2 (L-quartz, Rie-

[*] Priv.-Doz. Dr. M. Jansen
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)
Prof. Dr. H. H. Käs
FB Elektrotechnik der Fachhochschule
Schöfferstrasse 3, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0505-386 $ 02.50/0

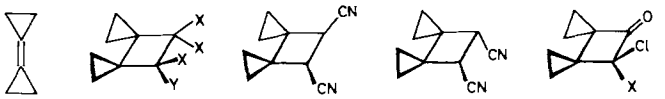
del-de Haen) were fused in corundum thimble crucibles under oxygen at ≥1800 bar and 600 °C (Ag/Si ratios 1, 2, 3, 4, 6, and 8). The cooled crucibles containing the solidified masses were cut into slices of *ca.* 1 mm thickness (diamond disk) and polished plane-parallel to a thickness of 0.4 mm.—During forming and switching the samples thus prepared are spring-mounted between hemispherical gold electrodes.

Received: October 26, 1979 [Z 443 IE]
German version: Angew. Chem. *92*, 386 (1980)

CAS Registry numbers:
Ag_2O, 20667-12-3; silver silicate, 42613-24-1

[1] a) *M. Jansen*, Acta Crystallogr. *B 33*, 3584 (1977); b) to be published; c) *M. Jansen, H.-L. Keller*, Angew. Chem. *91*, 500 (1979); Angew. Chem. Int. Ed. Engl. *18*, 464 (1979).
[2] *M. Jansen*, Habilitationsschrift, Universität Giessen 1978; J. Less Common Met., in press.
[3] *H. H. Käs, W. Platzer, J. Tille*, Glastech. Ber. *52*, 25 (1979).
[4] *H. H. Käs*, Naturwissenschaften *64*, 434 (1977); *H. H. Käs, H. Herwig*, Sci. Electr. *24*, 124 (1978).

proceeds in two steps *via* a 1,4-diradical or, in the second case, perhaps a 1,4-zwitterion[3], for reaction with fumarodinitrile analogously leads to a mixture of 78% *trans- (4)* and 22% *cis*-dispiro[2.0.2.2]octane-7,8-dicarbonitrile *(5)*. In this case the ring-closure of the intermediate is reversible; under the reaction conditions, gas-chromatographically purified *(4)* isomerizes back to a mixture of 78±3% *(4)* and 22±3% *(5)*. Chloro- and dichloroketene[4] also react in this way to give the [2+2]-cycloadducts *(6)* and *(7)*, respectively (see Table 1).



(1) *(2)* X=Cl, Y=H; *(3)* X=H, Y=CN; *(4)* *(5)* *(6)* X=H; *(7)* X=Cl

Table 1. Cycloadditions to bicyclopropylidene and characteristic data of the products [a].

Reaction conditions	Yield [%]	Product (m.p.) [°C]	^{1}H-NMR- (δ values and IR data) (ṽ [cm^{-1}])
4 d, 180 °C	18	*(2)* (−)	0.29—1.27 (m, 8H), 5.02 (s, 1H); 3080, 3000 (νC–H cyclopropyl.)
2 h, 180 °C	90	*(3)* (32)	0.18—0.82 (m, 8H), 3.25 (AB part of ABX, 1H), 2.40—2.58 (dd, 2H); 2230 (νC≡N)
2 h, 180 °C	56	78% *(4)* (88—90) 22% *(5)*	0.15—0.89 (m, 8H), 3.53 (s, 2H); 2240 (νC≡N) 0.17—0.89 (m, 8H), 3.40 (s, 2H); 2240 (νC≡N)
17 h, 34 °C, Et_2O	63	*(6)* (30)	0.58 (m, 2H), 0.73 (m, 2H), 0.92 (m, 1H), 1.00 (m, 1H), 1.38 (m, 3H); 1790 (νC=O)
17.5 h, 34 °C, Et_2O	59	*(7)* (74)	0.79 (m, 2H), 1.02 (m, 2H), 1.32 (m, 2H), 1.56 (m, 2H); 1800 (νC=O)
20 min, −78 °C, then 2 h, 25 °C CH_2Cl_2, hydrolysis	65	15% *(9b)* (120) 85% *(10b)* (87)	0.59 (m, 2H), 0.73 (m, 2H), 0.93 (m, 2H), 1.23 (m, 2H), 5.83 (br. s, 1H); 3220 (νN–H), 1740 (νC=O) 1.02 (m, 2H), 1.49 (m, 2H), 4.16 (m, 2H), 4.56 (m, 1H), 4.77 (m, 1H), 6.90 (br. s, 1H); 3210 (νN–H), 1695 (νC=O)
10 min, 0 °C, $CHCl_3$	83	*(12)* (228—230)	0.80 (m, 4H), 2.25 (dd, 2H), 3.18 (dd, 2H, ^3J=7.8, 8.6 Hz), 7.48 (m, 5H); 1760 (νC=O)
0.5 h, 60 °C C_6H_6	80	56% *(14)* (192) 22% *(15)* (140—145) 22% *(16)*	1.30 (m, 2H), 1.57 (m, 2H), 3.51 (m, 2H), 4.81 (m, 1H), 5.09 (m, 1H); 2260 (νC≡N), 1660 (νC=C) 0.85 (m, 4H), 1.20 (m, 4H); 2260 (νC≡N) 0.67 (m, 2H), 1.41 (m, 2H), 2.39 (m, 2H), 2.64 (m, 2H); 2260 (νC≡N)
12 d, 20 °C, CD_3CN	57	*(17* (92)	0.80 (m, 2H), 1.00 (m, 2H), 1.29 (m, 4H); 2250 (νC≡N), 1672 (νC=N)
2 d, 100 °C $(CH_3)_2CO$	60	*(19)* (99—102)	1.15 (m, 2H), 1.64 (m, 2H), 1.82 (s, 6H), 4.40 (m, 2H), 5.56 (m, 1H), 5.63 (m, 1H); 2250 (νC≡N), 1640 (νC=C)

[a] All the new compounds gave satisfactory elemental analyses and/or mass spectrometrically determined molecular weights.

Three Variants of the [2+2]-Cycloaddition of Bicyclopropylidene[**]

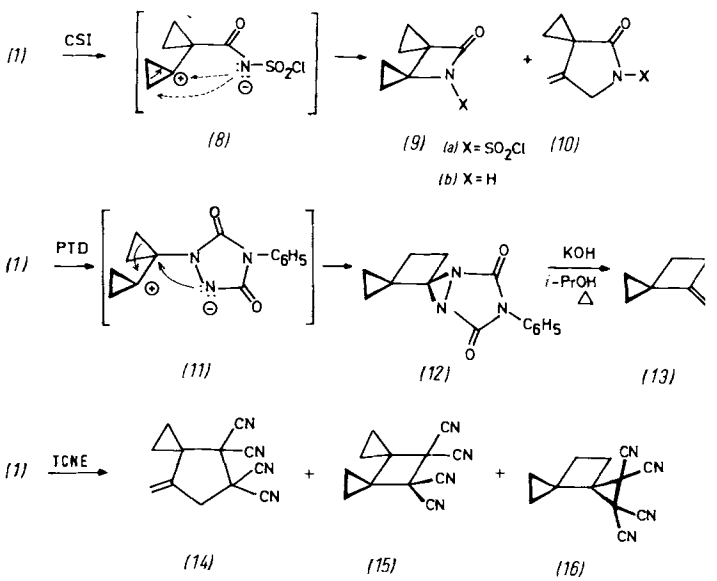
By *Walter Weber, Ihsan Erden,* and *Armin de Meijere*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Bicyclopropylidene *(1)*, whose [2+2]- and [2+4]-cycloadditions to conjugated dienes were reported in an earlier communication[1], has recently been shown to be relatively easily accessible[2] and can be used as a synthon for the preparation of compounds which contain the bicyclopropyl group as part of a dispiro system. We have now found that *(1)* does not react with electron-rich olefins, yet undergoes very smooth cycloadditions with a series of electron-deficient double-bond systems.

Thus, reaction of *(1)* with trichloroethylene affords the trichlorodispiro compound *(2)* (see Table 1), while reaction with acrylonitrile furnishes the cyano derivative *(3)* in more than 90% yield after 2 h at 180 °C. Presumably, the addition

Chlorosulfonyl isocyanate (CSI)[5], however, which is well-known for its [2+2]-cycloadditions to olefins, gives only small amounts (15%) of the β-lactam *(9a)* on reaction with



(1) CSI → *(8)* → *(9)* (a) X=SO_2Cl, (b) X=H + *(10)*

(1) PTD → *(11)* → *(12)* KOH, *i*-PrOH, Δ → *(13)*

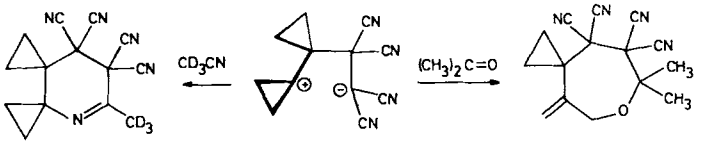
(1) TCNE → *(14)* + *(15)* + *(16)*

[*] Prof. Dr. A. de Meijere, Dipl.-Chem. W. Weber, Dr. I. Erden
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Hoechst AG.

(1) at −78 to +20 °C; the main product (85%) is the γ-lactam *(10a)* (see Table 1). This finding is best explained in terms of an intermediary 1,4-zwitterion *(8)*, which cyclizes predominantly with a concomitant cyclopropyl-to-allyl opening of its cationic end group. 4-Phenyl-1,2,4-triazoline-3,5-dione[6] (PTD) also reacts rapidly with *(1)* at 0 °C, surprisingly enough, however, in a mode completely different from that of CSI: the diaziridine derivative *(12)* was the sole product isolated (83%). In this case, the cyclization of the intermediate *(11)* apparently takes place only after or concomitantly with a cyclopropylmethyl—cyclobutyl ring enlargement. Alkaline hydrolysis of *(12)* does not give the expected diaziridine, but cleaves off the whole urazole moiety and forms the spiro[2.3]hexan-4-one *(13)*[7].

(1) reacts with tetracyanoethylene (TCNE) in benzene only in the absence of oxygen; nevertheless, with this reagent all three types of cycloaddition were realized, as demonstrated by the products *(14)* (56%), *(15)* (22%) and *(16)* (22%) isolated. The 1,4-zwitterion *(18)* apparently formed in this reaction can be trapped with CD_3CN to give *(17)*[8], which



(17) *(18)* *(19)*

contains a dispiro system with a six-membered ring and an unrearranged bicyclopropyl group; with acetone, on the other hand, the trapping product *(19)* containing a seven-membered ring was formed. *Noyori et al.*[9], however, maintain that formation of a 1,4-zwitterionic intermediate in the cycloaddition of TCNE to a methylenecyclopropane is unlikely, taking into account the very small solvent effect on the reaction rate.

Received: October 30, 1979 [Z 444 IE]
German version: Angew. Chem. *92*, 387 (1980)

CAS Registry numbers:
98-0; *(7)*, 105-53-3; *(8)*, 69564-05-2; *(9)*, 69564-06-3; *(10)*, 73481-58-0; 2-methoxyethanamine, 109-85-3; β-phenylethylamine, 64-04-0
(1), 27567-82-4; *(2)*, 73496-17-0; *(3)*, 73496-18-1; *(4)*, 73496-19-2; *(5)*, 73496-20-5; *(6)*, 73496-21-6; *(7)*, 73496-22-7; *(9a)*, 73496-23-8; *(10a)*, 73496-24-9; *(12)*, 73496-25-0; *(13)*, 20571-15-7; *(14)*, 73506-17-9; *(15)*, 73506-18-0; *(16)*, 73496-26-1; *(17)*, 73496-27-2; *(19)*, 73496-28-3; trichloroethylene, 79-01-6; acrylonitrile, 107-13-1; fumaronitrile, 764-42-1; chloroketene, 29804-89-5; dichloroketene, 4591-28-0; CSI, 1189-71-5; PDT, 4233-33-4; TCNE, 670-54-2; CD_3CN, 2206-26-9; acetone, 67-64-1

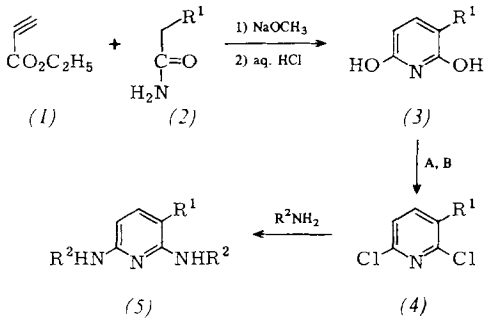
[1] *D. Kaufmann, A. de Meijere*, Angew. Chem. *85*, 151 (1973); Angew. Chem. Int. Ed. Engl. *12*, 159 (1973).
[2] a) *A. H. Schmidt, U. Schirmer, J.-M. Conia*, Chem. Ber. *109*, 2588 (1976); b) *W. Weber, A. de Meijere*, Synthesis, in press.
[3] The influence of different solvents on the steric course and rate of the reaction has not been investigated so far.
[4] Generated from dichloro- or trichloroacetyl chloride, respectively, and zinc according to the method of *D. A. Bak, W. T. Brady*, J. Org. Chem. *44*, 107 (1979).
[5] *R. Graf*, Angew. Chem. *80*, 179 (1968); Angew. Chem. Int. Ed. Engl. *7*, 172 (1968).
[6] *R. C. Cookson, S. S. H. Gilani, I. D. R. Stevens*, Tetrahedron Lett. *1962*, 615.
[7] *J. M. Denis, P. L. Perchec, J. M. Conia*, Tetrahedron *33*, 399 (1977).
[8] On the trapping of 1,4-zwitterions cf. *R. Schug, R. Huisgen*, J. Chem. Soc. Chem. Commun. *1975*, 60.
[9] *R. Noyori, H. Hayashi, M. Katô*, J. Am. Chem. Soc. *93*, 4949 (1971).

Aminopyridines

By *Werner Jünemann, Hans-Joachim Opgenorth*, and *Horst Scheuermann*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

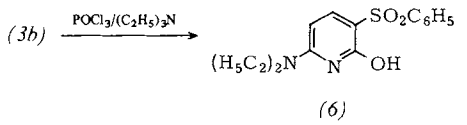
A versatile method for the synthesis of substituted pyridines consists in the condensation of 1,3-dicarbonyl compounds with acetic acid amides whose methylene group is additionally activated by an electron-withdrawing substituent[1]. The pyridines prepared in this way contain, besides this substituent in the 3-position, also one or more hydroxy groups in the 2-, 4- and/or 6-position, usually together with further substituents in the 4- or 5-position. We report here on the preparation of 4,5-unsubstituted pyridinediols *(3)* from propiolic ester *(1)*, and on the synthesis of the novel 3-phenylsulfonylpyridinediols *(3b)* and -triols *(8)* and their transformation into the corresponding chloro- and aminopyridines.



(1) *(2)* *(3)* *(5)* *(4)*

(a), R^1 = CN; *(b)*, R^1 = $SO_2C_6H_5$

On reaction of ethyl propiolate *(1)* with cyano- *(2a)* or phenylsulfonylacetamide *(2b)* in methanolic sodium methoxide solution at 60 °C one obtains 3-substituted 2,6-pyridinediols *(3)*. The hydroxy groups can be replaced by chlorine by reaction with $POCl_3$ at 140 °C in the presence of tertiary amines. Triethylamine proved to be a particularly suitable base in the case of *(3a)*→*(4a)* (Method A), while *(3b)* could be converted only with *s*-collidine into the dichloro compound *(4b)* (Method B). Reaction of *(3b)* with $POCl_3$/triethylamine gives the aminopyridinol *(6)*.



(6)

Replacement of the chlorine atoms in *(4)* to give the diaminopyridine *(5)* was achieved in the presence of excess amine above 100 °C. At lower temperatures one obtains only a mixture of isomeric monoamino compounds, whose isolation was not attempted.

Reaction of diethyl malonate *(7)* with phenylsulfonylacetamide *(2b)* analogously affords the triamino compound *(10)* *via* the pyridinetriol *(8)* and the trichloro derivative *(9)* (Method B). The pyridines so prepared are listed in Tables 1 and 2.

[*] Dr. W. Jünemann, Dr. H.-J. Opgenorth, Dr. H. Scheuermann
BASF AG, Farbenlaboratorium WF
D-6700 Ludwigshafen (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0505-388 $ 02.50/0*

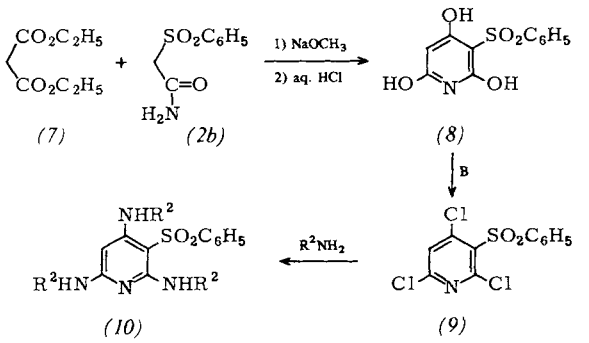


Table 1. Properties of the synthesized pyridines.

Cpd. [a]	R^1	R^2	Yield [%]	M.p. [°C]	Recryst. from
(3a)	CN		79	>200 dec.	Glycol/
(3b)	$SO_2C_6H_5$		48	>200 dec.	EtOH
(4a) [b]	CN		76	124—126	*c*-C_6H_{12}
(4b) [c]	$SO_2C_6H_5$		51	149—151	*c*-C_6H_{12}
(5a)	CN	$(CH_2)_2OCH_3$	80	102	*i*-BuOH
(5b)	$SO_2C_6H_5$	$(CH_2)_2C_6H_5$	81	118	*i*-BuOH
(6) [b]			98	238—243	BuOH
(8)			36	>256 dec.	EtOH/H_2O
(9) [c]			60	91	*c*-C_6H_{12}
(10)		$(CH_2)_2C_6H_5$	66	128	*i*BuOH

[a] All compounds gave correct elemental analyses. [b] Prepared according to Method A. [c] Prepared by Method B.

Table 2. ^{1}H-NMR [a] and IR data [b] of the synthesized pyridines.

(3a): ([D_6]-DMSO) 5.7 (d, 1H, H_β), 7.8 (d, 1H, H_γ), 10.5 (s, 2H, OH); 2250 (CN)

(3b): ([D_6]-DMSO) 5.85 (d, 1H, H_β), 7.5—8.2 (m, 5H, C_6H_5), 8.2 (d, 1H, H_γ), 12.5 (s, 2H, OH); 2420 (OH), 1300, 1160 (SO_2)

(4a): ($CDCl_3$) 7.4 (d, 1H, H_β), 7.95 (d, 1H, H_γ); 2260 (CN)

(4b): ($CDCl_3$) 7.5 (d, 1H, H_β), 7.2—8.2 (m, 5H, C_6H_5), 8.55 (d, 1H, H_γ); 1325, 1140 (SO_2)

(5a): ($CDCl_3$) 3.4 (s, 6H, CH_3), 3.1—3.9 (m, 8H, CH_2), 5.35 (br. s, 2H, NH), 5.65 (d, 1H, H_β), 7.25 (d, 1H, H_γ); 3350 (NH), 2180 (CN)

(5b): ($CDCl_3$) 2.85 (m=2 tr, 4H, CH_2), 3.6 (m, 4H, CH_2), 4.9 (tr, 1H, NH), 5.6 (d, 1H, H_β), 6.8 (tr, 1H, NH), 6.9—7.8 (m, 15H, C_6H_5), 7.6 (d, 1H, H_γ); 3400 (NH), 1130 (SO_2)

(6): ([D_6]-DMSO) 1.1 (tr, 6H, CH_3), 3.45 (q, 4H, CH_2), 5.85 (d, 1H, H_β), 7.3–8.1 (m, 5H, C_6H_5), 7.85 (d, 1H, H_γ), 11 (br. s, 1H, OH); 1270, 1130 (SO_2)

(8): ([D_6]-DMSO) 5.25 (s, 1H, H_β), 7.2–8.2 (m, 5H, C_6H_5), 11.5 (s, 3H, OH); 2350 (OH), 1305 (SO_2)

(9): ($CDCl_3$) 7.4 (s, 1H, H_β), 7.2–8.2 (m, 5H, C_6H_5); 1350, 1170 (SO_2)

(10): ($CDCl_3$) 2.6—3.9 (m, 12H, CH_2), 4.5 (tr, 1H, NH), 4.9 (s, 1H, H_β), 6.9—7.6 (m, 22H, C_6H_5, NH); 3380 (NH), 1350, 1130 (SO_2)

[a] TMS internal, δ values. [b] In KBr, $\tilde{\nu}$ in cm^{-1}.

Procedure

(3): A suspension of *(2)* (1 mol) in CH_3OH (190 ml) is treated, firstly with a solution of $NaOCH_3$ (54 g, 1 mol) in CH_3OH (160 ml) and then dropwise with 84 g (1 mol) of *(1)*. After heating under reflux for 1 h [in the case of *(3b)*] or 3 h [in the case of *(3a)*], the mixture is cooled, filtered, and the residue dissolved in warm water. The precipitate of *(3)* obtained on acidification with HCl is filtered off, washed with water, and dried.

(4a), Method A: A mixture of *(3a)* (136 g, 1 mol) with $POCl_3$ (160 ml) is treated dropwise below 95 °C with 227 ml of triethylamine. After 10 hour's stirring at 140 °C the mixture is poured into ice-water; the precipitate is filtered off and dried. The crude product (150 g; Cl: 38.8%) is purified by extraction with cyclohexane in a Soxhlet apparatus; yield 132 g (76%), m.p. 124—126 °C (119—121 °C[2]).

(4b), Method B: A suspension of *(3b)* (251 g, 1 mol) in $POCl_3$ (400 ml) is treated dropwise with 50 ml of *s*-collidine and the mixture stirred for 2 h at 120 °C and then for 5 h at 150 °C. After cooling, the mixture is poured into ice-water; the precipitate is washed with water, dried in air, and recrystallized from isobutyl alcohol; yield 147 g (51%), m.p. 149—151 °C.

(5b): (4b) (28.8 g, 0.1 mol) is transferred portionwise to 72.6 g (0.6 mol) of β-phenylethylamine at 110–120 °C. After 4.5 hours' stirring at 145 °C the mixture is treated with 42 ml of dimethylformamide with subsequent cooling. The resulting solution is added dropwise to a mixture of 33 ml conc. HCl and 830 ml H_2O, and the crystals which precipitate are filtered off under suction and washed with H_2O, dried, and recrystallized from isobutyl alcohol; yield 37 g (81%), m.p. 118 °C.

(8): A mixture of a 30% solution of $NaOCH_3$ in CH_3OH (180 g, 1 mol), *(7)* (80 g, 0.5 mol), ethanol (800 ml) and *(2b)* (99.5 g, 0.5 mol) is heated in an autoclave at 110—120 °C for 10 h. The crystals are filtered off, dissolved in hot water, precipitated with conc. HCl, filtered off, washed with water, and dried; yield 95 g (36%), m.p. 256 °C (dec.).

Received: January 3, 1980 [Z 445 IE]
German version: Angew. Chem. *92*, 390 (1980)

CAS Registry numbers:
(1), 623-47-2; *(2a)*, 107-91-5; *(2b)*, 35008-50-5; *(3a)*, 35441-10-2; *(3b)*, 69563-94-6; *(4a)*, 40381-90-6; *(4b)*, 69563-96-8; *(5a)*, 56112-94-8; *(5b)*, 73481-57-9; *(6)*, 69563-98-0; *(7)*, 105-53-3; *(8)*, 69564-05-2; *(9)*, 69564-06-3; *(10)*, 73481-58-0; 2-methoxyethanamine, 109-85-3; β-phenylethylamine, 64-04-0

[1] a) *E. Klingsberg* in *A. Weissberger:* The Chemistry of Heterocyclic Compounds. Vol. 14, Part 1. Interscience, New York 1960, p. 355; b) *R. A. Abramovitch* in *A. Weissberger, E. C. Taylor:* The Chemistry of Heterocyclic Compounds. Vol. 14, Supplement Part 1. Wiley, New York 1974, p. 257; c) special instance: *H. N. Al-Jallo, J. A. Al-Biaty, F. N. Al-Azawi,* J. Heterocycl. Chem. *14*, 1347 (1977).

[2] *G. Lamm,* DOS 2307444 (1974), BASF AG.

Cyclophanes as Diene Components in Diels-Alder Reactions[1]

By *Aboul Fetouh Murad, Jürgen Kleinschroth,* and *Henning Hopf*[*]

Dedicated to Professor Virgil Boekelheide on the occasion of his 60th birthday

Non-annelated arenes normally do not undergo cycloaddition reactions; for example, they do not participate as diene components in Diels-Alder reactions. To overcome this lack of reactivity, which reflects the "aromatic character"[2] of these hydrocarbons, the overall reaction must be activated. This may be accomplished, from the side of the dienophile by using a particularly reactive reagent at elevated temperatures and/or Lewis acid catalysis[3], as well as from the diene side by the incorporation of bridging structural elements in the arenes[3,4].

In the present communication, the first comparative study on the chemical behavior of [2_n]cyclophanes, it is shown that the tendency of benzenoid arenes to cycloadd can be enhanced to such an extent by bridging that it begins to equal

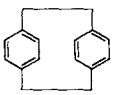
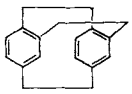
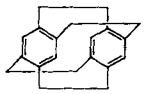
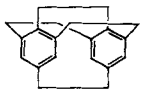
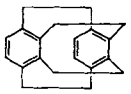
[*] Prof. Dr. H. Hopf, Dipl.-Chem. J. Kleinschroth, A. F. Murad, M. Sc., Institut für Organische Chemie der Universität Am Hubland, D-8700 Würzburg (Germany)

Present address: Institut für Organische Chemie der Technischen Universität, Schleinitzstrasse, D-3300 Braunschweig (Germany)

that of polyolefins: formally such molecules behave like cyclohexatriene derivatives.

In order to determine their diene activity the phanes *(1)*—*(5)* were allowed to react in benzene (internal standard) with dienophiles *(6)*—*(11)* which differ considerably in their reactivity (Table 1).

Table 1. Diels-Alder additions [5] with multiply bridged cyclophanes in benzene. NR: no reaction.

Dienophile \ Diene	 *(1)*	 *(2)*	 *(3)*	 *(4)*	 *(5)*
4-Phenyl-1,2,4-triazolin-3,5-dione *(6)*	20 °C, 138 h, 99% (1:2 adduct)	20 °C, 3 h, 79% (1:1 adduct); 20 °C, 24 h, 65% (1:2 adduct)	20 °C, 3 min, 100%	20 °C, 24 h, NR	20 °C, 24 h, NR
Tetracyanoethylene *(7)*	100 °C, 15 h, π-complex; 165 °C (in toluene), 13 h, NR	20 °C, 20 h, 59% (1:1 adduct) + 26% π-complex		20 °C, 20 h, π-complex	100 °C, 15 h, π-complex
Maleic anhydride *(8)*	180 °C (in toluene), 37 h, NR	100 °C, 10 h, 53% (1:1 adduct)		100 °C, 16 h, NR	100 °C, 17 h, NR
Dicyanoacetylene *(9)*	120 °C, 32% (1:1-) + 39% (1:2 adduct); 170 °C, 72% (1:2 adduct) [6]	20 °C, 14 d, 78% (1:1 adduct); 81 °C, 24 h, 30% (1:2 adduct)			
Dimethyl acetylenedicarboxylate *(10)*	NR at elevated temp. [7]	170 °C, 1 h, 61% (1:1 adduct) [7]			170 °C, 1 h, NR
Dimethyl maleate *(11)*	165 °C, 13 h, NR	100 °C, 10 h, NR			

As can be seen from the reaction of phanes *(1)*, *(2)* and *(3)* with dienophile *(6)*, the additivity is directly proportional to the degree of bridging, providing the phane contains at least one pair of *para*-hydrogen atoms. That the isomers *(4)* and *(5)*, which presumably hardly differ from *(3)* in their strain energy, do not cycloadd under comparable conditions is understandable if one remembers that the dienophile must attack the phanes from the "outside" and the substituents on the carbon atoms of the benzene rings are reoriented inwardly during the change from sp^2 to sp^3 hybridization. As long as the substituents are hydrogen atoms—as in *(1)* to *(3)*—there is ample room in the center of the molecule. In the case of *(4)* or *(5)* (and probably also in the case of still more highly bridged phanes), however, the bulky methylene groups of the bridges would not only have to be moved inwardly but also be strongly compressed towards each other. Evidently both molecules cannot fulfil these requirements.

With dienophiles less reactive than 4-*N*-phenyl-1,2,4-triazoline-3,5-dione *(6)* hydrocarbons *(1)*—*(5)* (Table 1) behave similarly; the cyclophane *(2)* forms the 1:1 adduct[7] even with dimethyl acetylenedicarboxylate *(10)* (which is *ca.* 10^6 times less reactive than *(6)*[8]). The limiting reactivity is reached with dimethyl maleate *(11)* (which is *ca.* 70 times less reactive than *(10)*[9]). With tetracyanoethylene *(7)*, only *(2)* could be converted into a (thermolabile) adduct, in all other cases π-complexes are formed, which decompose to the educts on heating.

That the high diene reactivity of *(1)*—*(3)* is not due to the activating effect of the alkyl substituents is shown by control experiments with the respective "halves" of these molecules: neither *p*-xylene, 1,2,4-trimethylbenzene nor durene nor any other polymethylated benzene reacts with *(6)* within 52 d at room temperature.

Received: July 2, 1979 [Z 446 IE]
supplemented: October 31, 1979
German version: Angew. Chem. 92, 388 (1980)

CAS Registry numbers:
(1), 1633-22-3; *(2)*, 58002-98-5; *(3)*, 54100-59-3; *(4)*, 61477-04-1; *(5)*, 69631-55-6; *(6)*, 4233-33-4; *(7)*, 670-54-2; *(8)*, 108-31-6; *(9)*, 1071-98-3; *(10)*, 762-42-5; *(11)*, 624-48-6

[1] Cyclophanes, Part 11. This work was supported by the Deutsche Forschungsgemeinschaft (Project Ho 534/16), the Fonds der Chemischen Industrie, and the van't Hoff Fonds.—Part 10: *J. Kleinschroth, H. Hopf*, Angew. Chem. *91*, 336 (1979); Angew. Chem. Int. Ed. Engl. *18*, 329 (1979).

[2] *G. Maier*, Chemie Unserer Zeit 9, 131 (1975).

[3] List of references in *S. Seltzer*, Adv. Alicycl. Chem. *2*, 1 (1968); *J. Sauer*, Angew. Chem. *78*, 233 (1966); Angew. Chem. Int. Ed. Engl. *5*, 221 (1966).

[4] *K.-L. Noble, H. Hopf, M. Jones, Jr., S. L. Kammula*, Angew. Chem. *90*, 629 (1978); Angew. Chem. Int. Ed. Engl. *17*, 602 (1978).

[5] All the new compounds gave correct elemental analyses and characteristic spectra.

[6] *E. Ciganek*, Tetrahedron Lett. *1967*, 3321.

[7] *D. J. Cram, E. A. Truesdale*, J. Am. Chem. Soc. *95*, 5825 (1973).

[8] *J. Sauer, B. Schröder*, Chem. Ber. *100*, 678 (1967); *M. E. Burrage, R. C. Cookson, S. S. Gupte, I. D. R. Stevens*, J. Chem. Soc. Perkin Trans. II *1975*, 1325.

[9] *J. Sauer, H. Wiest, A. Mielert*, Chem. Ber. *97*, 3183 (1964).

"Living Polymers" on Polymerization with Extremely Productive Ziegler Catalysts

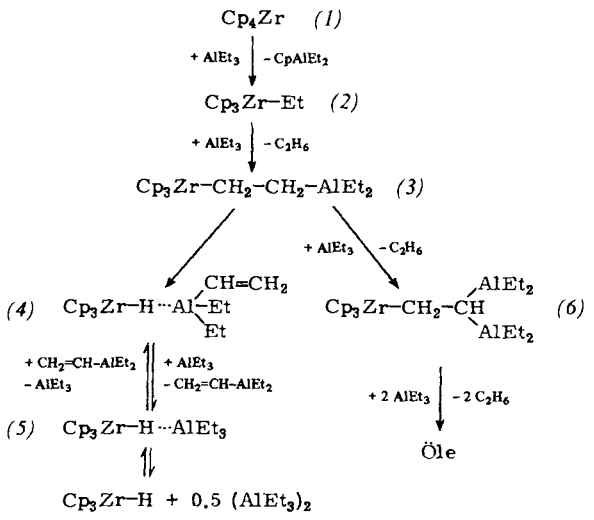
By *Hansjörg Sinn, Walter Kaminsky, Hans-Jürgen Vollmer,* and *Rüdiger Woldt*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The term "living polymers" was first applied by *Bier*[1] to the polymerization of α-olefins with Ziegler catalysts: He found that the polymerization can be interrupted for several hours after removal or consumption of monomer without diminishing the activity of the catalyst on renewed addition of monomer.

Such persistent activity is only possible if inactivation of the catalyst by side reactions involving hydrogen transfer is suppressed. The side reactions are therefore of special interest in connection with Ziegler catalysis[2]. On attempting to synthesize (see Experimental) the compound *(3)*, presumably formed as intermediate in the ethylene polymerization, we obtained a crystalline substance, which according to an X-ray structure analysis[3] was the zirconium hydride complex *(5)* (Fig. 1). The complex *(5)* can also be prepared directly from tris(cyclopentadienyl)zirconium and triethylaluminum.

[*] Prof. Dr. H. Sinn, Prof. Dr. W. Kaminsky [+], Dr. H.-J. Vollmer, Dipl.-Chem. R. Woldt
Institut für Anorganische und Angewandte Chemie der Universität, Abteilung für Angewandte Chemie
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
[+] Author to whom correspondence should be addressed.



Both halogen-free bis(cyclopentadienyl)zirconium compounds as well as the tris(cyclopentadienyl)zirconium compound *(5)* are, together with organoaluminum compounds, extremely long-lived catalysts for the polymerization of ethylene[4]. Longer-chain α-olefins can inhibit the ethylene polymerization—as distinguished from analogous titanium systems, which, *e.g.*, enable smooth ethylene-propene copolymerizations[5].

The polymerization activity is particularly enhanced by addition of water. We have therefore synthesized from trialkylaluminum and water the alkyl aluminoxanes, presumably formed in various degrees of oligomerization, and used them as organoaluminum components. The productivity increases with the cryoscopically determined degrees of oligomerization of 10 to 16 (checked in the titanium system with methyl aluminoxane *(7)*[6], see Table 1).

$$n\,Al(CH_3)_3 + n\,H_2O \rightarrow \text{-}[Al(CH_3)\text{—}O]_n\text{-} + 2n\,CH_4$$
(7)

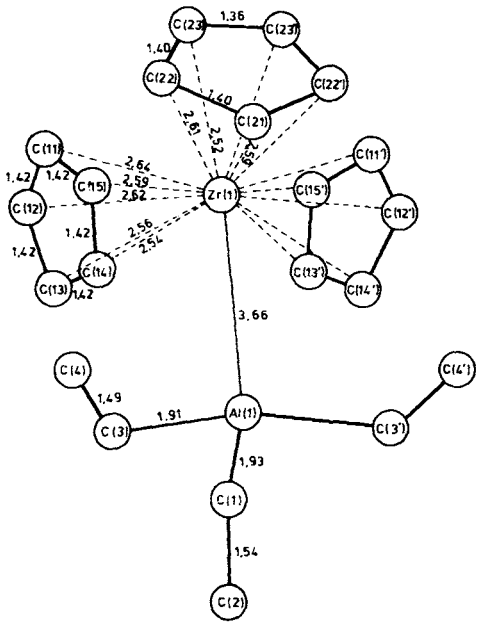


Fig. 1. Crystal structure of the zirconium-aluminum complex *(5)*. Distances in Å.

Table 1. Polymerization of ethylene with 1.34×10^4 mol/l bis(cyclopentadienyl)-dimethyltitanium(IV) and methylaluminoxane *(7)* of various degrees of condensation in 300 ml toluene at 20 °C.

Polyethylene yield [g]	$\bar{M}_n$	*(7)*, *n*	*t* [h]
2	—	2	20
51	360000	5	2
62.1	120000	>10	2

With the system bis(cyclopentadienyl)dimethylzirconium and methyl aluminoxane *(7)*, productivities (g polyethylene per g Zr) of over 10^8 were found. At concentrations of *(7)* between 1.5×10^{-2} and 3×10^{-3} mol Al/l and $Cp_2Zr(CH_3)_2$ concentrations $< 10^{-6}$ mol/l the reaction is sufficiently slow that diffusion no longer plays a decisive role and the reaction rate depends linearly on the zirconium concentration. In this concentration range productivities (g polyethylene per g Zr and 2 h) of around 10^7 were found (Table 2). The changeover time (interval between two insertion steps) is consequently smaller than 0.3 ms and thus comparable to the changover time of the fastest enzymes[7].

The molecular weights, which can be relatively easily varied by choice of temperature, are 10^6 to 10^3 at 0—100 °C[4]. Even under the assumption that each zirconium atom is part of an active center it follows that at least 10000 polymer molecules are formed at productivities of 10^8.

Table 2. Polymerization of ethylene with bis(cyclopentadienyl)dimethylzirconium and methylaluminooxane *(7)* ($n \approx 12$) in 330 ml toluene; ethylene pressure 8 bar, 1 l autoclave.

Polyethylene yield [g]	Activity g PE / g Zr·2 h	$\bar{M}_n$	$Cp_2Zr(CH_3)_2$ [mol/l]	*(7)* [mol Al-units/l]	*t* [h]	*T* [°C]
4.2	$1.4 \cdot 10^6$	173000	10^{-7}	$6.76 \cdot 10^{-3}$	2	60
0.9	$3.0 \cdot 10^6$	111000	10^{-8}	$6.61 \cdot 10^{-3}$	2	70
2.7	$8.9 \cdot 10^6$	177000	10^{-8}	$1.58 \cdot 10^{-2}$	2	70
13.3	$4.4 \cdot 10^6$	142500	10^{-7}	$9.25 \cdot 10^{-3}$	2	70
17.7	$11.6 \cdot 10^6$	142600	10^{-7}	$1.48 \cdot 10^{-2}$	1	70
15.4		216000	$2.2 \cdot 10^{-9}$	$1.45 \cdot 10^{-2}$	26	70
5			?	$1.45 \cdot 10^{-2}$	16	70 [c]
0.56	*ca.* $10 \cdot 10^6$	216000	$2.2 \cdot 10^{-9}$	$1.45 \cdot 10^{-2}$	2	70 [d]
19.0	$12.5 \cdot 10^6$ [a]	166000	10^{-7}	$1.53 \cdot 10^{-2}$ [b]	1	70
18.8	$14.9 \cdot 10^6$ [a]	149000	10^{-7}	$1.53 \cdot 10^{-2}$ [b]	0.83	70
0.4			?	$1.53 \cdot 10^{-2}$ [b]	20	70 [c]

[a] Extrapolated value. [b] $n \approx 14$. [c] Blank. [d] Corrected with blank.

If ethylene is again added to a system interrupted by withdrawal of monomer and in which the catalyst, though homogeneous in itself has been made heterogeneous by precipitated polyethylene, the polymerization resumes at a rate proportionate with the zirconium concentration and the polyethylene granules begin to swell.

Remarkably, a relatively large excess of organoaluminum component *(7)* is necessary. Preliminary kinetic investigations show that the reaction rate depends linearly on the zirconium concentration and quadratically on the aluminoxane concentration. This is consistent with our concept that a molecule of the organozirconium compound diffuses into an associate of aluminoxanes and forms the catalytically active center. No decomposition reactions take place. Hydrogen transfer leads to formation of zirconium hydrides [cf. *(5)*], from which the alkyl compounds and thus the reactive centers are formed by addition of olefin.

Experimental

(5): A stirred suspension of *(1)* (35 g, 0.1 mol) in *n*-heptane (300 ml) is treated at 40 °C with 70 ml (0.51 mol) triethylaluminum. After *ca.* 15 min the solution is homogeneous, and subsequently white [*(5)*] and dark-red [*(6)*] crystals precipitate with concomitant evolution of ethane. After 3 d the mixture is warmed to 60 °C and filtered. The residue (white crystals) is completely dissolved in toluene at 80 °C, cooled to 0 °C, and recrystallized twice; 40% yield of analytically pure *(5)*.

Polymerization: Toluene (330 ml) is transferred to a 1 l glass autoclave fitted with a thermostat and previously baked out and purged with argon. After warming to 70 °C, oligomeric methylaluminoxane (300 mg, 5.1 mmol Al) is added, the mixture stirred for 3 minutes and then treated with $(C_5H_5)_2Zr(CH_3)_2$ (3.33×10^{-8} mol) in toluene; after a further 3 minutes ethylene is introduced at a pressure of 8 bar. Approximately 120 s later white polyethylene precipitates out. After 1 h the catalyst is destroyed, by addition of methanol, since the polyethylene can no longer be stirred. The polyethylene is filtered off, washed several times with methanol and dried; yield 19.0 g, average molecular weight (viscometric) 166000.

Received: February 7, 1980 [Z 448 IE]
German version: Angew. Chem. *92*, 396 (1980)

CAS Registry numbers:
(7), 1273-01-4; *(5)*, 73505-54-1; triethylaluminum, 97-93-8; polyethylene, 9002-88-4; bis(cyclopentadienyl)dimethyltitanium(IV), 1271-66-5; bis(cyclopentadienyl)dimethylzirconium(IV), 12636-72-5.

[1] *G. Bier*, Makromol. Chem. *70*, 44 (1964).
[2] *E. Heins, H. Hinck, W. Kaminsky, G. Oppermann, P. Raulinat, H. Sinn*, Makromol. Chem. *134*, 1 (1970); *W. Kaminsky, H. Sinn*, Justus Liebigs Ann. Chem. *1975*, 424; *W. Kaminsky, H.-J. Vollmer, ibid. 1975*, 438; *W. Kaminsky, H.-J. Vollmer, E. Heins, H. Sinn*, Makromol. Chem. *175*, 443 (1974); *W. Kaminsky, J. Kopf, H. Sinn, H.-J. Vollmer*, Angew. Chem. *88*, 688 (1976); Angew. Chem. Int. Ed. Engl. *15*, 629 (1976).
[3] *J. Kopf, H.-J. Vollmer, W. Kaminsky*, Cryst. Struct. Commun., in press.
[4] *A. Andresen, H.-G. Cordes, J. Herwig, W. Kaminsky, A. Merck, R. Mottweiler, J. Pein, H. Sinn, H.-J. Vollmer*, Angew. Chem. *88*, 689 (1976); Angew. Chem. Int. Ed. Engl. *15*, 630 (1976).
[5] *J. Herwig*, Dissertation, Universität Hamburg 1979.
[6] The oligomeric pentamethylcyclopentaaluminoxane *(7)*, $n = 5$, was purified by recrystallization and characterized mass spectrometrically: $m/e = 289$ (2%, $M^+ - 1$), 275 (13), 217 (10), 177 (25), 159 (23), 101 (51), 72 (100), 58 (94), 57 (98), 56 (36), 44 (15), 43 (76), 42 (98), 41 (40), 40 (17), *etc.*
[7] *H. U. Bergmeyer:* Methoden der Enzymatischen Analyse, 3rd Edit. Verlag Chemie, Weinheim 1974.

Phthalocyaninatoiron with Pyrazine as a Bidentate Bridging Ligand[**]

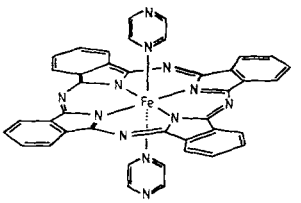
By *Otto Schneider* and *Michael Hanack*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

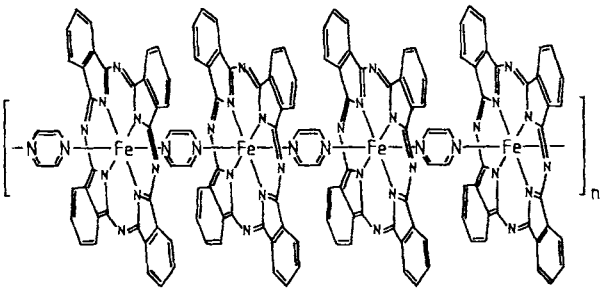
We recently described a new type of one-dimensional conductor consisting of square-planar metal complexes which are linked bisaxially *via* linear bidentate ligands with one or two crossed longitudinal π-systems to form linear polymeric chains[1a]. The square-planar metal complexes may be metal-phthalocyanines (PcM)[1a,c], metal-hemiporphyrazines (HpM)[1c], or metal-tetraphenylporphines (TPPM)[1d]. Linkage with $:C{\equiv}C:^{2\ominus}$ as a bidentate bridging ligand affords polymeric $[PcM(C{\equiv}C)]_n$ or $[HpM(C{\equiv}C)]_n$ which are predicted by EHMO calculations to have pronounced electrical conductivity[1b].

Monomeric octahedral metal-phthalocyanines with bisaxial alkyne substituents $PcM(C{\equiv}CR)_2$ (R = H, CH_3, C_6H_5, *t*Bu; M = Si, Ge, Sn), $HpGe(C{\equiv}CR)_2$ (R = H, C_6H_5, *t*Bu), and $TPPGe(C{\equiv}CR)_2$ (R = C_6H_5, *t*Bu) have recently been described[1c-e], as have some of the polymers $[PcM(C{\equiv}C)]_n$[1f].

We now report the preparation of phthalocyaninatobis(pyrazine)iron(II) *(1)* and the first successful attempts to synthesize a polymeric metal-phthalocyanine having pyrazine as bridging ligand.



(1)



(2)

Monomeric octahedral $PcFeL_2$ compounds with L = pyridine[2], imidazole and piperidine (pip)[3a], and benzyl[4] and tolyl isocyanide[3b] have been synthesized and the structure is known in the case of bis(4-methylpyridine)phthalocyaninatoiron(II)[5]. The $PcFeL_2$ compounds[3] could be obtained by reaction of solid PcFe[6] in the β-modification (β-PcFe) with the dissolved ligand.

The analogous reaction of β-PcFe with an excess of pyrazine (pyz) (molar ratio 1:5) in boiling chlorobenzene leads

[*] Prof. Dr. M. Hanack, Dipl.-Chem. O. Schneider
Institut für Organische Chemie der Universität
Lehrstuhl für Organische Chemie II
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Synthesis and Properties of Novel One-Dimensional Conductors, Part 6. This work was supported by the Stiftung Volkswagenwerk. We are grateful to Prof. Dr. *D. Krug*, Institut für Anorganische Chemie der Universität Tübingen, for the thermogravimetric analyses.—Part 5: *W. Hiller, J. Strähle, M. Hanack, K. Mitulla*, Justus Liebigs Ann. Chem., in press.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0505-392 $ 02.50/0*

not to the monomer *(1)* but immediately to polymeric blue phthalocyaninato(μ-pyrazine)iron(II) *(2)*. Compound *(2)* is also formed when chlorobenzene is co-distilled with pyrazine on pure β-PcFe.

It proved more difficult to synthesize the violet compound $PcFe(pyz)_2$ *(1)*. However, this can be accomplished by reacting β-PcFe with molten pyrazine for 24 h and then rapidly removing the excess of pyrazine with methanol. Platelet-shaped single crystals of *(1)*, which appear violet by reflected light, can also be obtained by ligand exchange from $PcFe(pip)_2$[3a] dissolved in $CHCl_3$ with a large excess of pyrazine after addition of light petroleum (b.p. 60—90 °C) over a period of one week.

Attempted purification of *(1)* by extraction with chlorobenzene also gave *(2)* with loss of pyrazine. After extraction with $CDCl_3$ the pyrazine liberated from *(1)* can be detected by a sharp singlet at 8.6 ppm in the ^{1}H-NMR spectrum.

The compounds *(1)* and *(2)* are stable to air and moisture; they have been identified by elemental and thermogravimetric analysis. Thermogravimetric studies show *(1)* to be less stable than *(2)*: both pyrazine ligands of *(1)* are eliminated in a single step between 150 and 240 °C. Compound *(2)* undergoes the loss of mass expected for elimination of one pyrazine moiety between 240 and 290 °C[7]. The residue in each case is β-PcFe.

The mass spectra of *(1)* and *(2)* show only $PcFe^{\oplus}$ as the ion of highest mass. The IR and FIR of samples of *(2)* obtained by different routes are identical and contain far fewer bands than the spectra of *(1)* (Table 1).

Table 1. Physical data of phthalocyaninatobis(pyrazine)iron(II) *(1)* and phthalocyaninato(μ-pyrazine)iron(II) *(2)*.

	$PcFe(pyz)_2$ *(1)*	$[PcFe(pyz)]_n$ *(2)*
Thermogravimetric loss of pyrazine	150—240 °C	240—290 °C
UV/VIS λ_{max} [nm], (log ε)	653 (5.07), 626 sh (4.60), 593 (4.54), 570 sh (4.14), 552 sh (3.95), 482 (4.06), 401 (4.09), 344 (4.85) [a]	788 (4.20), 723 (4.17), 714 (4.17), 697 sh (4.15), 628 sh (4.02), 400 sh (3.88), 353 (4.11), 342 (4.11) [b]
UV/VIS λ_{max} [nm] [c]	664, 600 sh, 499 sh, 400, 335, 264	770, 665, 600 sh, 400 sh, 333, 266
FIR [cm^{-1}] [d]	642 m, 624 m, 572 s, 524 s, 494 m, 442 vs, 414 m, 392 vw, 367 s, 330 s [e], 302 s, 239 w, 222 s, 194 s, 168 vs [f], 132 s, 88 vw, 74 vw	642 w, 572 vs, 542 s, 517 w, 438 vs, 409 m, 396 w, 362 w, 327 vw [e], 301 m, 270 s, 180 s, 160 vw [f], 130—118 w, 74 w
Conductivity [Ω^{-1} cm^{-1}] [g]	2×10^{-12}	1×10^{-7} [h] 2×10^{-6} [i]

[a] In a 1 M solution of pyrazine in 1-chloronaphthalene. [b] In 1-chloronaphthalene, log ε calculated for $[PcFe(pyz)]_1$. [c] Apparent extinction, 1% of *(1)* or *(2)* in $BaSO_4$ rel. to $BaSO_4$ as std. white. [d] Polyethylene disk. [e] and [f] Fe N_{Pc} stretching and N_{Pc} Fe N_{Pc} deformation mode after [5]. [g] Polycrystalline material, measured at 3 kbar pressure. [h] Prepared in chlorobenzene. [i] Prepared in $CHCl_3$.

The UV/VIS spectrum of *(1)* in a 1 M solution of pyrazine in 1-chloronaphthalene expectedly resembles that of phthalocyaninatobis(pyridine)iron(II) in the wavelength of the absorption maxima and in the extinction coefficients[8]. In contrast, the electronic spectrum of *(2)* in 1-chloronaphthalene, 1,2,4-trichlorobenzene, and benzene exhibits new intense bands at 714, 723, and 788 nm (Table 1), while the intense band of monomeric octahedral phthalocyaninatoiron(II) derivatives around 650 nm is no longer observed.

Reflection spectra of *(2)* recorded with a 1% finely ground mixture in $BaSO_4$ relative to $BaSO_4$ as a standard white show an apparent extinction in the long wave region at 770 nm which is observed neither for *(1)* nor for β-PcFe. The formation of the polymer *(2)* from *(1)* can be followed qualitatively in the electronic excitation spectrum in benzene as solvent. At room temperature the UV spectrum of *(2)* is still observed even in the presence of a 10^6-fold excess of pyrazine; partial regeneration of *(1)* is observed at higher temperature.

We conclude from the results of elemental analysis and the molar ration of PcFe:pyrazine (1:1) determined by thermogravimetry that *(2)* is oligomeric or polymeric; the degree of polymerization is still unknown.

The conductivities of *(2)* measured with polycrystalline samples at 3 kbar are up to 10^6 times higher than for *(1)* (Table 1). This is also indicative of pronounced electron delocalization over the pyrazine bridges[9] in *(2)*. Preliminary doping experiments with iodine in *(2)* indicate a significant increase in conductivity.

General procedure:

(1): Pyrazine (30 mmol) is fused under N_2. After addition of β-PcFe (1 mmol) with stirring the reaction mixture is kept at 80—100 °C for 24 h. The cooled melt is crushed, digested with methanol, and filtered immediately; the violet residue is washed repeatedly with methanol and dried at 80 °C (yield 90%).

(2), Route A: Compound *(1)* (1.4 mmol) is extracted in a Soxhlet apparatus under N_2 for 3 h with anhydrous chlorobenzene (50 ml). The extraction solution is initially blue-green but becomes colorless after a few minutes. The blue residue in the extraction vessel is washed with light petroleum (b.p. 60—90 °C), filtered, and dried at 80 °C (yield 84%).—*Route B:* β-PcFe (2 mmol) is slurried in anhydrous chlorobenzene (180 ml) and boiled under reflux with pyrazine (10 mmol) for 24 h. The blue residue is treated as in route A (yield 86%).

Received: January 2, 1980;
supplemented: April 1, 1980 [Z 449 IE]
German version: Angew. Chem. *92*, 391 (1980)

[1] a) *M. Hanack, F. F. Seelig, J. Strähle,* Z. Naturforsch. *A 34*, 983 (1979); b) *F. F. Seelig, ibid. 34*, 986 (1979); c) *M. Hanack, K. Mitulla, G. Pawlowski, L. R. Subramanian,* J. Organomet. Chem., in press; d) *M. Mezger, M. Hanack,* unpublished; e) *M. Hanack, K. Mitulla, G. Pawlowski, L. R. Subramanian,* Angew. Chem. *91*, 343 (1979); Angew. Chem. Int. Ed. Engl. *18*, 322 (1979); f) *M. Hanack, K. Mitulla,* Z. Naturforsch., in press.
[2] *P. A. Barrett, D. A. Frye, R. P. Linstead,* J. Chem. Soc. *1938*, 1157.
[3] a) *B. W. Dale, R. J. P. Williams, P. R. Edwards, C. E. Johnson,* Trans. Faraday Soc. *64*, 620 (1968); b) *R. Taube,* Pure Appl. Chem. *38*, 427 (1974).
[4] *D. V. Stynes,* Inorg. Chem. *16*, 1170 (1977).
[5] *F. Cariati, F. Morazzoni, M. Zocchi,* J. Chem. Soc. Dalton Trans. *1978*, 1019.
[6] *E. G. Meloni, L. R. Ocone, B. P. Block,* Inorg. Chem. *6*, 424 (1967).
[7] Complete elemental analysis of *(2)* gives the composition $[PcFe(pyz)\cdot 1/2C_6H_5Cl]_n$. Loss of chlorobenzene as crystal solvent between 120 and 220 °C could be detected by TGA.
[8] *M. Whalley,* J. Chem. Soc. *1961*, 866.
[9] *M. S. Haddad, D. N. Hendrickson, J. P. Cannady, R. S. Drago, D. S. Bieksza,* J. Am. Chem. Soc. *101*, 898 (1979).

Direct Observation of the Dibenz[*b,g*]oxocinide Ion; A Non-Aromatic $(4n+2)\pi$ Species[**]

By *A. G. Anastassiou* and *H. S. Kasmai*[*]

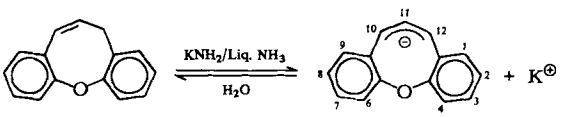
The acidity of 10*H*-dibenz[*b,g*]oxocin *(1)* exceeds that of xanthene *(3)* by *ca.* 1.9 pK_a units[11]. Assuming *(3)* to repre-

[*] Prof. Dr. A. G. Anastassiou
Department of Chemistry, Syracuse University
Syracuse, New York 13210 (USA)
Prof. Dr. H. S. Kasmai
Department of Chemistry, Shiraz University
Shiraz (Iran)

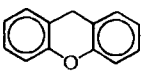
[**] Work at Syracuse was supported by the National Science Foundation, that at Shiraz by the Iranian Ministry of Higher Education.

sent a properly structured model compound for *(1)* it was reasonably concluded that the oxocarbanion derived from *(1)*, *i.e.* *(2)*, may be regarded as a 10π-arene.

Recent findings in our own laboratories[2], however, appeared to cast some doubt on the inference of an aromatically stabilized ion *(2)* insofar as *(3)*, the substance previously employed as an acidity standard[1], was shown to produce a decidedly paratropic anion and, hence, one which might reasonably be regarded as being antiaromatically delocalized[2].



(1) *(2)*



Ph–CH_2–Ph ⟶ Ph–$\overset{\ominus}{C}$H–Ph

(3) *(4)* *(5)*

In view of this controversial situation we decided to check whether *(2)*, the anion of *(1)*, is aromatically delocalized or not. To this end, *(1)* was allowed to react with potassium amide in liquid NH_3 at *ca.* $-30\,^{\circ}C$ in an NMR tube to give *(2)*[3] [(^{1}H-NMR, 60 MHz, NH_3, $\approx 34\,^{\circ}C$): $\delta = 6$—7 (8H, m), 5.6 (1H, t, H-11, $J = 11$ Hz), 4.0 (2H, d, H-10, H-12, $J = 11$ Hz); (^{13}C-NMR, 20 MHz, NH_3, $\approx 30\,^{\circ}C$, TMS): $\delta = 87.92$ (C-10, C-12), 115.62 (C-11), 124.3, 126.15, 128.10, 133.87, 145.50, 157.2]. The ^{1}H-NMR data of *(2)* are consistent with the presence of an unusual π-system—and not with a diatropic 10π- or 18π-system. Especially remarkable in this connection is the *upfield* shift of the signals of all benzenoid protons on transformation of *(1)* into *(2)* (Fig. 1); the signals of

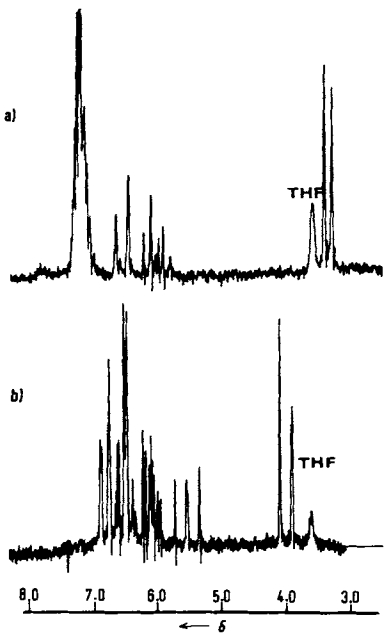


Fig. 1. 60 MHz ^{1}H-NMR spectrum of a) 10*H*-dibenz[*b*,*g*]oxocin *(1)* and b) the dibenz[*b*,*g*]oxocinide ion *(2)* at *ca.* 34 °C in liquid ammonia containing some tetrahydrofuran (< 1%, internal standard) as solvent.

the latter come into the same region as that occupied by the corresponding "benzenoid" resonances in the spectrum of a properly structured acyclic model without the central ring, *e.g.* of the diphenylmethanide ion *(5)* ($\delta = 5.6$—6.8)[2]. Further, the downfield shift of H-10, H-12 (*ca.* 0.6 ppm) on transformation of *(1)* into *(2)* may rationally be attributed simply to rehybridization insofar as a similar shift (*ca.* 0.4 ppm) is also observed for the benzylic proton of the anion *(5)* generated from diphenylmethane *(4)*[2]. This viewpoint is also supported by the close similarity of the ^{13}C-NMR signals of the "benzylic" C-atoms in the anions *(2)* ($\delta = 87.92$) and *(5)* ($\delta = 81.33$).

From the NMR findings it thus follows that the oxocarbanion *(2)* must largely be regarded as a conventional system, *i.e.* one in which the negative charge is primarily localized in the allylic moiety of the eight-membered ring. In conclusion, it is interesting to briefly note that while *(2)* somehow fails to realize its "$(4n+2)\pi$" potential ($n = 2$ or 4) for "aromatic" delocalization, the oxocarbanion derived from xanthene[2] readily realizes its "$4n\pi$" potential ($n = 2$ or 4) by yielding to what may best be described as "antiaromatic" delocalization. This interesting paradox undoubtedly arises from the controlling influence of skeletal (σ-frame) factors which are such as to impose a flat or nearly flat frame to the heterocycle in the xanthenide ion, and a heavily buckled one to that of *(2)*[4].

Received: October 17, 1979 [Z 450 IE]
German version: Angew. Chem. *92*, 402 (1980)

CAS Registry numbers:
(1), 24974-26-3; *(2)*, 73557-53-6

[1] *H. S. Kasmai, H. S. Whitlock, Jr.*, J. Org. Chem. *37*, 2161 (1972).

[2] *A. G. Anastassiou, H. S. Kasmai*, Angew. Chem. *92*, 53 (1980); Angew. Chem. Int. Ed. Engl. *19*, 43 (1980).

[3] The ^{1}H-NMR spectrum of *(2)* (Fig. 1b) shows no qualitative or quantitative deterioration upon prolonged (11 h) exposure to ambient temperature. Subsequent water quench of *(2)* produced *(1)* quantitatively.

[4] Besides being supported by simple inspection of a "Dreiding" molecular model the notion of a heavily buckled eight-membered unit in *(2)* receives added confirmation from the magnitudes of key C–H coupling constants $J_{(C\text{-}10)\ H} = 154$ Hz and $J_{(C\text{-}11)\ H} = 156$ Hz, which are inconsistently high for a planar eight-membered ring [5].

[5] *A. G. Anastassiou, E. Reichmanis*, J. Am. Chem. Soc. *98*, 8366 (1976).

4-Sulfobenzyl, a New Carboxy Protecting Group[**]

By *Arnulf Hubbuch, Roland Bindewald, Josef Föhles, Vinod Kumar Naithani*, and *Helmut Zahn*[*]

A cardinal problem in peptide synthesis is the sparing solubility of larger, protected peptide fragments[1]. A solubilizing, polar protecting group[2–5] provides a way out from this preparative bottle-neck. We report here on the combination of the solubilizing sulfo-function[2,5,6] with the benzyl group, a type of protecting group very frequently employed in peptide synthesis[7].

For incorporation of the 4-sulfobenzyl group in amino acids the reagent chosen was sodium 4-(bromomethyl)benzenesulfonate ("4-sulfobenzyl bromide") *(4)*, which should permit preparation of the corresponding ester- and ether-functions. Starting from benzylamine *(1)*, compound *(4)* is

[*] Prof. Dr. H. Zahn [+], Dr. A. Hubbuch, R. Bindewald, Dr. J. Föhles, Dr. V. K. Naithani
Deutsches Wollforschungsinstitut an der Technischen Hochschule
Veltmanplatz 8, D-5100 Aachen (Germany)

[+] Author to whom correspondence should be addressed.

[**] Part of a lecture delivered at the 1st European Symposium on Organic Chemistry, Köln, August 22, 1979.—This work was supported by the Deutsche Forschungsgemeinschaft (Za 5/32). We thank Prof. Dr. *R. G. Lawton*, Michigan University, for valuable discussions.

readily accessible on a 50—100 g scale in a three-step reaction without recourse to tedious purification steps[8] (see Procedure and Table 1).

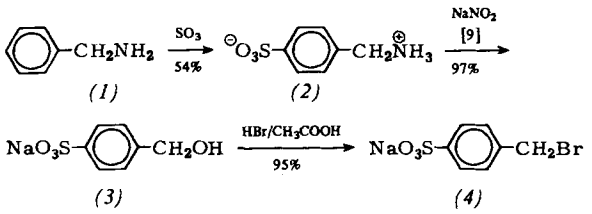
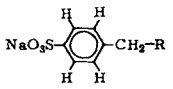


Table 1. ^{1}H-NMR spectroscopic data (90-MHz, [D$_6$]dimethyl sulfoxide, TMS, δ-values) of 4-sulfobenzyl derivatives.



R	$H_{A/A'}$	$H_{X/X'}$	CH_2	other H
NH_2 [a]	7.53	7.22	3.69 (s)	2.72 (s)
OH	7.58 (d)	7.25 (d)	4.48 (d)	5.2 (t)
BR	7.59 (d)	7.38 (d)	4.69 (s)	—
OR' [b]	7.61 (d)	7.35 (d)	5.1—5.2 (s)	—

[a] As zwitterion. [b] R = *e.g.* Ala-, Leu-.

The preparation of *N*-protected amino acid 4-sulfobenzyl esters was accomplished by alkylation of cesium-[7] or dicyclohexylammonium salts of *N*-benzyloxycarbonyl- (Z-) or *N*-*tert*-butyloxycarbonyl- (Boc) protected amino acids with the sodium salt *(4)*. The 4-sulfobenzyl group can be incorporated in peptides in yields equally as good as in amino acids:

Z-Leu-Val-Leu-OH + *(4)* →
Z-Leu-Val-Leu-$OCH_2C_6H_4SO_3Na(p)$
(5a), 80% yield

A characteristic feature of the amino acid 4-sulfobenzyl ester is its zwitterionic structure:

$H_3\overset{\oplus}{N}$—CHR—CO—O—$CH_2C_6H_4\overset{\ominus}{S}O_3(p)$ *(5)*

It facilitates purification by recrystallization and/or "filtration" on a mixed-bed exchanger. The multistep synthesis of the protected hydrophobic hexapeptide Z-Leu-Ala-Leu-Leu-Val-Leu-OH with the new ester protection strategy demonstrates the advantages of this protecting function in peptide synthesis. As in the case of cysteic peptides[2,6] the sulfo group considerably increases the solubility in polar solvents: the methyl ester of the above mentioned hexapeptide is insoluble in methanol and dimethylformamide; in contrast the 4-sulfobenzyl ester could be purified on Sephadex LH 20 with methanol.

Incorporation of the sulfo function in the benzyl group considerably increases the stability of the benzyl ester bond towards acids. The selective deblocking of Z-protected peptide-4-sulfobenzyl esters is far less problematical than in the case of unsubstituted benzyl esters (cf. Table 2).

4-Sulfobenzyl esters can be readily cleaved by catalytic hydrogenation or alkaline hydrolysis. The simple synthesis, high acid-stability, and solubilizing properties make the new protective function an attractive alternative to the benzyl- and *p*-nitrobenzyl groups. Moreover, the directed application of 4-sulfobenzyl esters, for example in combination with cationic protecting groups[4,10] or basic amino acids (histidine, arginine), ensures effective purification of protected peptide fragments by ion-exchange chromatography.

Table 2. Properties of amino acid 4-sulfobenzyl esters *(5)*.

a) Cleavage
catalytic hydrogenation: Pd/H_2
alkaline hydrolysis: $NaOH/H_2O$/dioxane
b) Stability towards acids

	Cleavage of leucine		
	benzyl-	4-sulfobenzyl- ester	4-nitrobenzyl-
Trifluoroacetic acid/17 h	12%	0.2%	—
2.5 N HBr/AcOH/24 h	100%	20%	10%

Procedure

(2): *(1)* (100 ml, 915 mmol) was added dropwise to 100 ml of ice-cooled concentrated sulfuric acid. The reaction mixture was then allowed to warm to room temperature and treated with 300 ml 30% oleum, whereupon the temperature increased to about 80 °C. After cooling the mixture was poured into ice-water and the resulting precipitate filtered off, washed with water, methanol and ether, and finally dried over P_2O_5. The yield of crude *(2)* was 92.8 g (54%). The crude product can be purified by recrystallization from water; decomposition above 300 °C.

(3) (cf. [9]): A suspension of *(2)* (18.72 g, 100 mmol) in 500 ml of a 0.04 M solution of sodium acetate was adjusted to pH 3.3 with acetic acid and treated dropwise at 40 °C (bath temperature) with a solution of sodium nitrite (6.9 g, 100 mmol) in 30 ml water. After 1 hour's stirring at the same temperature the solution was evaporated down, the residue taken up in water, transferred onto a cationic exchanger IRC-50 (Amberlite), and the eluate freeze-dried. This was dissolved in methanol, treated with ether, and the precipitate filtered off and dried; yield 20.4 g (97%) *(3)*.

(4): 10.5 g (50 mmol) of *(3)* was treated at room temperature with 110 ml 40% hydrogen bromide in acetic acid and the mixture stirred for 48 h. The residue obtained on evaporation was taken up in methanol, treated with ether, and the precipitate filtered off and dried over P_2O_5; yield 12.9 g (95%) *(4)*.

L-Leucyl-4-sulfobenzyl ester (5b): A mixture of Boc-L-Leu-DCHA (DCHA = dicyclohexylammonium) (4.1 g, 10 mmol) and *(4)* (4 g, 15.3 mmol) in 30 ml anhydrous dimethylformamide was stirred for 24 h at room temperature. After removal of dicyclohexylammonium bromide by filtration and of solvent by evaporation, the resulting residue was stirred for 30 min in trifluoroacetic acid. After evaporation in a vacuum the colorless solid was digested with 50 ml ether and filtered. The crude product was dissolved in 50 ml 5% acetic acid, warmed briefly to 50 °C, cooled, filtered and washed with 5% acetic acid. Recrystallization from water/methanol (2:1 v/v) afforded 1.3 g *(5b)* (m.p. 249 °C; $[\alpha]_D^{20} = -5.8$, $c = 30\%$ AcOH). The combined mother liquors were evaporated down to *ca.* 50 ml and transferred to a mixed-bed exchanger (Dowex 50 WX 8, Dowex 44, NH_4OAc form). A further 1.1 g of *(5b)* was isolated from the freeze-dried eluate; overall yield 80%.—Corresponding esters of L-phenylalanine, L-alanine and benzyloxycarbonyl-L-arginine were prepared analogously.—The products *(2)*—*(4)* and *(5b)* were characterized by ^{1}H-NMR spectroscopy and elemental analysis.

Received: December 20, 1979 [Z 451 IE]
German version: Angew. Chem. *92*, 394 (1980)

CAS Registy numbers:
(1), 100-46-9; *(2)*, 2393-24-0; *(3)*, 73506-14-6; *(4)*, 32014-22-5; *(5a)*, 73506-15-7; *(5b)*, 73506-16-8; Z-Leu-Val-Leu-OH, 7801-71-0; Boc-Leu-DCHA, 52657-56-4

[1] *E. Wünsch*, Angew. Chem. *83*, 773 (1971); Angew. Chem. Int. Ed. Engl. *10*, 786 (1971); *K. Lübke, E. Schröder, G. Kloss:* Chemie und Biochemie der Aminosäuren, Peptide und Proteine. Vol. I. Thieme, Stuttgart 1975, p. 169 ff.

[2] *A. Hubbuch, W. Danho, H. Zahn* in *M. Goodman, J. Meienhofer:* Proceedings of the Fifth American Peptide Symposium. Wiley, New York 1977, p. 540.

[3] *Th. Wieland*, Acta Chim. Acad. Sci. Hung. *44*, 5 (1965); *I. G. Tesser, I. C. Balvert-Geers*, Int. J. Pept. Protein Res. *7*, 295 (1975); *H. Anzinger, M. Mutter, E. Bayer*, Angew. Chem. *91*, 747 (1979); Angew. Chem. Int. Ed. Engl. *18*, 686 (1979).

[4] *H. Kunz*, Chem. Ber. *109*, 2670 (1976).

[5] *U. T. Rüegg, D. Jarvis, J. Rudinger*, Biochem. J. *179*, 127 (1979).

[6] *A. Hubbuch, E. Büllesbach, W. Danho, A. Schüttler, H. Zahn* in *E. Wünsch:* Proceedings of the Second FRG-USSR Symposium on Chemistry of Peptides and Proteins. München 1978, p. 144.

[7] *S. S. Wang, B. F. Gisin, D. P. Winter, R. Makofske, I. D. Kulesha, C. Tzougraki, J. Meienhofer*, J. Org. Chem. *42*, 1286 (1977).

[8] *R. Bindewald*, Diplomarbeit, Technische Hochschule Aachen 1980.

[9] *J. Meisenheimer, J. Link*, Justus Liebigs Ann. Chem. *479*, 211 (1930).

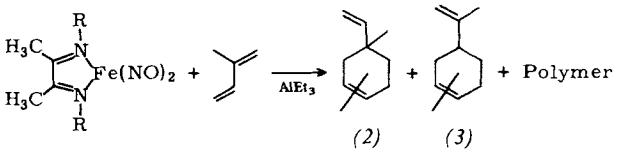
[10] *R. Camble, R. Garner, G. T. Young*, J. Chem. Soc. *C 1969*, 1911.

Rigid Phenyl-Group Conformation in Complexes[**]

By *Heindirk tom Dieck, Horst Bruder, Kurt Hellfeldt*, and *Dieter Leibfritz* and *Martin Feigel*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Chelate ligands of the diazadiene type, R—N=C(R′)—C(R′)=N—R (dad), especially when complexed with iron, have acclaimed special interest as directive ligands for homogeneous catalytic reactions. Thus, *e.g.*, the dimerization of butadiene or isoprene can be accomplished with $(dad)_2Fe$[1], the product distribution between six- and eight-membered ring compounds depending on the size and conformation of the groups R. 2,2′-Bipyridyl and 2-pyridinealdimines coordinated to iron also give interesting catalytic systems[2]. With complexes $(dad)Fe(NO)_2$ *(1)* we found not only the known dimerization of isoprene to 1,4- and 2,4-dimethyl-4-vinyl-1-cyclohexene *(2)*[3] but, depending upon R,R′, also polymerization at room temperature, predominantly to 3,4-polyisoprene[4] (Table 1).



(2) *(3)*

(1a), R = C_6H_5; *(1b)*, R = i-C_3H_7

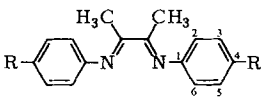
To obtain information about the stereochemical conditions in the coordination sphere of the iron, we have also investigated the complexation of bulky dad-ligands in the tris-chelate complex ion $[(dad)_3Fe]^{2+}$, known previously only with R = *n*-alkyl[5]. Such ions, however, can also be synthesized with secondary alkyl substituents (*e.g.* R = isopropyl, cyclohexyl)[1], while tertiary alkyl groups hinder *cis*- or *trans*-arrangements of two dad-ligands at the octahedrally coordinated metal, as at the trigonal-bipyramidal arrangement. The typical reactions of $(dad)_2Fe$ (reversible addition of CO to give $(dad)_2FeCO$, irreversible addition of $(CN)_2$ to give $(dad)_2Fe(CN)_2$) fail in the case of R = *tert*-butyl.

Table 1. Reactions of $(dad)Fe(NO)_2$ *(1)* with isoprene; ratio Fe:Al: isoprene: tetrahydrofuran = 1:1:150:150.

	T [°C]	*t* [h]	Conversion [%]	Products *(2)* : *(3)* : Polymer
(1) [a]	120	20	40	62 : 19 : 19
(1a)	80	20	30	65 : 7 : 28
(1b) [b]	25	24	100	0 : 0 : 100

[a] No $AlEt_3$ added. [b] The mixture solidified despite the amount of tetrahydrofuran.

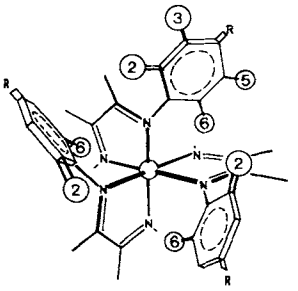
Surprisingly, however, tris-chelates can also be prepared with the, supposedly bulky, phenyl derivatives, *e.g.* with *(4a)* and *(4b)*. With tetracarbonyliron iodide as starting compound one obtains the tris-chelates as iodides *(5a)* and *(5b)*, respectively. The rigid conformation of these close-packed compounds is reflected in a unique pattern of the ^{1}H-NMR signals of the aromatic protons.



(4a) → $(dad)_3FeI_2$ *(5a)*
(4b) → $(dad)_3FeI_2$ *(5b)*

(4a), R = H; *(4b)*, R = OCH_3

Figure 1 shows only the region of the aromatic protons of the 270-MHz ^{1}H-NMR spectrum of *(5b)*. The *o*-hydrogen atoms H-2 and H-6 are non-equivalent, as are also the *m*-H atoms H-3 and H-5. H-6 shows a distinct upfield shift, while H_2 shows an exceptional one. With the tabulated parameters for the shielding caused by ring currents[6] and with known structural data of other dad-complexes[7], a maximum upfield shift of H-2 of about $\Delta\delta = 2.5$ ppm can be calculated for a torsional angle θ of the phenyl groups of *ca.* 60° and otherwise ideal octahedral coordination; this value is in satisfactory agreement with the observed values ($\Delta\delta$ for *(5a)* 3.0, for *(5b)* 2.8 ppm). For the remaining protons, especially H-6, on the other hand, the calculation gives no change. The upfield shift of H-6 *must* therefore be caused by the anisotropic



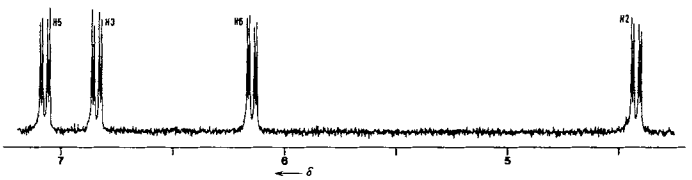


Fig. 1. 270-MHz ^{1}H-NMR spectrum of *(5b)* in CD_3CN (phenyl proton region). For the sake of clarity only three of the six *N*-substituents are shown in the structural diagram.

[*] Prof. Dr. H. tom Dieck [+], Dr. H. Bruder [***], Dipl.-Chem. K. Hellfeldt
Institut für Anorganische und Angewandte Chemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
Prof. Dr. D. Leibfritz, Dr. M. Feigel
Fachbereich Chemie und Biologie der Universität
D-2800 Bremen (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft (special program "homogeneous catalysis") and BASF AG. We are grateful to Prof. *Gütlich* and his co-workers for measuring the Mössbauer spectra.

[***] Present address: BASF AG, D-6700 Ludwigshafen (Germany).

shielding of the 4π electron system of the dad ligand and/or by the 6π electron system of the Fe-dad chelate ring. The mean torsional angle of 60° calculated for the position of H-2 relative to a neighboring phenyl group does in fact give a position for H-6 directly above a neighboring chelate ring (see Fig. 1). The remaining assignments are easily made by double resonance experiments.

An explanation of the unusual chemical shifts in terms of paramagnetic effects can be ruled out. As expected, in the ^{13}C-NMR spectrum[8] a signal is observed for each ring C-atom, but without any unusual shifts. The Mössbauer data of the solid compounds show typical values for low-spin complexes[8,9]. At 80 °C the exchange of H-2/6 and H-3/5 is detectable by means of saturation transfer. All these findings demonstrate the unusual packing density of the six *N*-substituents and at the same time underscore the influence of a single dad ligand on the remaining coordination sites of an octahedral complex.

Procedure

(1): $Fe(CO)_2(NO)_2$ reacts with a *ca.* 0.5 M solution of the relevant dad in toluene at room temperature to give almost quantitative yields of *(1)* as glistening green crystals, which appear brown in transmitted light.

(5): A mixture of $Fe(CO)_4I_2$ and the corresponding dad (molar ratio 1:3) in acetonitrile is stirred for 20 h at 40 °C. The deep-blue-violet crystals, obtained in quantitative yield, are stable to air.

Received: January 7, 1980 [Z 452 IE]
German version: Angew. Chem. *92*, 395 (1980)

CAS Registry numbers:
(1a), 73523-15-6; *(1b)*, 73523-16-7; *(2)*, 65025-40-3; *(3)*, 60735-00-4; *(4a)*, 5393-49-7; *(4b)*, 19215-52-2; *(5a)*, 73523-13-4; *(5b)*, 73523-14-5; isoprene, 78-79-5; $Fe(CO)_4I_2$, 14878-30-9; $Fe(CO)_2(NO)_2$, 13682-74-1

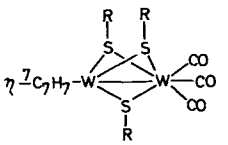
[1] *H. tom Dieck, H. Bruder*, Chem. Commun. *1977*, 24; *H. Bruder*, Dissertation, Universität Frankfurt 1977.
[2] *A. Yamamoto, K. Morifuji, S. Ikeda, T. Saito, Y. Uchida, A. Misono*, J. Am. Chem. Soc. *90*, 1878 (1968); *C. Y. Wu, H. E. Swift*, J. Catal. *24*, 510 (1972); *S. Wanatabe, K. Suga, H. Kikuchi*, Aust. J. Chem. *23*, 385 (1970).
[3] *D. Huchette, B. Thery, F. Petit*, J. Mol. Catal. *4*, 433 (1978); *D. Ballivet-Tkatchenko, M. Riveccie, N. El Murr*, J. Am. Chem. Soc. *101*, 2763 (1979).
[4] *K. Hellfeldt*, Diplomarbeit, Universität Hamburg 1980.
[5] *P. Krumholz, O. A. Serra, M. A. DePaoli*, Inorg. Chim. Acta *15*, 25 (1975) and earlier work.
[6] *J. W. Emsley, J. Feeney, L. H. Sutcliffe:* High Resolution NMR Spectroscopy. Pergamon Press, Oxford 1965, Appendix Vol. I.
[7] *H. tom Dieck, H. Bruder, K. Hellfeldt, A. Kinzel, J. Klaus, A. Lauer, B. Runge, M. Svoboda*, J. Pure Appl. Chem., in press; Section Lecture s 16, IXth I.C.O.C., Sept. 1979, Dijon.
[8] *(5a):* ^{13}C-NMR (ref. to TMS): 183.7 (C≡N), 146.8 (C1); 130.3, 128.6 (C3, C4, C5); 121.3, 119.4 (C2, C6). Mössbauer data (ref. to ^{57}Co/Rh): $\delta = 0.19$ mm/s; $\Delta E_Q = 0.55$; $\Gamma = 0.30$. *(5b):* ^{13}C-NMR: 183.3 (C≡N); 158.9 (C4); 139.7 (C1); 122.6, 120.5 (C2, C6); 115.8, 114.4 (C3, C5).
[9] *E. Baggio-Saitovich, M. A. DePaoli*, Inorg. Chim. Acta. *17*, 59 (1976).

Unusually Bridged Tungsten Complexes with $W(ER)_2W(ER)_3W$ Skeleton (E = S or Se; R = C_2H_5, *n*-C_4H_9, or C_6H_5)

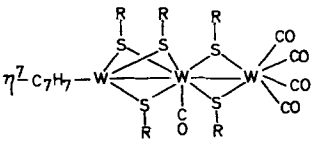
By *Luise R. Krauth-Siegel, Wolfgang Schulze,* and *Manfred L. Ziegler*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Reaction of the thiolates $Pb(SR)_2$ or the selenol $HSeC_6H_5$ with η^7-$C_7H_7W(CO)_2I$ gives, *inter alia,* the dinuclear *(1)* and the trinuclear coordination compounds *(2)* or their analogues *(3)* and *(4)* with SePh in place of SR. Compounds of type *(1)* correspond on the basis of their spectroscopic data to the molybdenum complexes η^7-$C_7H_7Mo(ER)_3Mo(CO)_3$[1a], of which those with E = S and R = *n*Bu, *t*Bu have been characterized by X-ray methods[1b]. Compounds of type *(2)* are novel "noncyclic trinuclear clusters". The analogous complexes *(2)* and *(4)* were characterized[2] by elemental analysis and by their IR and ^{1}H-NMR spectra. The last mentioned spectra show the C_7H_7 ring to be η^7 bonded and that five different SC_2H_5 groups are present in the case of *(2a)*. The unusual molecular structure could be determined by X-ray analysis of *(2b)*.



(1a), R = C_2H_5
(1b), R = *n*-C_4H_9
(3), SeC_6H_5 statt SR



(2a), R = C_2H_5
(2b), R = *n*-C_4H_9
(4), SeC_6H_5 statt SR

In the trinuclear tungsten complex *(2b)* the W atoms which are not in a linear arrangement are doubly and triply bridged by *n*BuS (Fig. 1). Such a combination of bridges has not previously been observed.

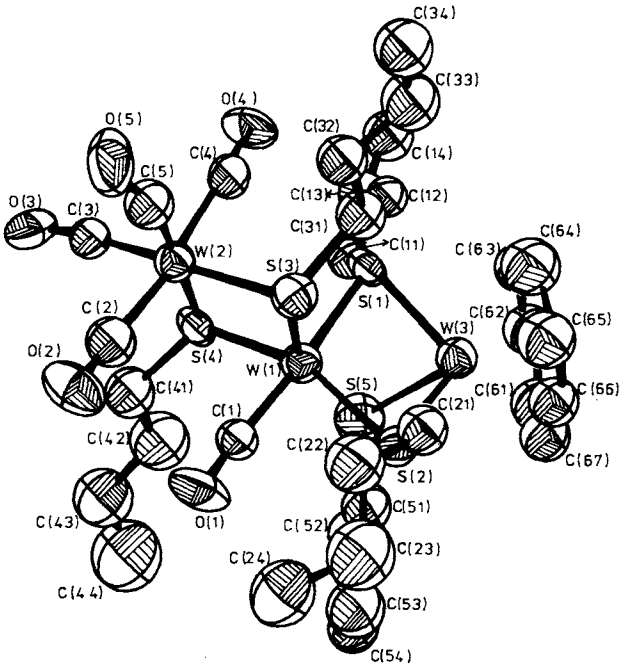
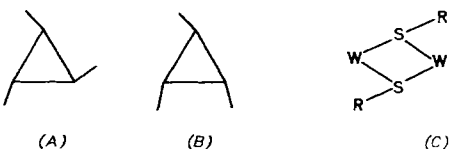


Fig. 1. Crystal structure of the $W(ER)_2W(ER)_3W$ complex *(2b)*.

The W—W distances, the WSW and SWS interior angles[4], and the 18-electron rule call for metal-to-metal bonds between neighboring W atoms. Thus the central W atom is eightfold coordinated and the two outer ones sevenfold coordinated. In the $W(SR)_3W$ moiety of *(2b)* the *n*-butylthio



(A) *(B)* *(C)*

[*] Prof. Dr. M. L. Ziegler, Dipl.-Chem. L. R. Krauth-Siegel, Dipl.-Chem. W. Schulze
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

groups are arranged in the same way as in *(A)* while the $W(SR)_2W$ moiety has the *anti* configuration *(C)*. We have detected only the arrangement *(B)* in previously examined dinuclear species *(1)* and their Mo homologues[1b,5].

Procedure

η^7-$C_7H_7W(CO)_2I$ (1 mmol) and $Pb(SR)_2$ (0.6 mmol) are stirred together in anhydrous CH_2Cl_2 (30 ml) under N_2 at room temperature for 20 h. The green reaction solution turns red-brown with precipitation of PbI_2. The concentrated filtrate is chromatographed on a silica gel column (0.05—0.2, CH_2Cl_2). The fastest migrating red-brown zone contains compounds *(1)* and *(2)* which are separated by preparative TLC (silica gel, CH_2Cl_2/cyclohexane 1:2, double development). *(2)* (brown) migrates in front of *(1)* (yellow). The fractions are dissolved out of the layer material with CH_2Cl_2 and precipitated at $-70\,^\circ C$ from pentane. Compound *(1b)* forms red-brown crystals (m.p. $>270\,^\circ C$, yield 31%) and *(2b)* forms black-green crystals (m.p. 110 °C (dec.), yield 37%).

The seleno complex *(4)* is obtained by stirring (3 h, 20 °C) of a suspension of η^7-$C_7H_7W(CO)_2I$ (1 mmol) in triethylamine (1.2 mmol), $HSeC_6H_5$ (1.2 mmol), and CH_2Cl_2 (30 ml) under argon. In addition to *(4)* this affords the dinuclear complexes *(3)* and $(CO)_4W(\mu\text{-SePh})_2W(CO)_4$ and the mononuclear complex η^7-$C_7H_7W(CO)_2SePh$; the products can be separated by column chromatography (silica gel) in several steps (CH_2Cl_2, acetone) and TLC (silica gel, CH_2Cl_2/*n*-pentane 1:1). Yield 2.2 mg of *(4)*, m.p. 140 °C (dec.).

Received: September 6, 1979 [Z 454 IE]
German version: Angew. Chem. *92*, 403 (1980)
Publication delayed at authors' request

CAS Registry numbers:
(1a), 73557-33-2; *(1b)*, 73557-32-1; *(2a)*, 73557-31-0; *(2b)*, 73557-30-9; *(3)*, 73557-29-6; *(4)*, 73557-28-5; η^7-$C_7H_7W(CO)_2I$, 12082-10-9; $(CO)_4W(\mu\text{-SePh})_2W(CO)_4$, 73544-65-7; η^7-$C_7H_7W(CO)_2SePh$, 73557-27-4; $Pb(SEt)_2$, 32812-83-2; $Pb(SBu)_2$, 32812-85-4

[1] a) *D. Mohr, H. Wienand, M. L. Ziegler*, J. Organomet. Chem. *134*, 281 (1977); b) *K. Weidenhammer, M. L. Ziegler*, Z. Anorg. Allg. Chem. *455*, 29 (1979).

[2] IR. ν_{CO} [cm^{-1}]: *(2a)* 2010 vs, 1905 vs; *(2b)* 2010 vs, 1910 vs; *(4)* 2020 vs, 1925 vs (CH_2Cl_2). — ^{1}H-NMR (90 MHz, $CDCl_3$, TMS int., δ values): *(2a)* 1.03(3) t, $J=7.5$ Hz; 1.30(3) t, $J=7.5$ Hz; 1.53(6) t, $J=7.5$ Hz; 1.59(3) t, $J=7.5$ Hz [CH_3]; 2.15(4) q, $J=7.5$ Hz; 2.89—3.33(6) m [CH_2]; 5.16(7) s [C_7H_7]. *(2b)* 5.15(7) s [C_7H_7]; 0.75—3.25 non-resolved, superposed multiplets [*n*-C_4H_9]; intensity ratio $C_7H_7:C_4H_9=1:6.5$.

[3] *(2b)* forms monoclinic crystals from *n*-pentane, C_{2h}^5-$P2_1/c$, $a=1156.9(7)$, $b=1680.9(4)$, $c=2083.9(5)$ pm, $\beta=92.26(2)^\circ$, $Z=4$. 4313 independent reflections, $R=0.087$.

[4] *L. F. Dahl, E. R. DeGil, R. D. Feltham*, J. Am. Chem. Soc. *91*, 1653 (1969).

[5] *M. Hohmann*, Diplomarbeit, Universität Heidelberg 1978.

OH Clusters with Homodromic Circular Arrangement of Hydrogen Bonds

By *Wolfram Saenger* and *Klaus Lindner*[*]

The general significance of circular hydrogen bonds[1] for the structure of water and the structure of the hydration sheaths of macromolecules[2] was underscored in a recent article. Three kinds of circular H bonds were distinguished, depending upon whether the interactions between OH groups act in the same sense *(homodromic)*, in an opposing sense *(antidromic)*, or in irregular fashion *(heterodromic)* (Fig. 1). As discussed in reference[1], rings and "infinite" chains with homodromic H bonds are stabilized by the cooperative effect[3]; as a consequence of this effect, an OH group which is already an H bond donor/acceptor exhibits enhanced acceptor/donor properties.

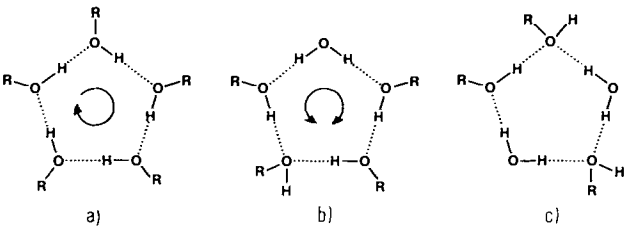


Fig. 1. Three types of circular H bonds: a) having the same sense (homodromic); b) opposing sense (antidromic); c) not having any particular direction (heterodromic) [1].

In a subsequent discussion[4] it was mentioned that, by virtue of its special topography, the water molecule must favor a circular arrangement of H bonds, and the contribution of the cooperative effect therefore appears questionable. However, on the other hand, quantum chemical calculations[4b,5] show (i) that cooperativity leads to a considerable gain in energy and (ii) that rings with homodromic H bonds possess considerably smaller dipole moments than other cyclic and catenary structures. Two further rings with homodromic H bonds will now be considered which support these results.

While the previous study[1] was based on a neutron diffraction analysis of α-cyclodextrin hexahydrate (modification *A*), a detailed and well refined ($R=3.7\%$ for 4500 data) X-ray structure analysis is now available for a second modification (*B*) of α-CD · $6H_2O$ which exhibits a different molecular packing and hence differing H bonds in the crystal lattice from modification *A*. The unit cell contains a total of four $C_{36}H_{60}O_{30}\cdot 6H_2O$ [*i.e.* $(C_6H_{10}O_5)_6\cdot 6H_2O$] units, which are stabilized by $4\times(18+12)=120$ O H···O H bonds. Since all the H atoms except one on water molecule W(5) (see Fig. 2 for nomenclature) could be localized, the H bonds are unequivocally defined. Figure 2 shows a small section from the crystal structure. Primary (O(6)—H) and secondary (O(2)—H; O(3)—H) hydroxy groups of the cyclodextrins are

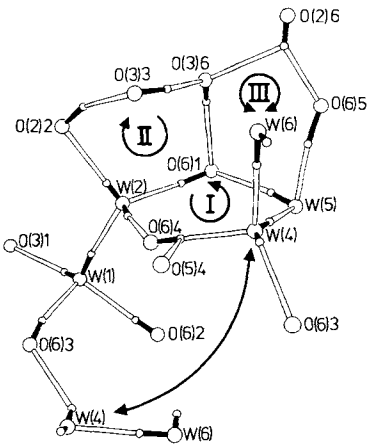


Fig. 2. The OH cluster in α-CD · $6H_2O$ (modification *B*). The rings with homodromic H bonds are designated I and II; the arrows show the directions of the O H···O bonds. Ring III having antidromic H bonds contains a bifurcated H bond emanating from O(2)6 H. An "infinite" chain of homodromic H bonds shown by a double arrow from water molecule W(4) to the symmetrically equivalent W(4) goes through the crystal lattice. Water molecules are indicated by W(1) to W(6), and hydroxy groups of α-cyclodextrins by O(2)*n*, O(3)*n*, O(6)*n*, where *n* (= 1 to 6) is the number of glucose units in the α-CD molecule. O(5)4 refers to the ring O atom in glucose unit No. 4. O═o=O H bond, o⊃O=H···O bond.

[*] Prof. Dr. W. Saenger, Dipl.-Phys. K. Lindner
Max-Planck-Institut für experimentelle Medizin, Abteilung Chemie
Hermann-Rein-Strasse 3, D-3400 Göttingen (Germany)

shown, which together with the water molecules W(1), W(2), W(4), W(5), W(6) form a H-bond stabilized cluster. This is a component of a homodromic chain structure W(4) H···O(6)3 –H···W(1)– H··· *etc.*, which continues infinitely through the crystal lattice and reveals the influence of the cooperative effect.

The actual OH cluster is formed by two "five-membered" rings (I and II) with homodromic H bonds. The two rings share the O(6)1 –H···W(2) interaction and must therefore run in a mutually opposing sense, as indicated by the arrows. A particular feature is ring III, which contains a bifurcated H bond emanating from O(2)6– –H. This initiates two chains of H bridges, which meet at the O(6)1 atom. Thus while in the previously described rings with antidromic H bonds (cf. Fig. 1b) opposing chains emanated from a water molecule, an H atom is to be regarded as origin in the present case.

The O···O distances of the H bonds systems shown in Figure 2 lie in the "normal" region of 2.67 to 2.97 Å. The H···O distances lie between 1.87 and 2.13 Å and are thus significantly shorter than the sum of the van der Waals distances for H and O (2.6 Å)[6]. The bifurcated bridge is unsymmetrical: H···O(6)5 is 2.00 Å and H···O(3)6 is 2.41 Å. These data are consistent with the results of neutron diffraction analyses[3a].

The angle in a regular pentagon is 108°, and the sum of the angles is therefore 540°. The O···O···O angles in rings I and II lie between 96 and 118° and between 89 and 112°, respectively; however, the sum of the angles only approaches the ideal value in ring I (533°); that in ring II (495°) shows considerable deviation and thus reveals puckering. The coordination tetrahedra around the water molecules W(2), W(4), and W(5) are well formed with O···O···O angles of 84 to 125° while the angles around W(1) range between 82 and 157°. Viewed overall, these geometric data meet expectations more closely than those for modification *A*[1] in which one of the water molecules shows trigonal-planar coordination.

The present cluster structure of circular homodromic H bonds clearly shows that the cooperative effect has a decisive influence on the formation and direction of the H bonds. If this effect were inoperative then an almost random distribution of H bonds would be present such as is found neither in modification *A*[1] nor in modification B. Thus not only the topological effects discussed in ref.[4a] come into play on assembly of water molecules themselves or with hydroxy groups, but cooperativity makes a decisive contribution to stabilization of the aggregates[4b]. Rings with five or six O atoms are formed preferentially. This has mainly topological reasons, since the corresponding endocyclic O···O···O angles lie between 100 and 120 °C and thus correspond to the orientation of the H atoms and the orbitals of the hydroxy groups. Smaller and larger rings would require less favorable geometries and tend to rearrange to the preferred rings.

Received: November 8, 1979 [Z 455 IE]
German version: Angew. Chem. 92, 404 (1980)

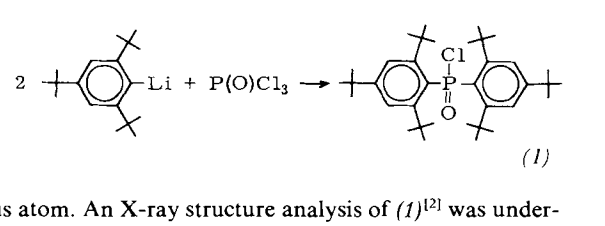
CAS Registry numbers:
α-Cyclodextrin hexahydrate, 37913-57-8

[1] *W. Saenger*, Nature *279*, 343 (1979).
[2] *J. L. Finney*, Phil. Trans. R. Soc. *B 278*, 3 (1977); *P. Barnes* in *C. A. Croxton*: Progress in Liquid Physics. Wiley, Chichester 1978, p. 381.
[3] a) *G. A. Jeffrey, S. Takagi*, Acc. Chem. Res. *11*, 264 (1978); b) *J. E. Del Bene, J. A. Pople*, J. Chem. Phys. *52*, 4858 (1970); *58*, 3605 (1973).
[4] a) *J. L. Finney*, Nature *280*, 848 (1979); b) *W. Saenger, ibid. 280*, 848 (1979).
[5] *B. Lesyng, W. Saenger*, to be published.
[6] Handbook of Chemistry and Physics. CRC Press, Cleveland 1977, p. D 178.

A Very Crowded Molecule: X-Ray Crystallographic Analysis of Bis(2,4,6-tri-*tert*-butylphenyl)phosphinic Chloride[**]

By *Masaaki Yoshifuji, Ichiro Shima, Naoki Inamoto, Ken Hirotsu,* and *Taiichi Higuchi*[*]

We have recently synthesized the highly substituted title compound *(1)* from 2,4,6-tri-*tert*-butylphenyllithium and phosphorus oxide trichloride[1]. In *(1)*, two very bulky 2,4,6-tri-*tert*-butylphenyl groups are attached to the same phosphorus atom. An X-ray structure analysis of *(1)*[2] was undertaken in order to investigate the large steric congestion expected around the phosphorus atom. As can be seen from Figure 1 and Table 1, the two benzene rings assume unusual distorted boat forms; each "boat" is almost an image of the other.



(1)

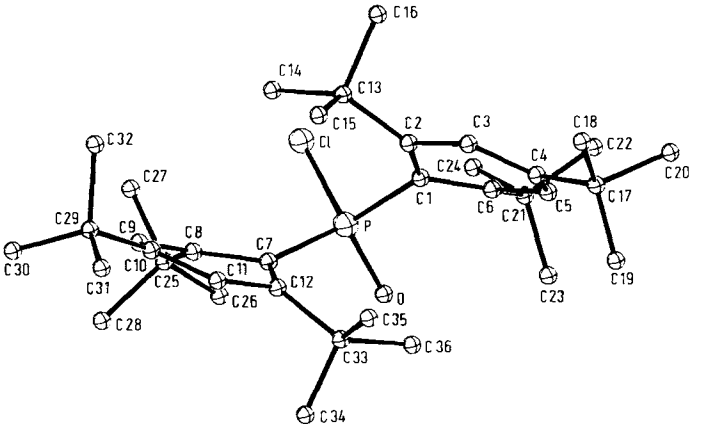


Fig. 1. Molecular structure of *(1)* in the crystal. Bond angles:
C(1) C(2) C(13) = 130.4°, C(3) C(2) C(13) = 112.0°,
C(1) C(6) C(21) = 129.0°, C(5) C(6) C(21) = 112.3°,
C(7) C(8) C(25) = 127.8°, C(9) C(8) C(25) = 115.0°,
C(7) C(12) C(33) = 125.1°, C(11) C(12) C(33) = 116.1°.

The interplanar angles of 17.8° between planes 1 and 2 and of 19.1° between planes 4 and 5 are even larger than the corresponding average values of 13.7° in [2.2]paracyclophane diolefin[4] and of 16.8° in [7]paracyclophane-3-carboxylic acid[5]. Moreover, the exocyclic bonds C(1) P and C(7)—P form angles of 10.9° and 9.1° to the planes 2 and 5, respectively, while planes 3 and 6 are bent at angles of 9.8° and 10.8°, respectively, to the planes 1 and 4. In the case of the *tert*-butyl groups, C(13) is situated 0.21 Å above the plane defined by C(1), C(2), and C(3); in addition, C(21),

[*] Prof. Dr. N. Inamoto [+], Dr. M. Yoshifuji [***], Dipl.-Chem. I. Shima
Department of Chemistry, Faculty of Science
The University of Tokyo, Hongo, Tokyo 113 (Japan)
Dr. K. Hirotsu [+], Prof. Dr. T. Higuchi
Department of Chemistry, Faculty of Science
Osaka City University, Sumiyoshi, Osaka 558 (Japan)
[+] Authors to whom correspondence should be addressed.

[**] This work was supported in part by the Scientific Research Fund of the Ministry of Education of Japan (No. 464163). We thank Prof. Dr. *K. Nakatsu* for the use of the automatic diffractometer at Kwansei Gakuin University (Hyogo, Japan).

[***] Present address: Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, Universitätstrasse 16, CH-8006 Zürich (Switzerland).

Table 1. Deviations of atoms from mean planes, interplanar angles, and intramolecular short contacts in *(1)*.

Plane	Atoms defining plane	Deviations [Å]
1	C(2), C(3), C(5), C(6)	C(2), 0.02; C(3), −0.02; C(5), 0.02; C(6), −0.02; C(1), 0.22; C(4), 0.12; C(13), −0.40; C(21), −0.42; P, 1.12
2	C(1), C(2), C(6)	P, 0.35
3	C(3), C(4), C(5)	C(17), −0.11
4	C(8), C(9), C(11), C(12)	C(8), −0.01; C(9), 0.01; C(11), −0.01; C(12), 0.01; C(7), 0.25; C(10), 0.14; C(25), −0.52; C(33), −0.52; P, 1.13
5	C(7), C(8), C(12)	P, 0.30
6	C(9), C(10), C(11)	C(29), −0.09

Interplanar angles between

1 and 2 = 17.8°;	1 and 3 = 9.8°;	4 and 5 = 19.1°;	4 and 6 = 10.8°

Intramolecular short contacts [Å]

Cl/C(14) = 3.16;	Cl/C(24) = 3.28;	Cl/C(25) = 3.33;	Cl/C(26) = 3.30;
Cl/C(27) = 3.22;	O/C(23) = 3.01;	O/C(24) = 3.06;	O/C(36) = 3.03;
C(1)/C(36) = 3.22;	C(7)/C(14) = 3.24		

C(25), and C(33) deviate by 0.08, 0.21, and 0.31 Å, respectively, from the corresponding planes. The angle C(1)—C(2)—C(13) is opened to a value of 130.4° with a consequent compression of the angle C(3)—C(2)—C(13) to 112.0°. Similar deformations were found for the exocyclic bond angles at positions C(6), C(8), and C(12). The intramolecular distances given in Table 1 are 0.4—0.5 Å shorter than the expected van der Waals distances ($CH_3/C_{aromatic}$ = 3.7, CH_3/Cl = 3.8, and CH_3/O = 3.4 Å). These short contacts are indicative of the high strain within the molecule *(1)* and lead to the remarkable boat forms of the two benzene rings and to the deformation of the bond angles[6]. To our knowledge this is the first example where non-bridged benzene rings prefer a boat form because of strong intramolecular repulsion.

Received: February 18, 1980 [Z 457 IE]
German version: Angew. Chem. *92*, 405 (1980)

CAS Registry number:
(1), 73557-52-5

[1] *M. Yoshifuji, I. Shima, N. Inamoto*, Tetrahedron Lett. *1979*, 3963.

[2] *(1)* monoclinic single crystals grown slowly from pentane, space group $P2_1$, a = 14.939(6) Å, b = 10.924(2) Å, c = 11.136(4) Å, β = 101.8(1)°, Z = 2 [3]; 2444 diffractometer data measured by ω scan with $Mo_{K\alpha}$ radiation up to 2θ = 46°, of which 473 were regarded as unobserved ($I < 2\sigma(I)$). The structure was solved by heavy atom methods and refined to a standard crystallographic residual of R = 0.08 by least squares methods.

[3] An arbitrary single crystal was removed and its optical activity was measured: $[\alpha]_D^{30} = 106.6°$ (c, 0.15, hexane). It should be noted that resolution occurs on slow recrystallization of *(1)*.

[4] *C. L. Coulter, K. N. Trueblood*, Acta Crystallogr. *16*, 667 (1963).

[5] *N. L. Allinger, T. J. Walter, M. G. Newton*, J. Am. Chem. Soc. *96*, 4588 (1974).

[6] ^{1}H- and ^{13}C-NMR spectra were complicated owing to decreased molecular symmetry of *(1)* because of large steric hindrance (cf. [1]).

α-D-Glucuronides of 1-(*N*-Alkyl-*N*-nitrosoamino)alkyl Alcohols[**]

By *Horst Braun* and *Manfred Wiessler*[*]

1-(*N*-Alkyl-*N*-nitrosoamino)alkyl alcohols are now designated as proximate carcinogens of *N*-nitrosodialkylamines[1]. It is known that xenobiotics are hydroxylated in the organism and after conjugation with glucuronic acids are excreted *via* the kidney as β-*O*-glucuronides. This process is regarded as detoxification, but there are indications that glucuronides may also be transport forms of highly reactive proximate or ultimate carcinogens[2]. Since their release, due to pH or content of β-glucuronidase, can be organ-specific, the *O*-glucuronides of α-hydroxylated *N*-nitrosodialkylamines might be responsible for their pronounced organotropic action[3]. We now report the first synthesis of the title compounds, *i.e.* the glucuronides of α-hydroxylated *N*-nitrosodialkylamines.

Since stable α-hydroxylated *N*-nitrosodialkylamines are still unknown, while the corresponding α-chlorinated compounds have been reported[4], only an inverse Königs-Knorr reaction[5] was feasible; the nature of the linkage (α or β) should depend upon the glucuronic acid employed. We used methyl 2,3,4-tri-*O*-acetyl-D-glucuronate *(2)*[6], which exists in the α form[7].

Reaction of *(1b)*[4] with *(2)* at 0 °C in the presence of a molar amount of $BF_3 \cdot Et_2O$ and with addition of pyridine[8] gave the α-D-glucuronide *(3a)* in 20% yield (see Table 1) after work-up and chromatography on silica gel (CH_2Cl_2/ether/hexane, 10:7:5). Compounds *(3b)* and *(3c)* are obtained analogously. The coupling constants of 1-*H* and 2-*H* show the compounds *(3)* to belong to the α-series. All attempts to prepare *(3d)*, *(3e)*, or *(3f)* under the same conditions have been unsuccessful[9].

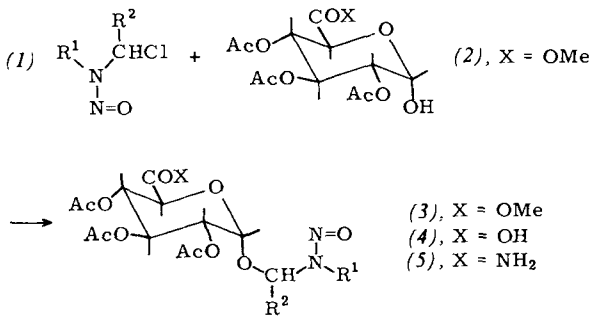


Table 1. Selected properties of products of types *(3)*, *(4)*, and *(5)*. *d*: $R^1 = CH_3$, R^2 = H; *e*: $R^1 = C_2H_5$, $R^2 = CH_3$; *f*: R^1—R^2 = $(CH_2)_3$ [a].

	R^1	R^2	M.p. [°C]	^{1}H-NMR [b]
(3a)	*n*-C_3H_7	H	Oil	0.87 (3H, t, 7 Hz), 2.05 (9H, s), 3.77 (3H, s), 5.57 (1H, d, 2Hz)
(3b)	*i*-C_3H_7	H	Oil	1.20 (6H, d, 7 Hz), 2.05 (9H, s), 3.77 (3H, s), 5.73 (1H, d, 2 Hz)
(3c) [c]	*t*-C_4H_9	H	125 (Ether)	1.60 (9H, s), 2.00 (9H, s), 3.77 (3H, s), 5.33 (1H, d, 2 Hz)

	M.p. [°C]	UV [a]	^{1}H-NMR [b]
(4a)	Resin	300 (200), 230 (4300)	0.80 (3H, t), 1.50 (2H, q), 4.87 (1H, d, 2 Hz), 5.56 (2H, m)
(4b)	Resin	300 (350), 230 (4280)	1.17 (6H, d, 7 Hz), 5.63 (2H, s)
(4c)	86	300 (100), 234 (510)	1.55 (9H, s), 4.75 (1H, d, 2 Hz), 4.95 (2H, s)

	M.p. [°C]	UV [d]	^{1}H-NMR [b]
(5a)	128	300 (190), 230 (6000)	0.80 (3H, t, 7 Hz), 1.50 (2H, q), 4.80 (1H, d, 2 Hz), 5.65 (2H, m)

[a] Correct elemental analyses were obtained for all the new compounds. Only those NMR are included which could be unequivocally assigned. [b] In $CDCl_3$, δ values, coupling constants J. [c] ^{13}C-NMR ($CDCl_3$): δ = 95.8; UV (CH_3OH): λ = 300 (ε = 180), 234 nm (5150). [d] In CH_3OH, λ [nm] (ε).

[*] Priv.-Doz. Dr. M. Wiessler, H. Braun
Institut für Toxicologie und Chemotherapie,
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280, D-6900 Heidelberg (Germany)

[**] We wish to thank *G. Riethmüller*, Max-Planck-Institut für medizinische Forschung Heidelberg, for performing numerous analyses.

Since the same yields were obtained with pyridine alone as base (without addition of $BF_3 \cdot Et_2O$) we replaced the pyridine by a cross-linked polyvinylpyridine[10]; the reaction was accelerated without any loss of selectivity.

Hydrolysis with 10% methanolic KOH and chromatography on Dowex 50 WX (50—100 mesh, H^+ form/H_2O) led to the glucuronic acids *(4a)*, *(4b)*, and *(4c)* (see Table 1). The ^{1}H-NMR data again confirm that the compounds belong to the α-series.

That the acids *(4)* do not undergo any change under the acidic conditions of ion exchange was demonstrated in the following way: Reaction of *(3a)* with NH_3/CH_3OH gave the same amide *(5a)* (m.p. 128 °C) as was obtained on treatment of the glucuronic acid *(4a)* with an ethereal solution of diazomethane and subsequently with NH_3/CH_3OH.

Received: September 24, 1979 [Z 459 IE]
German version: Angew. Chem. *92*, 407 (1980)

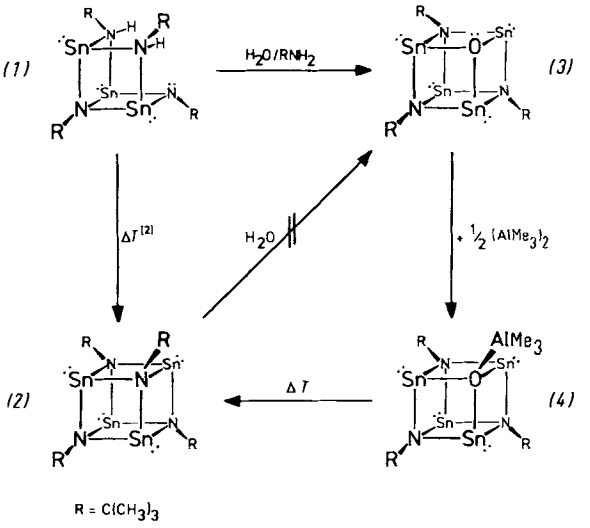
CAS Registry numbers:
(1a), 73558-95-9; *(1b)*, 73558-96-0; *(1c)*, 53198-40-6; *(2)*, 72692-06-9; *(3a)*, 73558-97-1; *(3b)*, 73558-98-2; *(3c)*, 73558-99-3; *(4a)*, 73559-00-9; *(4b)*, 73559-01-0; *(4c)*, 73559-02-1; *(5a)*, 73559-03-2

[1] *E. C. Miller*, Cancer Res. *38*, 1479 (1978); *R. E. Lyle, H. M. Fribush, S. Singh, F. E. Saavedra, G. G. Lyle, R. Barton, S. Yoder, M. K. Jacobson*, ACS Symp. Ser. *101*, 39 (1979).
[2] *K. W. Bock*, Arch. Toxikol. *39*, 77 (1977); see also *W. Forth, D. Henschler, W. Rummel:* Allgemeine und spezielle Pharmakologie und Toxikologie. Wissenschaftsverlag B.I., Mannheim 1977.
[3] *H. Druckrey, R. Preussmann, S. Ivankovic, D. Schmähl*, Z. Krebsforsch. *69*, 103 (1967).
[4] *M. Wiessler*, Angew. Chem. *86*, 817 (1974); Angew. Chem. Int. Ed. Engl. *13*, 743 (1974); ACS Symp. Ser. *101*, 57 (1979); see also *J. E. Baldwin, A. Scott, S. E. Branz, S. R. Tannenbaum, L. Green*, J. Org. Chem. *43*, 2457 (1978).
[5] Cf. *R. Brossmer, V. Eschenfelder*, Justus Liebigs Ann. Chem. *1974*, 967.
[6] *N. Pravdic, K. Keglevic*, J. Chem. Soc. *1964*, 4633; *W. D. S. Bowering, T. E. Timell*, J. Am. Chem. Soc. *82*, 2827 (1960).
[7] ^{1}H-NMR ($CDCl_3$): $\delta = 5.50$, $J = 2$ Hz; ^{13}C-NMR ($CDCl_3$): $\delta = 95.3$. The C-1 atom can also be unequivocally assigned in the ^{13}C-NMR Spectrum, for the ^{13}C signal for C-1 of the glucuronic acids is shifted by about 3 ppm upfield in the β series; methyl 2,3,4-tri-*O*-acetyl-1-*O*-benzyl-β-D-glucuronate: ^{13}C-NMR ($CDCl_3$): $\delta = 99.4$.

A Cubane-Type Sn_4N_3O Cage[1]

By *Michael Veith* and *Holger Lange*[*]

Having already synthesized the oligomeric "iminostannylenes" *(1)* and *(2)*[2] we have now succeeded in incorporating both tin(II) and nitrogen atoms as well as an oxygen atom into such cage molecules. As shown by the reaction scheme



it is surprisingly only the open cage *(1)*, and not the closed cage *(2)*, which can be transformed by incomplete hydrolysis into the oxa derivative *(3)*. The cubane-type structure of *(3)* is revealed by the ^{1}H-NMR spectrum (Table 1), which shows only one signal for the three *tert*-butyl groups. Proof of this structure is provided by the quantitative reaction of *(3)* with trimethylaluminum to form the Lewis acid-base adduct *(4)*, whose X-ray structure characterization showed it to crystallize isotypically to *(2)*[2] (Table 1).

Table 1. Physical data and lattice constants of the compounds *(3)* and *(4)*; those of compound *(2)* are also given for the sake of comparison [2].

		(3)	*(4)*	*(2)*
		orange-yellow crystals	colorless crystals	pale yellow crystals
M.p. [°C]		180 (dec.)	196 (dec.)	260 [a]
^{1}H-NMR (in benzene; δ values, integration in parentheses)		−1.43	0.2 (1.0); −1.29 (3.0)	−1.52
High-resolution mass spectrum		$^{120}Sn_2{}^{118}Sn_2ON_3C_{12}H_{27}$	$^{119}Sn^{118}Sn_3AlON_3C_{14}H_{33}(M-15)$	
		exp. 704.8277	exp. 758.8516	
		calc. 704.8230	calc. 758.8520	
Space group		P1 (P$\bar{1}$)	$P2_1/c$	$P2_1/c$
Lattice constants [pm, °]	*a*	1275(2)	1015(1)	1033(2)
	b	1017(2)	1488(2)	1458(8)
	c	1701(2)	1741(2)	1707(8)
	α	90.9(1)	90	90
	β	102.4(1)	91.4(1)	91.8(1)
	γ	106.6(1)	90	90
V (10^6 pm^3)		2057	2630	2570
Z		4	4	4
$\rho_{calc.}$ [g/cm^3]		2.27	1.96	1.96

[a] Solid/plastic phase transition at 228 °C.

[8] Cf. *M. Kühn, A. v. Wartburg*, Helv. Chim. Acta *51*, 1631 (1968).
[9] The same behavior is observed on reaction of *(1a)* to *(1f)* with 2,3,4,6-tetra-*O*-acetyl-β-D-glucose. Once again, only the glucosides corresponding to *(3a)*, *(3b)*, and *(3c)* could be isolated, which likewise belong to the α series. In contrast, the more nucleophilic 3,4-dichlorothiophenolate reacts with *(1a)* to *(1f)* to give the thioethers in yields of 50 to 60%.
[10] *M. L. Hallensleben, M. Wurm*, Angew. Chem. *88*, 192 (1976); Angew. Chem. Int. Ed. Engl. *15*, 163 (1976).

That *(2)* and *(4)* are isotypic is hardly surprising in view of the "isosteric character" of the two molecules. If a nitrogen

[*] Prof. Dr. M. Veith, Dipl.-Chem. H. Lange
Institut für Anorganische Chemie der Technischen Universität
Pockelsstrasse 4, D-3300 Braunschweig (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0505-401 $ 02.50/0*

atom of *(2)* is replaced by an oxygen then the tertiary carbon atom must be replaced by a Group 3 element (by a boron atom for true isosteric character[3]) in order to preserve the electron balance.

The smooth reaction *(3)*→*(4)* shows that the oxygen atom still exhibits Lewis basicity in spite of threefold coordination in the polycycle *(3)* (cf. also [4]); the reason for this reactivity possibly lies in the close proximity of four lone pairs owing to bonding to three Sn^{II} atoms. On addition of the acid $AlMe_3$ one of the electron pairs is coordinated, thus reducing the electronic interaction; the O atom becomes tetracoordinate.

Under conditions of thermolysis (200 °C), the cage *(4)* affords the cage *(2)*; the expected fragment ($SnOAlMe_3$) has not yet been intercepted.

The new compounds *(3)* and *(4)* are intermediate members in the series of cubane-type cages $(SnX)_4$ (X = N or O) of *(1)* and *(2)*[2] on the one hand and the cation $Sn_4O_3OH^+$ in $Sn_{21}Cl_{16}(OH)_{14}O_6$ on the other[5]. Owing to the *tert*-butyl groups on the nitrogen atoms, compound *(3)* differs from related SnNO polycycles of lower symmetry and with weaker steric shielding[6] by being soluble in nonpolar solvents.

Procedure

H_2O (0.049 ml, 2.7 mmol) in *tert*-butylamine (5 ml) is slowly added dropwise to *(1)*[2] (7.0 g, 10.9 mmol) in *tert*-butylamine (50 ml). The light yellow solution turns orange and a precipitate appears. After refluxing for 1.5 h the reaction mixture is filtered, *tert*-butylamine is distilled off, and the residue is crystallized from anhydrous benzene. On repeated recrystallization, orange crystals of *(3)* first grow which can thus be separated from *(1)*; yield 2.5 g (44%).

$AlMe_3$ (0.2 ml, 2.1 mmol) is added to *(3)* (1 g, 1.4 mmol) in benzene (10 ml). On concentration, 0.88 g (81%) of the adduct *(4)* crystallizes.

Received: October 15, 1979 [Z 460 IE]
German version: Angew. Chem. *92*, 408 (1980)

CAS Registry numbers:
(1), 71330-79-5; *(3)*, 73574-68-2; *(4)*, 73587-38-9

[1] Cyclic Diazastannylenes, Part 9. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 8: *M. Veith*, Z. Naturforsch. *B 35*, 20 (1980).

[2] *M. Veith, M.-L. Sommer, D. Jäger*, Chem. Ber. *112*, 2581 (1979).

[3] The cage is destroyed by substitution of the tin on reaction of *(3)* with $(BMe_3)_2$.

[4] *M. Veith*, Chem. Ber. *111*, 2536 (1978).

[5] *R. Nesper, H. G. von Schnering*, Acta Crystallogr. *A 34*, 158 (1978).

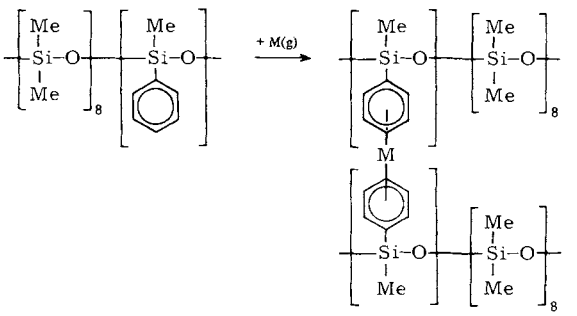
[6] *M. Veith, O. Recktenwald*, Z. Anorg. Allg. Chem. *459*, 208 (1979).

Synthesis of Organotrimetal Polymers Using Trimetal Vapor-Fluid Matrix Techniques[**]

By *Colin G. Francis, Helmut X. Huber,* and *Geoffrey A. Ozin*[*]

Supported trimetallic particle catalysts have been shown to exhibit certain advantages over their respective bimetallic counterparts, noteworthy features being enhanced stability towards segregation, sintering, and poisoning in hydrocarbon reforming processes[1]. These trimetallic compositions are usually prepared by salt impregnation techniques[2] although an attractive alternative would be to attach well-defined, organometallic clusters such as $FeRuOs_2H_2(CO)_{13}$[3] to functionalized polymers or oxide supports in a manner similar to that currently being developed for bimetallic catalyst systems[4]. However, as far as we are aware, neither polymer-anchored, three-component mononuclear nor trimetallic cluster systems have been reported previously in the open literature, although a number of two-component and bimetallic cluster analogues are known[5]. We wish to report that "organotrimetal polymers" containing three different mononuclear metal sites can be readily generated by the metal vapor-fluid matrix technique[6, 10, 11].

The fluid polymer chosen for this feasibility study was a poly(methylphenylsiloxane), Dow Corning DC510. This fluid was originally shown to react with the metal vapors of Ti, V, Cr, Mo, and W (in a metal vapor rotatory reactor) to give a liquid bisarene-organometallic polymer[9], as shown in Scheme 1.



Scheme 1.

We subsequently demonstrated[6, 10, 11] that the metal vapor-liquid polymer encounters that occur in such a reactor system (where one envisages both microscopic and macroscopic mobility in the polymer film) can be adequately simulated in a thin, static film experiment.

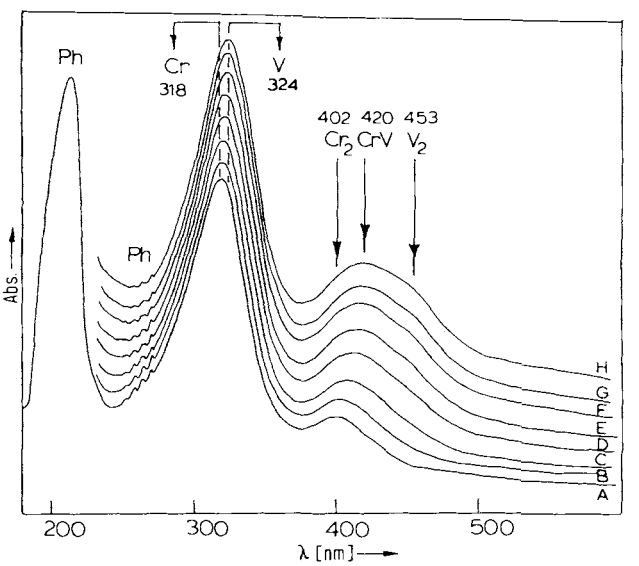


Fig. 1. UV/VIS spectra of the products of (A) a Cr vapor deposition into a thin, static film (*ca.* 10^{-6} m) of DC510 poly(methylphenylsiloxane) at 250 K, followed by (B H) roughly equal increments of V vapor. The spectra initially show the growth of polymer-attached bis(arene)chromium and polymer-stabilized dichromium, which is followed by the appearance of polymer-attached bis(arene)vanadium and polymer-stabilized divanadium and chromium-vanadium (see [10, 11]).

[*] Prof. Dr. G. A. Ozin, Dr. C. G. Francis, H. X. Huber
Lash Miller Chemical Laboratories and Erindale College
University of Toronto, Toronto, Ontario (Canada) M5S 1A1

[**] We would like to acknowledge the financial assistance of the National Research Council of Canada, Imperial Oil, the Connaught Foundation, Erindale College and the Lash Miller Chemical Laboratories. The assistance of Dr. *D. McIntosh* with the curve fitting computer analysis is greatly appreciated.

A useful probe of the extent and site of metal attachment is an intense UV metal-to-ligand charge transfer absorption associated with the polymer-anchored bis(arene)metal complex. Thus the Cr, V, and Ti/DC510 systems show MLCT absorptions at 318, 324, and 355 nm, respectively[6, 10, 11].

In a continuing effort to establish the general applicability of the multimetal vapor-liquid polymer technique, we will present initially data for the Cr/V/DC510 system followed by those for the Cr/V/Ti/DC510 system. The initial deposition of Cr into DC510 at 250 K is shown in Figure 1A, and is seen to display the MLCT band of polymer-supported bis(arene)chromium at 318 nm as well as polymer-stabilized dichromium at 402 nm.

Subsequent depositions of V into the DC510 at 250 K, close to the saturation loading, are depicted in Figures 1B—1H and show a small spectral shift of the original 318 nm band to 324 nm, corresponding to the growth of the polymer-anchored bis(arene)vanadium complex[10]. Concomitant with this growth in the MLCT region is the broadening and shifting of the polymer-stabilized dichromium band at 402 nm to eventually yield a structured band with maxima at 402, 420, and 453 nm, the latter being associated with the previously identified divanadium absorption. The new absorption, at energies intermediate between those of Cr_2 and V_2 absorptions, can be ascribed to the polymer-stabilized, bimetallic cluster CrV.

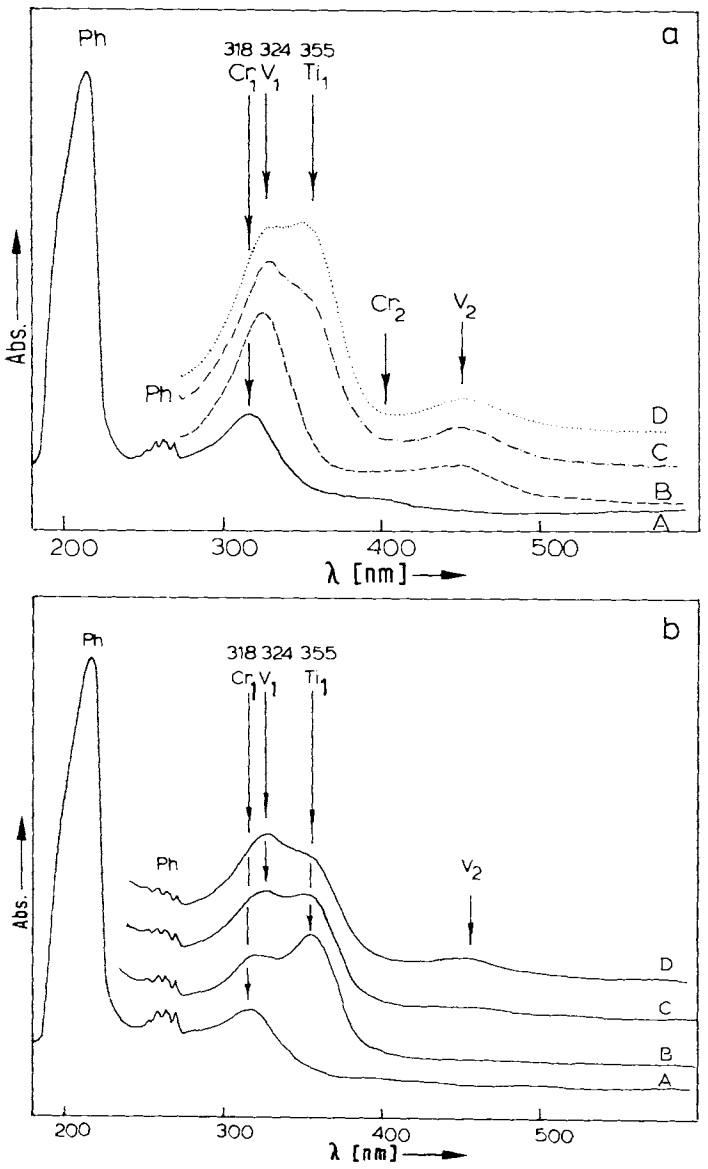


Fig. 2. UV/VIS spectra of a thin static film of DC510 held on a quartz optical window at 250 K following deposition of a) Cr (A), V (B), Ti (C, D) [10, 11] and b) Cr (A), Ti (B), V (C, D), in increments of approximately 2×10^{-6} gm.

Two kinds of experiment demonstrate the feasibility of extending the above methods to trimetallic systems. By working at least a factor of three below the saturation loading of the phenyl groups for each of the metals employed, one can turn to Figures 2a and 2b which illustrate the progress of sequentially depositing Cr/V/Ti or Cr/Ti/V respectively into a thin film of DC510 adhering to a quartz optical window maintained at 250 K. On depositing approximately 2×10^{-6} gm of chromium into the DC510, one observes the appearance of the characteristic 318 nm absorption of polymer-anchored bis(arene)chromium (Figure 2a: A) together with a small amount of the polymer-stabilized dichromium species as seen by the weak band at 402 nm[10, 11]. Deposition of a roughly equal increment of vanadium causes further growth of the MLCT absorption assigned to bis(arene)chromium but with the noticeable and anticipated red shift of the peak maximum to 324 nm (Figure 2a: B), the wavelength of anchored bis(arene)vanadium[10, 11]. Concurrently with the production of mononuclear vanadium sites, one observes the growth of some polymer-stabilized, divanadium sites indicated by the weak absorption around 453 nm[10]. Deposition of roughly equal increments of titanium into the polymer film (Figure 2a: C and D) causes additional growth in the MLCT region but with a new peak at 355 nm, depicting the generation of polymer-attached bis(arene)titanium[10, 11].

In an attempt to obtain clearer spectroscopic resolution of the bis(arene)chromium and vanadium sites, similar trimetal vapor depositions were conducted but using the deposition order Cr/Ti/V. An illustrative spectral trace is shown in Figure 2b. Following the sequential Cr/Ti depositions (Figure 2b: B), the coexistence of bis(arene)chromium and titanium on the polymer is easily discerned by the MLCT bands at 318 and 355 nm respectively[10, 11]. Further deposition of V clearly defines the continued growth in the MLCT region but with a new maximum at 324 nm (Figure 2c: C and D).

In order to resolve the existence of three absorption maxima within the envelope of Figure 2b: D, the observed spectrum was subjected to a computer curve-fitting procedure (Fig. 3)[12]. Three maxima were obtained with peak positions

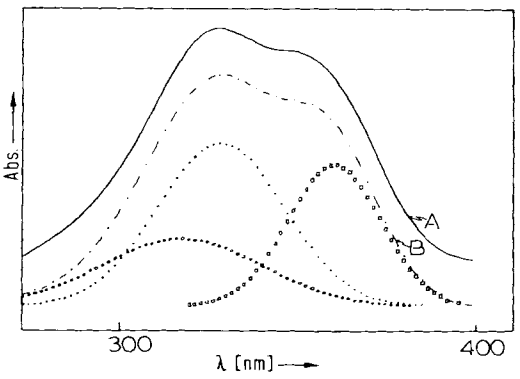


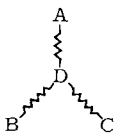
Fig. 3. A triple-Gaussian computer fit of the MLCT absorptions of polymer-anchored bis(arene)chromium, -vanadium, and -titanium. A, observed spectrum (see Fig. 2b, D); B, computer curve fitted spectrum.

corresponding to those for the MLCT absorptions of the individual bis(arene)metal complexes on the polymer.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0505-403 $ 02.50/0

Experimental

The method essentially involves the deposition of the three chosen metals into a thin, viscous film of a functionalized liquid polymer at close to room temperature. The creation of the distinct, polymer-anchored metal sites is conveniently monitored by means of UV-visible spectroscopy of the fluid sample adhering to a quartz optical window attached to the second stage of a Displex closed-cycle helium refrigeration system. The vacuum furnace employed for these trimetal vapor experiments has not been previously described but is a straightforward modification of the arrangement used for our earlier bimetal vapor work[7]. The device consisted of a water-cooled, four-electrode-flange assembly (illustrated below) having a triangular electrode configuration of live terminals (A, B, C) around a central ground terminal (D). The three different evaporation sources were connected radially (A—D, B—D, C—D) and heated directly and independently by passage of AC. The rate of deposition of the metals was monitored by three *in situ* quartz crystal microbalances[8] aligned behind each metal vapor source. Radiation shields were appropriately positioned between the evaporation sources, liquid polymer sample, and quartz crystals. The geometrical correction factor for this trimetal deposition configuration was determined by replacing the sample window by a fourth mass monitor, thereby permitting a calibration of the forward-to-backward flux for each metal. Chromium metal was vaporized from a tantalum Knudsen cell (wall thickness 0.010″, orifice diameter 0.020″) while vanadium and titanium metal depositions were achieved from thin (0.015″) filaments of the metal. All metals were better than 99.95% as supplied by A. D. McKay, New York.



Received: January 2, 1980 [Z 461 IE]
German version: Angew. Chem. 92, 409 (1980)

CAS Registry numbers:
Cr, 7440-47-3; Ti, 7440-32-6; V, 7440-62-2.

[1] *J. H. Sinfelt*, US Pat. 3953368 (April 27, 1976); Acc. Chem. Res. *10*, 15 (1977), and references cited therein.
[2] *J. J. Burton, R. L. Garten:* Advanced Materials in Catalysis. Academic Press, New York 1977, and references cited therein.
[3] *G. L. Geoffroy, W. L. Gladfelter*, J. Am. Chem. Soc. 99, 304 (1977).
[4] *M. Ichikawa*, J. Catal. *59*, 67 (1979), and references cited therein.
[5] *C. E. Carraher, Jr., J. E. Sheats, C. U. Pittman, Jr.:* Organometallic Polymers. Academic Press, New York 1978; *C. U. Pittman, Jr., L. R. Smith*, J. Am. Chem. Soc. 97, 1749 (1975); *R. Pierantozzi, K. J. McQuade, B. C. Gates, M. Wolf, H. Knözinger, W. Ruhmann*, J. Am. Chem. Soc. *101*, 5436 (1979); *J. M. Basset, A. K. Smith* in *M. Tsutsui, R. Ugo:* Fundamental Research in Homogeneous Catalysis, Vol. 1. Plenum Press, New York 1978, and references cited therein.
[6] *C. G. Francis, H. Huber, G. A. Ozin*, Inorg. Chem. *19*, 219 (1980).
[7] *W. Klotzbücher, G. A. Ozin, J. G. Norman, Jr., H. J. Kolari*, Inorg. Chem. *16*, 2871 (1977).
[8] *M. Moskovits, G. A. Ozin*, J. Appl. Spectrosc. *26*, 487 (1972).
[9] *C. G. Francis, P. L. Timms*, J. Chem. Soc. Chem. Commun. *1977*, 466; *C. G. Francis, P. L. Timms*, J. Chem. Soc. Dalton Trans., in press.
[10] *C. G. Francis, G. A. Ozin:* Proceedings of the EUCMOS Conference, Frankfurt, September 1979, in Spectroscopy in Chemistry and Physics. Elsevier, Amsterdam 1979; J. Mol. Struct. *59*, 55 (1980).
[11] *C. G. Francis, H. Huber, G. A. Ozin*, J. Am. Chem. Soc. *101*, 6250 (1979).
[12] A least squares analysis was performed using the SIMPLEX optimization method of *J. A. Nelder* and *R. Mead*, Computer J. 7, 308 (1965). The program used was that of *D. F. McIntosh* and *M. R. Peterson* (Program 3 of Program 342, Quantum Chem. Program Exchange, Indiana Univ.).

Distribution of Terminal and Bridging CO-Groups in an Anionic Carbonylmetal Cluster as a Result of Ion-Pair Formation. Crystal and Molecular Structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$[**]

By *Hans-Norbert Adams, Giuseppe Fachinetti,* and *Joachim Strähle*[*]

The interaction between highly acidic countercations and carbonyl groups of mononuclear carbonylmetalates in solvents of relatively poor coordinating ability has already been demonstrated[1], and examples are also known of interactions of this sort in the solid state[2]. The increased reactivity of mononuclear carbonyl metalates towards alkyl halides[3a] and molecular oxygen[3b] has been interpreted on this basis. Anionic carbonylmetalates, however, have not been studied under "acidic" conditions (*i.e.* in weakly coordinating solvents and with countercations of very high charge density), so comparable cation-anion interactions could previously not be observed[4].

We have now succeeded in preparing single crystals of diisopropyl ether solvated $LiCo_3(CO)_{10}$, as product of the reac-

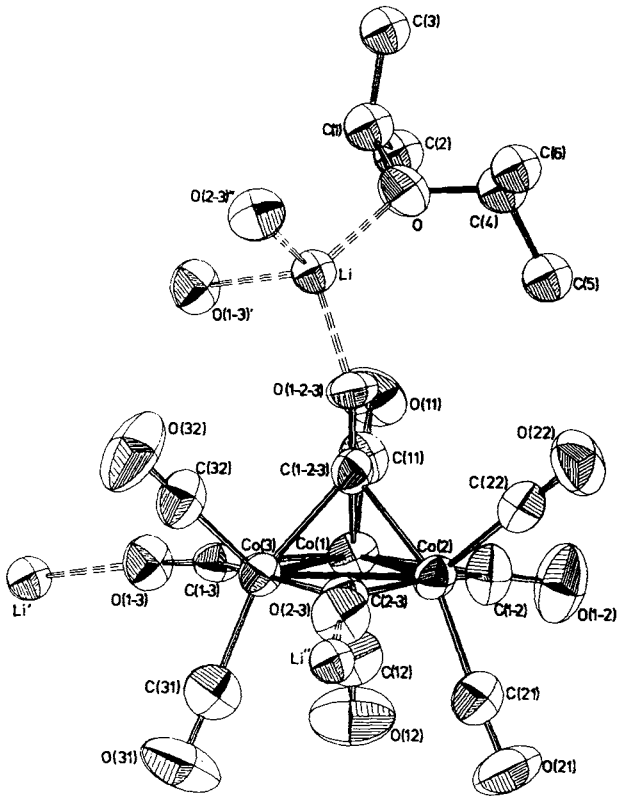


Fig. 1. Molecular structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$. Some important distances [Å] are: Co(1) Co(2) 2.489(1), Co(1) Co(3) 2.472(1), Co(2) Co(3) 2.462(1); average Co C(terminal) 1.800; average C O(terminal) 1.123; average Co C(bridging) 1.956; C(1-2) O(1-2) 1.137(8); C(1-3) O(1-3) 1.164(7); C(2-3) O(2-3) 1.164(7); average Co C(1-2-3) 2.013; C(1-2-3) O(1-2-3) 1.190(7).

[*] Prof. Dr. J. Strähle, Dipl.-Chem. H.-N. Adams
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Dr. G. Fachinetti [']
University of Pisa, Istituto di Chimica Generale
Via Risorgimento 35, I-56100 Pisa (Italy)
[']Author to whom correspondence should be addressed.

[**] This work was supported by the National Research Council (C.N.R., Roma), and by the Deutsche Forschungsgemeinschaft. We thank Prof. *Fausto Calderazzo* for helpful discussions.

tion of $LiCo(CO)_4$ with $Co_4(CO)_{12}$[5]. The molecular structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$ *(1)* has been solved by X-ray diffraction methods[6]. It consists of the ions $[Co_3(CO)_{10}]^-$ and Li^+. The cations are approximately tetrahedrally surrounded by one ether oxygen (1.910(12) Å) and by three carbonyl oxygens [one μ_3-CO, 1.859(10) Å, and two μ-CO, Li–O(2-3) 1.989(10), Li–O(1-3) 2.049(10) Å] of three different cluster units.

The three cobalt atoms form an almost regular triangle, forming the base of a tetrahedron having the face-bridging carbon, C(1-2-3), at an apex. The interatomic distances and angles of the Co_3C cluster are comparable with those found in other cluster compounds of the oxymethylidyne type[7].

The IR spectrum of *(1)* as Nujol mull shows strong absorptions around 1800 cm^{-1}, in agreement with the presence of edge-bridging carbonyl groups as established by the X-ray structure analysis. This contrasts with the weak carbonyl absorption observed at 1865 cm^{-1} in ether solution[5]. These observations can be rationalized in terms of small amounts of clusters with edge-bridging carbonyl groups in solvent-dependent equilibria with clusters containing terminal carbonyl groups only. Addition of tetrahydrofuran (1—3 vol-%) to a $n\text{-}Bu_2O$ solution of *(1)*, before decomposition takes place[5], considerably decreases the intensity of the 1865 cm^{-1} band and modifies the spectral pattern associated with the face-bridging carbonyl group at about 1580 cm^{-1}, while the terminal carbonyl stretching region around 2000 cm^{-1} remains essentially unchanged: under these conditions the acidity of Li^+ supposedly is decreased through coordination to the more basic tetrahydrofuran. In the solid state the acidity of Li^+ is greatly enhanced, thus promoting the structural change to the form containing the edge-bridging carbonyl groups.

Our investigations show that dramatic structural changes can occur in an anionic carbonyl cluster by apparently small changes of the acid-base properties of the system.

Experimental

Analytically pure $LiCo_3(CO)_{10}\cdot Et_2O$ (1.3 g) was dissolved in diisopropyl ether (20 ml) and the resulting solution was concentrated to about 5 ml under reduced pressure. On addition of *n*-hexane (100 ml) and filtration, the mother liquor slowly yielded 0.5 g of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$ as black crystals. All of the operations must be carried out under purified argon.

Received: October 15, 1979 [Z 462 IE]
German version: Angew. Chem. *92*, 441 (1980)

CAS Registry numbers:
(1), 73612-21-2; $LiCo_3(CO)_{10}$, 26248-45-3

[1] *W. F. Edgell, J. Lyford, A. Barbetta, C. I. Jose*, J. Am. Chem. Soc. *93*, 6403 (1971); *W. F. Edgell, J. Lyford, ibid. 93*, 64 (1971); *M. Y. Darensbourg, D. J. Darensbourg, D. Burns, D. A. Drew, ibid. 98*, 3127 (1976).

[2] *G. Fachinetti, C. Floriani, P. F. Zanazzi, A. R. Zanzari*, Inorg. Chem. *17*, 3002 (1978); *H. B. Chin, R. Bau*, J. Am. Chem. Soc. *98*, 2434 (1976).

[3] a) *J. P. Collman, R. G. Finke, J. N. Cawse, J. I. Brauman*, J. Am. Chem. Soc. *99*, 2515 (1977); b) *M. Darensbourg, H. Barros, C. Borman, ibid. 99*, 1647 (1977).

[4] *E. L. Muetterties, T. N. Rhodin, E. Band, C. F. Bricker, W. R. Pretzer*, Chem. Rev. *79*, 91 (1979); *P. Chini, G. Longoni, V. G. Albano*, Adv. Organomet. Chem. *14*, 98 (1976).

[5] *G. Fachinetti*, J. Chem. Soc. Chem. Commun. *1979*, 396.

[6] Monoclinic, $P2_1/c$, $a = 11.322(2)$, $b = 11.943(3)$, $c = 16.557(2)$ Å, $\beta = 91.72(1)^\circ$, $Z = 4$, $\rho_{calc} = 1.68$ g/cm³; single crystal diffractometer CAD 4, $Mo_{K\alpha}$ (graphite monochromator); data collection up to $2\theta = 50^\circ$ (half sphere, 8511 reflections), merging about equivalent reflections gives 3026 independent observed ones, 15 reflections suppressed because of asymmetric background, program for crystal structure determination: SHELX-76, refinement to $R = 0.0758$ ($R_w = 0.0487$, $w = 0.058/[\sigma^2(F) + 0.002\,F^2]$) for the observed reflections.

[7] *B. Stutte, V. Bätzel, R. Boese, G. Schmid*, Chem. Ber. *111*, 1603 (1978); *V. Bätzel*, Z. Naturforsch. *B 31*, 342 (1976); *V. Bätzel, U. Müller, R. Allmann*, J. Organomet. Chem. *102*, 109 (1975); *G. Schmid, V. Bätzel, B. Stutte, ibid. 113*, 67 (1976); *F. Klanberg, W. B. Asken, L. J. Guggenberger*, Inorg. Chem. *7*, 2265 (1968).

Triple-Decker Sandwich Complexes of 4d and 5d Metals with *cyclo*-Triphosphorus as μ,η^3-Ligand: Structural and Magnetic Properties

By *Claudio Bianchini, Massimo Di Vaira, Andrea Meli,* and *Luigi Sacconi*[*]

The recent synthesis of mononuclear and dinuclear 3d metal complexes containing the *cyclo*-triphosphorus (η^3-P_3) group as a ligand[1] prompted us to attempt the synthesis of the corresponding compounds of the 4d and 5d metals. On reaction of white phosphorus (P_4) with $[Rh(C_2H_4)_2Cl]_2$ *(1)* or $Ir(PPh_3)_2(CO)Cl$ in the presence of 1,1,1-tris(diphenylphosphinomethyl)ethane (triphos) we obtained the mononuclear complexes [(triphos)M(η^3-P_3)] with M = Rh *(2)* and M = Ir *(3)*, respectively[2]. These compounds react with *(1)* and cobalt(II) or nickel(II) tetrafluoborates in the presence of triphos (and, where appropriate, of $NaBPh_4$) yielding the dinuclear compounds

[(triphos)Rh-μ-(η^3-P_3)Co(triphos)]$(BPh_4)_2\cdot 2(CH_3)_2CO$ *(4)*
[(triphos)Rh-μ-(η^3-P_3)Ni(triphos)]$(BF_4)_2\cdot C_4H_8O$ *(5)*
[(triphos)Ir-μ-(η^3-P_3)Co(triphos)]$(BF_4)_2\cdot CH_2Cl_2$ *(6)*
[(triphos)Rh-μ-(η^3-P_3)Rh(triphos)]$BPh_4\cdot(CH_3)_2CO$ *(7)*

whose cations have a triple-decker sandwich structure with *cyclo*-triphosphorus acting as central bridge-forming *trihapto ligand*. The salts *(4)*, *(5)* and *(6)* behave as 1:2 electrolytes, whereas *(7)* is a 1:1 electrolyte. They are all air-stable in the solid state, but rather unstable in solution. Compounds *(4)* and *(6)* are paramagnetic with a magnetic moment corresponding to a doublet ground state. Compound *(7)* is essentially diamagnetic at room temperature, whereas *(5)* has a magnetic moment slightly dependent on the nature of the counterion and of the solvent in the lattice, decreasing from values of 1.3—1.6 μ_B at room temperature to *ca.* 0.7 μ_B at 100 K. The magnetic behavior of *(5)* and *(7)* differs considerably from that of the previously described complexes with 32 valence electrons, which have a magnetic moment corresponding to two unpaired electrons[1]. This difference in the magnetic properties may be traced to structural differences between the compounds[3]: the η^3-P_3 bridge in *(5)* is shifted from the line joining the two metal atoms (cf. Fig. 1) in such

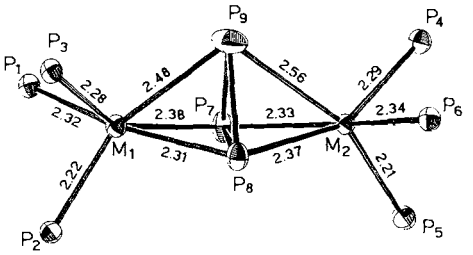


Fig. 1. Structure of the dication of *(5)*. Bond lengths in the η^3-P_3 ligand of the triple-decker complex: P7 P8 = 2.31, P7,8 P9 = 2.15 Å. Each metal site, M, has 50% Rh and 50% Ni (or 50% Co, in compound *(4)*) occupancy.—Bond lengths in complex *(4)*: M P_n = 2.21—2.22 (n = 1—6), 2.29—2.32 (n = 7—9); P_n P_m = 2.19—2.20 (n = 7, 8; m = 8, 9).

[*] Prof. Dr. L. Sacconi, Dr. C. Bianchini, Dr. M. Di Vaira, Dr. A. Meli
Istituto di Chimica Generale e Inorganica dell'Università,
Laboratorio CNR,
Via J. Nardi 39, I-50132 Firenze (Italy)

a way that the approximate C_3 symmetry existing in the structure of *(4)* as well as in those of all the analogous complexes previously investigated[1] is lost. As a consequence of this distortion the degeneracy of the highest-occupied 6e orbital[1] is lifted and a spin singlet, rather than triplet, ground state is attained. The residual paramagnetism of compound *(5)* may include a temperature independent (TIP) contribution but there may also be a contribution from partial occupation of the higher triplet state.

Procedure

Synthesis of *(4)*: A solution of *(2)* (410 mg, 0.50 mmol) in 40 ml of CH_2Cl_2 was added under nitrogen at room temperature to a mixture of $Co(BF_4)_2 \cdot 6H_2O$ (170 mg, 0.50 mmol) in 15 ml of ethanol and of the triphos ligand (320 mg, 0.50 mmol) in 20 ml of CH_2Cl_2. A solution of $NaBPh_4$ (350 mg, 1 mmol) in 10 ml of ethanol was then added. After concentration of the resulting solution brown crystals were obtained, which were recrystallized from acetone/ethanol. Yield 80%.

(5): A solution of *(2)* (410 mg, 0.50 mmol) in 80 ml of THF was added under nitrogen at room temperature to a mixture of $Ni(BF_4)_2 \cdot 6H_2O$ (170 mg, 0.50 mmol) in 30 ml of ethanol and of the triphos ligand (320 mg, 0.50 mmol) in 10 ml of THF. The resulting mixture was concentrated to 40 ml under vacuum. After standing overnight dark red crystals had separated. Yield 60%.

(6): Prepared by the same procedure as *(4)* except for substitution of compound *(3)* (450 mg, 0.50 mmol) for *(2)*. The reddish brown crystals were recrystallized from dichloromethane/ethanol. Yield 80%.

(7): Prepared by the same procedure as *(4)* except for substitution of *(1)* or $[Rh(CO)_2Cl]_2$ (0.30 mmol) for the cobalt salt; triphos (0.60 mmol), $NaBPh_4$ (0.50 mmol) in 30 ml of ethanol. Orange-red crystals; yield 70%.

Received: November 20, 1979 [Z 463 IE]
German version: Angew. Chem. 92, 412 (1980)

[1] *M. Di Vaira, S. Midollini, L. Sacconi*, J. Am. Chem. Soc. *101*, 1757 (1979), and references therein.

[2] *C. Bianchini, C. Mealli, A. Meli, L. Sacconi*, Inorg. Chim. Acta *37*, L543 (1979).

[3] Philips PW 1100 automated diffractometer. Crystallographic data of *(4)*: $a = 17.55(1)$, $b = 15.90(1)$, $c = 13.81(1)$ Å, $\alpha = 111.5(1)$, $\beta = 91.1(1)$, $\gamma = 115.4(1)°$, triclinic, space group P1, $Z = 1$; and of *(5)*: $a = 20.02(1)$, $b = 15.72(1)$, $c = 16.33(1)$ Å, $\alpha = 126.6(1)$, $\beta = 91.0(1)$, $\gamma = 93.5(1)°$, triclinic, space group P$\bar{1}$, $Z = 2$. Determination of structures with respectively 3760 and 4440 observed ($I \geq 3\sigma(I)$) structural amplitudes, refined to R values of 0.079 *(4)* and 0.065 *(5)* [Rh, Ni, Co, P, F anisotropic, Ph rigid groups].

Calcium Isotope Separation on an Exchange Resin Having Cryptand Anchor Groups[**]

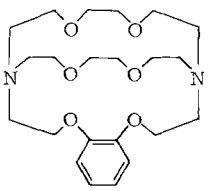
By *Klaus G. Heumann* and *Hans-Peter Schiefer*[*]

The stable heavy calcium isotopes ^{46}Ca and ^{48}Ca are of interest primarily for labeling purposes in medical research[1]. In 1977 a French research team reported the enrichment of ^{235}U by crown ethers[2]; *Jepson* and *DeWitt* were able to enrich ^{44}Ca relative to ^{40}Ca with the aid of dibenzo[18]crown-6[3]. Since some of the cryptands are known to form strong complexes with alkaline earth metals[4], we have examined calcium isotope separation on an exchange resin containing the cryptand $[2_B.2.2]$ as anchor group.

[*] Prof. Dr. K. G. Heumann, Dr. H.-P. Schiefer [***]
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[***] Present address: Centre de Recherches sur les Macromolecules, F-67083 Strasbourg (France).

$[2_B.2.2]$ 

The experiments were performed in a thermostated column of 60 cm length and 1.2 cm i.d. packed with 19 g of exchanger resin ("$[2_B.2.2]$ polymer", E. Merck). In each run 40 mg of calcium of natural isotopic composition was applied to the column as $CaCl_2$ dissolved in 1 ml of $CH_3OH/CHCl_3/H_2O$ (70:30 v/v + 1.65 vol% H_2O) and eluted at −21, 0, and 20 °C with this solvent system (*ca.* 0.5 ml/min). The calcium content of the eluate fractions was determined by flame atomic absorption spectrometry and the $^{44}Ca/^{40}Ca$ and the $^{48}Ca/^{40}Ca$ isotope ratio determined by thermionic mass spectrometry[5].

In the case of the isotope exchange reaction between $^{48}Ca^{2+}$ and $^{40}Ca^{2+}$ we find (L = solution; R = resin monomer unit):

$$R\ [2_B.2.2, {}^{48}Ca]^{2+} + {}^{40}Ca_L^{2+} \rightleftharpoons R\ [2_B.2.2, {}^{40}Ca]^{2+} + {}^{48}Ca_L^{2+} \quad (1)$$

The equilibrium constant K_c corresponds to the elementary separation factor $\alpha = 1 + \varepsilon$.

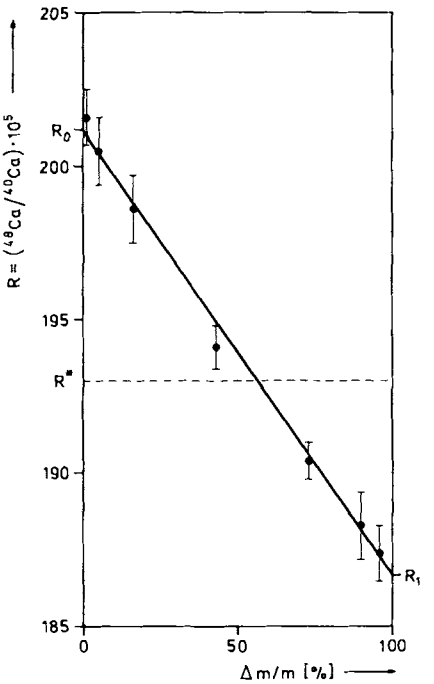


Fig. 1. Calcium isotope separation as function of the eluted amount of substance $\Delta m/m$ at 20 °C. R^* = initial isotopic ratio, R_0 and R_1 = extrapolated isotope ratio at $\Delta m/m = 0$ or 1.

Figure 1 shows the dependence of the isotopic ratio $R = {}^{48}Ca/{}^{40}Ca$ upon the amount of substance eluted $\Delta m/m$ at 20 °C. The relationship between R and $\Delta m/m$ is linear at all the temperatures investigated; unlike comparable isotope exchange reactions[7] the isotope separation increases with increasing temperature (Table 1).

In the first fractions eluted, R is higher than the initial isotopic ratio R^*, and lower in the final fractions. We therefore have an enrichment of the heavier relative to the lighter calcium isotopes in the solution. The direction of this isotopic enrichment is in accord with that of other cation exchanger/aqueous solution systems[6].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0505-406 $ 02.50/0

Table 1. Isotope separation effects in column chromatography with "[2$_B$.2.2] polymer" as function of temperature. γ (maximum separation efficiency of column) $= (R_0/R_1) - 1$; ε (isotope separation effect) $= \alpha - 1$.

T [°C]	$\gamma(^{44}Ca/^{40}Ca)$	$\gamma(^{48}Ca/^{40}Ca)$	$\varepsilon(^{44}Ca/^{40}Ca)$	$\varepsilon(^{48}Ca/^{40}Ca)$
−21	1.5×10^{-2}	2.5×10^{-2}	0.26×10^{-2}	0.45×10^{-2}
0	2.6×10^{-2}	4.9×10^{-2}	0.42×10^{-2}	0.77×10^{-2}
20	4.4×10^{-2}	7.9×10^{-2}	0.57×10^{-2}	1.04×10^{-2}

Table 1 contains the ε values determined by an approximation method commonly employed in isotope chemistry[8]. They are in good agreement with the values determined in a static experiment at 20 °C [$\varepsilon(^{44}Ca/^{40}Ca) = 0.55 \times 10^{-2}$ and $\varepsilon(^{48}Ca/^{40}Ca) = 1.21 \times 10^{-2}$].

The value of ε determined at 20 °C is by far the greatest known calcium isotope separation effect in an equilibrium step on an ion exchanger; the ε values obtained on sulfonic acid resin exchangers are up to two orders of magnitude smaller[9]. Only the isotopic separation reported for $^{44}Ca/^{40}Ca$ in an extraction system with a crown ether (*i.e.* $\varepsilon = 0.4 \times 10^{-2}$) is comparable[3]. On average $\varepsilon(^{48}Ca/^{40}Ca)$ is greater than $\varepsilon(^{44}Ca/^{40}Ca)$ by a factor of 1.8 (Table 1). This corresponds to the ratio of the relative mass difference (8/48):(4/44) = 1.83. If the logarithm of the K_c values [eq. (1)] is plotted against the reciprocal absolute temperature, then all the values lie on a van't Hoff reaction isobar whose slope gives $\Delta H(^{44}Ca/^{40}Ca) = 46$ J/mol and $\Delta H(^{48}Ca/^{40}Ca) = 87$ J/mol. The few ΔH values known so far for isotope exchange reactions on cation or anion exchangers in aqueous systems are smaller: $\Delta H(^{7}Li/^{6}Li) = -9.6$ J/mol[7b]; $\Delta H(^{37}Cl/^{35}Cl) = -5.4$ J/mol[7a].

The separation results demonstrate for the first time that the chemical pre-enrichment of heavy calcium isotopes can be realized in amounts of interest on a technical scale. For example, use of the above mentioned solvent mixture in the elution makes isolation of the enriched material a practicable proposition; the linearity between isotope separation and amount of substance eluted (Fig. 1) enables isolation of larger amounts of enriched isotope.

In a preliminary experiment, we have been able to isolate 30 mg of calcium in which ^{48}Ca was enriched by 3.3% at 0 °C from 210 mg of calcium having a natural isotope abundance[10].

Received: November 19, 1979 [Z 458 IE]
German version: Angew. Chem. 92, 406 (1980)

CAS Registry numbers:
^{44}Ca, 14255-03-9; ^{40}Ca, 14092-94-5; ^{48}Ca, 13981-76-5; cryptands [2$_B$.2.2], 31250-18-7

[1] *J. Knop, K.-H. Reichstein, R. Montz*, Eur. J. Nucl. Med. *2*, 35 (1977).
[2] Press release at Conference of Nuclear Energy, Salzburg, May 1977 (*e.g.* Frankfurter Allgemeine Zeitung, May 18, 1977).
[3] *B. E. Jepson, R. DeWitt*, J. Inorg. Nucl. Chem. *38*, 1175 (1976).
[4] *J. M. Lehn, J. P. Sauvage*, Chem. Commun. *1971*, 440.
[5] *K. G. Heumann, E. Kubassek, W. Schwabenbauer*, Z. Anal. Chem. *287*, 121 (1977).
[6] a) *K. G. Heumann, F. Gindner, H. Klöppel*, Angew. Chem. *89*, 753 (1977); Angew. Chem. Int. Ed. Engl. *16*, 719 (1977); b) *K. G. Heumann, K. H. Lieser*, Z. Naturforsch. *B 27*, 126 (1972).
[7] a) *K. G. Heumann, R. Hoffmann*, Angew. Chem. *89*, 118 (1977); Angew. Chem. Int. Ed. Engl. *16*, 114 (1977); b) *D. A. Lee*, J. Phys. Chem. *64*, 187 (1960).
[8] *E. Glueckauf*, Trans. Faraday Soc. *54*, 1203 (1958).
[9] a) *J. Aaltonen*, Suom. Kemistil. *B 44*, 1 (1970); b) *G. D. Klinskii, D. A. Knyazev, G. I. Vlasova*, Russ. J. Phys. Chem. *48*, 380 (1974); c) *D. A. Lee*, J. Inorg. Nucl. Chem. *38*, 161 (1976).
[10] *H.-P. Schiefer*, Thesis, Universität Regensburg 1979.

Acetaldehyde as Main Product of the Oxidation of Ethylene Oxide on a Silver Catalyst[**]

By *Günther Prauser, Guillermo Fischer*, and *Kurt Dialer*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

In the direct oxidation of ethylene to ethylene oxide on silver catalysts acetaldehyde is formed at most in traces. In the absence of oxygen or with substoichiometric amounts of oxygen, however, ethylene oxide also partially reacts on silver to give acetaldehyde[1,2]; thus, *e.g.*, for complete conversion of ethylene oxide at 200 °C without oxygen in the gas phase a product ratio of $CH_3CHO : C_2H_4 : CO_2 = 3 : 1 : 1.2$ was found[2]. In the presence of an excess of oxygen at 200–320 °C, on the other hand, only the total oxidation of ethylene oxide to CO_2 and H_2O has been observed[1,3].

We have studied the kinetics of the oxidation of ethylene oxide in a continuously circulating reactor between 190 and 300 °C with the aim of determining separately the undesired combustion of ethylene oxide in the direct oxidation of ethylene, and thus to be able to formulate a model for the overall reaction. To our amazement we found that acetaldehyde is formed as main product with a selectivity of up to 70% on an unmodified silver catalyst[4], even in the presence of a very large excess of oxygen (molar ratio $O_2 : C_2H_4O$ up to 50:1). In addition, CO_2 and H_2O were formed together with further by-products, of which acetic acid and crotonaldehyde were identified.

As example, Figure 1 shows a plot of the yields of acetaldehyde (Y_{AcH}) and carbon dioxide (Y_{CO_2}), as well as the yield of the remaining by-products (Y_{BP}) calculated from ($C_{EO} - Y_{AcH} - Y_{CO_2}$), over the modified residence time τ^* (where C_{EO} = ethylene oxide conversion). In this series of experiments the reaction temperature was 270 °C.

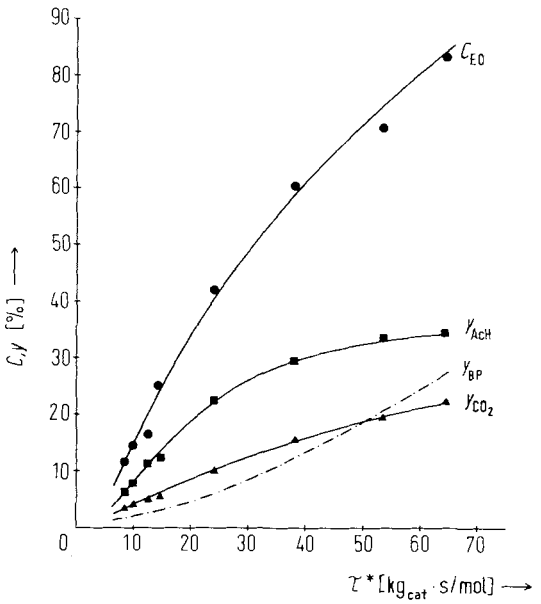


Fig. 1. Dependence of the ethylene oxide conversion (C_{EO}) and the product yields (Y) on the modified residence time τ^*. $T_R = 270$ °C, $p_R = 1.3$ bar, $x^a_{EO} = 0.0223$, $x^a_{O_2} = 0.20$, rest He.

[*] Prof. Dr. K. Dialer, Dr. G. Prauser
Institut für Technische Chemie der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)
Dr. G. Fischer
Present address: Frauenhofer Gesellschaft
D-7000 Stuttgart (Germany)

[**] This work was supported by the Max-Buchner-Forschungsstiftung.

The selectivity referred to carbon dioxide $S_{CO_2} = Y_{CO_2}/C_{EO}$ for temperatures $\leq 270\,^{\circ}C$ over a wide range of residence time is about 27%, independent of the conversion C_{EO} and of the concentration of the ethylene oxide feed. In contrast, the selectivity of the acetaldehyde $S_{AcH} = Y_{AcH}/C_{EO}$ decreases with increasing reaction temperature, increasing residence time, and increasing ethylene oxide conversion. From this behavior it can be concluded that the isomerization of the ethylene oxide runs parallel to its total oxidation and that acetaldehyde undergoes very little, if any, further combustion to CO_2 and H_2O at $T_R \leq 270\,^{\circ}C$, but reacts in a secondary reaction, predominantly to give acetic acid.

As investigations on the carrier and on mixtures of carrier and silver catalyst ($A_{spec} = 0.92\ m^2/g$) at a dilution ratio of 5:1 have shown, under the chosen reaction conditions an isomerization of ethylene oxide on the carrier material α-Al_2O_3 ($A_{spec} = 0.06\ m^2/g$) can be ruled out. Similarly, an isomerization in the gas phase during recirculation in the reactor can also be considered as unlikely. Acetaldehyde was also the main product obtained in a simple flow-through tubular reactor, even at *ca.* 300 °C and brief contact times[5].

The observed isomerization is apparently limited to unmodified silver catalysts; for example it does not take place on barium-containing catalysts[4]. Moreover, it is decisive that the ethylene oxide is re-purified by passage over silver at *ca.* 50 °C before being fed into the reactor, whereby the removal of halogen compounds would appear to play an important role.

In parallel investigations on the partial oxidation of ethylene to ethylene oxide on the same catalyst only traces of acetaldehyde were found. It can therefore be assumed that ethylene, and most likely also halogen compounds, block the sites on the surface of the catalyst where ethylene oxide isomerizes. Experience gained with oxygen-free systems would suggest the assumption of silver sites which are not covered by oxygen. Presumably, such sites are met with on unmodified silver catalysts even at high oxygen concentrations.

The demonstrated influence of ethylene on the isomerization of ethylene oxide clearly indicates that the isolated kinetic investigation of a heterogeneous catalytic partial reaction—in this case the oxidation of ethylene oxide—can lead to false conclusions regarding the relevance of this partial reaction for the overall reaction.

Received: January 2, 1980 [Z 447 IE]
German version: Angew. Chem. 92, 389 (1980)

[1] *G. H. Twigg*, Proc. R. Soc. London *A 188*, 92, 105, 123 (1946); *Y. Ide, T. Takoji, T. Keii*, Nippon Kagaku Zasshi *86*, 1249 (1965).
[2] *R. E. Kenson, M. Lapkin*, J. Phys. Chem. *74*, 1493 (1970).
[3] *A. Orzechowski, K. E. MacCormack*, Can. J. Chem. *32*, 432 (1954); *Y. V. Jonov, V. Y. Rastaturin, Y. Y. Kurochin*, Zh. Prikl. Khim. *44*, 606 (1971).
[4] *G. Fischer*, Dissertation, Technische Universität München 1979.
[5] *K. D. Wiese*, Dissertation, Technische Universität München 1979.

New Aspects of the Reaction of Difluorosulfur Imides with Fluorine[**]

By *Ingo Stahl, Rüdiger Mews*, and *Oskar Glemser*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

In fluorination reactions the product composition often depends very strongly on the reaction conditions. Thus difluorosulfur imides react with fluorine in metal autoclaves[1] (catalysis by metal fluorides) according to

$$RN{=}SF_2 + F_2 \longrightarrow RN(F){-}SF_2{-}NR{-}NR(F){-}SF_5 + \cdots$$
$$\xrightarrow{CsF} RN(F){-}SF_5 + \cdots$$

$R = CF_3, C_2F_5$

In pyrex vessels, on the other hand, reaction takes place at room temperature only on irradiation with UV light:

$$\underset{(1)}{F_5C_2N{=}SF_2} + F_2 \xrightarrow{h\nu} \underset{(2)}{\{F_5C_2NSF_3^{\oplus}\}} \rightarrow \underset{(3)}{F_5C_2N{=}SF_4} \rightarrow \underset{(4)}{F_5C_2N(F){-}SF_5}$$

$$\downarrow$$

$$\underset{(5)}{F_5C_2N{=}SF_2{-}NC_2F_5} \rightarrow \underset{(6)}{F_5C_2N(F){-}SF_4{-}NC_2F_5}$$

In this case, the simultaneous occurrence of *(3)* and *(5)* is observed IR spectroscopically—from which it can be concluded that a common intermediate (such as *(2)*) is formed. These primary products are slowly further fluorinated. If, however, the irradiation is interrupted at the correct time one obtains maximum yields of 30% of *(3)*, which is only difficultly accessible *via* alternative routes.

Addition of a further molecule of F_2 to the SN double bond of *(3)* affords the well-known[1] *N*-fluoramine *(4)*. The fluorination sequence *(1)*→*(3)*→*(4)* corresponds to that of $O{=}SF_2$ *via* $O{=}SF_4$ to $FO{-}SF_5$[2].

With the reaction step *(5)*→*(6)* it was possible for the first time to convert a tetracoordinated sulfur(VI) compound into a hexacoordinated one by F_2-addition. This addition leads stereospecifically to *trans-(6)*. An analogous reaction in the SO system to give bishypofluorites $FO{-}SF_4{-}OF$ is unknown.

Pentacoordinated tetrafluorosulfur imides such as *(3)* are of special interest on account of their stereochemistry[3]; owing to their reactivity (similar to that of $O{=}SF_4$) they should also be useful as synthetic building blocks. The hexacoordinated *N*-fluoramines *(4)* and *(6)*, on the other hand, are chemically very resistant, *e.g.* they are not attacked by water at room temperature.

Experimental

A mixture of *(1)* (100 torr) and F_2 (100—400 torr) in a 2 l pyrex flask is irradiated with a Hg high-pressure lamp (Philips 500 W; distance ≈1 cm). The duration of irradiation is dependent upon the amount of F_2, the desired products, and

^{19}F-NMR data (δ values, coupling constants in Hz) and boiling points of the compounds *(3)*, *(4)* and *(6)*.

	(3) [a]		*(4)* [b]	*(6)*
$\delta(CF_3)$	−87.4		−81.7	−81.8
$\delta(CF_2)$	−92.8		−109.95	−109.5
$\delta(NF)$			−51.0	−49.3
$\delta(SF)$	78.3	$^3J = 150$	58.7 (a)	63.9
			61.3 (e)	
$^3J(CF_3\text{-}CF_2)$	< 0.5		1.25	1.2
$^3J(CF_2\text{-}NF)$			28.3	27.8
$^3J(SF_4\text{-}NF)$			2.4	1.5
$^3J(SF\text{-}NF)$			2.5	
$^4J(CF_2\text{-}SF)$	8.9		1.7 (a)	14.0
			13.5 (e)	
$^4J(CF_3\text{-}NF)$			18.5	18.5
$^5J(CF_3\text{-}SF)$	< 1.5		< 0.2 (a)	0.5
			< 0.3 (e)	
B.p. [°C]	25		39	111

[a] Room temperature. [b] Coupling constants and b.p. of *(4)* are not given in [1].

[*] Prof. Dr. O. Glemser, Dr. I. Stahl, Priv.-Doz. Dr. R. Mews
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

the quality of the lamp. The reaction mixture was monitored semi-continuously by gas-phase IR (sampling every 2—5 min). The products were purified by fractional condensation. Besides the given products, SF_6 is also formed

(3): IR: 1315 (s), 1237 (s), 1162 (s), 1066 (m), 895 (m), 847 (s), 836 (s), 742 (m), 605 cm^{-1} (w); EI-MS: $m/e = 222$ (16%) $(M-F)^+$.—*(6):* IR: 1348 (w), 1275 w (sh), 1253 vs, 1240 s, 1222 (s), 1187 (m), 1139 (w), 1096 (s), 1066 (w), 1029 (w), 941 (w), 907 (m), 853 (w), 825 (w), 783 (vw), 755 (vw), 714 (w), 695 (m), 660 (s), 629 (vw), 613 cm^{-1} (vw); EI-MS: $m/e = 393$ (2%) $(M-F)^+$.—The data for *(4)*[1] and *(5)*[1,4] are in complete agreement with those given in the literature.

Irradiation of *(5)* (6.0 g) in the presence of an excess of fluorine affords, within 48 h, 2.5 g of *(6)* (36% yield) besides 2.0 g of *(4)* (40% yield).

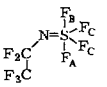
Received: January 10, 1980 [Z 453 IE]
German version: Angew. Chem. *92*, 393 (1980)

CAS Registry numbers:
(7), 4101-37-5; *(3)*, 73557-54-7; *(4)*, 4101-58-0; *(5)*, 4101-59-1; *(6)*, 73557-55-8

[1] *M. Lustig, J. K. Ruff*, Inorg. Chem. *4*, 1444 (1965).

[2] Cf. *H. Jonas*, Z. Anorg. Allg. Chem. *265*, 273 (1951); *F. B. Dudley, G. H. Cady, D. F. Eggers Jr.*, J. Am. Chem. Soc. *78*, 1553 (1956); *J. K. Ruff, M. Lustig*, Inorg. Chem. *3*, 1422 (1964).

[3] The $X_3K_2A_4$ spectrum (room temperature) converts at low temperature (coalescence point $-65\,^{\circ}C$) into a spectrum of the type $X_3K_2ABC_2$. This temperature-dependence has already been observed in the case of the trifluoromethyl- [*E. L. Muetterties, W. Mahler, K. J. Packer, R. Schmutzler*, Inorg. Chem. *3*, 1298 (1964)] and the methyl-derivative [*R. Mews*, Angew. Chem. *90*, 561 (1978); Angew. Chem. Int. Ed. Engl. *17*, 530 (1978)], but an exact interpretation of the spectra has not been reported. For the ABC_2 part of *(3)* we found:



$\delta_A = 98.5$, $\delta_B = 77.2$, $\delta_C = 66.7$; $^2J_{AB} = 31.2$, $^2J_{AC} = 210.6$, $^2J_{BC} = 208.0$, $^4J_{A\text{-}CF_2} = 21.6$, $^4J_{B\text{-}CF_2} = 3.6$, $^4J_{C_2\text{-}CF_2} = 3.0$ Hz.

[4] *I. Stahl, R. Mews, O. Glemser*, J. Fluorine Chem. *7*, 55 (1976).

BOOK REVIEWS

Polarography of Molecules of Biological Significance. Edited by *W. F. Smyth.* Academic Press, New York 1979. xix, 326 pages, bound, $ 47.50.

In ten chapters, written by twelve authors, this book deals with the more recent developments in polarographic (voltammetric) techniques in the field of biological analysis, with particular emphasis on the period since about 1965. Two introductory chapters serve as a brief outline of the principles and rudiments of general and special working techniques, and indicate how the best possible method can be selected. Brief reference is made to the possible applications of computer-assisted electrochemical analysis, where substantial improvements have taken place on the instrumental side. The main part of the book is devoted to applications in pharmacy, pharmacology, medical research, and in environmental research. The bibliography lists sometimes very diverse processes for the determination of a wide variety of medically, pharmacologically, or environmentally toxicologically interesting compounds, the arrangement of the references being designed for easy orientation. The greatest attention is given to the determination of drugs and their metabolites.

The book provides the analyst familiar with electrochemical working methods with a great deal of inspiration and would be difficult to beat as a reference for rapid orientation on more recent work.

Gerhard Eisenbrand [NB 503 IE]

Foundations of Molecular Pharmacology, Vol. 1 and 2. By *J. B. Stenlake.* The Athlone Press, London 1979. xi, 936 pages, bound, £ 36.00 (Vol. 1). xii, 318 pages, bound, £ 18.50 (Vol. 2).

The first of the two volumes of this work concentrates on the physical and chemical properties of medical substances, pharmaceutical additives, and cell components. As the author explains in the introduction, the contents originate from lectures and courses for students of pharmaceutical and medical chemistry. Essentially, the subject is organic chemistry, presented in a systematic arrangement, with brief references to the relationships with biology and medicine. The descriptions of biologically important reaction prerequisites, structural characteristics, and biochemical reaction pathways are particularly valuable. After some general sections on the types of chemical bonds, on radicals, and on other rudiments of chemistry, all the essential classes of organic compounds are dealt with in 21 chapters, ranging from alkanes through alcohols, acids, phenols, amines and amino acids to carbohydrates, vitamins, and heterocyclics of special biological significance (pyridines, purines, and nucleic acids).

The work provides a compressed and detailed summary of biologically and medically important compounds and compound classes that can serve as a textbook and course book for students of pharmaceutical chemistry. For the organic chemist it can also act as a source of rapid information in the field of medicinal chemistry. In this sense the subtitle "Medicinal and Pharmaceutical Chemistry" is in fact more appropriate than the main title.

For pharmacologists, especially those concerned with the basics of the interactions between chemical substances and biological substrates, the second volume, subtitled "The Chemical Basis of Drug Action" is a suitable textbook and source of information. The pharmaceutical chemist will find here information on substance-receptor interactions, on biochemical bonding, on the biological significance of stereochemistry and on the fundamentals of pharmacokinetics and drug metabolism.

The value of the book lies in the fact that it offers the newcomer to the field of drug research, particularly the pharmaceutical chemist, a comprehensive and systematic compendium of knowledge clarified further by many schemes, tables, and figures. The advanced student can rapidly extract information on less familiar fields. A comprehensive bibliography is provided for going further into the subject. The book will prove a valuable aid in the teaching of pharmaceutical chemistry.

H. G. Kroneberg [NB 504 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Trivialnamenkartei. 6th supplementary instalment. 1024 additional cards. Verlag Chemie, Weinheim 1979. DM 268.00.

Angewandte Klebtechnik. By *G. Fauner* and *W. Endlich.* Carl Hanser Verlag, München 1979. 227 pp., bound, DM 68.00.—ISBN 3-446-12767-4

Annual Reports on Fermentation Processes, Vol. 3. Edited by *D. Perlman.* Academic Press, New York 1979. xiv, 346 pp., sewed, $ 22.00.—ISBN 0-12-040303-X

Huminstoffe. By *W. Ziechmann.* Verlag Chemie, Weinheim 1980. xi, 408 pp., sewed, DM 95.00.—ISBN 3-527-25839-6

Phase Transfer Catalysis. By *E. V. Dehmlow* and *S. S. Dehmlow.* Verlag Chemie, Weinheim 1980. xi, 316 pp., bound, DM 138.00.—ISBN 3-527-25820-5

Molybdenum Chemistry of Biological Significance. Edited by *W. E. Newton* and *S. Otsuka.* Pergamon Press, New York 1980. x, 425 pp., bound, $ 39.50.—ISBN 0-306-40352-8

Electronic Structure and Magnetism of Inorganic Compounds, Vol. 6. Senior Reporter: *P. Day.* The Chemical Society, London 1980. x, 313 pp., bound, DM 132.30.—ISBN 0-85186-610-7.—A volume of the series "Specialist Periodical Reports"

General and Synthetic Methods, Vol. 3. Senior Reporter: *G. Pattenden.* The Chemical Society, London 1980. xiv, 382 pp., bound, DM 156.80.—ISBN 0-85186-730-8.—A volume of the series "Specialist Periodical Reports"

Carbohydrate Chemistry, Vol. 11. Senior Reporter: *J. S. Brimacombe.* The Chemical Society, London 1979. xv, 546 pp., bound, DM 191.10.—ISBN 0-85186-102-4.—A volume of the series "Specialist Periodical Reports"

Dynamics of Synergetic Systems. Edited by *H. Haken.* Springer-Verlag, Berlin 1980. v, 271 pp., bound, DM 68.00.—ISBN 3-540-09918-2

Chemistry for the Engineering and Applied Sciences. By *W. Steedman, R. B. Snadden,* and *I. H. Anderson.* Pergamon Press, Oxford 1980. viii, 449 pp., sewn, $ 17.95.—ISBN 0-08-022852-6

Topics in Current Physics. Theory of Chemisorption. Edited by *J. R. Smith.* Springer-Verlag, Berlin 1980. xi, 240 pp., bound, DM 58.00.—ISBN 3-540-09891-7

Advances in Heterocyclic Chemistry. Vol. 25. Edited by *A. R. Katritzky* and *A. J. Boulton.* Academic Press, New York 1979. vi, 397 pp., bound, $ 41.00.—ISBN 0-12-020625-0

Reactive Intermediates, Vol. 1. Edited by *R. A. Abramovitch.* Plenum Press, New York 1980. xiii, 522 pp., bound, $ 49.50.—ISBN 0-306-40220-3

Advances in Chemical Physics, Vol. XL. Edited by *I. Prigogine* and *St. A. Rice.* John Wiley & Sons, New York 1979. 504 pp., bound, £ 27.55.—ISBN 0-471-03884-9

Synthetic Aspects of Biologically Active Cyclic Peptides. Gramicidin S and Tyrocidines. By *N. Izumiya, T. Kato, H. Aoyagi, M. Waki,* and *M. Kondo.* Kodansha Ltd., Tokio 1979/Halsted Press, New York 1979. xii, 166 pp., bound, £ 18.25.—ISBN 0-470-26863-8

Springer Series in Chemical Physics. Vol. 9. Secondary Ion Mass Spectrometry SIMS II. Edited by *A. Benninghoven, C. A. Evans, Jr., R. A. Powell, R. Shimizu,* and *H. A. Storms.* Springer-Verlag, Berlin 1979. xiii, 298 pp., bound, DM 58.00.—ISBN 3-540-09843-7

Organic Reaction Mechanisms. By *A. C. Knipe* and *W. E. Watts.* John Wiley & Sons, Chichester 1980. 719 pp., bound, £ 50.00.—ISBN 0-471-27613-8

Biochemie. By *K. Jungermann* and *H. Möhler.* Springer-Verlag, Berlin 1980. xii, 733 pp., bound, DM 98.00.—ISBN 3-540-09302-8

Biochemie. Übungen und Prüfungsfragen. By *K. Jungermann* and *H. Möhler.* Springer-Verlag, Berlin 1980. xi, 229 pp., sewn, DM 19.80.—ISBN 3-540-09300-1

Physiologische Chemie. By *G. Löffler, P. E. Petrides, L. Weiss,* and *H. A. Harper.* Springer-Verlag, Berlin 1979. xvi, 940 pp., bound, DM 98.00.—ISBN 3-540-09332-X

Angewandte chemische Thermodynamik und Thermoanalytik. Edited by *E. Marti, H. R. Oswald,* and *H. G. Wiedemann,* Birkhäuser Verlag, Basel 1979. viii, 385 pp., bound, DM 79.00.—ISBN 3-7643-1142-8

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar,* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 6
June 1980
Pages 411–494

The Kinetic and Mechanistic Evaluation of NMR Spectra

New analytical methods (18)

By Gerhard Binsch and Horst Kessler[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In addition to the static parameters of the chemical shifts and coupling constants, which serve as a source of knowledge for molecular structure and stereochemistry, an NMR spectrum can frequently furnish dynamic quantities characterizing relaxation and exchange phenomena. The information about nuclear switching processes has proved to be particularly useful in practice for the detection of internal molecular motions and for the estimation or determination of the corresponding energy barriers. A plethora of studies of this nature has in the past been performed on simple proton spectra. Methodological developments of recent years have led to a significant reduction of the effort required for the quantitative dynamic evaluation of NMR spectra arising from complex spin systems or involving other nuclei. In many cases it has, moreover, become possible to extract detailed mechanistic information inaccessible by other means. The practical execution of such analyses will be explained and illustrated by a selected number of applications.

1. Introduction

For spectroscopic investigations in the ultraviolet, visible and infrared domains only thermal light sources had been available until quite recently. In contrast, coherent electromagnetic radiation has been employed in magnetic resonance from the very outset. This peculiarity offers the unique possibility of quantitative studies of dynamic processes at the molecular level, notwithstanding the fact that the measurements themselves are performed on samples in thermodynamic equilibrium. The coherence of the radiation imposes a phase relationship on the quantum-mechanical state functions of the microscopic subsystems, giving rise to a macroscopic observable by constructive interference. On the other hand, the random motions of the molecules in fluids and gases tend to reestablish the statistical phase distribution. The spectroscopy devoted to this interplay is referred to as dynamic spectroscopy[1], to distinguish it from the conventional kind in which one is only concerned with the quantum statics of the relevant energy levels and the transition probabilities between them. For most applications it is appropriate to differentiate further between relaxation and exchange processes in regard to the physical origins of the observed effects. The terminology of "dynamic NMR" or "DNMR" spectroscopy suggested 12 years ago[2] has come to be generally adopted, especially for the study of exchange phenom-

[*] Prof. Dr. G. Binsch
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)
Prof. Dr. H. Kessler
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-0411 $ 02.50/0

ena, and has recently been canonized by the title of a monograph[3].

The potential of DNMR spectroscopy for chemical applications was recognized at an early date[4-8] and has subsequently been exploited so frequently that the typical phenomena of exchange broadening and coalescence of NMR lines are nowadays familiar to every chemist. Already at the qualitative level the method can be very useful in practice. As a reminder we cite the proof of fluxionality for molecules such as bullvalene. In the simplest and frequently encountered case of two equally intense singlets merging in a single broad band on increase of the exchange rate it is, furthermore, trivially easy to perform a quantitative analysis applicable to the singular temperature T_c of the coalescence point. One only needs the chemical shift difference Δ of the singlets in frequency units. On conversion to the rate constant k of the exchange by means of the formula $k = 2^{-1/2}\pi\Delta$ and substitution of k and T_c into the Eyring equation one obtains the free energy of activation $\Delta G_c^{\ddagger}$ of the underlying chemical process at the coalescence temperature with a typical accuracy of 0.2 kcal mol^{-1}. A graphical procedure[9] may be used for the corresponding analysis involving two singlets of unequal intensity. Even when one is dealing with a binary exchange problem involving first-order multiplets, for which a coalescence "point" can naturally no longer be defined, the mechanical application of the cited formula to the vaguely specifiable "temperature of maximum broadening" permits the estimation of a $\Delta G^{\ddagger}$ value that deviates from the true value by not more than 1 kcal mol^{-1}. Another very convenient method for determining a rate constant, which furthermore has the advantage of remaining valid in more complicated cases and which does not even require the knowledge of a chemical shift difference, is based on measurements of the incipient line broadening. After subtraction of the natural linewidth the resulting number (in Hz) yields the k value directly on multiplication by π.

Some 10 years ago we wrote a couple of review articles[2,10] on the applications of DNMR spectroscopy to conformational interconversions, atomic inversions, ring reversals and valence isomerizations, for which the overwhelming majority of the free energies of activation had been calculated or estimated in one of these simple ways. Much of the dynamic information in the most recent literature[3,11-14] still stems from elementary methods of analysis. With the latest advances in methodology it is now feasible, however, to treat complex systems quantitatively on a routine basis, and thus to obtain detailed mechanistic information frequently not accessible from simple systems. In this article we propose to present these developments to a chemical readership and to subject the time-honored and still widely used methods to a critical scrutiny from a modern vantage point.

An explicit bandshape analysis is advisable especially if there are several nuclei in different magnetic environments participating in the exchange, if the spectra exhibit strong spin coupling or if one is dealing with some subtle mechanistic issue. With certain provisos this already applies to the simple binary exchange problems alluded to above if it is desired to determine rate constants at a series of temperatures in order to dissect the free energies of activation into their enthalpic and entropic components $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. The theory of exchange-broadened NMR spectra is highly developed in a formal as well as computational sense, but is not our primary concern in this article. We merely cite some recent expositions[15-17] and confine ourselves to the explanation of those concepts indispensable also for the practitioner. The emphasis of the subsequent discussion will be on the general analysis techniques and the applications of the numerical methods. It will be unavoidable, however, to devote some space to the discussion of those specific experimental and computational aspects through whose frequent neglect in the past DNMR spectroscopy has acquired the reputation of being a quantitatively unreliable technique. For the selection of examples we have preferentially taken recourse to results from our own laboratories.

2. Exchange Types and Spin Systems

DNMR spectroscopy is equally suited for the study of intermolecular as well as intramolecular chemical processes in which a magnetic nucleus exchanges its position with another of the same kind or migrates into a new magnetic environment. Even in the latter case it is still appropriate to speak of an "exchange". As mentioned in the Introduction, DNMR measurements are performed on macroscopic samples in thermodynamic equilibrium. The maintenance of the equilibrium is evidently only guaranteed if there is a concurrent countermigration of a nucleus of the same species from another molecule or from another isomer of the same molecule. Although similar NMR investigations can in principle also be performed on systems suffering a macroscopic change during measurement, the required generalization of the theory has been worked out only very recently[18] and applications[18] have not yet progressed very far.

Intermolecular chemical processes amenable to a DNMR investigation include proton jumps between acidic molecules of the same or of different kinds, ligand exchanges involving inorganic complexes or organometallic compounds, the dissociation of covalent compounds into ions or the reverse process of ion recombination, and those exchange processes of particular importance for biochemistry in which a small substrate molecule or an inorganic ion is in equilibrium between its free form in aqueous solution and its protein-bound state.

Far more frequently still, DNMR spectroscopy has been applied to the problem of the internal mobility of molecules, on which we shall therefore focus our main attention in the following discussion. If the elementary step only leads to a permutation of the nuclear sites, the corresponding chemical process is called a topomerization[19]. The same spectral type is also realized for enantiomerizations, provided that the compounds are investigated in achiral solvents, as is usually the case. Such enantiomerizations become detectable through the presence of prochiral groups (*e.g.* $-CX_2Y$) in the molecule, since the elementary act exchanges the diastereotopic positions of the nuclei X[20]. In diastereomerizations and constitutional isomerizations, on the other hand, each spin is transported to a new magnetic environment. A single spin thus suffices for the identification of the latter exchange type. A consistent exploitation of this differentiability of molecular processes with due regard to symmetry considerations has, for instance, permitted the mechanistic distinction be-

tween inversion and rotation for *syn-anti* isomerizations of imines[21].

It may of course also happen that inter- and intramolecular exchange processes proceed simultaneously[22].

2.1. Computer Programs

The complete bandshape analysis of an exchange-broadened NMR spectrum is not practicable economically without a computer, although a desk calculator will do for the simplest cases. Pertinent computer programs exist in large numbers (at least 50). One has to distinguish between two basic types:

— The NMR computer programs for spectral synthesis—commonly, albeit somewhat inappropriately, called simulation—only produce a theoretical trial spectrum from given spectral parameters (chemical shifts, coupling constants, natural linewidths, populations, exchange rate constants) on the basis of the specified model (exchange type, spin system, permutational mechanism), usually in the form of a computer-drawn tracing. It is then the task of the user to modify the parameters by trial and error until a visual comparison of the newly synthesized curve shows satisfactory agreement with the experimental spectrum.

— With the analysis programs proper, on the other hand, the optimum fit is calculated internally by an iterative process. Their applicability requires, of course, that in addition to the starting parameters the experimental spectrum itself is supplied to the computer in a suitable fashion. Hand digitization is easily possible for strongly exchange-broadened spectra, but in the presence of comparatively sharp lines becomes not only tedious but, above all, too inaccurate. Some kind of automated procedure is in any case to be preferred. A convenient method, for example, consists in copying the raw spectral data, initially recorded to a magnetic disk as commonly practiced, to a magnetic tape which can then serve as an input medium for a large and efficient number cruncher. Regrettably, many laboratories are at present still lacking the necessary equipment.

Most computer programs had originally been designed for special exchange types and simple spin systems and are now principally of historical interest only, since their tasks can also be performed by general programs. There are about a dozen synthesis programs of the latter type. Although the majority of them has not been published, some have been distributed on a personal basis; from acknowledgments and footnotes in relevant papers published in the last decade it can be gleaned that this must have been the case especially for the versions developed by *M. Saunders* (Yale University) and *G. M. Whitesides* (Massachusetts Institute of Technology). Two published synthesis programs for the intramolecular exchange of coupled spin systems[23,24] are available from the organization of the Quantum Chemistry Program Exchange at Indiana University (Bloomington, Indiana 47401, USA).

The latter versions are now also rendered obsolete by recent developments. The analysis program DNMR5[25] emerged from a systematic comparison study[26] of a variety of minimization algorithms and is characterized by high efficiency and absolute stability of the iteration procedure; in other words, divergence is logically impossible by design. This program is also capable of utilizing raw spectral data taken directly from the spectrometer and of performing a complete error analysis on the results. The analysis of exchange-broadened NMR spectra has thereby been automated to a large extent. The modular program structure enables the nonspecialist user to adapt the program by the simple redimensioning of arrays or the incorporation of mechanistic constraints to those intramolecular exchange problems which have not been provided for as standard features.

There is no difference in the computational treatment between intra- and intermolecular exchange if spin coupling is absent from the spectra or if the fine structure has been eliminated by decoupling. This is no longer true, however, for coupled spin systems. Although the theory has long been known also for the general intermolecular case and minor discrepancies in the original formulations have recently been eradicated[17,27], it appears that corresponding computer programs have so far been written only for special exchange types. In this area the potential user might therefore still find himself confronted with the necessity of having to invest some programming work of his own.

2.2. Exchange between Singlets

The simplest case is realized if the exchanging nuclei or groups of nuclei give rise to two singlets of equal or unequal intensity in the NMR spectrum below a certain temperature. From a purely computational standpoint the analysis of the spectra covering the entire temperature range of exchange-broadening presents no difficulty even if the singlets exhibit different natural linewidths. An iterative calculation using the DNMR5 program consumes only a fraction of a second per spectrum on a modern computer, starting for example from 10000 spectral points automatically recorded on a spectrometer and transmitted to a computing facility. That does not answer the question, however, which of the parameters can or should be determined iteratively, and also does not provide any guarantee for the quality of the dynamic results. We shall return to these problems later.

For n exchanging singlets there can be up to $n(n-1)/2$ independent first-order or pseudo-first-order rate constants k_{ij}. The corresponding constants k_{ji} of the reverse reactions are fixed by the relative populations p of the molecular species through the relationships $p_i k_{ij} = p_j k_{ji}$. (Note that in some programs the term "population" is used in a different, purely computational sense for the specification of the number of nuclei per magnetic environment. In the presence of experimental artifacts, such as differential nuclear Overhauser effects in ^{13}C-DNMR spectroscopy, these computational quantities have moreover to be chosen such as to reproduce the actually observed signal intensities.) The full kinetic complexity is indeed occasionally observed in intermolecular exchange, but is atypical for the intramolecular case. The chemical constraints customarily admit of only few possibilities and the DNMR spectra can then lead to valuable mechanistic conclusions. In the extreme case there remains only a single possibility whose mechanism is known beforehand.

A fascinating and frequently investigated example is provided by bullvalene *(1)*, in which a sequence of Cope rearrangements ultimately renders all nuclei of the same species equivalent. Only the $\{^1H\}$-noise-decoupled ^{13}C-PFT-NMR

spectra[28-30] are of interest in the present context. At low temperature one observes four singlets, for which one expects the idealized intensity ratios of 3:3:3:1 in the absence of differential nuclear Overhauser and/or longitudinal relaxation effects. Dynamic spectra for two separate temperature ranges are shown in Figures 1 and 2[29]. In the intermediate region

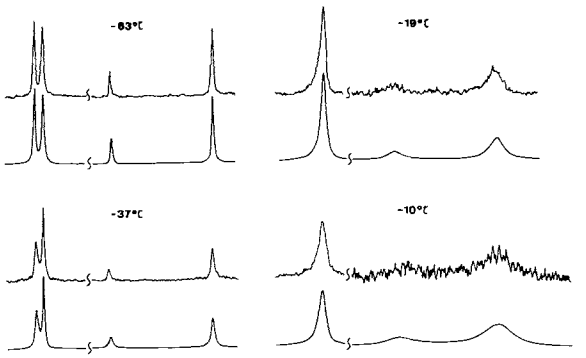


Fig. 1. Observed and computed ^{13}C-DNMR spectra of bullvalene *(1)* at slow exchange [29].

the spectra are so broad that they remain buried in the noise even on accumulation of 6000 transients[29]. By extending the acquisition period to 24 hours or more *Oth et al.*[30] succeeded, however, in obtaining spectra of superb quality also in this domain.

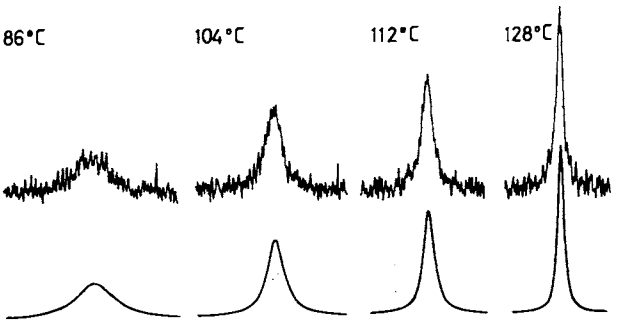
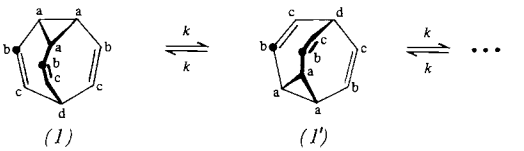


Fig. 2. Observed and computed ^{13}C-DNMR spectra of bullvalene *(1)* at fast exchange [29].

For the calculations one needs the exchange matrix $\mathbf{X}$[15,31], which in the present case of a constitutional topomerization[19] can be written as a product $\mathbf{X}=k\mathbf{Q}$ of a single rate constant k pertinent to the elementary chemical step *(1)*→*(1')*, and a statistical matrix $\mathbf{Q}$. A foolproof method consists in first figuring the off-diagonal elements column-wise. An element q_{ij} represents the probability that a jump out of site j of formula *(1)* ends up in site i of formula *(1')*. Finally the column sums are entered with a negative sign in the diagonal positions. Figure 3 shows the result for the idealized intensity ratios. The indicated procedure pertains to the theoretical standard formulation[15] of exchange-broadened NMR spectra. The nonexpert should be aware that some computer programs are based on classical precursors of the general quantum mechanical theory[32,33] and require instead the transpose $\mathbf{Q}^T$. We also mention that in the iterative program DNMR5[25] only symmetric $\mathbf{X}$ matrices are used internally. They are automatically generated from the unsymmetric standard form of the input by means of a similarity transformation[34]; with this trick the numerical computations can be speeded up considerably[34].

	a	b	c	d
a	−1	0	$\frac{2}{3}$	1
b	0	$-\frac{1}{3}$	$\frac{1}{3}$	0
c	$\frac{2}{3}$	$\frac{1}{3}$	−1	0
d	$\frac{1}{3}$	0	0	−1

Fig. 3. Statistical $\mathbf{Q}$ matrix for bullvalene *(1)* in the standard formulation.

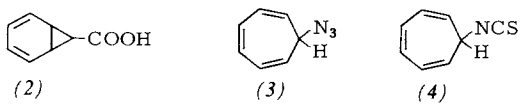


A quantitative bandshape analysis requires in addition that the signal assignments be known. The correct assignment may on first sight not be obvious for the closely spaced singlets of the olefinic ^{13}C nuclei at low fields (Fig. 1), but the missing piece of information is immediately supplied by the spectrum at −37 °C. A straightforward perturbation-theoretical argument leads to the conclusion that the effect of the off-diagonal $\mathbf{X}$ matrix elements can be neglected as long as the lines have not yet started to run together.

The diagonal elements X_{ii} then play the role of an effective transverse relaxation time T_2^{eff}, which according to theory[15] appears as $-1/T_2^{\text{eff}}$ on the diagonal and is related to the linewidth W by the formula $T_2^{\text{eff}}=(\pi W)^{-1}$. Inspection of the $\mathbf{Q}$ matrix (Fig. 3) reveals that the exchange contribution to the incipient broadening of the b signal is smaller by a factor of 3 than for the other singlets. Alternatively, it becomes clear also on examination of the structural formulas that except for two of the three olefinic carbons in the positions b of *(1)* all nuclei change places in the course of a single Cope rearrangement. In other words, with each rearrangement only 1/3 of the b spins depart from their sites, which manifests itself in a diminished broadening of the nonoverlapping b signal. The correct assignment can thus be established already on a qualitative basis. After subtraction of the natural linewidths the effect can be analyzed quantitatively as well, to a good approximation[30]. Of even greater importance in practice is the reverse application of this simple criterion to problems where the assignments are known from other arguments, but the exchange mechanism remains to be ascertained. In Section 5 we shall discuss the further techniques of saturation transfer and 2D spectroscopy, which in the case of exchanging singlets are also suited for obtaining mechanistic information without the necessity of an explicit bandshape calculation.

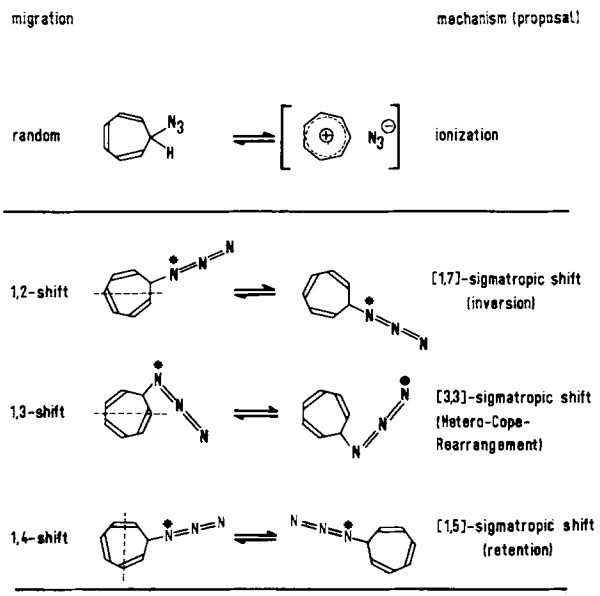
Selective line broadenings are of great practical importance also in a somewhat different context. In binary isomerizations M⇌N it may happen that the population p_N is insufficient for the direct NMR-spectroscopic detection of species N at low temperature, but still large enough to influence the lines of the major species M dynamically. The selective broadenings or sharpenings of the M lines as a function of temperature can then yield information about the nature of

the N form. With this elegant technique *Günther et al.*, for example, succeeded in adducing indirect evidence for bicyclic valence isomers of substituted cycloheptatrienes[35,36] and azepines[37]; for instance, the existence of the Buchner acid *(2)*, having remained elusive for decades, could in this way be established experimentally[35].



(2) *(3)* *(4)*

Tropylium azide *(3)* provides a pertinent example of an exchange for which the mechanism was not known beforehand. This case was discovered in the course of a systematic DNMR investigation of reversible dissociation processes[38-43] and was studied by dynamic ^1H, ^{13}C and ^{15}N spectroscopy and by the saturation transfer method[43]. In the polar solvent SO_2, *(3)* is found to be almost completely ionized at 203 K. On addition of $CDCl_3$ the covalent form can be detected as well. The ^{13}C-DNMR spectra of Figure 4 are in agreement with theoretical curves calculated on the basis of an azide migration proceeding through the symmetric ion pair. Dynamic effects can still be observed in less polar solvents such as CD_3CN, but the ionic species is no longer detectable and the DNMR spectra are at variance with a random azide migration. In contrast, the migration of the thiocyanate residue in tropylium isothiocyanate *(4)* remains statistical even in



Scheme 1.

Quantitative bandshape analyses were performed for the ^{13}C spectra of *(3)* and the ^1H spectra of $[^2H_6]$-*(3)* (Fig. 5); both agree in that for solutions in CD_3CN the selective 1,2-, 1,3- and 1,4-shifts participate to the extent of 30%, 60% and 10%, respectively, whereas there is no noticeable contribution from the intermolecular exchange through ions. In less

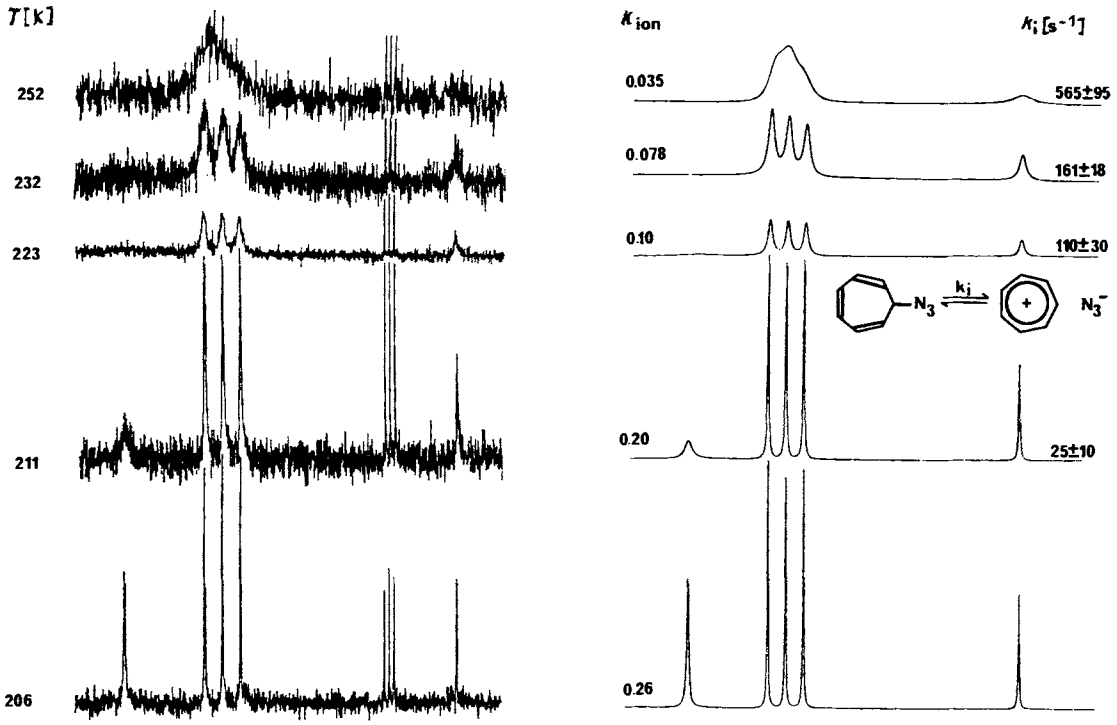


Fig. 4. Observed and computed ^{13}C-DNMR spectra of tropylium azide *(3)* in $SO_2/CDCl_3$ (4:5).

$CS_2/CDCl_3$ solution, where again only the covalent form can be observed[42]. A preferred 7→2 migration (1,3-shift) in *(3)* is proved by saturation transfer experiments at carefully selected temperatures (cf. Section 5). Calculations reveal, however, that none of the pure alternative mechanisms of Scheme 1 is compatible with the observed bandshapes. The exchange matrix must hence be formulated as a linear combination $\mathbf{X} = \sum_i k_i \mathbf{Q}_i$.

polar solvents ($CDCl_3$, THF) the percentage of the 1,3-shift increases still further at the expense of the other possibilities of migration. As a consequence of an isotope effect the isotopomers of $[^2H_6]$-*(3)* are no longer strictly isoenergetic and this has to be taken into account when setting up the **Q** matrices for $[^2H_6]$-*(3)*. As is the case for all mechanistic studies of this kind, DNMR spectroscopy can yield information only about permutational mechanisms; the "chemical" mecha-

nisms also listed in Scheme 1 are therefore to be regarded merely as palpable suggestions.

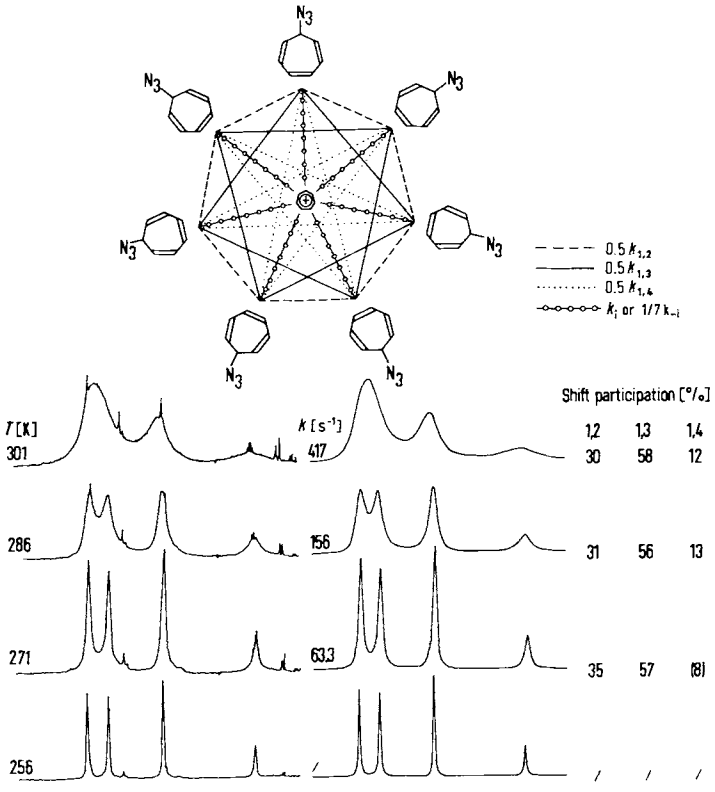
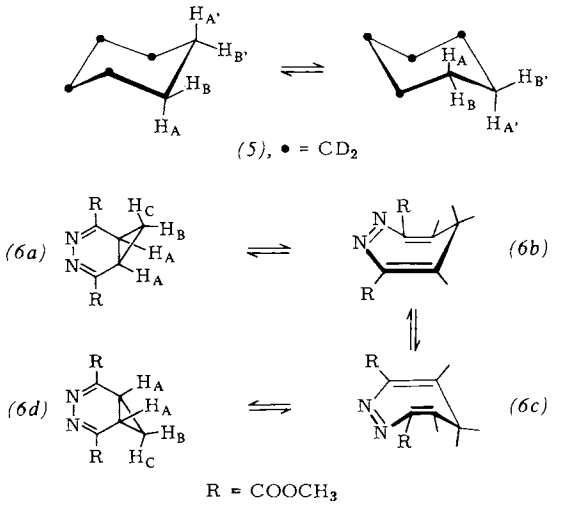


Fig. 5. Isomerization graph for tropylium azide *(3)* and observed and computed 270-MHz ^{1}H-DNMR spectra of $[^2H_6]$-*(3)* in CD_3CN.

2.3. Binary Exchange of Coupled Spin Systems

Spin-Spin coupling causes a quantum-mechanical mixing of the nuclear spin product functions and it is therefore no longer possible to assign a certain line in the spectrum to a single nucleus in the molecule. In the present context the kinetic process must always be formulated as an exchange between "nuclear configurations". If this is done correctly at input time for a computer calculation, the user need no longer concern himself with the details of the **X** matrices required for the general quantum-mechanical theory[15,32,33]; in programs of sufficient generality[23 25] the rate constants are automatically put into their correct locations by the computational algorithm.



The prototype is the mutual exchange AB⇌BA, and is represented by numerous examples in the literature. The remarks made at the beginning of Section 2.2 apply to this case accordingly.

Two slightly more complicated cases of mutual exchange are shown in Figures 6 and 7. In the first we are dealing with the well-known ring reversal of cyclohexane, exemplified by the $^1H\{^2H\}$-DNMR (type AA'BB'⇌BB'AA') spectra of the octadeuterio derivative *(5)*[44], in the second with the successive valence isomerizations and ring reversals of the diazanorcaradiene *(6)*[45,46].

Because of their high energy content the monocyclic forms *(6b)* and *(6c)* do not appear directly in the spectra and the dynamic effects therefore arise from an overall topomerization. It can be seen (Fig. 7) that the A spins are only indirectly involved in the $A_2BC⇌A_2CB$ exchange by virtue of their couplings to the B and C nuclei and that the relevant signals undergo very slight changes throughout the entire temperature range. At first sight it might thus appear as if the A spins merely represent a superfluous complication, which could for instance be chemically removed by specific deuteration, in which case the $^1H\{^2H\}$-spectra would collapse to a singlet on fast exchange. But apart from the fact that there is really no need for such a simplification from the point of view of computational expense, it will become apparent from arguments to be presented later that the presence of such "supernumerary" spins in the system can be distinctly advantageous (cf. Section 4.3).

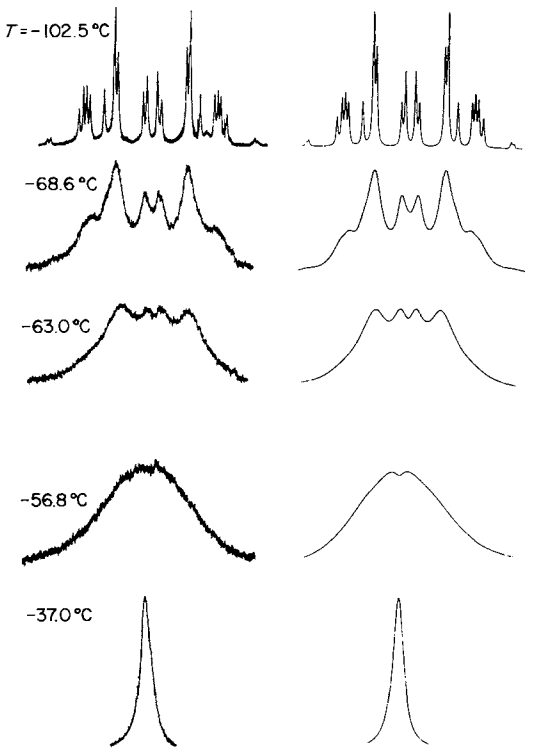


Fig. 6. Observed and computed $^1H\{^2H\}$-DNMR spectra of the octadeuteriocyclohexene *(5)*.

By studying nonmutual exchange processes one not only obtains the kinetic parameters, but in addition the thermodynamic quantities for the equilibria involved. The potential of

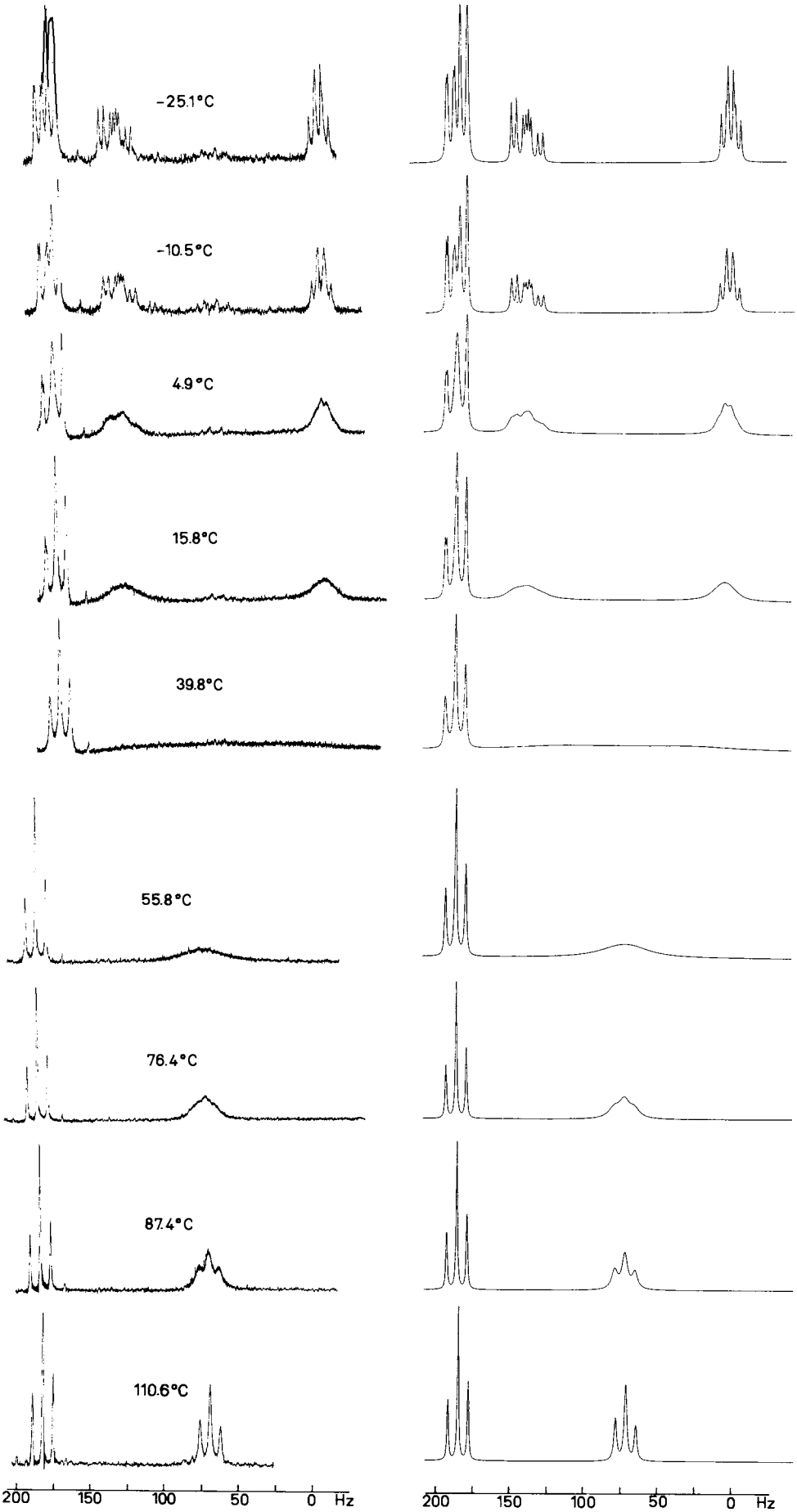
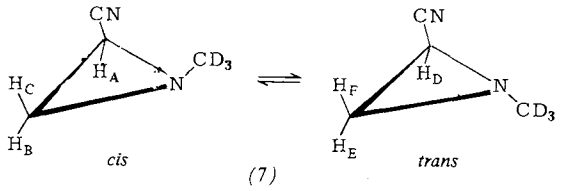


Fig. 7. Observed and computed ^{1}H-DNMR spectra of the diazanorcaradiene *(6)*.



(7)

the ABC⇌DEF type for chemical applications has recently been subjected to a systematic scrutiny[44,47]. The nitrogen inversion in the aziridine derivative *(7)* may serve as an example.

At room temperature and below, one observes the superposed, but easily distinguishable static spectra of the separate diastereomers (Fig. 8), of which the *trans* form predominates. In the range from −40.3 to 23.2 °C the temperature dependence of the equilibrium constant could be determined directly by comparison with synthesized spectra. A further data point can be obtained by extrapolation from the averaged spectrum at 158.9 °C (Fig. 9). Since the latter still exhibits fine structure, characterized by three chemical shifts and

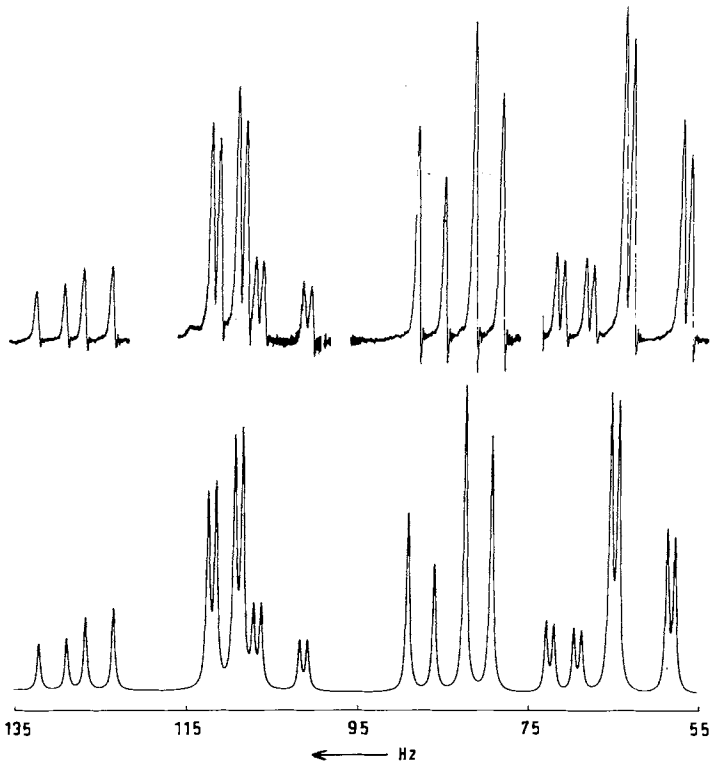


Fig. 8. Observed and computed ^{1}H-NMR spectrum of the aziridine *(7)* at −40.3 °C.

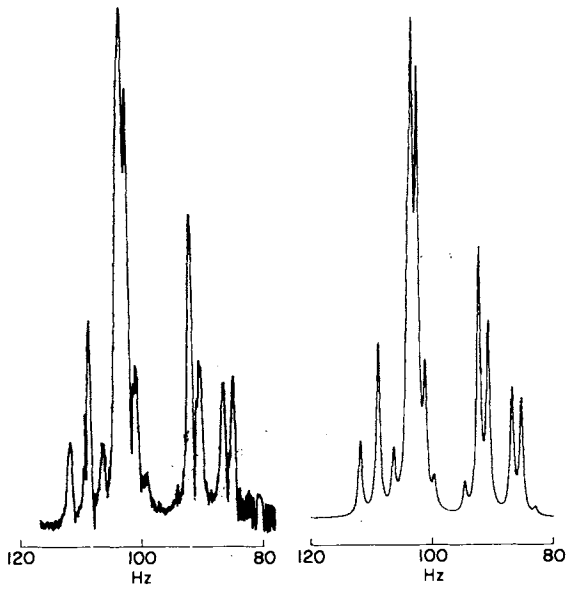


Fig. 9. Observed and computed ^{1}H-NMR spectrum of the aziridine *(7)* at 158.9 °C.

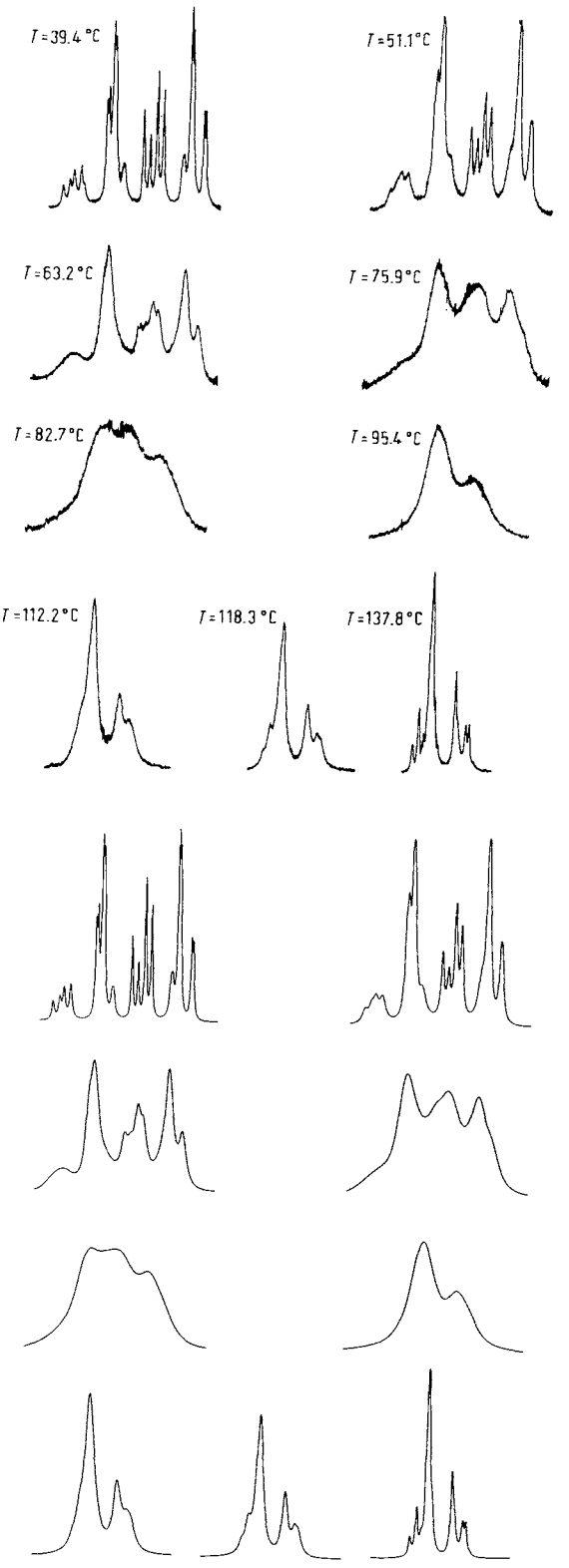
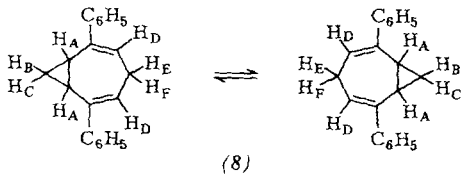


Fig. 10. Observed and computed ^{1}H-DNMR spectra of the aziridine *(7)*.

three coupling constants, there exists the possibility of checking this extrapolation for internal consistency in six different ways. Some of the dynamic spectra are displayed in Figure 10; the nature of these DNMR spectra is such as to permit the determination of an activation entropy for an atomic inversion with high precision (cf. Sections 4.2 and 4.3). It is encouraging that this number can be understood quantitatively on the basis of the principles of statistical thermodynamics[47].

A more complicated situation is encountered in the homotropylidene derivative *(8)*[48]. Chemically speaking, we are dealing with an overall topomerization, again passing through a sequence of valence isomerizations and ring reversals (Fig. 11), but if one neglects the small cross-ring cou-



(8)

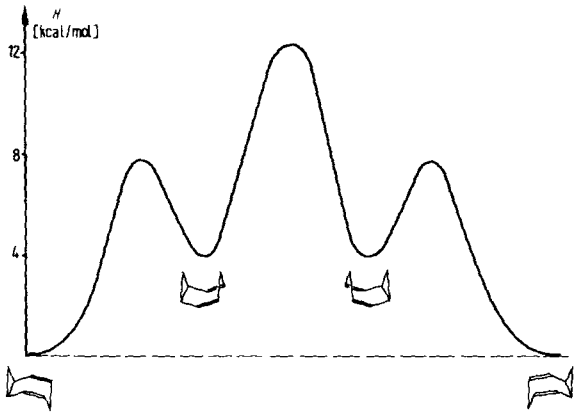


Fig. 11. Free energy profile for the valence topomerization of homotropylidene.

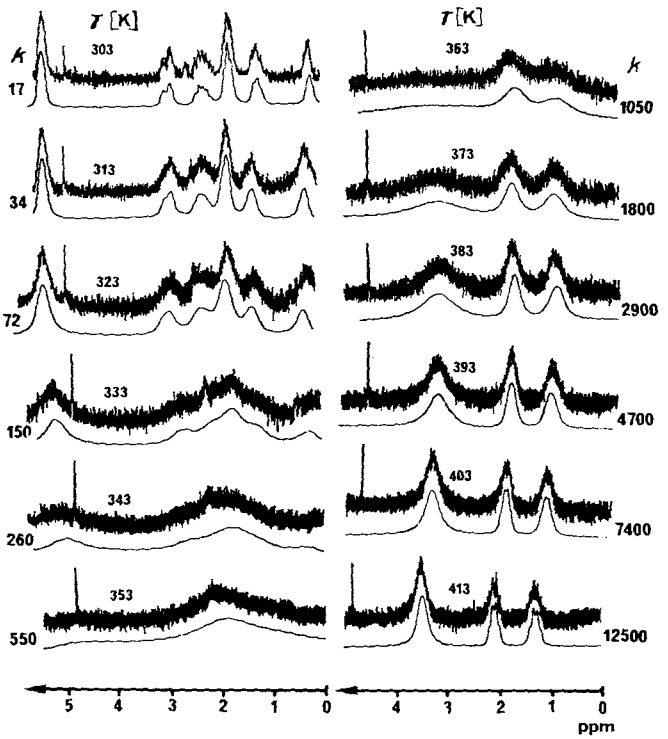
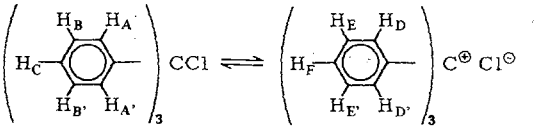


Fig. 12. Observed and computed ^{1}H-DNMR spectra of the homotropylidene *(8)*.

plings the case can be treated computationally as an $A_2BC \rightleftharpoons D_2EF$ nonmutual exchange between two chemically different, albeit of course equally populated nuclear configurations. Dynamic spectra are reproduced in Figure 12. A comparison of the activation parameters with those of analogously substituted derivatives led to conclusions concerning the nature of the transition state of the Cope rearrangement[48].

A very complex example of a quantitatively analyzed binary exchange is provided by the ionization of trityl chloride *(9)* in $SO_2/CDCl_2$[49]. Although the covalent and ionic forms



(9)

are connected *via* an intermolecular process, the theoretical DNMR spectra of the type AA'BB'C$\rightleftharpoons$DD'EE'F (Fig. 13)

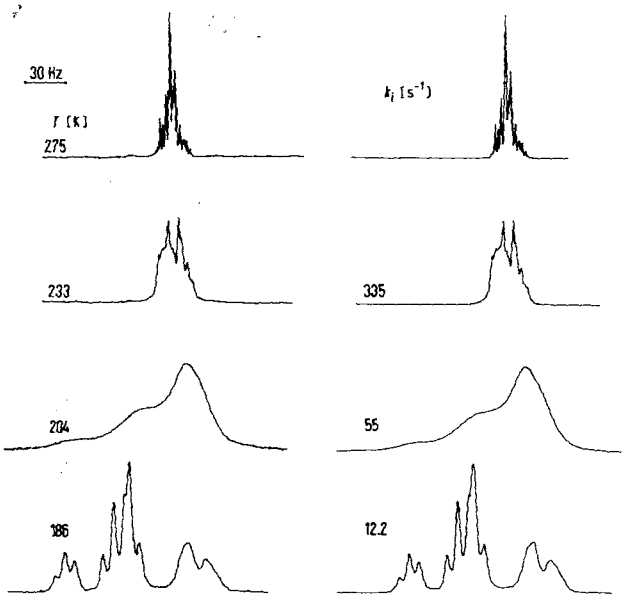


Fig. 13. Observed and computed ^{1}H-DNMR spectra of trityl chloride *(9)* in $SO_2/CDCl_2$ (10:1).

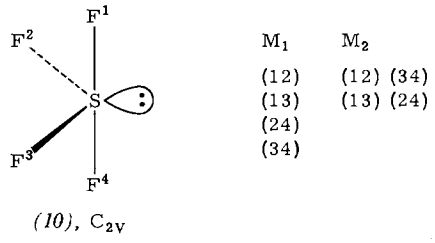
could be calculated[49] using a redimensioned standard program[24], since the aromatic protons show no spin coupling to the departing chloride ligand. Even an iterative determination of the exchange rate constant would still be perfectly feasible. It is true, however, that the complexity is now so high that it becomes quite tedious to determine the numerous static parameters and their temperature dependence from the slow-exchange spectra if one has to rely on conventional techniques. With the recently reported[50-52] automated analysis procedure for complex static spectra this obstacle has now disappeared as well.

2.4. Multiple Exchange of Coupled Spin Systems

As was the case for exchanging singlets, the most intriguing examples are also found in the realm of coupled systems if the chemical constraints are loose enough to permit the exchange between more than two nuclear configurations, at

least in principle. For n spins of the same kind there can be as many as $(n!-1)$ different topomerizations and/or enantiomerizations; the number of exchange possibilities increases further if diastereomers and/or constitutional isomers are involved. This does not mean, however, that all these possibilities necessarily give rise to different DNMR spectra. The number of differentiable processes, for the designation of which there unfortunately exists a bewildering variety of nomenclature suggestions, is often drastically curtailed by molecular symmetry. Before embarking on a bandshape analysis it is therefore first necessary to ascertain the fundamental exchange possibilities with regard to number, nature and degeneracy. The complexity may easily exceed the bounds of chemical intuition and it then becomes unavoidable to resort to group-theoretical techniques. A voluminous formalistic literature has been accumulating on this subject in recent years, but its exposition would go beyond the limits of the present review. We can do no more than cite a few review articles[53-55], in which the aspects relevant to DNMR spectroscopy are treated in some detail. Corresponding applications experienced a sudden upsurge at the beginning of the past decade especially in inorganic chemistry[3,56,57].

The pseudorotation in the repeatedly studied sulfur tetrafluoride, which could finally be clarified by *Whitesides et al.*[58] by the investigation of a carefully purified sample, is transparent enough so as not to require an elaborate group-theoretical machinery and may therefore serve as an illustration of the principles. At low temperature one observes a ^{19}F-NMR spectrum of the type A_2B_2 (or A_2X_2), in agreement with the theoretically expected C_{2v} structure *(10)*. By inspection one finds that of the $4!=24$ permutations (including the identity) of the ^{19}F nuclei there only remain the two differentiable mechanisms M_1 and M_2 of degeneracy 4 and 2, respec-



(10), C_{2v}

Scheme 2.

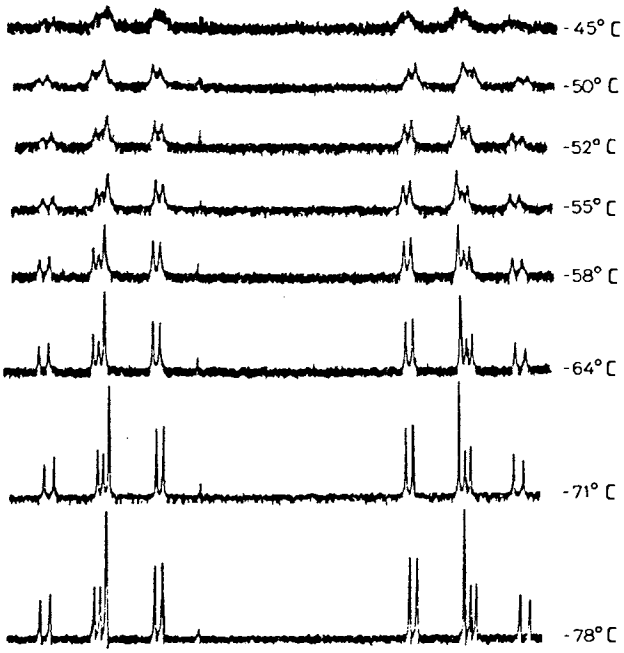


Fig. 14. ^{19}F-DNMR spectra of sulfur tetrafluoride *(10)* at 9.2 MHz [58].

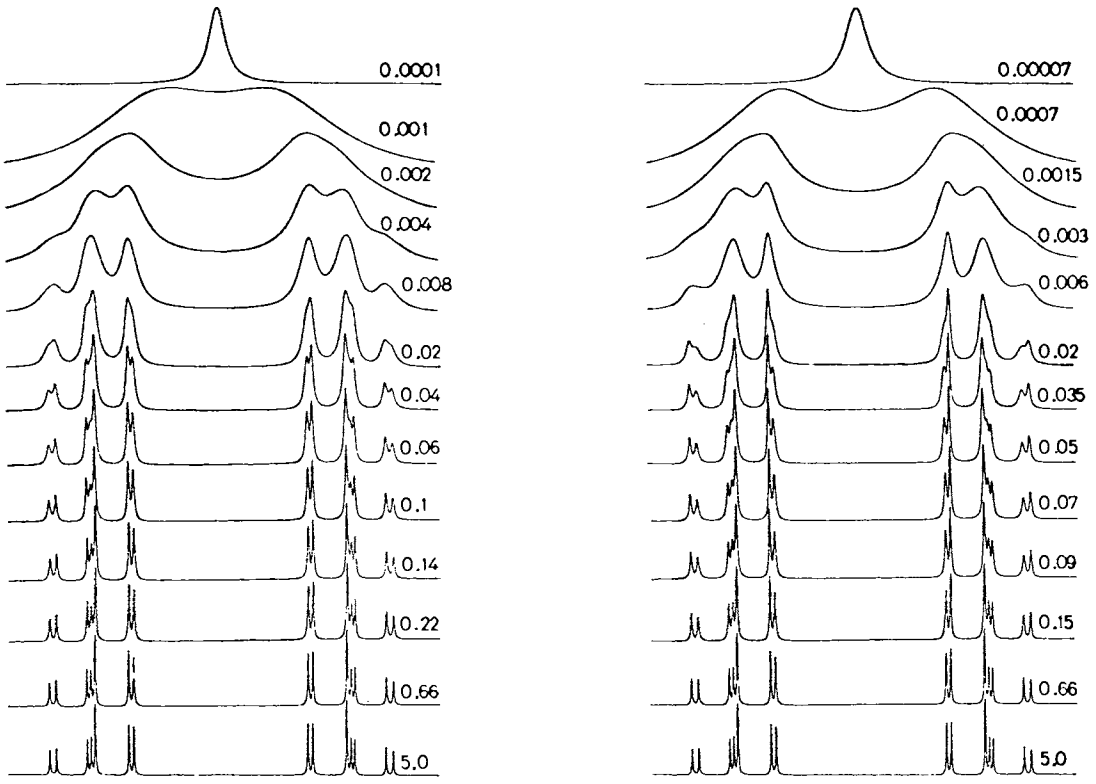
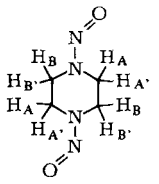


Fig. 15. Computed DNMR spectra for Fig. 14, corresponding to the mechanisms M_1 (right) and M_2 (left) [58].

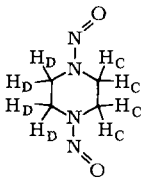
tively (Scheme 2). The exchange of the axial and equatorial ligands proceeds sequentially in M_1 and concertedly in M_2.

A careful examination of the curves in Figure 15, synthesized on the basis of the permutational schemes shown, reveals that M_2 matches the experimental DNMR spectra of Figure 14 more closely than M_1. This result is in agreement with a process known as Berry pseudorotation, but would equally well be compatible with any other chemical mechanism giving rise to the same nuclear permutations. It cannot be overlooked, however, that the differences between the two sets of theoretical spectra are exceedingly subtle. In fact, when the spectra were recorded at "normal" field strengths, an unambiguous distinction could no longer be made at all. *Whitesides et al.*[58] were forced to reduce the field strength of the spectrometers used in this study to about 10% of their nominal value. This casts an interesting spotlight on the rampant misconception regarding the *universality* of the advantages to be expected from the high-field spectrometers which are becoming so popular these days.

The same difficulty of not being able to differentiate convincingly between alternative mechanisms with the conventional procedure of spectral synthesis has frequently arisen in other studies of this kind and provided the motivation for a further development of the methodology[25,26]. The molecule 1,4-dinitrosopiperazine *(11)* served as a test case[59]. At room temperature one records the superposed spectra of two diastereomeric forms in equilibrium: the AA'BB' pattern of *(11a)* and the two four-proton singlets C_4 and D_4 of *(11b)*. At elevated temperature one observes the onset of internal rotations about the N—N bonds of the *N*-nitroso groups. In calculating the dynamic spectra it has to be remembered that the two singlets also require a full quantum-mechanical treatment, since their equivalence is destroyed in the course of the diastereomerizations. The problem was formulated theoretically as an exchange between four nuclear configurations involving three independent rate parameters, according to the mechanisms of Scheme 3. In the iterative analysis, starting from 10200 raw spectral points fed to the computer, the parameters k_{II} and k_{III} converged to zero. That is to say, the mechanistic conclusion emerged here as a *result* from the analysis. The preprocessed experimental DNMR spectrum at 130 °C reproduced in Figure 16, which was computer-generated from the raw data by smoothing and reduction to 999 points as a preparation for analysis, and the calculated curve plotted on top of it furthermore illustrate the degree of agreement between theory and experiment that can be achieved with this automated procedure. The new technique is clearly the method of choice especially in those cases where the contribution of a "pure" mechanism in a mixture of several mechanisms needs to be determined quantitatively.



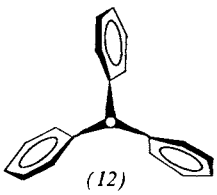
(11a), trans



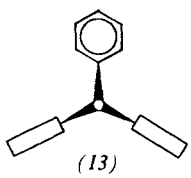
(11b), cis

	I	$[AA'BB'\|BB'AA'] \rightleftharpoons [C_4\|D_4]$
	II	$AA'BB' \rightleftharpoons BB'AA'$
Scheme 3.	III	$C_4 \rightleftharpoons D_4$

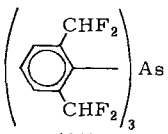
We briefly sketch an enticing application of this technique to the problem of correlated motions in triaryl derivatives of the type Ar_3XY, where Y stands for a ligand of conical symmetry or a free electron pair[60]. A restricted internal rotation in trimesityl derivatives of phosphorus and arsenic had already been detected by DNMR spectroscopy in 1969[61]. More recently, the mechanism of this dynamic process has been extensively investigated especially by *Mislow et al.* The theoretical and experimental results communicated in about 20 lengthy papers[62] are overwhelmingly in favor of the chiral (C_3) propeller conformation *(12)* in solution and of the operation of the so-called two-ring flip mechanism, whose transition state is indicated schematically in *(13)*. Surprisingly enough, an iterative DNMR analysis of a single model type with three structurally identical aryl groups can furnish the conclusive proof. The synthesis of the conceived model compounds has recently been successful in four cases[60]; here we



(12)



(13)



(14)

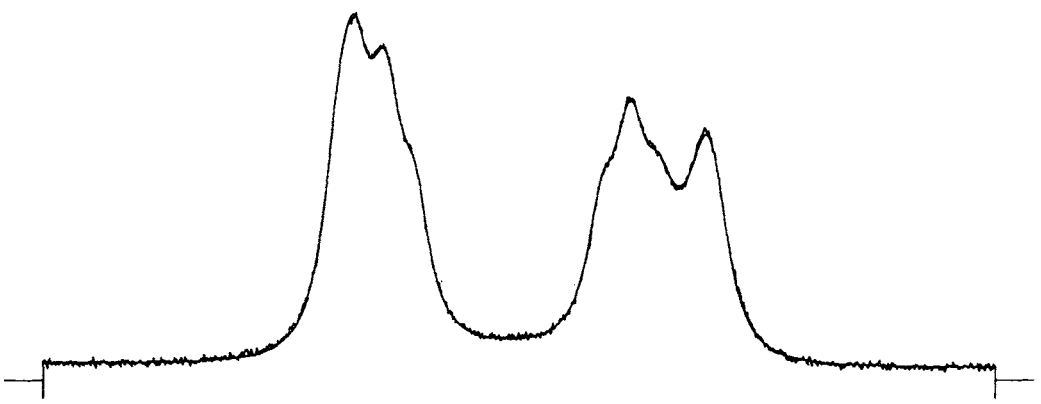


Fig. 16. ^{1}H-DNMR spectrum of 1,4-dinitrosopiperazine *(11)* at 130 °C and superposed computed spectrum.

show the spectra of the arsenic derivative *(14)*. The ^{19}F sensor nuclei serve the double purpose of responding to the "edge interchange"[62b] e *as well as* the "helicity reversal"[62b] h, *provided* that the molecule assumes a chiral C_3 equilibrium conformation in solution. That this is indeed the case follows immediately, and rigorously, from the ^{19}F-NMR spectrum at $-91.7\,^{\circ}C$ (Fig. 17). The large chemical shift differences and

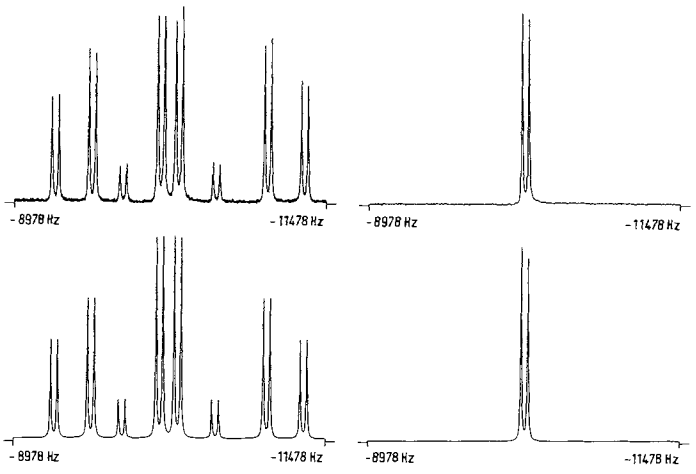


Fig. 17. Observed and computed static ^{19}F-NMR spectra of the triphenylarsane derivative *(14)* at $-91.7°$ (left) and $+60.6\,^{\circ}C$ (right).

Table 1. Permutational mechanisms for *(14)* in simplified notation and their consequences.

Mechanism	Type	Degeneracy	Elementary Act	Fast-Exchange Limit Spectra
M_1	e	3	[CDAB][ABCD]$_2$	1 AB type
M_2	e^2	3	[CDAB]$_2$[ABCD]	1 AB type
M_3	e^3	1	[CDAB]$_3$	1 AB type
M_4	h	1	[BADC]$_3$	2 singlets
M_5	eh	3	[DCBA][BADC]$_2$	1 singlet
M_6	e^2h	3	[DCBA]$_2$[BADC]	1 singlet
M_7	e^3h	1	[DCBA]$_3$	1 AB type [a]

[a] The parameters of this AB spectrum differ from those of the other AB types.

the cleanly separated signals of ^{19}F subspectra of the two ABX systems simultaneously confirm the working hypothesis underlying this project, namely that the ^{19}F nucleus is really the only sensor spin suitable for a successful study of this kind. The chemical constraints permit seven differentiable mechanisms for this $[ABXCDY]_3$ spin system[63], whose nature and consequences are collected in Table 1, where the XY nuclei have been suppressed for simplicity and the (anyway unobservable) long-range couplings disregarded. It can be seen that the high-temperature spectrum of Figure 17 already eliminates all pure mechanisms with the exception of M_5 and M_6. The latter can now be distinguished on the basis of the DNMR spectra, formulated theoretically[60] as an exchange between four ABX-type nuclear configurations with two independent rate parameters. Note, however, that there is still a choice between two alternative relative assignments of the chemical shifts, about which nothing is known initially. This decision can also be left to the computer. The iterative calculation with one of these assignments results in an acceptable fit to the dynamic spectra, but leads to a linear

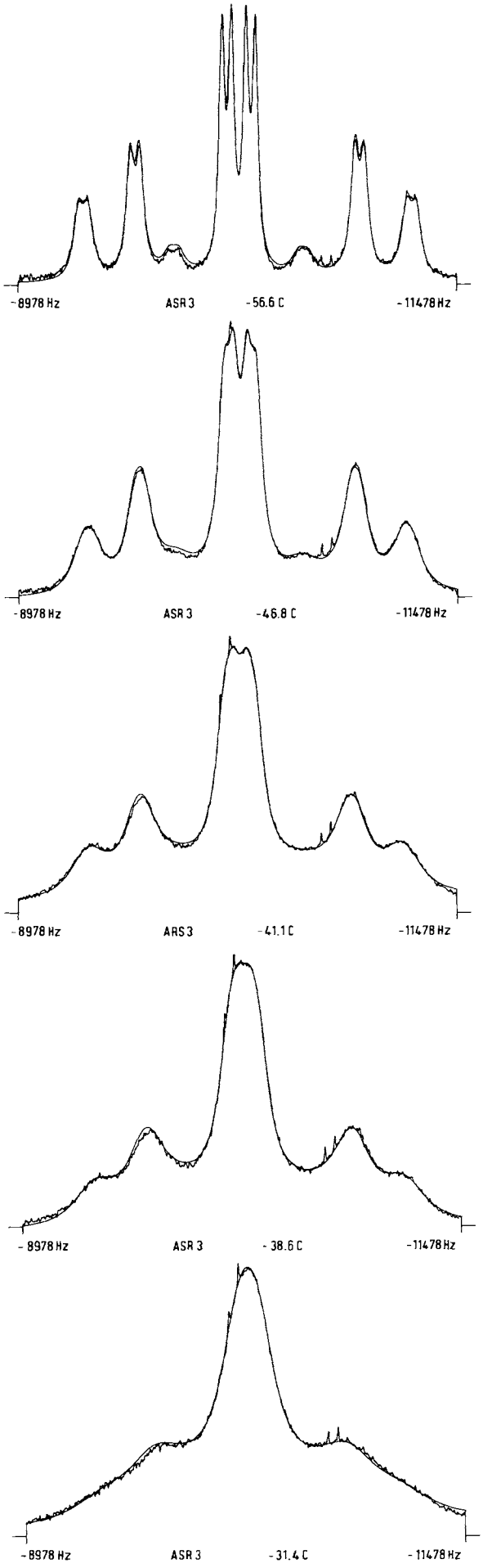


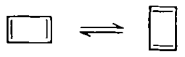
Fig. 18. ^{19}F-DNMR spectra of the triphenylarsane derivative *(14)* and superposed computed spectra (see right-hand column).

combination of M_5 and M_6 in which one of the rate constants decreases drastically with increasing temperature. This physically nonsensical result can only mean that the incorrect assignment was chosen. With the other assignment one obtains the fits shown in Figure 18 and the results listed in Table 2. This completes the proof of mechanism M_5.

Table 2. Iteratively calculated rate constants for the processes M_5 and M_6 of *(14)* and their standard deviations.

Temperature [°C]	k_5 [s^{-1}]	k_6 [s^{-1}]
−56.6	161.3 ± 4.1	5.1 ± 3.3
−46.8	415.8 ± 5.6	0.9 ± 4.7
−41.1	654.6 ± 5.9	0.7 ± 4.3
−38.6	805.3 ± 8.0	0.8 ± 5.2
−31.4	1366 ± 13	0.6 ± 6.5

Finally, we mention the interesting possibility of mechanistic DNMR studies in nematic phases. In the hypothetical case of cyclobutadiene, for example, a singlet would be observed in the ^1H- (or $^{13}C\{^1H\}$-) spectrum in isotropic solution even if the valence topomerization *(15a)* ⇌ *(15b)* were slow on the NMR time scale, but this would not be the case in a liquid crystal solvent. The technique has already been



(15a) *(15b)*

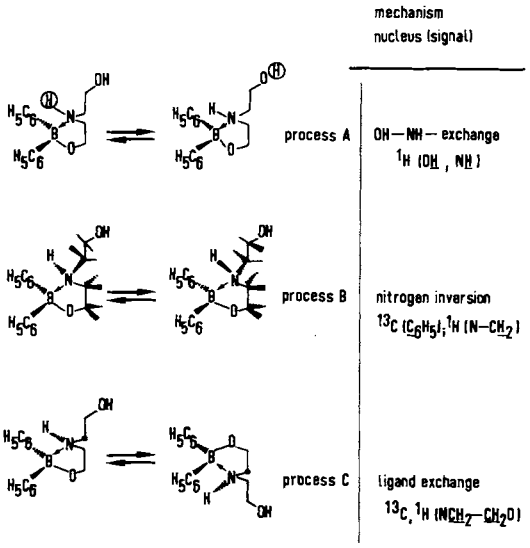
applied[64] to the bond-shift process in cyclooctatetraene, previously studied by way of the ^{13}C satellite DNMR spectra[65,66] and on substituted cyclooctatetraenes[67-69]. General computer programs are presently being developed[70] and one may look forward to exciting applications in the future.

3. Choice of Sensor Nucleus

There is no choice at all if the molecule contains only one kind of magnetically active nucleus or if for theoretical or practical reasons (*e.g.* spin > 1) only one kind is suited for a DNMR study. For example, dynamic processes in metal carbonyls can frequently be studied only by ^{13}C-DNMR spectroscopy[13,71].

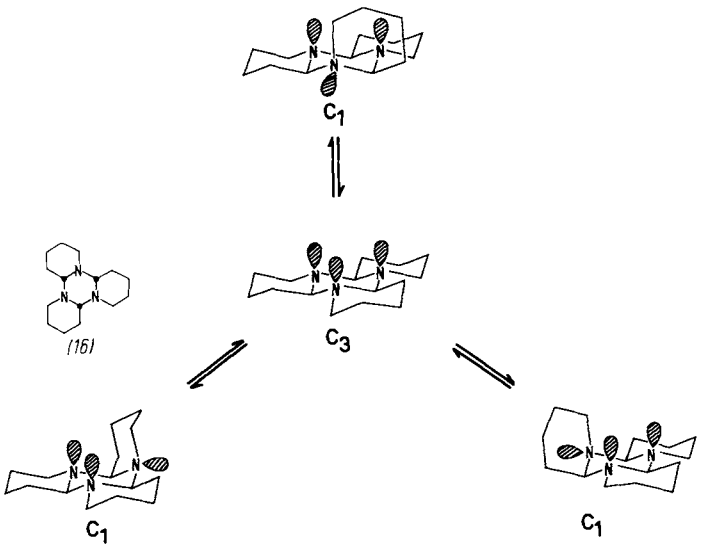
In other cases the mechanistic details of a specific process may manifest themselves more clearly by the judicious choice of a sensor nucleus. In the example of the tropylium azide already alluded to in Section 2.2 we have focused attention on the seven-membered ring. The preferred 1,3-shift in nonpolar solvents may be interpreted (Scheme 1) as a [3,3]-sigmatropic rearrangement (hetero Cope rearrangement) in which the terminal nitrogen atoms of the azide ligand are interchanged as well. In the ^{15}N-NMR spectrum of an isotopically enriched sample one indeed observes the exchange in the expected temperature range; unfortunately, a quantitative analysis was prevented by the low signal-to-noise ratio of the exchange-broadened ^{15}N-DNMR spectra[43,72].

In the presence of several processes proceeding concurrently one occasionally succeeds in differentiating them by appropriately choosing the sensor nucleus. We have recently investigated a case in which three different processes occur in the temperature interval from −50 to +50 °C[22] (Scheme 4).



Scheme 4.

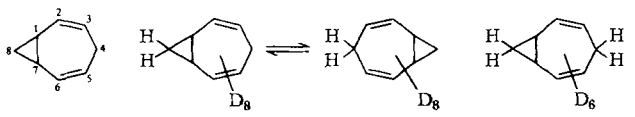
In the situation most frequently encountered in practice, however, several magnetically active nuclear species respond to one and the same chemical process. Practical aspects such as NMR sensitivity, magnitude of the shift differences and complexity of the spin system then determine the choice. Owing to its superior sensitivity the proton will often be preferred, since it yields an acceptable signal-to-noise ratio even in the highly exchange-broadened region. Exceptions are indicated if the shift differences in the static spectra are too small to permit a quantitative bandshape analysis or if the spin system is too complex even on the basis of present criteria. A pertinent example is *cis*-decalin, for which one observes a sharp singlet in the ^1H-NMR spectrum down to −120 °C, whereas the expected dynamic behavior is easily detectable in the ^{19}F spectrum of 2,2-difluoro-*cis*-decalin[73] or in the ^{13}C spectrum of the parent compound[74]. Similarly, the ^1H-NMR spectrum of tripiperidein *(16)* is too complex (strongly coupled 9-spin system) and too poorly resolved even at 270 MHz, whereas the ^{13}C-NMR spectra establish at once that only the asymmetric C_1 form is populated at low temperature. The dynamics of the molecule (Scheme 5)



Scheme 5.

could be studied without difficulty by means of the three-site exchanges in the ^{13}C-DNMR spectra[75].

The advantages and disadvantages of the various nuclear species and/or spin systems can be demonstrated with the homotropylidene *(17)*. An exact bandshape calculation for the exchanging 10-proton system is at present not feasible. *Günther et al.* have therefore decided to investigate the octadeuterio derivative *(18)* (AB⇌CD exchange with unequal populations owing to the isotope effect in the $^1H\{^2H\}$-DNMR spectrum)[76]. A later analysis[77] of the hexadeuterio derivative *(19)* (AB⇌CD exchange with equal populations) fully corroborated their results.



(17) *(18a)* *(18b)* *(19)*

At this point the question arises as to how much the barrier in the parent compound is changed by a secondary kinetic deuterium isotope effect. The kinetic evaluation of the ^{13}C-DNMR spectra of *(17)* indeed yielded slightly different ΔH^+ and ΔS^+ values[78] and thus provided the motivation for a subsequent reinvestigation of *(17)* by ^{1}H-NMR spectroscopy at 270 MHz. Because of the very large chemical shift differences in the high-field ^{1}H spectrum it is now a good approximation to neglect the couplings to the protons 2-H and 6-H and the small cross-ring couplings[79], so that the exchange can be treated computationally as an $ABC_2 \rightleftharpoons DEF_2$ system[80]. The results are in agreement with the ^{13}C-DNMR (Table 3). The error situation is still marginal, but the internal consistency of the values of Table 3 does suggest the presence of a detectable isotope effect[80].

Table 3. Activation parameters of homotropylidene and its deuterated derivatives.

Cpd.	Method	ΔH^+ [kcal mol^{-1}]	ΔS^+ [cal mol^{-1} K^{-1}]	ΔG^+_{298} [kcal mol^{-1}]
(17)	$^{13}C\{^1H\}$-DNMR	12.34 ± 0.09	−5.9 ± 0.6	14.10 ± 0.09
(17)	270-MHz ^{1}H-DNMR	12.31 ± 0.09	−6.2 ± 0.3	14.158 ± 0.001
(18) *(a→b)*	100-MHz ^{1}H-DNMR	12.03 ± 0.18	−7.5 ± 0.6	14.265 ± 0.001
(18) *(b→a)*	100-MHz ^{1}H-DNMR	11.84 ± 0.17	−8.0 ± 0.6	14.224 ± 0.009
(19)	270-MHz ^{1}H-DNMR	11.86 ± 0.11	−7.8 ± 0.4	14.184 ± 0.009

4. Experimental and Computational Aspects

The determination of a free energy of activation makes quite modest demands on the accuracy of a rate constant and consequently on the quality of the experimental DNMR spectra and on the validity of the approximations employed in their dynamic evaluation. The reason for this insensitivity resides in the fact that k enters logarithmically into the calculation of a ΔG^+ value by means of the Eyring equation, which for the convenience of the experimentalist shall be reproduced with the currently valid numerical constants:

$$\Delta G^+ \text{[kcal mol}^{-1}\text{]} = 1.9872\,T\,(23.7600 + \ln T - \ln k).$$

Even a temperature error of 3 K can readily be tolerated; the aforementioned (cf. Section 1) typical precision of ±0.2 kcal mol^{-1} remains untouched. The situation changes abruptly, however, as soon as the temperature dependence of k is to be evaluated quantitatively as well[15]. Reliable ΔH^+ and ΔS^+ values, and in particular activation entropies *explicable in a chemically meaningful fashion,* may realistically be expected only if careful attention is paid to the various aspects to be detailed in the following Sections.

4.1. Instrumental Problems

The temperature problem presents itself in three facets: constancy, uniformity and measurement. A convincing instrumental solution (±0.01 K even at −170 °C!) has been reported at least once[81], but is unfortunately not available commercially. With sufficient care the difficulties can, however, be largely overcome with most spectrometers in current use, at least for the temperature range from about −100 to +150 °C. Such care is mandatory, to be sure! If one is not willing to inform oneself about the possibilities of error and to invest the minimum expenditure of effort, it is preferable to abstain altogether from any attempt at evaluating the temperature dependence of k quantitatively; expecially with regard to activation entropies the pertinent literature is already burdened with such a heavy load of ballast that we can easily do without more of the same.

The temperature dial readings of commercial control units cannot be trusted; even a single calibration is by no means sufficient. This is not the place to enter into technical details of the numerous suggested and/or practiced methods and their advantages and disadvantages. We merely indicate the two procedures presumably employed most commonly. In the first method the sample tube is substituted by an open tube partially filled with a suitable solvent (if possible the same that was used in dissolving the compound to be investigated) and containing a thermocouple immersed to the height of the receiver coil; after allowing for adequate equilibration the temperature is recorded before and after performing a DNMR measurement. Alternatively, one may use an "NMR thermometer liquid" (*e.g.* CH_3OH or $HOCH_2CH_2OH$ for ^{1}H-DNMR) which shows a temperature-dependent chemical shift difference for the DNMR sensor nucleus, either also contained in a replacement tube or preferably in a sealed capillary added to the sample solution. A careful recalibration has recently been performed for the ethylene glycol curve[82], making elegant use of the sharply defined and almost instantly regulatable clearing point of liquid crystals. NMR thermometers have also been suggested for other sensor nuclei; the relevant literature can be traced back from a paper published not long ago[83].

In recording the spectra by the CW technique, as commonly practiced in the past, attention has to be paid to the bandshape distortions caused by saturation effects and finite sweep rates; happily, these experimental difficulties have vanished with the FT technique now used almost universally. There has been no change, of course, in the requirement of aiming for a field homogeneity that is as high as possible. It also should not be overlooked that the FT technique has created new problems. The baseline artifacts and signal distortions caused by pulse breakthrough and nonlinear phase

effects are much more serious and also more difficult to avoid for strongly exchange-broadened DNMR spectra than for static spectra consisting of sharp lines; they certainly deserve the careful attention of the experimentalist and may even require modifications of the commercial system software. It hardly needs to be stressed that the most sophisticated band-shape calculation becomes illusory if the quality of the experimental DNMR spectra falls below an acceptable standard. If the spectra are to be evaluated by visual comparison with synthesized DNMR spectra it is therefore good policy to insist from the outset that they be recorded in a sufficiently large format (at least 30 × 30 cm appears to be a normal requirement).

4.2. Static NMR Parameters and Thermodynamic Quantities

A dynamic bandshape calculation requires that the chemical shifts and coupling constants be known at the respective temperature. Using modern programs[25] the static parameters can be determined iteratively as long as the DNMR spectra still exhibit sufficient fine structure. A decision concerning this point may be made on the basis of the correlation coefficients produced by the program. In general, however, one will have to rely on extrapolations. A fit to a linear function of the temperature has been perfectly adequate in virtually all cases studied so far. If the barriers are not too small, the required information can be obtained by static analysis of the spectra in a temperature range below the onset of appreciable exchange broadening[84]. The latest developments[50, 52] have drastically reduced the effort of such analyses for complicated spectra. The reliability of the extrapolations is expected to increase with the temperature range in which static analyses are feasible. In favorable cases[44,47], where the exchange takes place between *chemically* distinct nuclear configurations resulting in averaged spectra still exhibiting fine structure (Fig. 12), the validity of the extrapolations can be subjected to detailed cross-checks.

It may of course also happen that a temperature trend is not detectable within the limits of experimental error or that it makes such a small *percentage* contribution to the crucial frequency differences that it becomes safe to work with constant numbers in a bandshape calculation. This is indeed the normal situation for coupling constants and is, *with the exception of the proton,* often realized for the chemical shift parameters of other sensor nuclei as well. Furthermore, it is clear that only a possible temperature trend of the chemical shift *differences* of the exchanging spins is of interest in the present context; an absolute shift, *e.g.* with respect to an internal reference, is of no relevance for the dynamic analysis. In modern programs[25] this feature is taken into account by the introduction of an additional parameter specifying the spectral origin.

Analogous low-temperature measurements are required if one is dealing with isomerizations or with the intermolecular exchange between chemically different molecules, except that it is now necessary to determine in addition the temperature dependence of the populations. An iterative calculation is to be preferred over a simple integration also for this purpose, even if (and especially if) there are only singlets. The analysis according to van't Hoff yields the ΔH^0 and ΔS^0 values of the equilibria, from which the populations at other temperatures can be back-calculated. An additional data point can be extracted from the exchange-averaged spectrum. In the presence of large chemical shift differences Δ between the species and in the absence of an appreciable temperature dependence of the static parameters, the precision of such a number can be quite high even for singlets[78,85], but decreases hyperbolically with Δ according to the laws of error propagation. As already mentioned in Section 2.3 in connection with the aziridine example *(7)*, fine structure in the spectrum in the fast-exchange limit then offers the possibility of improving the situation by taking the weighted average of several alternatives. This remark also applies to the case of trityl chloride[49] (Fig. 13).

4.3. Natural Line Widths

A generally vastly underestimated problem in connection with the quantitative evaluation of DNMR spectra as a function of temperature is raised by the natural width W_0 of the lines. In conjunction with the aspects to be discussed subsequently, it embodies the principal cause for the overwhelming percentage of worthless $\Delta S^{\neq}$ values in the literature. A statistical analysis[15] demonstrates that for obtaining reliable activation enthalpies and entropies a large temperature interval is a necessary *but not sufficient* requirement. Of decisive importance are almost exclusively only the data in the two extremes of the range, and it is here that the DNMR spectra are least sensitive to the exchange rate. As already pointed out in the Introduction and again in the discussion of bullvalene (Section 2.2), exchanging singlets show up as broadened Lorentzian lines in these regions. Since the natural width is dominated by field inhomogeneity broadening in the absence of special effects, it appears plausible to extract it from an internal reference signal at the respective temperature and subtract it from the exchange-broadened lines or use it as a constant in an explicit bandshape calculation. If field inhomogeneity is no longer dominant, that is to say if there are genuine transverse relaxation effects or unresolved residual splittings, the natural line widths can be extrapolated into the dynamic region from measurements at temperatures below or above detectable exchange broadening[86]. These procedures are indeed perfectly satisfactory for the determination of a free energy of activation even if the exchanging lines are, say, only three times as broad as the standard; a k error of 20%, caused by experimental imperfections, by approximations in the calculations or indirectly by a temperature error, is of absolutely no consequence for the calculation of a $\Delta G^{\neq}$ value from a chemical standpoint. Experience shows, however, and a statistical analysis proves it, that such an error in k in most cases totally prevents the determination of an activation entropy that can be *meaningfully interpreted chemically*[44,46,47].

For exchanging singlets or an AB$\rightleftharpoons$BA exchange no remedy is to be expected for these difficulties from an iterative bandshape analysis either. Because of virtually complete correlation it is clearly impossible to determine k and W_0 separately[87]. A rule of thumb for the nonexpert is to refrain from using a DNMR rate constant for the analysis of its temperature dependence if it stems from an A$\rightleftharpoons$X or AB$\rightleftharpoons$BA DNMR spectrum in which the line widths were less than

about 6 W_0. But this already restricts the available temperature range so severely for the chemical shift differences typical for ^{1}H-DNMR spectroscopy that it is preferable to abstain from any attempt at dissecting a $\Delta G^{\neq}$ value for $\Delta < 50$ Hz if the spin system is too simple.

Of the currently known procedures for avoiding these difficulties we shall discuss the nonstationary methods in Section 5; two further techniques are to be mentioned in the present context. For very large chemical shift differences, as they are typically encountered for many nuclei with the exception of the proton, it is possible to cover such a large temperature interval even when observing the cited rule of thumb that reliable results are to be expected in principle, provided that the sensitivity suffices for spectra of good quality and that other complications are absent. That this expectation could in the past often not be realized for ^{13}C-DNMR spectroscopy becomes depressingly apparent on inspection of the tables in a recently published survey[12]. Another technique exploits the advantages of spin systems of *sufficient* complexity. Whereas the field inhomogeneity affects all lines equally, the exchange may lead to *differential* line broadenings even in the extremes of the temperature range as a consequence of quantum-mechanical mixing, provided of course that fine structure can be observed in both regimes. This condition can be satisfied by the presence of "supernumerary" spins as in *(6)* (Fig. 7) or by chemically different nuclear configurations like in *(7)* (Fig. 10). A distinction of these differential effects from W_0 is already feasible by means of the conventional method of spectral synthesis, but is more profitably carried out using the iterative procedures that have recently become available[25,26], since in this way one automatically also obtains the objective error information required for an unbiased calculation of $\Delta H^{\neq}$ and $\Delta S^{\neq}$. If for lack of the proper equipment one still needs to resort to the synthetic evaluation, it is necessary to determine in each case the upper and lower bounds of the rate constant that lead to unequivocally ascertainable disagreements with the experimental spectrum. In this way one obtains realistic estimates of the rate errors that are required for the calculations to be discussed in the following section.

4.4. Activation Parameters

The quantitative evaluation of the temperature dependence of the rate constants can be performed according to the Arrhenius or Eyring equations. Owing to its lack of easy explicability in chemical terms it is fitting that the former alternative is on the retreat in the modern literature. The popular graphical evaluation is to be rejected for the same reason, as are all numerical procedures in which the statistical weights of the data points cannot be taken into account. For, even if the errors in k and T were the same over the entire range, the laws of error propagation would then demand that they be different for the functions $\ln(k/T)$ and $(1/T)$ of the linearized treatment. In reality, however, the errors in k are normally much higher at the extremes of the temperature range than around the coalescence point. Even the most frequently used standard computer programs for weighted adjustment are not fully appropriate to the DNMR situation, since they only allow for the variances of the dependent variable in the linearized treatment; the errors of the independent variable $(1/T)$ should also enter into the calculation. The correct formalism was first given by *Deming*[88], but is surprisingly still unknown even to many specialists. A typical calculation of this kind for a simple exchange problem, carried out with the program ACTPAR[89], is reproduced graphically in Figure 19.

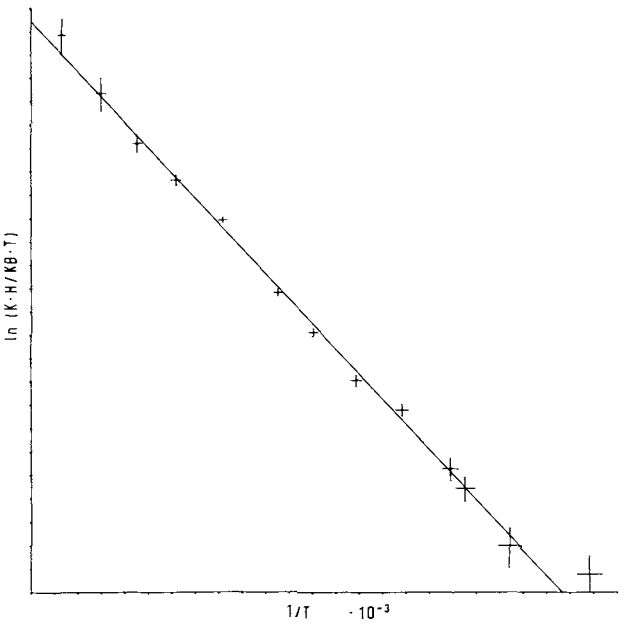


Fig. 19. Graphical Representation of a typical ACTPAR calculation of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ for the exchange of two singlets.

The neglect of elementary principles of statistics has, *inter alia,* often led to an underestimation of the *purely statistical* errors in $\Delta H^{\neq}$ and $\Delta S^{\neq}$, not infrequently by more than an order of magnitude[90]. On the other hand, it is commonly found that the errors in $\Delta G^{\neq}$ back-calculated from those of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ have been *overestimated.* It is almost invariably overlooked that the covariance $\mathrm{cov}(\Delta H^{\neq}, \Delta S^{\neq})$ plays a decisive role. The correct formula reads

$$\sigma^2(\Delta G^{\neq}) = \sigma^2(\Delta H^{\neq}) + T^2\sigma^2(\Delta S^{\neq}) - 2T\rho(\Delta H^{\neq}, \Delta S^{\neq})\sigma(\Delta H^{\neq})\sigma(\Delta S^{\neq}),$$

and since the correlation coefficient $\rho(\Delta H^{\neq}, \Delta S^{\neq})$ can here be equated to 1 without further ado, in simplified form

$$\sigma^2(\Delta G^{\neq}) \approx \sigma^2(\Delta H^{\neq}) + T^2\sigma^2(\Delta S^{\neq}) - 2T\sigma(\Delta H^{\neq})\sigma(\Delta S^{\neq})$$

or

$$\sigma(\Delta G^{\neq}) \approx |\sigma(\Delta H^{\neq}) - T\sigma(\Delta S^{\neq})|$$

5. Nonstationary Methods

We have already emphasized that the distinction between exchange broadening and natural line width in the extremes of slow and fast exchange is rendered particularly difficult for singlets. It is gratifying that the nonstationary methods of magnetization transfer offer an alternative especially suited for such simple spectra. They permit the determination of a rate constant in the temperature region below the onset of noticeable line broadening.

The method of saturation transfer goes back to classic papers of *Forsén* and *Hoffman*[91] and is usually applied to CW spectra in the experimental version of *Anet* and *Bourn*[92]. Irradiation at the resonance frequency of *one* of the nuclei causes the occupation numbers of the respective energy levels to become equalized. The signals of the other nuclei involved in the exchange thus experience a time-varying intensity change, provided the effect is not extinguished by rapid relaxation. It is of course also possible to monitor the time variation of the signal intensities by means of the FT technique[12,93,94], which is the method of choice especially for ^{13}C-NMR spectra[12,93].

Modern pulse spectrometers allow an even more sensitive version of this experiment. The level populations are inverted by a selective 180° pulse, followed by a delay time τ and a nonselective 90° observing pulse; the evaluation of the signal intensities as a function of τ then yields the desired dynamic information[95-97]. The generation of a selective 180° pulse is a little tricky, but by exploiting the latest techniques[98] it is possible to replace it by m identical $180°/m$ pulses[99] whose separation τ determines the pulse frequency.

Not unexpectedly, these techniques are also subject to a multitude of error sources, about whose influence on the determination of activation parameters systematic experience is at present still largely lacking. Their great practical value for qualitative mechanistic studies has, however, already been established beyond doubt. For tropylium azide *(3)* it was possible, for instance, to prove the preferred 1,3-shifts in relatively nonpolar solvents by saturation transfer experiments at carefully selected temperatures[43,100] (cf. Section 2.2). Recently, it has also been shown[101] that qualitative information of this kind can elegantly be obtained by two-dimensional NMR spectroscopy.

We mention in passing that quantitative DNMR analyses of isomerizations can often be supplemented by classical chemical equilibration studies at sufficiently low temperatures (about 100 K below the coalescence temperature). A discussion of the extensive literature on this topic, however, does not fall within the purview of the present essay.

6. Conclusion and Perspectives

In the arsenal of methods at the disposal of the experimentalist DNMR spectroscopy has long been firmly entrenched as a convenient diagnostic for the detection of molecular rate processes. The quantitative determination of a free energy of activation is routinely possible as well and often calls for less effort than commonly supposed. An estimate of the coalescence temperature or the measurement of an incipient line broadening is in many cases all that is required.

The possibility of exploiting DNMR spectroscopy for the elucidation of reaction mechanisms has been fully appreciated only during the last decade. One may no doubt anticipate further interesting applications in the future.

Although DNMR spectroscopy is also suited for a quantitative determination of activation enthalpies and entropies, experience shows that activation entropies of an accuracy indispensable for a meaningful chemical interpretation are no longer obtained routinely. The number of careful studies has increased in recent years, but still constitutes a small percentage of the total body of investigations. If one limits oneself to those in which a detailed interpretation based on the principles of statistical thermodynamics has been seriously attempted, their number shrinks considerably further. Recent methodological developments and the accumulated experience about sources of error lead to the conclusion, however, that DNMR spectroscopy can be perfected to the point where it becomes a precision method also for activation entropies. This opens up broad avenues for future applications. After a sufficient amount of reliable material has been gathered, it might well turn out that activation entropies are sometimes easier to interpret theoretically than the corresponding energy quantities and that they yield novel information about dynamic properties of transition states inaccessible by direct observation. The first indications of such a possibility have been obtained. One thing is certain already: the tools of classical chemical kinetics, to whose application to mechanistic problems of organic chemistry *Rolf Huisgen* has contributed so brilliantly, have been supplemented and materially amplified by DNMR spectroscopy.

We owe a great debt of gratitude to our coworkers named in the cited publications. Financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: March 20, 1980 [Z 322 IE]
German version: Angew. Chem. *92*, 445 (1980)

[1] *J. D. Macomber:* The Dynamics of Spectroscopic Transitions. Wiley, New York 1976.
[2] *G. Binsch*, Top. Stereochem. *3*, 97 (1968).
[3] *L. M. Jackman, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975.
[4] *E. L. Hahn, D. E. Maxwell*, Phys. Rev. *88*, 1070 (1952).
[5] *H. S. Gutowsky, D. W. McCall, C. P. Slichter*, J. Chem. Phys. *21*, 279 (1953).
[6] *H. S. Gutowsky, A. Saika*, J. Chem. Phys. *21*, 1688 (1953).
[7] *H. S. Gutowsky, C. H. Holm*, J. Chem. Phys. *25*, 1228 (1956).
[8] *A. T. Bottini, J. D. Roberts*, J. Am. Chem. Soc. *78*, 5126 (1956).
[9] *H. Shanan-Atidi, K. H. Bar-Eli*, J. Phys. Chem. *74*, 961 (1970).
[10] *H. Kessler*, Angew. Chem. *82*, 237 (1970); Angew. Chem. Int. Ed. Engl. *9*, 219 (1970).
[11] *T. Drakenberg, H. Wennerström* in *R. K. Harris:* Nuclear Magnetic Resonance (Specialist Periodical Reports), Vol. 5. The Chemical Society, London 1976, p. 163.
[12] *B. E. Mann*, Prog. Nucl. Magn. Reson. Spectrosc. *11*, 95 (1977).
[13] *S. Aime, L. Milone*, Prog. Nucl. Magn. Reson. Spectrosc. *11*, 183 (1977).
[14] *F. G. Riddell* in *R. J. Abraham:* Nuclear Magnetic Resonance (Specialist Periodical Reports), Vol. 8. The Chemical Society, London 1979, p. 285.
[15] *G. Binsch* in *L. M. Jackman, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975, p. 45.
[16] *P. D. Buckley, K. W. Jolly, D. N. Pinder*, Prog. Nucl. Magn. Reson. Spectrosc. *10*, 1 (1975).
[17] *S. Szymanski, M. Witanowski, A. Gryff-Keller*, Annu. Rev. NMR Spectrosc. *8*, 227 (1978).
[18] *R. O. Kühne, T. Schaffhauser, A. Wokaun, R. R. Ernst*, J. Magn. Reson. *35*, 39 (1979).
[19] *G. Binsch, E. L. Eliel, H. Kessler*, Angew. Chem. *83*, 618 (1971); Angew. Chem. Int. Ed. Engl. *10*, 570 (1971).
[20] Cf. *e.g. H. Kessler, W. Rundel*, Chem. Ber. *101*, 3350 (1968); *H. Kessler, W. Rundel, A. Rieker*, Chem. Commun. *1968*, 475; *H. Kessler*, Tetrahedron *24*, 1857 (1968).
[21] *H. Kessler, D. Leibfritz*, Chem. Ber. *104*, 2143 (1971).
[22] See, *e.g. H. Kessler, G. Zimmermann, H. Fietze, H. Möhrle*, Chem. Ber. *111*, 2605 (1978).
[23] *G. Binsch, D. A. Kleier*, Quantum Chem. Progr. Exch. *10*, 140 (1969).
[24] *D. A. Kleier, G. Binsch*, Quantum Chem. Progr. Exch. *10*, 165 (1970).
[25] *D. S. Stephenson, G. Binsch*, Quantum Chem. Progr. Exch. *10*, 365 (1978).
[26] *D. S. Stephenson, G. Binsch*, J. Magn. Reson. *32*, 145 (1978).
[27] *H. H. Limbach*, J. Magn. Reson. *36*, 287 (1979).
[28] *H. Nakanishi, O. Yamamoto*, Tetrahedron Lett. *1974*, 1803.

[29] *H. Günther, J. Ulmen,* Tetrahedron *30*, 3781 (1974).
[30] *J. F. M. Oth, K. Müllen, J. M. Gilles, G. Schröder,* Helv. Chim. Acta *57*, 1415 (1974).
[31] For an easily comprehensible introduction to the determination of exchange matrices, see *C. S. Johnson, C. G. Moreland,* J. Chem. Educ. *50*, 477 (1973).
[32] *G. Binsch,* J. Am. Chem. Soc. *91*, 1304 (1969).
[33] *D. A. Kleier, G. Binsch,* J. Magn. Reson. *3*, 146 (1970).
[34] *D. S. Stephenson, G. Binsch,* J. Magn. Reson. *30*, 625 (1978).
[35] *R. Wehner, H. Günther,* J. Am. Chem. Soc. *97*, 923 (1975).
[36] *M. Balci, H. Fischer, H. Günther,* Angew. Chem. *92*, 316 (1980); Angew. Chem. Int. Ed. Engl. *19*, 301 (1980).
[37] *H. Günther, J. B. Pawliczek, B. D. Tunggal, H. Prinzbach, R. H. Levin,* Chem. Ber. *106*, 984 (1973).
[38] *H. Kessler,* Chimia *27*, 444 (1973).
[39] *H. Kessler, A. Walter,* Angew. Chem. *85*, 821 (1973); Angew. Chem. Int. Ed. Engl. *12*, 773 (1973).
[40] *M. Feigel, H. Kessler,* Angew. Chem. *89*, 266 (1977); Angew. Chem. Int. Ed. Engl. *16*, 256 (1977).
[41] *M. Feigel, H. Kessler,* Chem. Ber. *111*, 1659 (1978).
[42] *M. Feigel, H. Kessler, A. Walter,* Chem. Ber. *111*, 2947 (1978).
[43] *M. Feigel, H. Kessler, D. Leibfritz, A. Walter,* J. Am. Chem. Soc. *101*, 1943 (1979).
[44] *D. Höfner, S. A. Lesko, G. Binsch,* Org. Magn. Reson. *11*, 179 (1978).
[45] *D. A. Kleier, G. Binsch, A. Steigel, J. Sauer,* J. Am. Chem. Soc. *92*, 3787 (1970).
[46] *A. Steigel, J. Sauer, D. A. Kleier, G. Binsch,* J. Am. Chem. Soc. *94*, 2770 (1972).
[47] *D. Höfner, I. Tamir, G. Binsch,* Org. Magn. Reson. *11*, 172 (1978).
[48] *H. Kessler, W. Ott,* J. Am. Chem. Soc. *98*, 5014 (1976).
[49] *M. Feigel, H. Kessler,* Chem. Ber. *112*, 3715 (1979).
[50] *D. S. Stephenson, G. Binsch,* J. Magn. Reson. *37*, 395, 409 (1980).
[51] *D. S. Stephenson, G. Binsch,* Quantum Chem. Progr. Exch. *11*, 378 (1979).
[52] *G. Binsch* in *J. Bargon:* Computational Methods in Chemistry. Plenum Press, New York, in press.
[53] *J. P. Jesson, P. Meakin,* Acc. Chem. Res. *6*, 269 (1973).
[54] *W. G. Klemperer* in *L. M. Jackman, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975, p. 23.
[55] *A. Steigel* in *P. Diehl, E. Fluck, R. Kosfeld:* NMR Basic Principles and Progress, Vol. 15. Springer, Berlin 1978, p. 1.
[56] *G. Binsch* in *R. K. Harris:* Nuclear Magnetic Resonance (Specialist Periodical Reports), Vol. 3. The Chemical Society, London 1974, p. 223.
[57] *T. Drakenberg, H. Wennerström* in *R. K. Harris:* Nuclear Magnetic Resonance (Specialist Periodical Reports), Vol. 4. The Chemical Society, London 1975, p. 141.
[58] *W. G. Klemperer, J. K. Krieger, M. D. McCreary, E. L. Muetterties, D. D. Traficante, G. M. Whitesides,* J. Am. Chem. Soc. *97*, 7023 (1975).
[59] *D. Höfner, D. S. Stephenson, G. Binsch,* J. Magn. Reson. *32*, 131 (1978).
[60] *E. E. Wille, D. S. Stephenson, P. Capriel, G. Binsch,* unpublished.
[61] *A. Rieker, H. Kessler,* Tetrahedron Lett. *1969*, 1227.
[62] For reviews see a) *K. Mislow, D. Gust, P. Finocchiaro, R. J. Boettcher,* Top. Curr. Chem. *47*, 1 (1974); b) *K. Mislow,* Acc. Chem. Res. *9*, 26 (1976).
[63] The notation of *Haigh* has been used here; see *C. W. Haigh,* J. Chem. Soc. *A 1970*, 1682.
[64] *Z. Luz, S. Meiboom,* J. Chem. Phys. *59*, 1077 (1973).
[65] *F. A. L. Anet,* J. Am. Chem. Soc. *84*, 671 (1962).
[66] *J. F. M. Oth,* Pure Appl. Chem. *25*, 573 (1971).
[67] *F. A. L. Anet, A. J. R. Bourn, Y. S. Lin,* J. Am. Chem. Soc. *86*, 3576 (1964).
[68] *D. E. Gwynn, G. M. Whitesides, J. D. Roberts,* J. Am. Chem. Soc. *87*, 2862 (1965).
[69] *J. F. M. Oth, R. Merényi, T. Martini, G. Schröder,* Tetrahedron Lett. *1966*, 3087.
[70] *Z. Luz, R. Naor, E. Meirovitch,* private communication.
[71] *R. D. Adams, F. A. Cotton* in *L. M. Jackman, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975, p. 489.
[72] *M. Feigel,* Dissertation, Universität Frankfurt 1978.
[73] *J. T. Gerig, J. D. Roberts,* J. Am. Chem. Soc. *88*, 2791 (1966).
[74] *D. K. Dalling, D. M. Grant, L. F. Johnson,* J. Am. Chem. Soc. *93*, 3678 (1971).
[75] *H. Kessler, G. Zimmermann,* Chem. Ber. *110*, 2306 (1977); *H. Kessler, H. Möhrle, G. Zimmermann,* J. Org. Chem. *42*, 66 (1977).
[76] *H. Günther, J. B. Pawliczek, J. Ulmen, W. Grimme,* Chem. Ber. *108*, 3141 (1975).
[77] *M. Kempf,* Dissertation, Universität Frankfurt 1978.
[78] *R. Bicker, H. Kessler, W. Ott,* Chem. Ber. *108*, 3151 (1975).
[79] *H. Günther, J. Ulmen,* Chem. Ber. *108*, 3132 (1975).
[80] *H. Kessler, M. Kempf,* unpublished.
[81] *F. R. Jensen, C. H. Bushweller, B. H. Beck,* Rev. Sci. Instrum. *43*, 145 (1972); *F. R. Jensen, L. A. Smith, C. H. Bushweller, B. H. Beck, ibid. 43*, 894 (1972); *R. A. Neese,* Ph. D. Thesis, University of California, Berkeley 1971.
[82] *H. Friebolin, G. Schilling, L. Pohl,* Org. Magn. Reson. *12*, 569 (1979).
[83] *G. C. Levy, J. T. Bailey, D. A. Wright,* J. Magn. Reson. *37*, 353 (1980).
[84] The fact that, at the coalescence point of two equally intense singlets, the total width equals the sum of the static splitting and the natural width, cannot be exploited for bandshape analyses, although it is unquestionably very useful for an estimation of a ΔG^{+} value.
[85] *R. W. Hoffmann, N. Hauel, F. Frickel, M. Kempf, H. Kessler,* Chem. Ber. *112*, 2894 (1979).
[86] See *e.g. H. Kessler, M. Molter,* J. Am. Chem. Soc. *98*, 5969 (1976).
[87] An iterative calculation for an experimental test example of two exchanging singlets with a chemical shift difference of about 50 Hz and $W \approx 3\,W_0$, in which the dynamic parameters k and W_0 were confined to the expected domain of 0—5 s^{-1} by means of reflective boundaries [26], yielded the value of $k = 1.26 \pm 96424\ s^{-1}$ (correlation coefficient $\rho(k, W_0) = -0.999998$); a result that speaks for itself!
[88] *W. E. Deming:* Statistical Adjustment of Data. Wiley, New York 1943.
[89] *G. Binsch,* 1969, unpublished. Modern versions of this program, which is also suitable for the determination of the thermodynamic quantities ΔH^0 and ΔS^0, were written by *M. Feigel* (Universität Frankfurt) und *T. Dürst* (Universität München).
[90] A classic paper, in which a careful study of the possibilities of *systematic* errors was performed for the first time, is constantly cited in this connection: *A. Allerhand, H. S. Gutowsky, J. Jonas, R. A. Meinzer,* J. Am. Chem. Soc. *88*, 3185 (1966). Now there can indeed be no doubt about the crucial importance of systematic errors in practical applications of DNMR spectroscopy, as has also been emphasized in the above discussion. But it would appear to the authors that one can begin to talk about systematic errors only when the statistics is in order.
[91] *S. Forsén, R. A. Hoffman,* Acta Chem. Scand. *17*, 1787 (1963); J. Chem. Phys. *39*, 2892 (1963); *40*, 1189 (1964); *R. A. Hoffman, S. Forsén, ibid. 45*, 2049 (1966).
[92] *F. A. L. Anet, A. J. R. Bourn,* J. Am. Chem. Soc. *89*, 760 (1967).
[93] *B. E. Mann,* J. Magn. Reson. *21*, 17 (1976); *25*, 91 (1977); J. Chem. Soc. Chem. Commun. *1977*, 626.
[94] *C. L. Perrin, E. R. Johnston,* J. Magn. Reson. *33*, 619 (1979).
[95] *F. W. Dahlquist, K. J. Longmuir, R. B. Du Vernet,* J. Magn. Reson. *17*, 406 (1975).
[96] *J. R. Alger, J. H. Prestegard,* J. Magn. Reson. *27*, 137 (1977).
[97] *I. D. Campbell, C. M. Dobson, R. G. Ratcliffe, R. J. P. Williams,* J. Magn. Reson. *29*, 397 (1978).
[98] *G. Bodenhausen, R. Freeman, G. A. Morris,* J. Magn. Reson. *23*, 171 (1976); *G. A. Morris, R. Freeman, ibid. 29*, 433 (1978).
[99] *M. F. Grenier-Loustalot, R. K. Harris, C. J. Macdonald,* Third European Experimental NMR Conference, Elsinore, Denmark 1977.
[100] Careful selection of the temperature is critical. The exchange should still be fast enough so as not to be swamped by relaxation, but not so fast that saturation is transferred indiscriminately also to the other positions not connected to the irradiated line by an elementary step.
[101] *B. H. Meier, R. R. Ernst,* J. Am. Chem. Soc. *101*, 6441 (1979); *J. Jeener, B. H. Meier, P. Bachmann, R. R. Ernst,* J. Chem. Phys. *71*, 4546 (1979).

Towards an Understanding of the Carbon-Carbon Bond

By Christoph Rüchardt and Hans-Dieter Beckhaus[*]

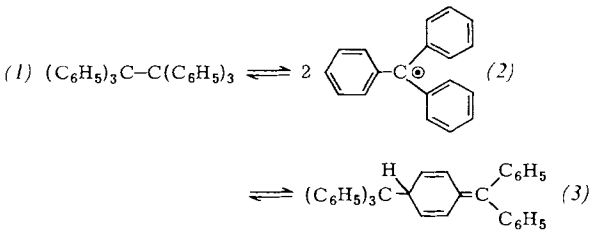
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In this essay, the classical question of "the influence of the number and kind of substituents on the strength of the C—C bond", is pursued with the modern tools of contemporary physical organic chemistry. Based on the work of *Karl Ziegler,* the products and kinetics of thermolysis of a large number of highly branched aliphatic hydrocarbons and phenyl- or cyano-substituted derivatives were investigated. For each class of compounds, a linear relationship was found between the free enthalpy of activation of the homolytic cleavage of the weakest C—C bond and the strain energy in the ground state. These relationships permitted a *quantitative* separation of steric and electronic effects on the cleavage of C—C bonds. The influence of the size of the substituent groups on bond angles, bond lengths, and the conformational behavior of model compounds was studied by means of experimental structure determinations and force field calculations. C—C bond lengths up to 164 pm, bond angles at tetracoordinate carbon as large as 126°, and unusual eclipsed and *gauche* preferred conformations were found.

1. Introduction

In the last 35 years, the study of organic reaction mechanisms has experienced a golden age which has led not only to the development of new experimental methods and theoretical models but also to elucidation of the mechanisms of most organic reactions and to the discovery of many new ones. *Rolf Huisgen* is one of the scientists who has made authoritative contributions to this development.

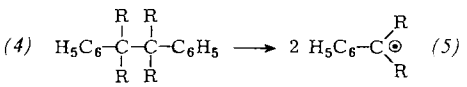
In 1949, *Karl Ziegler* wrote a paper on trivalent carbon[1] starting from the question: "Why is the central C—C bond in the Gomberg hydrocarbon hexaphenylethane *(1)*[2] so weak that the hydrocarbon spontaneously decomposes in solution to give a measurable equilibrium concentration of triphenylmethyl radicals *(2)*?"



Ziegler determined the rates of thermolysis of a series of hydrocarbons *(4)* as well as other compounds, and established that their thermal stability follows the series

$$R = CH_3 > C_2H_5 > C_3H_7 > C_4H_9$$

i.e. their stability decreases rapidly with the size of R[1].

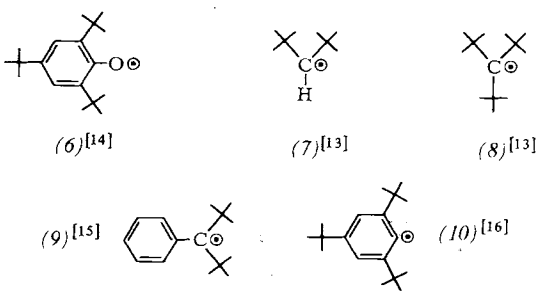


Consequently, the instability of hexaphenylethane *(1)* could no longer be attributed solely to the *electronic stabilization* of the resulting triphenylmethyl radicals *(2)* as had been previously believed. The *"steric acceleration"* of thermolysis, established by studies on *(4)*, also had to be accepted in the case of *(1)*. The fact that the Gomberg hydrocarbon is now known to be the α,*p*-dimer *(3)* which is less crowded than the α,α-dimer *(1)*[3,4], does not, in principle, alter *Ziegler*'s argument. The key point is that all the repulsive forces between atoms and groups of atoms in *(1)*, *(3)*, or *(4)* decrease during the dissociation process as the central C—C bond becomes longer and as the bond angles at the central tetracoordinate carbon atoms increase[5].

On the basis of simple kinetic experiments and considerations of skeletal models, *Ziegler* postulated[1] the principle of "steric acceleration"[6] long before the definition of precise stereochemical concepts such as back strain[6,7], front strain[6-8], steric substituent constants[9], or conformational analysis[10]. Moreover, the modern methods of precise structural analysis were not available at that time.

Meanwhile, steric effects have been firmly established in many reactions[6,11,12]; in particular, many examples of the influence of bulky groups on the persistence of radicals have been recognized[13]. For example, the *tert*-butyl groups in radicals *(6)*—*(10)* hinder their dimerization, because the repulsive van der Waals forces give rise to large activation energies for recombination.

Because the interpretation of the effects discussed so far is still only qualitative, the question of different bond strengths



[*] Prof. Dr. Ch. Rüchardt, Dr. H.-D. Beckhaus
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0606-0429 $ 02.50/0*

in branched and substituted alkanes is just as real today as it has ever been. The effects are so large that they demand a quantitative interpretation; for example, there is a difference of 76 kcal mol^{-1} between the bond dissociation enthalpy in ethane[17a-c] and that of the Gomberg dimer *(3)*[17d]! Ethane decomposes to methyl radicals with $\tau_{1/2}=1$ h only at 690 °C; in contrast, *(3)* dissociates at the same rate at 0 °C.

$$CH_3{-}CH_3 \xrightarrow{690\,^{\circ}C} 2\,CH_3^{\bullet} \qquad H_D = 88 \text{ kcal mol}^{-1}\text{[17a-c]}$$

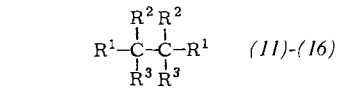
$$(3) \xrightarrow{0\,^{\circ}C} 2(C_6H_5)_3C^{\bullet} \quad H_D \approx 12 \text{ kcal mol}^{-1}\text{[17d]}$$

On extrapolation, the two dissociation reactions are seen to differ in their rates by a factor of about 10^{30}. Hardly any other chemical reaction is more drastically influenced by substituents than carbon-carbon bond cleavage.

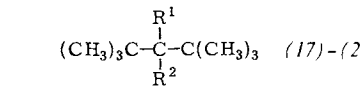
2. Synthesis and Thermolysis of Highly Branched Hydrocarbons

At the beginning of our work 10 years ago[18], the region between these two extremes of thermal stability had been

Table 1. Thermal stability and strain enthalpy H_{sp} [a] of the hydrocarbons of types *(11)—(16)* and *(17)—(21)*.



(11)-(16)



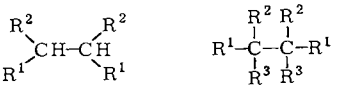
(17)-(21)

No.	R^1	R^2	R^3	Form	T ($\tau_{1/2}=1$ h) [°C]	$\Delta G^{\ddagger}$ (300 °C) [kcal mol^{-1}]	$\Delta H^{\ddagger}$ [kcal mol^{-1}]	$\Delta S^{\ddagger}$ [cal mol^{-1} K^{-1}]	H_{sp} [a] [kcal mol^{-1}]	Ref.
(11)	H	H	H		695	79 [b]	87	14	0	[17]
(12)	CH_3	H	H		590	69 [b]	78	16	0	[20]
C,C, alkanes (13)										
a	CH_3	CH_3	H		565	68	75	12	2.7	[21]
b	CH_3	*c*-C_6H_{11}	H	*meso*	453	59	67.5	15 [c]	9.6	[23]
c	*c*-C_6H_{11}	*c*-C_6H_{11}	H		384	52.2	62.9	18.4	17.0	[24]
d	*c*-C_6H_{11}	*t*-C_4H_9	H	D,L	329	46.7	55.5	15 [c]	28.1	[25]
e	*c*-C_6H_{11}	*t*-C_4H_9	H	*meso*	285	42.6	53.4	18.9	34.5	[25]
f	*t*-C_4H_9	*t*-C_4H_9	H		141	29.6	36.4	11.8	57.7	[27]
C_qC_q alkanes (14)										
a	CH_3	CH_3	CH_3		470	60 [b]	67.4	13	6.9	[21]
b	CH_3	CH_3	C_2H_5		424	55.3	62.1	11.9	12.3	[28]
c	CH_3	CH_3	*n*-C_3H_7		411	53.6	57.8	7.3	11.8	[28]
d	CH_3	CH_3	*i*-C_3H_7		329	47.3	62.2	26.3	22.4	[28]
e	CH_3	CH_3	*n*-C_4H_9		412	53.9	59.0	9.0	11.2	[28]
f	CH_3	CH_3	*i*-C_4H_9		384	51.9	60.7	15.3	17.2	[28]
g	CH_3	CH_3	*t*-C_4H_9		195	33.7	44.0	17.7	45.3	[28]
h	CH_3	CH_3	$(CH_3)_3CCH_2$		321	46.1	57.8	20.4	25.3	[28]
i	CH_3	CH_3	*i*-C_5H_{11}		412	53.8	58.3	7.9	12.5	[28]
k	CH_3	CH_3	*c*-C_6H_{11}		315	45.7	61.2	27.0	24.5	[28, 29]
l	CH_3	C_2H_5	C_2H_5		364	50.2	60.7	17.5	20.2	[28]
m	CH_3	C_2H_5	*c*-C_6H_{11}	*meso*	250	39.3	52.1	22.4	34.8	[28, 30]
n	C_2H_5	C_2H_5	C_2H_5		285	42.8	51.0	14.4	32.6	[28, 29]
Phenyl-substituted C,C, alkanes (15)										
a	C_6H_5	CH_3	H	*meso*	365	50.0	58.1	14.1	3.6 [d]	[26]
b	C_6H_5	C_2H_5	H	*meso*	360	49.7	59.4	16.9	4.8 [d]	[26]
c	C_6H_5	*i*-C_3H_7	H	*meso*	335	47.4	57.4	17.4	8.4 [d]	[26]
d	C_6H_5	*t*-C_4H_9	H	D,L	308	44.6	53.5	15 [c]	19.3 [d]	[26]
e	C_6H_5	*t*-C_4H_9	H	*meso*	281	42.1	50.4	14.2	22.2 [d]	[26]
f	4-ClC_6H_4	*t*-C_4H_9	H	D,L	300	44.0	50.0	10.4	19.3 [e]	[32, 33]
g	4-ClC_6H_4	*t*-C_4H_9	H	*meso*	279	42.2	47.2	8.8	22.2 [e]	[32, 33]
h	C_6H_5	*t*-C_5H_{11}	H	*meso*	258	40.3	44.3	6.8	27.0 [f]	[26]
Phenyl-substituted C_qC_q alkanes (16)										
a	C_6H_5	CH_3	CH_3		233	37.9	45.7	13.7	18.4 [d]	[1, 34]
b	C_6H_5	CH_3	C_2H_5	*meso*	211	34.9	48.8	24.3	23.7 [d]	[34]
c	C_6H_5	CH_3	*n*-C_3H_7	*meso*	194	33.3	46.3	22.7	23.2 [d]	[35]
d	C_6H_5	CH_3	*i*-C_3H_7	*meso*	114	26.7	35.1	14.6	40.9 [d]	[19a]
e	C_6H_5	CH_3	*i*-C_4H_9	*meso*	156	30.1	40.5	18.2	26.3 [d]	[35]
f	C_6H_5	C_2H_5	C_2H_5		134	25.4	44.7	33.6	37.1 [d]	[34]
g	4-*t*-BuC_6H_4	C_2H_5	*n*-C_3H_7	*meso*/D,L	130	27.7	37.8	17.6	36.5 [d]	[35]
h	C_6H_5	*n*-C_3H_7	*n*-C_3H_7		119	27.5	34.9	13.0	35.8 [d]	[1, 36]
i	C_6H_5	*n*-C_4H_9	*n*-C_4H_9		118	25.7	38.5	22.4	34.6 [d]	[35]
Other hydrocarbons [g]										
(17)	H	H			502	63.9	74.6	18.9	7.4	[37]
(18)	CH_3	H			426	55.8	64.4	15.0	13.9	[37]
(19)	CH_3	CH_3			350	48.8	58.9	17.8	21.6	[37]
(20)	H	*t*-C_4H_9			243	38.6	47.3	15.1	37.1	[38]
(21)	CH_3	*i*-C_3H_7			258	40.1	48.3	14.3	40.1	[39]

[a] $H_{sp}=\Delta H_f^{\circ}(\text{gas})-\Delta H_f^{N}$. Unless otherwise noted, the enthalpy of formation, ΔH_f°(gas) was calculated with the force field MM2 [22] (computer program STRAIN 65 [27a]). The specific reference value ΔH_f^{N} was calculated from group increments [40]. Incremental corrections [22] for free rotation around C—C bonds were added for *(13a—c)*, *(14b—f, h, i)* and *(17)*. [b] Gas phase. [c] Assumed value (see [25] and [26]). [d] ΔH_f°(gas) was calculated with the Allinger force field, supplemented with the phenyl parameters, SET B, of *Mislow* [31] (see [26]). [e] Values for the compounds *(15d, e)* without chlorine substituents. [f] Value determined from heat of combustion measurements (see [26]). [g] A C—*tert*-butyl bond is broken during thermolysis. When there are several equivalent bonds, the kinetic data are statistically corrected.

barely explored, with the exception of the results of *Ziegler*[1] and a few complementary investigations[17d, 19a, b]. Work was subsequently published on the decomposition of phenyl-substituted alkanes[19c, d] and on the kinetics of pyrolysis of simple alkanes in the gas phase[17a-c, 20]. Since then, we have synthesized a great number of highly branched hydrocarbons whose thermal stabilities lie between the two extremes discussed above (see Table 1). In the main, classical dimerization methods such as the Wurtz synthesis and related techniques were used; of course, the yields decrease to a few percent for the highly branched representatives and the isolation of these compounds in gram quantities was therefore extremely laborious. Gas chromatography was an indispensable aid for purity control and occasionally also for isolation. Stepwise syntheses of the compounds in Table 1 were successful in only a few cases. Preparation of the cyclohexyl-substituted ethanes *(13b—e)* and *(14k, m)* was accomplished by high pressure hydrogenation of the corresponding phenyl derivatives.

We divide the symmetrical ethane derivatives which we have studied into two classes designated as the C_t—C_t series *(13), (15)* or the C_q—C_q series *(14), (16)* according to whether the two central C atoms are tertiary or quaternary.



C_t–C_t $\qquad$ C_q–C_q

In addition, a few highly branched unsymmetrical alkanes were prepared and thermolyzed. In the C_q—C_q- and C_t—C_t series, both the alkanes [*(13)* and *(14)*] and the phenyl derivatives [*(15)* and *(16)*] were studied (see Table 1).

The products of thermolysis of a large number of typical representatives were quantitatively determined by gas chromatography[23, 25, 27, 30, 34, 38, 39]. In all cases the major, and usually the only, decomposition pathway was homolytic cleavage of the central C—C bond or of the most substituted C—C bond in the other kinds of molecules *(17)—(21)*.

The kinetics of thermolysis were studied under N_2 using ampoule techniques, and were generally followed by gas chromatographic determination of the decrease in concentration of the starting material. A thermostat utilizing molten tin as the bath liquid was developed for the high temperature measurements. A few kinetic measurements were conducted with other methods, such as radical scavenging techniques with chloranil[1] or other radical traps. In general, aromatic hydrocarbons such as ethylbenzene, toluene, or mesitylene served as solvents; occasionally, decalin or *n*-alkanes with added scavenger such as mercaptan was used. Induced decomposition is recognizable under the specific reaction conditions, *e.g.* by strongly negative entropies of activation, and was not a serious drawback[29] under the conditions of measurement chosen by us.

The results of the kinetic measurements are given in Table 1. The Eyring activation parameters are recorded because the rates of reaction can only be compared at equivalent temperatures and because the actual reaction temperatures are very different. In most cases, the activation parameters were calculated from rate constants measured over a 50-degree temperature range. The temperatures at which $\tau_{1/2} = 1$ h are also listed, in order to permit an easy comparison of the thermal stability of these hydrocarbons.

Application of the Exner test showed that, at least within a series of comparable compounds, isokinetic and even isoentropic relationships exist; a discussion of the relationship between structure and activity in terms of the precisely determined free enthalpies of activation, $\Delta G^{\neq}$, or in terms of the linearly related temperatures for $\tau_{1/2} = 1$ h is therefore permissible[23, 26, 37].

A qualitative examination of the kinetic results in Table 1 supports the findings of *Ziegler*[1]: the thermal stability of the central C—C bond in substituted ethanes is decreased not just by radical-stabilizing α-phenyl substituents, but also especially by increasing size of the groups in the alkyl side chain. This steric acceleration of the homolytic bond dissociation is especially clear in the thermolysis of 3,4-di-*tert*-butyl-2,2,5,5-tetramethylhexane ("tetra-*tert*-butylethane"), *(13f)*[27], which dissociates into ordinary secondary radicals with no special stabilization[43]. The C—C bond of *(13f)* is cleaved at approximately the same rate as the O—O bond in di-*tert*-butyl peroxide ($\Delta H^{\neq} = 37$ kcal mol^{-1}, $\Delta S^{\neq} = 12$ cal mol^{-1} K^{-1} in cyclohexane)[42].

The discovery that the cyclohexyl-substituted compounds *(13d, e)*[25] have $\tau_{1/2} = 1$ h at almost the same temperature as the corresponding phenyl-substituted compounds *(15d, e)*[26], in spite of the fact that the latter decompose into radicals of the benzyl type, points to the same conclusion. Finally, it is striking that the diastereomers *(13d, e)*[22], *(15d, e)*[26], or *(15f, g)*[32, 33] are remarkably different in stability. Since thermolysis of the diastereomeric hydrocarbons gives the same radicals, the heat of formation of the diastereomeric hydrocarbons themselves must be very different. This is apparently the case when the ethane moiety is substituted on both C atoms with *tert*-butyl groups.

Finally, the finding[11, 12, 23, 26, 28, 29] that the rates of thermolysis of the four symmetrical compound types *(13)—(16)* all give good correlations with the steric substituent constants E_s^c or $\mathscr{S}_f$[9d] indicates that, within each series, the different ground state strain of the hydrocarbons is the factor which determines the reactivity.

2.1. Thermal Stability and Strain Enthalpy

We calculated the ground state strain enthalpies, H_{sp}, for the hydrocarbons *(11)—(21)* (see Table 1) in order to be able to *quantitatively* analyze the steric acceleration of the decomposition of these compounds. By definition, H_{sp} corresponds to the difference between the standard enthalpy of formation in the gas phase, ΔH_f^0(gas), and a strain-free "normal heat of formation", ΔH_f^N. The latter is calculated from group increments[40]. We calculated the heat of formation of the hydrocarbons with empirical force field techniques[44], which also give agreement with structural data (see below).

Since the available force fields are not parameterized for highly strained compounds[44], their suitability for such compounds must be tested by comparison with experimental data. This was accomplished by comparison of calculated structural data with the results of X-ray analyses (see Section 3). In addition, we determined the heat of formation from

experimental thermochemical data, *i.e.* heats of combustion, heats of fusion, and heats of sublimation[25-27], for a few of the most highly strained compounds. Their strain enthalpies, H_{sp}, based on the experimentally determined heats of formation of the most highly strained compounds, tetra-*tert*-butylethane *(13f)* (exp. $H_{sp} = 57 \pm 4$ kcal mol^{-1})[45] and 3,4-dimethyl-3,4-dicyclohexylhexane *(14m)* (exp. $H_{sp} = 35 \pm 0.5$ kcal mol^{-1})[30] are in excellent agreement with the values calculated with *Allinger*'s force field MM2[22] (see Table 1). Because the other force fields did not give the same uniformly high precision of agreement, we used the MM2 values for the alkanes *(13)*, *(14)*, and *(17)—(21)* in Table 1. However, since this force field[22] is not yet parameterized for aromatic hydrocarbons, we used the older force field of *Allinger* (71)[44,46] with the phenyl parameters (SET B) of *Andose* and *Mislow*[31] for the phenyl-substituted compounds in Table 1. This choice of force field was fully justified by the structural data (see Section 3).

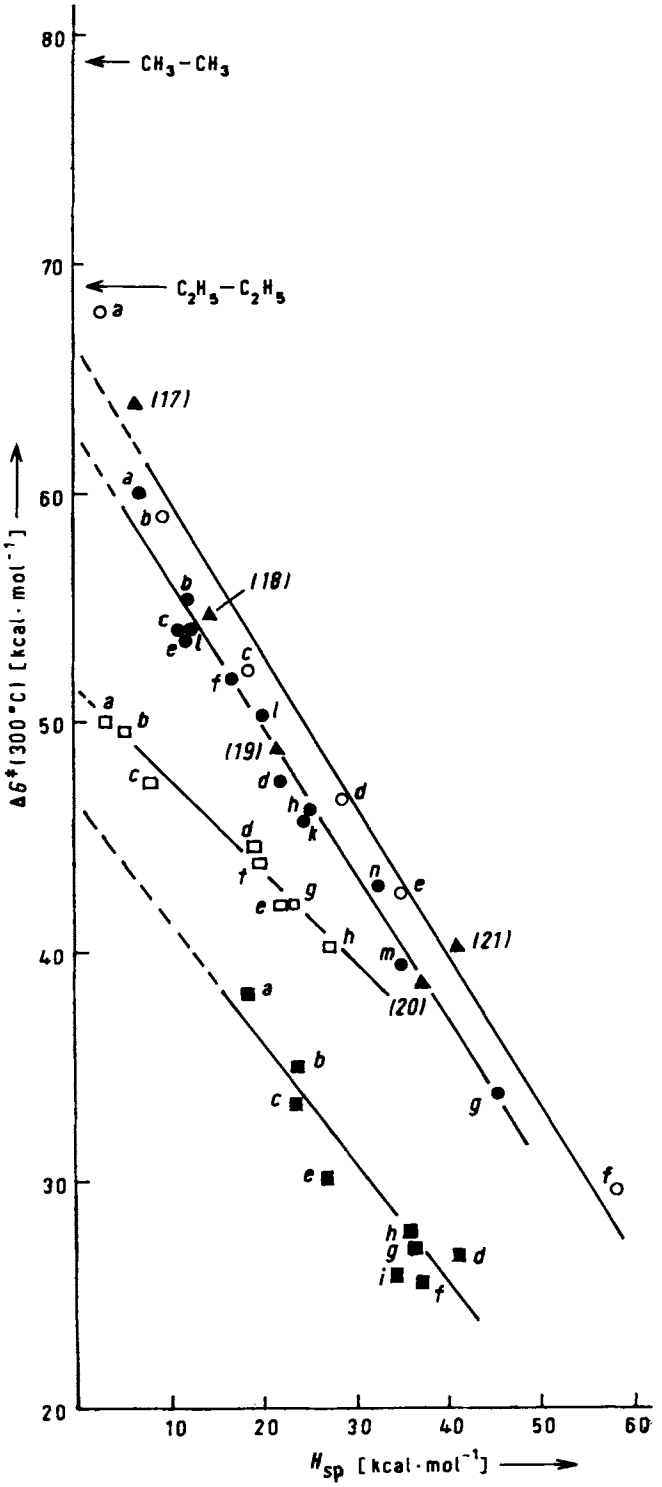


Fig. 1. Correlation between the free enthalpy of activation, $\Delta G^{\ddagger}$ (300 °C), of the thermolysis and the strain enthalpy, $H_{sp} = \Delta H_f^{\circ}(\text{gas}) - \Delta H_f^{N}$ [40], for the hydrocarbons *(13)—(21)* (see Table 1).
The correlation lines yield the following equations:

○ *(13a—f)*: $\Delta G^{\ddagger} = 66.5\ (\pm 1.6) - 0.67\ (\pm 0.05)\ H_{sp}$ kcal mol^{-1}
● *(14a—h)*: $\Delta G^{\ddagger} = 62.4\ (\pm 0.7) - 0.64\ (\pm 0.03)\ H_{sp}$ kcal mol^{-1}
□ *(15a—h)*: $\Delta G^{\ddagger} = 51.4\ (\pm 0.4) - 0.40\ (\pm 0.02)\ H_{sp}$ kcal mol^{-1}
■ *(16a—i)*: $\Delta G^{\ddagger} = 46.2\ (\pm 2.4) - 0.52\ (\pm 0.07)\ H_{sp}$ kcal mol^{-1}
▲ *(17)—(21)*
(Standard deviation in parentheses.)

Can a relationship be established between the strain enthalpies of the hydrocarbons and their thermal stabilities? If $\Delta G^{\ddagger}$ (300 °C) for the thermolysis of *(13)—(16)* is plotted against the strain, H_{sp}, a far-reaching linear correlation with astoundingly little scatter obtains for each of the four types of compounds. The slopes of the calculated correlation lines permit conclusions about the sensitivity of the rate of decomposition of a class of compounds to increasing strain in the ground state. The displacements between the lines point to the influence of radical stabilizing substituents on the transition state of the reaction[47].

The correlation lines of the C_t—C_t series *(13)* and the C_q—C_q series *(14)* possess almost the same slope, but differ in intercept by about 4 kcal mol^{-1}. This difference was not established previously, when computational results from the Engler-Schleyer force field were used[37]. Experimental data verify that this older force field leads to excessively high strain enthalpies in the C_q—C_q series[30]. Since *(13)* gives secondary radicals and *(14)* gives tertiary radicals, the small difference in intercepts is now in agreement with the expectation[5,43] of different bond strengths at tertiary and quaternary C atoms. On the other hand, it is seen from Figure 1 that the linear correlations for *(13)* and *(14)* break down for very small strain energies; extrapolation to the intercepts is therefore somewhat questionable. The points for *(13a)* and *(14a)* lie clearly above the correlation lines. However, in contrast to the others, these points are literature values determined in the gas phase.

The trend to a higher stability than is understandable solely in terms of the strain energy is particularly apparent when ethane *(11)* and butane *(12)* are included in the picture. The high stability of their C—C bonds has not yet been satisfactorily explained: weak electronic stabilization of the resulting methyl and ethyl radicals is hardly or only partly responsible. There may be a special stabilization of the hydrocarbon ground state in these cases[5,11,12,43,48]. These minor deviations cast no doubt on the overall correlation which certainly does not have to be strictly linear in any case. Further conclusions can therefore be drawn: the intercepts of $\Delta G^{\ddagger} = 63$ or 66 kcal mol^{-1}, correspond to bond dissociation enthalpies, $H_D = 71.6$ [C_q—C_q alkanes *(14)*] or 74.6 kcal mol^{-1} [C_t—C_t alkanes *(13)*] for the unstrained prototypes, in full accord with expectation[49]. It is particularly impressive that the thermolysis data for the alkanes *(17)—(21)* are generally in line with the correlations in Figure 1. In these cases, the free enthalpies of activation for the thermolyses must be statistically corrected for the number of equivalent bonds and the

bond types must be taken into account [C_q—C_q: *(19)*, *(21)*; C_q—C_t: *(18)*, *(20)*; C_q—C_s: *(17)*] (s = secondary).

It is particularly interesting that the correlations for C_t—C_t and for C_q—C_q alkanes both show a slope of about 0.65. An increase in the ground state strain is therefore only about 65% effective in decreasing the activation enthalpy of C—C cleavage. Approximately 35% residual strain must remain in the transition state of the thermolysis. It is interesting that this rule holds, apparently independently of the total strain in the compound. According to the principle of microscopic reversibility, the recombination of two alkyl radicals must experience a strain in the transition state which corresponds to about 35% of the strain in the dimer. Assuming that the alkyl radicals are unstrained, or at most much less strained than their dimers[27,28], one obtains the reaction coordinate diagram shown in Figure 2.

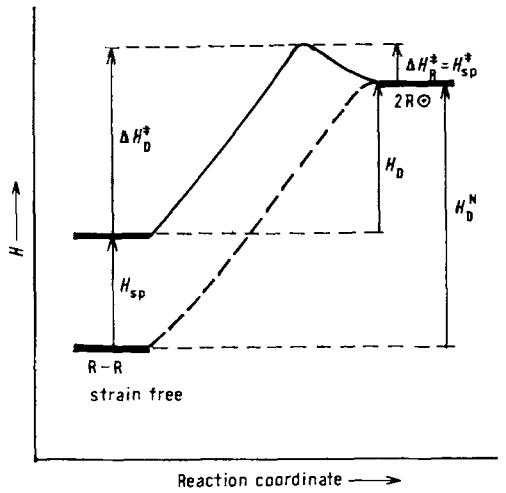
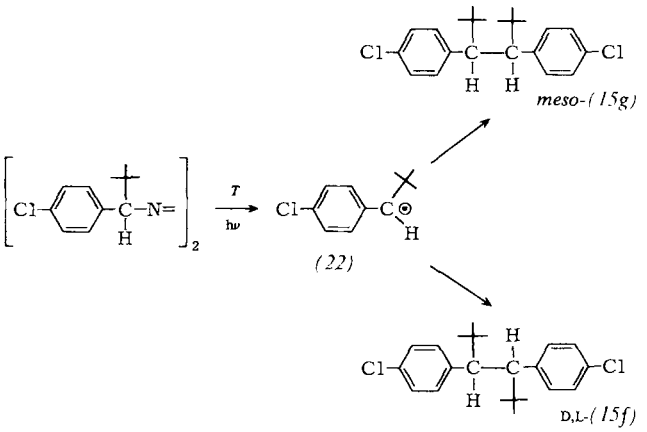


Fig. 2. Reaction coordinate for thermal C—C cleavage.

The bond dissociation enthalpy H_D^N of the unstrained compound, the strain enthalpy, H_{sp}, as well as the $\Delta H_D^{\ddagger}$ are accessible through experiment or calculation. By subtraction, one obtains $\Delta H_R^{\ddagger}$, the activation enthalpy for recombination of the radicals and H_D, the thermodynamic bond enthalpy. $\Delta H_R^{\ddagger}$ is diminished, of course, when a residual strain ultimately appears in the radicals themselves[27,28].

In contrast to small alkyl radicals whose recombination rates are diffusion controlled[32,50], hindered radicals have to overcome an activation barrier to dimerization. This is in agreement with the observed lack of dimerization of the hindered radicals *(6)*—*(10)*. Experiments to measure the recombination rates of selected radicals of moderate size by ESR spectroscopy are in progress[51]. For an independent test of this question, the diastereomeric pairs *(13d, e)*, *(15d, e)*, and *(15f, g)* are suitable; their different rates of thermolysis are explained by their different strain enthalpies. According to Figure 2, one anticipates that the formation of the *meso*- and D,L-diastereomers by radical recombination proceeds over different activation barriers. Therefore, the diastereomers should not be formed in 1:1 ratio, as is usually the case with the recombination of smaller radicals. The finding that the dimerization of 1-*p*-chlorophenylneopentyl radicals *(22)* proceeds diastereoselectively to give the more stable D,L-dimer *(15f)*, in preference to *(15g)*, appears to be in agreement with an activation barrier to dimerization of the radicals[32].



However, the product ratio, *(15f)*:*(15g)* = 1.66 was found to be independent of the temperature between −30 and +140 °C[33]. Therefore, in this case it cannot be that the differences in the rates of dimerization are caused by differences in strain enthalpy of the diastereomers. The significance of this diastereoselectivity must be examined with other models[52].

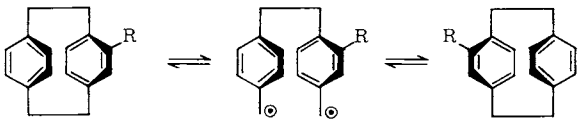
2.2. Influence of Phenyl Substituents

The correlation lines for the phenyl-substituted compounds *(15)* and *(16)* in Figure 1 resemble those for the alkanes *(13)* and *(14)* in several respects. In particular, the correlation lines for *(15)* (C_t—C_t series) and *(16)* (C_q—C_q series) again differ in their intercepts by about 4 kcal mol^{-1}. However, their slopes (0.40 and 0.52 respectively) are significantly smaller than the slopes for the alkanes *(13)* and *(14)* (0.67 and 0.64). The fact that the thermolyses of *(15)* and *(16)* give resonance-stabilized α-substituted benzyl radicals certainly plays an important role. This is also the reason that the correlation lines for the phenyl substituted compounds *(15)* and *(16)* in Figure 1 lie further down than the lines for the aliphatic compounds *(13)* and *(14)*. $\Delta G^{\ddagger}$ is decreased by that part of the resonance energy of the resulting radicals which is set free at the transition state. This resonance energy can be estimated from Figure 1. According to the above arguments, one can be certain that the transition state lies at the energy level of the resulting radicals only in the case of the thermolysis of unstrained hydrocarbons (see Fig. 2). For the dissociation of strained hydrocarbons, the transition state should be reached before the dissociation is complete (see Fig. 2); therefore, the full benzyl resonance cannot be effective in stabilizing the transition state. In order to estimate the benzylic resonance, we therefore compare the intercepts ($H_{sp} = 0$) of the correlation lines of the phenyl-substituted and the corresponding alkane compounds. For the C_t—C_t series [*(13)* and *(15)*], the difference is $\Delta\Delta G_0^{\ddagger} = 15.1$ (±1.7) kcal mol^{-1} and for the C_q—C_q series [*(14)* and *(16)*] $\Delta\Delta G_0^{\ddagger} = 16.2$ (±2.5) kcal mol^{-1}. To be sure, it should be noted that two different force fields were used for the alkanes *(13)* and *(14)* and for the phenyl derivatives *(15)* and *(16)*; the discrepancies caused by this are certainly not large, because the use

of the Engler-Schleyer[53] force field for *(13)* gave[26] a difference in intercepts [*(13)*:*(15)*] of 16 kcal mol^{-1}. Thus, the resonance energy per benzyl radical is *ca.* 8 kcal mol^{-1}, in good agreement with the most recent literature value of 10 ± 2 kcal mol^{-1}[54]. The qualitative estimation of the thermal stability of hydrocarbons in terms of radical stabilization and ground state strain, as intended by *Ziegler*, has thus been put on a *quantitative* basis.

In addition, the smaller slopes of the correlations for the phenyl derivatives are probably explained by the resonance energies of the radicals resulting from the thermolysis. As the strain in the hydrocarbon increases, the transition state of the thermolysis is reached sooner on the reaction coordinate (see Fig. 2), *i.e.* the bond breaking is not complete and the delocalization energy of the benzyl radicals is therefore only partially released. The separation between the correlation lines for the aliphatic and the phenyl substituted derivatives should, therefore, decrease in the region of high strain H_{sp}, as observed. It is not yet known why the effect is smaller in the C_q—C_q series than in the C_t—C_t series. A conclusion will only be possible when the strain enthalpies of the phenyl-substituted compounds have been calculated with the force field MM2 and this force field has been tested in this series against experimental, thermochemical data.

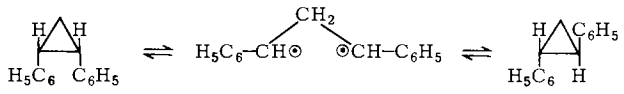
The results described here concerning the demarcation of steric and electronic effects have provided a substantially deeper insight into the laws concerning C—C bond cleavages and have stimulated a study of the reverse reaction, namely the recombination of radicals to give strained hydrocarbons. However, the results also have empirical significance for the prediction of the thermal stability of hydrocarbons. By means of simple force field calculations, these predictions are possible from Figure 1 with considerable precision. The finding that the rates of thermolysis of the unsymmetrical compounds *(17)*—*(21)* corresponds to expectation is especially important. In this regard, it is interesting to see that homolytic cleavage reactions associated with the release of ring strain, but not with the release of F-strain[8], as in our examples, are apparently also in qualitative agreement with the correlations of Figure 1. Thus, the rate of racemization of (−)-methyl [2.2]paracyclophane-4-carboxylate, (−)-*(23)*, which is formulated as a homolysis-recombination reaction ($\Delta G^{\neq} \approx 38$ kcal mol^{-1}; H_{sp} 31.3 kcal mol^{-1})[55] lies on the correlation line for the class of compounds of type *(15)* in Figure 1.



(−)-*(23)* R = $COOCH_3$ (+)-*(23)*

The same applies to the rate of *cis-trans* isomerization of 1,2-diphenylcyclopropane *(24)* [$\Delta G^{\neq}$ (300 °C) = 38.4 kcal mol^{-1}][56] or the rate of racemization of the optically active *trans* compound *(25)* [$\Delta G^{\neq}$ (300 °C) = 40.2 kcal mol^{-1}][57], if 27 kcal mol^{-1}[58] is used as the value for the ring strain.

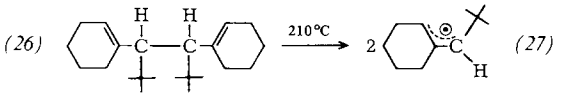
The activation energies for the ring opening of cyclopropane [$\Delta G^{\neq}$ (300 °C) = 56.4 kcal mol^{-1}][59], methylcyclopropane [$\Delta G^{\neq}$ (300 °C) = 54.5 kcal mol^{-1}][60] and 1,2-dialkylcyclopropanes [$\Delta G^{\neq}$ (300 °C) = 53—54 kcal mol^{-1}][61] correlate less satisfactorily, but still lie in the expected region of Figure 1 for 27 kcal mol^{-1} ring strain[58]. In addition, the homolytic ring opening of cyclobutane with 26 kcal mol^{-1} strain enthalpy[58] [$\Delta G^{\neq}$ (300 °C) = 56 kcal mol^{-1}][62] and methylcyclobutane [$\Delta G^{\neq}$ (300 °C) ≈ 55 kcal mol^{-1}][63] lie in the expected region of Figure 1.



(24) *(25)*

2.3. Further Substituent Effects

Using the methods described in this paper for the hydrocarbons, it should be possible to clarify the question of the stabilizing effect of substituents other than the phenyl group on a neighboring radical center and to clarify the associated question of the thermal stability of the corresponding substituted alkanes. Preliminary experiments with the first α-vinyl substituted compound, *meso*-3,4-di-(1-cyclohexenyl)-2,2,5,5-tetramethylhexane *(26)*[64] showed that the allyl resonance of the radicals *(27)* produced in the thermolysis once again lowers the thermal stability ($\tau_{1/2} = 1$ h at 210 °C)[64].



(26) *(27)*

The further exploration of this class of compounds is of particular interest because they are, in principle, suitable for Cope rearrangement. Can these two reaction possibilities be distinguished from each other?

More kinetic data are available in the tetraalkylated succinodinitrile series *(28)*[65] (see Table 2). Since strain enthalpies for these nitriles have not yet been measured experimentally, and also cannot yet be calculated with the force fields available[44], the strain enthalpy H_{sp} calculated for the corresponding hydrocarbon (CH_3 instead of CN) with the force field MM2[22] is listed for each compound in Table 2. Figure 3

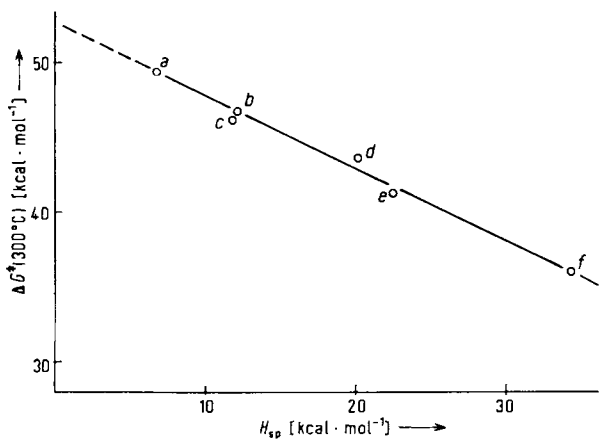


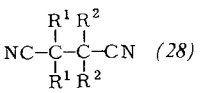
Fig. 3. Relationship between the free enthalpy of activation $\Delta G^{\neq}$ (300 °C) for the thermolysis of tetraalkyl-substituted succinonitriles *(28)* from Table 2 and the strain enthalpies H_{sp} of the hydrocarbons $CH_3CR^1R^2$–$CR^1R^2CH_3$, as calculated with the force field MM2 [22].

shows that an excellent linear correlation between the stability and the strain enthalpies again obtains; the correlation obeys the equation

$$\Delta G^{\neq}(300\,^{\circ}C) = 52.5\ (\pm 0.5) - 0.48\ (\pm 0.03)\ H_{sp}$$

The difference between the intercept of this line (52.5 kcal mol^{-1}) and that for the C_q—C_q alkanes *(14)* in Figure 1 (62.6 kcal mol^{-1}) is once again attributable to the resonance energy of the α-cyanoalkyl radicals. With the reservation that the strain enthalpies H_{sp} of the succinonitriles are only known by modeling, a resonance stabilization of α-cyanoalkyl radicals of 5 kcal mol^{-1} results, in unexpectedly good agreement with literature values which lie between 5 and 7 kcal mol^{-1}[66,67].

Table 2. Thermal stability of tetraalkylated succinonitriles *(28)* [65].



(28)

No.	R^1	R^2	T ($\tau_{1/2}$ = 1 h) [°C]	$\Delta G^{\neq}$ (300 °C) [kcal mol^{-1}]	$\Delta H^{\neq}$ [kcal mol^{-1}]	$\Delta S^{\neq}$ [cal mol^{-1} K^{-1}]	H_{sp} [a] [kcal mol^{-1}]
a	CH_3	CH_3	367	49.4	50.8	2.4	6.9
b	CH_3	C_2H_5	332	46.8	51.7	8.5	12.3
c	CH_3	n-C_3H_7	325	46.3	54.2	13.8	11.8
d	C_2H_5	C_2H_5	297	43.7	52.4	15.2	20.2
e	CH_3	i-C_3H_7	270	41.3	47.0	9.9	22.4
f	i-C_4H_9	i-C_4H_9	209	36.1	40.7	8.0	34.4

[a] Strain enthalpy of the corresponding hydrocarbons (with CH_3 in place of CN) calculated with force field MM2; see Table 1, footnote [a].

Further refinement of these conclusions by thermochemical measurements will show whether the techniques developed here are generally suited to the quantitative interpretation and prediction of the thermal stability of other substituted hydrocarbon frameworks and to the estimation of resonance energies of α-substituted alkyl radicals.

3. Structure and Strain of Highly Branched Hydrocarbons

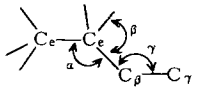
It was to be anticipated that strain enthalpies as high as 57 kcal mol^{-1}, as were found for compounds in Table 1, would also have consequences for the structures of these compounds. How do the reduced bond dissociation enthalpies influence the bond lengths? How do the hydrocarbons accommodate the steric pressures by angle deformation? What are the consequences for conformational analysis? To answer these questions the X-ray structure analyses of typical members of the C_t—C_t series [*(13c)*[24], *(13d, e)*[25], *(15d, e)*[68]] and the C_q—C_q series [*(14m)*[30] and *(16i)*[69]] were carried out by *H. J. Lindner* and by *W. Littke*; the applicability to the solution state was justified by NMR investigations[25]. The structural data for these ethanes, together with the structures described in the literature and determined by electron diffraction in the gas phase for *(13a)*[70] and *(14a)*[70], are found in Table 3. The experimentally determined structural data are set alongside the values calculated with the force field MM2. This comparison must show whether the results of these computational techniques also give trustworthy predictions for those structures which lie outside the limited region of parametrization of the actual force field with simple test compounds[44]. The use of the MM2 force field[22] for highly branched alkanes is justified by the precise agreement between experiment and calculation in Table 3, as well as by the comparison of experimental heats of formation with calculated values[71], as discussed above. The less reliable results of calculations with the older Allinger force field[31,44,45] which must be employed for the diphenylethanes *(15)* and *(16)*, give at least the correct trends of the structural deformations evoked by the strain [cf. *(15d, e)* and *(16i)* in Table 3).

The data in Table 3 and further data show that the strain engendered in the hydrocarbons by the steric pressure of the substituents is distributed over several internal coordinates and does not just lead to a stretching of the central C—C bond; rather, neighboring bonds are lengthened and particularly marked angle deformations result. Analysis of all the structural parameters for the hydrocarbons *(13)*—*(21)*, which are accessible through the force field calculations, permit the recognition of two general rules for the relationship between strain and structure:

1) Deformation of bond angles and lengths occur mainly at the C atoms of the weakest, *i.e.* the most highly substituted bond (C_e), and less distinctly at the immediately adjacent atoms (C_β).
2) Highly branched alkanes preferentially yield to the strong van der Waals repulsions between non-bonded groups by expansion of the CCC angles and simultaneous reduction of HCH or HCC angles at the same center. Bond stretching only appears as a secondary effect.

Rule 2 is understandable in terms of the smaller force constants for angle deformation than for bond stretching. From rule 2 it also follows that a marked expansion of CCC angles is possible only at secondary (C_s) and tertiary (C_t) centers because the increase of an angle at a quaternary carbon atom

Table 3. Selected structural parameters for some highly branched ethanes *(13)*—*(16)*. Comparison of experimental [a] and EFF results [b]. (e in C_e refers to ethane).



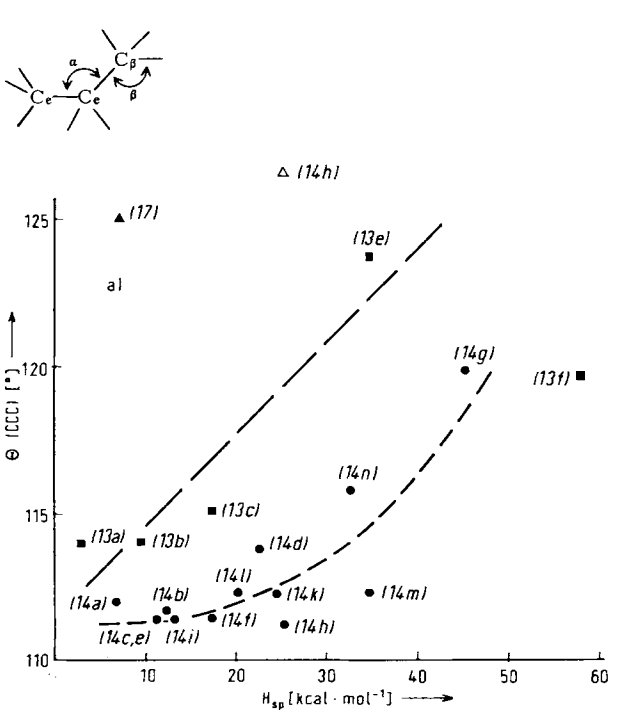
	R^1	R^2	R^3	Form	Method [a, b]	Point group	$d(C_e—C_e)$ [pm]	$d(C_e—R^x)$ [pm]	x	α	β [°] [c]	γ
(13a)	CH_3	CH_3	H		ED [70]	C_2	154.6	153.9	1	111.3	—	—
					EFF-MM2	C_2	154.9	154.0		114.0	109.2	—
(13c)	*c*-C_6H_{11}	*c*-C_6H_{11}	H		X [24]	C_1	157.7	156.1/158.0	1	112.1	115.2	117.5
					EFF-MM2	C_2	158.1	156.6		111.9	115.0	114.0
(13d)	*c*-C_6H_{11}	*t*-C_4H_9	H	D,L	X [25]	C_1	158.9	156.2/154.8	2	113.9	119.5	120.9
					EFF-MM2	C_2	158.0	157.5		115.9	119.4	119.3
(13e)	*c*-C_6H_{11}	*t*-C_4H_9	H	*meso*	X [25]	C_i	160.2	158.9/159.4	2	123.5	117.7	121.3
					EFF-MM2	C_i	158.4	158.4/157.9		123.8	119.8	118.2
(14a)	CH_3	CH_3	CH_3		ED [70]	D_3	158.2	154.2	1	111.0	—	—
					EFF-MM2	D_3	157.2	154.8		112.1	107.8	—
(14m)	CH_3	C_2H_5	*c*-C_6H_{11}	*meso*	X [30]	C_1	162.6	160.2	3	112.1	110.5	117.5
					EFF-MM2	C_1	163.0	159.2		112.3	110.6	117.4
(15d)	C_6H_5	*t*-C_4H_9	H	D,L	X [68]	C_1	158.9	158.3/156.9	2	116.2	113.1	114.4
					EFF-AM	C_2	157.2	156.9		120.1	114.0	114.0
(15e)	C_6H_5	*t*-C_4H_9	H	*meso*	X [68]	C_i	157.3	158.2	2	116.8	110.3	113.9
					EFF-AM	C_i	157.7	157.5		122.1	109.2	114.1
(16i)	C_6H_5	*n*-C_4H_9	*n*-C_4H_9		X [69]	C_i	163.8	158.2	3	111.9	109.8	119.1
					EFF-AM	C_1	159.5	157.5		114.5	108.6	124.9

[a] Experimental structure analysis by electron diffraction (ED) in the gas phase or by X-ray analysis (X) in the crystalline state. [b] Force field calculations for the gas phase with the Allinger MM2 force field [22] (EFF-MM2) or the Allinger-Mislow force field [31, 46] (EFF-AM). [c] Central C atom always tetracoordinate. Only the largest angles are given. The angle γ corresponds to β in Fig. 4.

would be tied to the simultaneous compression of another CCC angle.

3.1. Bond Angles and Bond Lengths

In order to facilitate an overview, the *largest* CCC angles α at the central bonds which are cleaved in the thermolysis of the hydrocarbons listed in Table 1 are indicated as *filled symbols* in Figure 4. With two exceptions *(14g, n)*, α at quaternary C atoms (●) is only slightly expanded to 112—114°. At tertiary C atoms (■), a mildly strained representative such as 2,3-dimethylbutane *(13a)* (H_{sp} = 2.7 kcal mol^{-1}) already has α = 114°. With increasing strain, α at the tetracoordinate C atom of the C_t—C_t series, increases to 120° and above [cf. *(13f)* and *(15d, e)*]. The largest angle deformation, α = 125°, is found at a secondary C atom (▲) in di-*tert*-butylmethane *(17)*, in spite of the relatively low strain enthalpy (H_{sp} = 7 kcal mol^{-1}) of this compound.



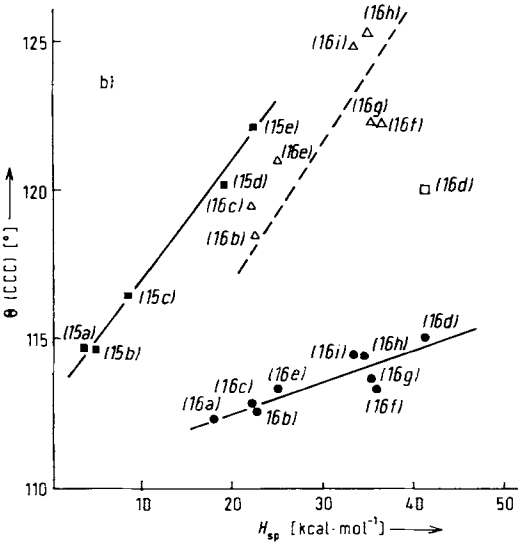


Fig. 4. CCC bond angles a) in the alkanes *(13)*, *(14)*, and *(17)* (calculated values from the force field MM2 [22]) and b) in the diphenylethanes *(15)* and *(16)* (calculated values from the force field of *Allinger-Mislow* [31, 46]) plotted against their strain enthalpy H_{sp} (see Table 1). Filled symbols: large angle α at a central C_e atom; open symbols: angle β at a neighboring C_β atom. ● angle at a quaternary C atom; ■, □ angle at a tertiary C atom; ▲, △ angle at a secondary C atom. The angle β corresponds to the angle γ in Table 3.

A similar picture emerges for the estimated angles β at the β-C atom to the central bond, shown in Figure 4 as *open symbols*. They are also consistently most strongly expanded in the case of secondary or tertiary C_β atoms. In some cases, C_β is unusually broadened; in the neopentyl side chain in *(14h)* ($H_{sp}=25.3$ kcal mol^{-1}), $\beta=126.5°$. Whether this considerable deformation from the tetrahedral angle of 109° is a consequence of a rehybridization of the C-atom or whether bent bonds[72] occur cannot be decided at the present time[73].

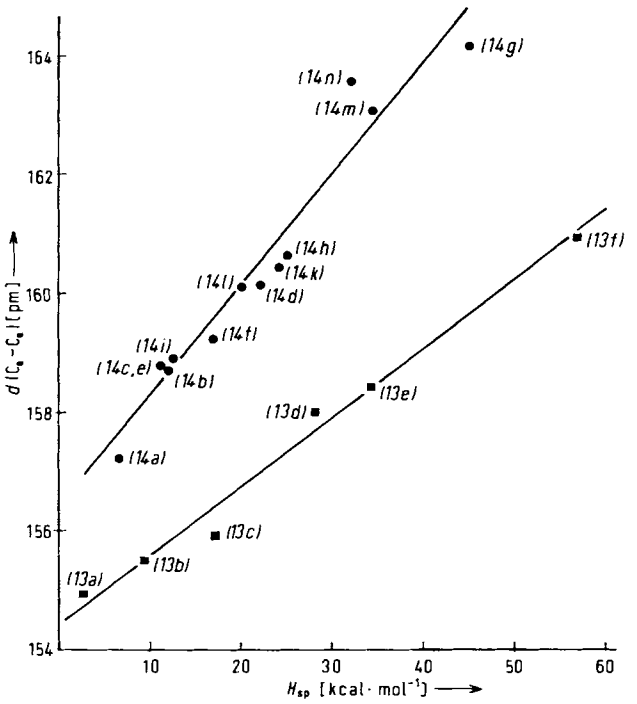


Fig. 5. C—C bond lengths for the central bonds in the alkanes *(13)* and *(14)* plotted against the strain calculated with force field MM2 [22]. ■ C_t—C_t series *(13)*; ● C_q—C_q series *(14)*.

The molecules yield to ground state strain not only through angle deformation, but also through bond stretching. This is recognizable in Figure 5, in which the length of the central, weak C—C bond in *(13)* and *(14)* is plotted against the strain enthalpy H_{sp}. The C_q—C_q alkanes *(14)* (●) have distinctly longer bonds than the C_t—C_t alkanes *(13)* (■). Because angle deformations are hardly possible in the C_q—C_q series, the central C—C bond is more strongly stretched with increasing strain than in the C_t—C_t series. This is expressed in the different slopes for the two lines shown in Figure 5. The extreme bond length in *(14m)* (163.0 pm)[30] and *(14g)* (164.1 pm) are among the longest C—C single bonds known in noncyclic hydrocarbon frameworks[74]. The C_q—C_q and C_t—C_t series of the 1,2-diphenylethanes[35,68,69] show a relationship between H_{sp}, bond angles, and bond lengths which is qualitatively similar to those in Figures 4 and 5.

3.2. Conformations

The broadening of the bond angles has consequences for the conformations of highly substituted ethanes. As a rule, one finds staggered conformations about the ethane bond with 60° torsion angles[75] as the energy minima. A Newman projection of the ethane bond (see Fig. 6) shows that an increase in the bond angle R^1—C—R^2 also leads to a considerable change in the torsion angle. This can have a great effect on conformational equilibria[76].

In the C_q—C_q series [*(14)* and *(16)*], even the strained members of the series show only small changes in the C_e—C_e—C_β and the C_β—C_e—C_β angle (see Fig. 4)[28,35]. Therefore, this series also shows normal staggered conformations with torsion angles between 40 and 80°. The rotamers with the largest side chains in the *anti* position possess energies similar to those with the residues in the *gauche* position, with the exception of the extreme case of *(14g)*[28] which only occurs in the *anti* conformation. *meso*- and D,L-diastereomers are likewise comparable in energy ($\Delta\Delta H<2$ kcal mol^{-1}).

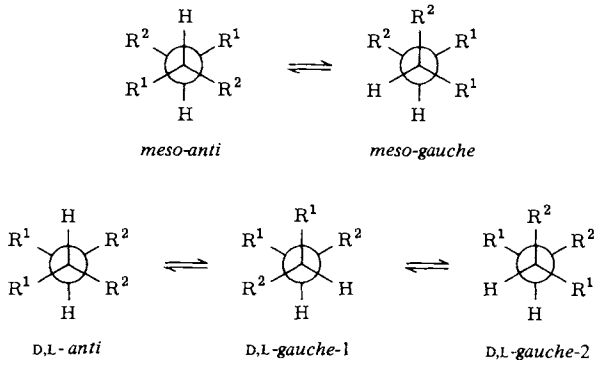


Fig. 6. Alternating conformations at the ethane bond in *(13)* and *(15)*.

The conformational situation in the series of the C_t—C_t alkanes *(13)* is completely different. There exist alternating $(FB)_3$ conformations[77] with the H atoms in the *anti*- or *gauche* positions. For a *meso* configuration ($R^1\neq R^2$), there are two rotamers: *meso-anti* and *meso-gauche*. For the D,L-configurations, there are one *anti*- and two *gauche* conformations (see Fig. 6). With normal torsion angles, one would expect from experience that the *anti* rotamers are the most stable, because they show only *two* skew interactions and not *three*, as do the *gauche* conformations. In addition, one usually ascribes a higher stability to the *meso* form because the two largest groups (R^1 or R^2) are in an *anti* disposition. These customary predictions are turned completely upside down in the C_t—C_t series *(13)*.

1) All tetraalkylethanes *(13)* prefer the *gauche* over the *anti* arrangement. The energy difference between these two conformations is only 0.1 kcal mol^{-1}[78] for 2,3-dimethylbutane *(13a)*, but grows dramatically with increasing size of the groups, as shown schematically in Figure 7.
2) When different configurations exist (*i.e.* $R^1\neq R^2$), the D,L form is more stable than the *meso* form.

These two unexpected findings follow directly from the *expansion of the geminal angle* R^1—C_e—R^2 in the C_t—C_t alkanes (see Fig. 4). NMR and EFF analysis of the conformations of the extreme member of the series, 3,4-di-*tert*-butyl-2,2,5,5-tetramethylhexane *(13f)* shows this quite clearly[27]:

The strong increase of the angle between the geminal *tert*-butyl groups in the *anti* conformation leads to a drastic increase in strain because of the decreasing distance between

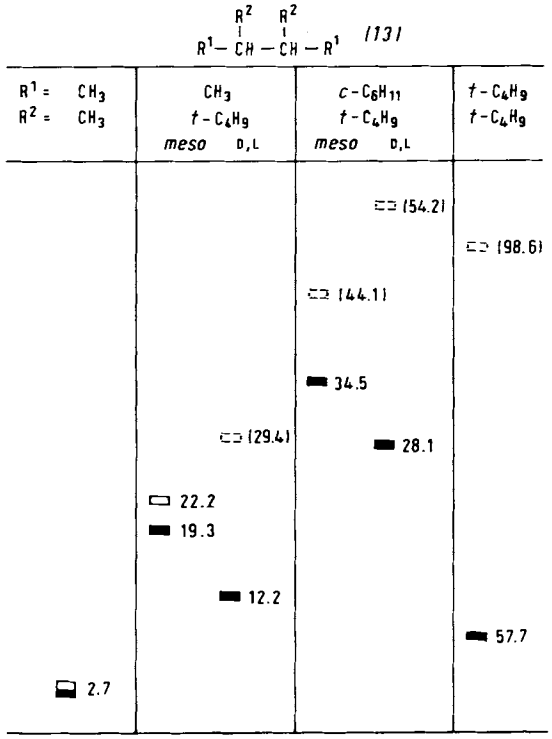
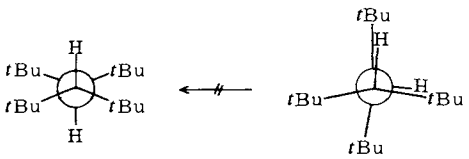


Fig. 7. Strain enthalpies for the C_t—C_t alkanes *(13)* in their various conformations (see Fig. 6) according to calculations with the force field MM2 [22]. ■ H, R^2 *gauche*, □ H *anti*. (Energy levels of rotamers printed as dashed lines are not minima, but are transition states for bond rotation.)

the vicinal *tert*-butyl groups. As a result, the *anti* conformation is a saddle point on the energy surface[27b]: The energy of the *anti* conformation lies higher than the transition state for the thermolysis of *(13f)*. For *(13f)*, there are only strongly



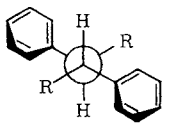
anti-(13f) FBE$_2$-*(13f)*

distorted *gauche*-like minima, in which the *tert*-butyl groups are at the maximum distance from each other. Two of these groups can avoid each other in the "steric hole" caused by the vicinal H atoms. The result is a nearly eclipsed FBE_2 conformation[77].

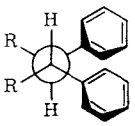
Similar conformations were found[25] by X-ray analysis for the two diastereomers *meso*- and D,L-3,4-dicyclohexyl-2,2,5,5-tetramethylhexane *(13d, e)*. The higher stability of the D,L diastereomer ($\Delta\Delta H_f^0 = 7.8$ kcal mol^{-1}) results because both the *tert*-butyl groups (R^2 = *tert*-butyl) in the *gauche*-1-conformation of the D,L compound can occupy the sterically preferred position opposite to the vicinal H atom (see Fig. 6). In the *gauche* rotamer of the *meso* form, this is possible for only one of the large *tert*-butyl groups and for the smaller cyclohexyl residue. In addition, tetracyclohexylethane *(13c)* exists exclusively in the *gauche* conformation[24], while both *gauche*- and *anti* conformations are populated[78] for 2,3-dimethylbutane *(13a)*. Apparently then, the rules indicated above are roughly valid even for ethanes *(13)* bearing small groups. Even the torsion angles $\Delta\Theta(RC_eC_eH)$ for these compounds are smaller than 60°.

Finally, it can be deduced that non-alternating conformations[77] can be expected as energy minima only for tetrasubstituted ethanes with unusually large geminal bond angles, *i.e.* when there are large repulsions between the geminal groups, or when the geminal angles are especially small as in dicyclopropyl[80].

The effects of various strong repulsions between geminal groups on conformational equilibria can also be studied in the 1,2-dialkyl-1,2-diphenylethanes *(15)*. The energies calculated with the Allinger-Mislow force field[31,46] for conformers of several compounds of type *(15)* are displayed in Figure 8 for the *meso*- and D,L configurations.



meso-(15)-anti



D,L-*(15)-anti*

The diphenylalkanes *(15)* with primary and secondary alkyl groups R *(15a—c)* behave "normally", *i.e.* they prefer the *anti* conformation. The flat disc shape of the phenyl ring and the associated small steric demand is responsible for this difference from the tetraalkylethanes *(13)*: methyl, ethyl, or isopropyl groups R can arrange themselves over the plane of a *geminally* oriented phenyl group and thereby produce little repulsion. The D,L-*(15)-anti* conformation is additionally favored because of the "stacking"[79] of the two *vicinal* rings. As a result, there is no expansion of the geminal bond angles in the *anti*-conformations of these compounds and the torsion

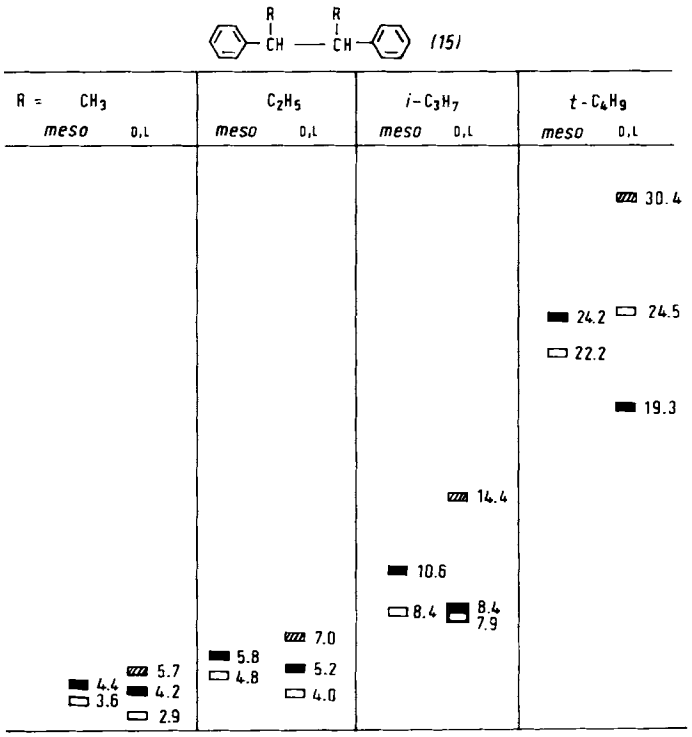


Fig. 8. Strain enthalpies H_{sp} [kcal mol^{-1}] for various conformations of the dialkyldiphenylethanes *(15)* (see Fig. 6) according to calculations with the Allinger-Mislow force field [31, 46]. ■ H, R *gauche*; ▨ H, Ph *gauche*; □ H *anti*.

angles are also normal at *ca.* 60°. The usual rules for the relative stability of the conformations *(anti > gauche)* remain valid.

Even *meso*-2,2,5,5-tetramethyl-3,4-diphenylhexane *(15e)* strongly prefers the *meso-anti* conformation over the *meso-gauche* orientation. In the *anti* conformation the bulky vicinal *tert*-butyl groups achieve the maximum separation, while in the *meso-gauche* arrangement (see Fig. 6, $R^1 = C_6H_5$, $R^2 = tert$-butyl) only one *tert*-butyl group can occupy the favorable position *gauche* to an H atom and even this must be purchased at the expense of a direct *gauche* interaction with the vicinal *tert*-butyl group. The situation is otherwise in *(15d)*: as a result of the geminal repulsion between the *tert*-butyl group and the phenyl ring the repulsion between the vicinal *tert*-butyl groups is increased. Thus, torsion around the central bond leading to the *gauche*-1 conformation (see Fig. 6, $R^1 = C_6H_5$, $R^2 = tert$-butyl) is associated with a decrease in energy. The vicinal *tert*-butyl groups reach an *anti* orientation and both take up the sterically preferred position *gauche* to a vicinal H atom.

The study of the structures of highly branched hydrocarbons has shown that increasing strain is preferentially countered by an increase in the geminal bond angle and that this, in turn, is often the source of a change in the relative stabilities of the rotamers. When expansion of the geminal angles is prohibited, or is possible only in small measure, as in the C_q—C_q series [*(14)* and *(16)*], then a marked bond stretching, particularly of the central C—C bond, is observed as the ground state strain increases.

4. Outlook

The results communicated in this essay confirm that *quantitative* investigations are rewarding and ultimately lead to novel qualitative information. The simple relationships found to exist between stability, strain, and structure are a fitting illustration. These results could not have been achieved without the availability of new experimental methods and theoretical models. The challenge remains to transfer these relationships, established for simple model hydrocarbons, to other classes of compounds. To this end, further refinement of the methodology will be necessary, particularly with regard to the development of suitable force fields.

We thank those co-workers who have participated in this work, Dr. G. Hellmann, Dipl.-Chem. G. Kratt, Dr. R. Winiker, Dipl.-Chem. S. Weiner, Dipl.-Chem. W. Barbe, Mrs. J. Geiselmann, Mrs. K. Lay, for their experimental effort, for continuing critical discussion, and for considerable stimulation. Thanks are also due to Prof. H. J. Lindner, Dr. W. Littke, Prof. H. Fritz for their close cooperation in the work on structural problems. We are indebted to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Dr. Otto Röhm Memorial Foundation for financial support, and the Computer Center of the University of Freiburg for generous allocation of computer time.

Received: March 17, 1980 [A 319 IE]
German version: Angew. Chem. *92*, 417 (1980)
Translated by Prof. *J. A. Kampmeier*

[1] *K. Ziegler*, Angew. Chem. *61*, 168 (1949).
[2] See *J. M. McBride*, Tetrahedron *30*, 2009 (1974).
[3] a) See *W. D. Hounshell, D. A. Dougherty, J. P. Hummel, K. Mislow*, J. Am. Chem. Soc. *99*, 1916 (1977) for force field calculations on *(1)*; b) *M. Stein, W. Winter, A. Rieker*, Angew. Chem. *90*, 737 (1978); Angew. Chem. Int. Ed. Engl. *17*, 692 (1978).
[4] *H. Lankamp, W. Th. Nauta, C. MacLean*, Tetrahedron Lett. *1968*, 249; *H. A. Staab, H. Brettschneider, H. Brunner*, Chem. Ber. *103*, 1101 (1970); *H. Volz, W. Lotsch, H. W. Schnell*, Tetrahedron *26*, 5343 (1970).
[5] See *C. Rüchardt*, Angew. Chem. *82*, 845 (1970); Angew. Chem. Int. Ed. Engl. *9*, 830 (1970).
[6] See *T. T. Tidwell*, Tetrahedron *34*, 1855 (1978).
[7] See *H. C. Brown:* Boranes in Organic Chemistry. Cornell University Press, Ithaca, N. Y. 1972.
[8] *J. Slutsky, R. C. Bingham, P. von R. Schleyer, W. C. Dickason, H. C. Brown*, J. Am. Chem. Soc. *96*, 1969 (1974).
[9] a) *O. Exner* in *N. B. Chapman, J. Shorter:* Correlation Analysis in Chemistry. Plenum Press, New York 1978, p. 448; b) *M. Charton, B. I. Charton*, J. Org. Chem. *44*, 2284 (1979) and references cited therein; c) *J. A. MacPhee, A. Panaye, J.-E. Dubois*, Tetrahedron Lett. *1978*, 3297; d) *H.-D. Beckhaus*, Angew. Chem. *90*, 633 (1978); Angew. Chem. Int. Ed. Engl. *17*, 592 (1978).
[10] a) *D. H. R. Barton:* Theoretical Organic Chemistry (Kekulé Symposium). Butterworths, London 1959, p. 127; b) *N. L. Allinger, E. L. Eliel*, Top. Stereochem. *6*, 1 (1971).
[11] *C. Rüchardt*, Zh. Vses. Khim. O-va *24*, 121 (1979); C. A. *91*, 4705k (1979).
[12] *C. Rüchardt*, Top. Curr. Chem. *88*, 1 (1980).
[13] *D. Griller, K. U. Ingold*, Acc. Chem. Res. *9*, 13 (1976).
[14] *E. Müller, L. Ley*, Z. Naturforsch. *B 8*, 694 (1953); *C. D. Cook*, J. Org. Chem. *18*, 261 (1953).
[15] a) *H. Regenstein, W. Ahrens, A. Berndt*, Tetrahedron *31*, 2837 (1975); b) *K. Schreiner, A. Berndt*, Angew. Chem. *87*, 285 (1975); Angew. Chem. Int. Ed. Engl. *14*, 366 (1975).
[16] *G. Brunton, D. Griller, L. R. C. Barclay, K. U. Ingold*, J. Am. Chem. Soc. *98*, 6803 (1976).
[17] a) *A. Burcat, G. B. Skinner, R. W. Crossley, K. Scheller*, Int. J. Chem. Kinet. *5*, 345 (1973); b) *D. B. Olson, W. C. Gardiner, Jr.*, J. Phys. Chem. *83*, 922 (1979). c) See also *A. B. Trenwith*, J. Chem. Soc. Faraday Trans. I *1979*, 614; d) *F. S. D'iachkowskii, M. N. Bubnov, A. E. Shilov*, Dokl. Akad. Nauk SSSR *122*, 629 (1958).
[18] *H.-D. Beckhaus*, Diplomarbeit, Universität Münster 1970/71.
[19] a) *P. D. Bartlett, J. M. McBride*, Pure Appl. Chem. *15*, 89 (1967); b) *L. I. Peterson*, J. Am. Chem. *89*, 2677 (1967); c) *W. P. Neumann, F. Werner*, Chem. Ber. *111*, 3904 (1978), and references cited therein; d) *H. A. P. de Jongh, C. R. H. I. de Jonge, H. J. M. Sinnige, W. J. De Klein, W. G. B. Huysmans, W. J. Mijs, W. J. van den Hoek, J. Smidt*, J. Org. Chem. *37*, 1960 (1972), and references cited therein.
[20] *T. Berces, L. Seres, F. Manta*, Acta Chim. Acad. Sci. Hung. *71*, 31 (1973) with corrections according to *J. F. Large, R. Martin, M. Niclause*, Bull. Soc. Chim. Fr. *1972*, 961.
[21] *W. Tsang*, J. Chem. Phys. *43*, 352 (1965).
[22] *N. L. Allinger*, J. Am. Chem. Soc. *99*, 8127 (1977).
[23] *G. Hellmann*, Dissertation, Universität Freiburg 1977.
[24] *S. G. Baxter, H. Fritz, G. Hellmann, B. Kitschke, H. J. Lindner, K. Mislow, C. Rüchardt, S. Weiner*, J. Am. Chem. Soc. *101*, 4493 (1979).
[25] *H.-D. Beckhaus, G. Hellmann, C. Rüchardt, B. Kitschke, H. J. Lindner, H. Fritz*, Chem. Ber. *111*, 3764 (1978).
[26] *G. Hellmann, H.-D. Beckhaus, C. Rüchardt*, Chem. Ber. *112*, 1808 (1979).
[27] a) *H.-D. Beckhaus, G. Hellmann, C. Rüchardt*, Chem. Ber. *111*, 72 (1978); b) *E. Osawa, H. Shirahama, T. Matsumoto*, J. Am. Chem. Soc. *101*, 4824 (1979).
[28] *R. Winiker, H.-D. Beckhaus, C. Rüchardt*, Chem. Ber., in press.
[29] *H.-D. Beckhaus, J. Schoch, C. Rüchardt*, Chem. Ber. *110*, 878 (1977).
[30] *H.-D. Beckhaus, G. Kratt, K. Lay, J. Geiselmann, C. Rüchardt*, Chem. Ber., in press.
[31] a) *J. D. Andose, K. Mislow*, J. Am. Chem. Soc. *96*, 2168 (1974). b) Basis set for calculation of ΔH_f^0: $C_{Ph}(-H) = 2.87$, $C_{Ph}(-C_q) = 0.32$, $C_{Ph}(-C_t) = 1.51$ kcal mol^{-1}. Basis values for alkyl C: *D. F. DeTar, C. J. Tenpas*, J. Am. Chem. Soc. *98*, 4567 (1976).
[32] *K.-H. Eichin, K. J. McCullough, H.-D. Beckhaus, C. Rüchardt*, Angew. Chem. *90*, 987 (1978); Angew. Chem. Int. Ed. Engl. *17*, 934 (1978).
[33] *K.-H. Eichin, H.-D. Beckhaus, C. Rüchardt*, unpublished.
[34] *H.-D. Beckhaus*, Dissertation, Universität Freiburg 1975.
[35] *G. Kratt*, planned Dissertation, Universität Freiburg.
[36] *K. Ziegler, W. Deparade*, Justus Liebigs Ann. Chem. *567*, 123 (1950).
[37] *C. Rüchardt, H.-D. Beckhaus, G. Hellmann, S. Weiner, R. Winiker*, Angew. Chem. *89*, 913 (1977); Angew. Chem. Int. Ed. Engl. *16*, 875 (1977).
[38] *C. Rüchardt, S. Weiner*, Tetrahedron Lett. *1979*, 1311.
[39] *S. Weiner*, planned Dissertation, Universität Freiburg.
[40] For the calculation of the strain-free "normal heat of transformation" ΔH_f^N, the following group increments were used: CH_3 −10.05; CH_2 −5.13; CH −2.16; C −0.30 (cf. Ref. [41]); C_6H_5:$C_{Ar}(-H)$ 3.28; $C_{Ar}(-C)$ 5.62 kcal mol^{-1} (cf. Ref. [26].

[41] *P. von R. Schleyer, J. E. Williams, K. R. Blanchard*, J. Am. Chem. Soc. *92*, 2377 (1970).
[42] *E. S. Huyser:* Free Radical Chain Reactions. Wiley-Interscience, New York 1970, p. 272.
[43] *C. Rüchardt, H.-D. Beckhaus, J. Bonnekessel, H. Böck, E. Dempewolf, F. A. Groeger, V. Golzke, G. Hamprecht, K. Herwig, J. Hinz, P. Lorenz, I. Mayer-Ruthardt, J. Müller, A. Oberlinner, E. Schacht:* Structure Reactivity-Relationships in the Chemistry of Aliphatic Free Radicals. XXIII Int. Congr. Pure Appl. Chem. Vol. 4. Special Lectures, Butterworths, London 1971, p. 223.
[44] *N. L. Allinger*, Adv. Phys. Org. Chem. *13*, 1 (1976).
[45] This value is derived from the heat of combustion [27a] and from the heat of sublimation ($\Delta H^0_{sub} = 17.75 \pm 0.13$ kcal mol^{-1}) measured by *M. Månsson* and *G. Grantz* (Lund).
[46] *N. L. Allinger, M. T. Tribble, M. A. Miller, D. H. Wertz*, J. Am. Chem. Soc. *93*, 1637 (1971).
[47] Because different force fields were used for the alkanes *(11)—(14)* and *(17)—(21)* than for the diphenylalkanes, *(15)—(16)*, comparisons of strain enthalpies between the two classes of compounds are less reliable than comparisons within a class.
[48] The direct relationship between IR frequencies and C—H bond energies supports this assumption. Cf. *D. C. McKean*, Chem. Soc. Rev. *7*, 399 (1978).
[49] For the central bond of 2,3-dimethylbutane ($H_{sp} = 2.7$ kcal mol^{-1}) a dissociation energy $D = 78.2$ kcal mol^{-1} was determined: *K. W. Egger, A. T. Cooks*, Helv. Chim. Acta *56*, 1516, 1537 (1973).
[50] *M. J. Gibian, R. C. Corley*, Chem. Rev. *73*, 441 (1973).
[51] *H.-D. Beckhaus, J. H. Kaiser*, unpublished.
[52] See, *e.g., H. H. Schuh, H. Fischer*, Helv. Chim. Acta *61*, 2463 (1978).
[53] *E. M. Engler, J. D. Andose, P. von R. Schleyer*, J. Am. Chem. Soc. *95*, 8005 (1973).
[54] *M. Rossi, D. M. Golden*, J. Am. Chem. Soc. *101*, 1230 (1979).
[55] *H. J. Reich, D. J. Cram*, J. Am. Chem. Soc. *91*, 3517 (1969); *R. H. Boyd*, Tetrahedron *22*, 119 (1966).
[56] *L. B. Rodewald, C. H. DePuy*, Tetrahedron Lett. *1964*, 2951.
[57] *R. J. Crawford, T. R. Lynch*, Can. J. Chem. *46*, 1457 (1968).
[58] *J. F. Liebman, A. Greenberg*, Chem. Rev. *76*, 311 (1976).
[59] *B. S. Rabinovitch, E. W. Schlag, K. B. Wiberg*, J. Chem. Phys. *28*, 504 (1958).
[60] *D. W. Setser, B. S. Rabinovitch*, J. Am. Chem. Soc. *86*, 564 (1964).
[61] *H. C, Flowers, H. M. Frey*, Proc. R. Soc. London *A 257*, 123 (1960); *C. S. Elliott, H. M. Frey*, J. Chem. Soc. *1964*, 900.
[62] *H. O. Pritchard, R. G. Sowden, A. F. Trotman-Dickenson*, Proc. R. Soc. London *A 217*, 563 (1953); *H. M. Frey*, Adv. Phys. Org. Chem. *4*, 147 (1966).
[63] *M. N. Das, W. D. Walters*, Z. Phys. Chem. (Frankfurt am Main) *15*, 22 (1958); *T. A. Babcock*, J. Am. Chem. Soc. *91*, 7622 (1969).
[64] *H.-D. Beckhaus, G. Hellmann, C. Rüchardt, B. Kitschke, H. J. Lindner*, Chem. Ber. *111*, 3780 (1978).
[65] *W. Barbe*, Diplomarbeit, Universität Freiburg 1978; planned Dissertation, Universität Freiburg.
[66] *J. C. Martin, J. E. Schultz*, J. W. Timberlake, Tetrahedron Lett. *1967*, 4629; *K. D. King, R. D. Goddard*, J. Am. Chem. Soc. *97*, 4504 (1975); Int. J. Chem. Kinet. *10*, 453 (1978), references cited therein; *D. Bellus, G. Rist*, Helv. Chim. Acta *57*, 194 (1974); *S. F. Sarner, D. M. Gale, H. K. Hall, Jr., A. B. Richmond*, J. Phys. Chem. *76*, 2817 (1972).
[67] *D. A. Luckraft, P. J. Robinson*, Int. J. Chem. Kinet. *5*, 137 (1973).
[68] *H.-D. Beckhaus, K. J. McCullough, H. Fritz, C. Rüchardt, B. Kitschke, H. J. Lindner, D. A. Dougherty, K. Mislow*, Chem. Ber. *113*, 1867 (1980).
[69] *W. Littke, U. Drück*, Angew. Chem. *91*, 434 (1979); Angew. Chem. Int. Ed. Engl. *18*, 406 (1979).
[70] *L. S. Bartell, T. L. Boates*, J. Mol. Struct. *32*, 379 (1976).
[71] See also ref. [38] for a comparison of experimentally determined structural data with computational results for *(20)*.
[72] Cf. *C. L. Reichel, J. M. McBride*, J. Am. Chem. Soc. *99*, 6758 (1977).
[73] The normal coupling constant, $^{13}J_{(H,C)} = 123$ Hz [27a], argues for a normal sp^3 hybridization of the *tert*-C atom in *(13f)*, $\Theta(C_t—C_t—C_q) = 119.5°$.
[74] *W. D. Hounshell, D. A. Dougherty, J. P. Hummel, K. Mislow*, J. Am. Chem. Soc. *99*, 1916 (1977); *P. T. Cheng, C. Thankachan, T. T. Tidwell, S. C. Nyburg*, Angew. Chem. *89*, 658 (1977); Angew. Chem. Int. Ed. Engl. *16*, 654 (1977); *T. T. Tidwell*, Tetrahedron Report No. 53, Pergamon Press, Oxford 1978.
[75] Summary: *C. A. Kingsbury*, J. Chem. Educ. *56*, 431 (1979).
[76] *N. L. Allinger, J. A. Hirsch, M. A. Miller, J. Tyminski, F. A. Van-Catledge*, J. Am. Chem. Soc. *90*, 1199 (1968).
[77] For nomenclature (F = front, B = back, E = eclipsed) of alternating and non-alternating conformations, see *W. D. Hounshell, D. A. Dougherty, K. Mislow*, J. Am. Chem. Soc. *100*, 3149 (1978).
[78] Determined by NMR spectroscopy: *W. Ritter, W. Hull, H.-J. Cantow*, Tetrahedron Lett. *1978*, 3093; *F. Heinrich, W. Lüttke*, Chem. Ber. *110*, 1246 (1977).
[79] *D. A. Dougherty, F. M. Llort, K. Mislow, J. F. Blount*, Tetrahedron *34*, 1301 (1978).
[80] According to an electron diffraction study [81] and EFF-calculation, dicyclopropyl preferentially adopts a conformation with *gauche* H atoms ($\Delta H_{rel.}$ for the *anti* form = +0.5 kcal mol^{-1}). Because of the smaller bond angles in cyclopropane, dicyclopropyl adopts a non-alternating FBF_2B_2-structure: cf. *H. Braun, W. Lüttke*, J. Mol. Struct. *31*, 97 (1976).
[81] *O. Bastiansen, A. de Meijere*, Angew. Chem. *78*, 142 (1966); Angew. Chem. Int. Ed. Engl. *5*, 124 (1966).

The Role of Pyridoxal Phosphate in the Catalysis of Glycogen Phosphorylases

By Ernst J. M. Helmreich and Helmut W. Klein[*]

Dedicated to Professor Otto H. Wieland on the occasion of his 60th birthday

Glycogen phosphorylases catalyze the degradation of glycogen by phosphate (or arsenate) to glucose 1-phosphate (or glucose + arsenate). All glycogen phosphorylases that have been studied so far contain pyridoxal 5'-phosphate, a vitamin B_6-derivative, as cofactor. Removal of the cofactor results in an inactive apoenzyme. However, reduction of the azomethine bond linking pyridoxal phosphate to an ε-aminolysyl side chain of the enzyme with $NaBH_4$ does not inactivate glycogen phosphorylase. If therefore the cofactor should be involved in catalysis in glycogen phosphorylase it must function differently from all other classical pyridoxal phosphate dependent enzymes, for these are inactivated by reduction. ^{31}P-NMR spectroscopy has revealed that the 5'-phosphate group of pyridoxal phosphate is present in catalytically active forms of glycogen phosphorylases as dianion in a hydrophobic environment shielded from aqueous solvent. Covalent and/or allosteric *activation* of muscle glycogen phosphorylases is accompanied by a transition of the monoprotonated form to the dianionic form of the phosphate group of the cofactor. We now report on such ionization changes in unregulated *active* potato- and *E. coli* maltodextrin phosphorylases on binding of glucose and oligosaccharides and following catalytic turnover, *i. e.* arsenolysis of α-1,4-glycosidic bonds. (Like glycogen phosphorylases, maltodextrin phosphorylases belong to the class of α-glucan phosphorylases.) The results of experiments carried out by our group together with recent findings on the three dimensional structure of crystalline muscle glycogen phosphorylases indicate a participation of the dianionic phosphate group as proton acceptor for the glucosyl transfer to and from the glucosyl acceptor. Although other interpretations are not excluded, at present little doubt remains that in the case of glycogen phosphorylases the dianionic phosphate group of the cofactor functions in catalysis.

1. Introduction

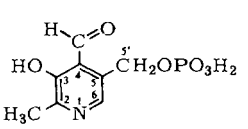
1.1. Properties of Phosphorylase

Glycogen is a highly branched animal reserve carbohydrate made up of α-1,4-D-glucose residues. Glycogen phosphorylases [EC 2.4.1.1] catalyze the phosphorolytic cleavage and formation of α-1,4-glycosidic bonds of glycogen starting from the nonreducing end of the polysaccharide:

$$(\text{Glycogen})_n + P_i \rightleftharpoons (\text{Glycogen})_{n-1} + \text{Glucose 1-phosphate} \quad (1)$$

P_i = inorganic phosphate

The reaction is reversible *in vitro* ($K_{eq} = [P_i]/[\text{glucose 1-phosphate}] = 3.6$ at pH 6.8). In the living cell, however, phosphorylases catalyze glycogen degradation, because of the high concentration of P_i and the relatively small concentration of glucose 1-phosphate (P_i : glucose 1-phosphate = 300 : 1)[1]. All



(1)

glycogen phosphorylases so far studied contain covalently bound pyridoxal 5'-phosphate *(1)*, a derivative of vitamin B_6. Pyridoxal phosphate is linked *via* its aldehyde group with the ε-amino group of a lysine moiety in the phosphorylase. On reduction of this azomethine bond with sodium borohydride the cofactor is irreversibly bound to the enzyme, but as has been shown by *E. H. Fischer et al.*, its activity is retained[2]. Hence, glycogen phosphorylases differ from the "classical" pyridoxal phosphate dependent enzymes which are inactivated by reduction.

1.2. Structure

Phosphorylases from rabbit skeletal muscle, potato and *E. coli* (with which we obtained the data reported here) are dimeric molecules made up of identical subunits. The molecular weight of the subunit of muscle phosphorylase is 97412 as determined by sequence analysis (the polypeptide chain contains 841 amino acids)[3–5]. The molecular weight of the subunit of potato tuber phosphorylase is reported as 103000[6,7], that of the subunit of *E. coli* phosphorylase 81000 and thus considerably smaller than the others[8]. Rabbit skeletal muscle phosphorylase exists in a phosphorylated form (phosphorylase *a*) and an unphosphorylated form (phosphorylase *b*). In both forms subunits may form tetramers. The enzymatically active forms are however the dimeric phosphorylases *a* active without AMP and the dimeric phosphorylases *b* active only in the presence of AMP[9]. Tetramers and monomers are inactive[23 25] or according to others partially active[18,26]. Formation of tetramers is facilitated by low temperature, Mg^{2+}, Ca^{2+}, F^- and other ions,

[*] Prof. Dr. E. J. M. Helmreich, Dr. H. W. Klein
Physiologisch-chemisches Institut der Universität
Koellikerstrasse 2, D-8700 Würzburg (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0606-0411 $ 02.50/0*

the presence of the allosteric effector, AMP and of the substrates, P_i and glucose 1-phosphate[10 14]. Tetrameric phosphorylases dissociate to dimers in the presence of glucose, glycogen, caffeine and α-1,4-glucans (hepta- and pentaamyloses)[19 22]. The dimer-tetramer equilibrium of phosphorylase *a* is mainly dependent on ionic strength and the nature of ions, on pH and temperature ($-\Delta H = 60$ kcal/mol)[15 18]. Phosphorylase *a* is tetrameric even at fairly low concentrations and at elevated temperatures. Phosphorylase *b* forms tetramers only at high concentrations, low temperatures and in the presence of AMP[9].

The dimensions of dimeric phosphorylase were estimated by electron microscopy as about $110 \times 65 \times 55$ Å. This agrees with small angle X-ray diffraction curves which gave dimensions of $110 \times 60 \times 55$ Å for an ellipsoidal body. More detailed information became available with the progress of X-ray crystal structure analysis[27-32]. Rabbit muscle phosphorylases *a* and *b* crystallize isomorphously in the presence of glucose or inosinic acid (IMP) respectively in the space group $P4_32_12$ with the unit cell dimensions $a = 128$ Å and $c = 116$ Å[29,30]. These crystals contain a monomer per asymmetric unit. A dimer is formed through the interactions of two monomers across a twofold crystallographic axis of symmetry. The arrangement of the monomers in this space group precludes tetrameric crystals. A detailed and complete interpretation of the electron density maps was only possible after the complete amino acid ("primary structure") sequence of rabbit skeletal muscle phosphorylase was determined by *Titani et al.*[3 5]. The chemical information helped to identify the various parts of the polypeptide chain and to determine the spatial arrangement and structure. Especially the assignment of the ε-aminolysyl-Schiff base with pyridoxal phosphate to position 679 in the enzyme permitted exact location of the cofactor in phosphorylase[27,28]. The polypeptide chain is built to about 50% as α-helix and to about 30% as β-sheet.

The phosphorylase monomer can be divided into three domains: An N-terminal domain with about 320, a central domain with 160 and a C-terminal domain with 360 amino acids. The three domains are arranged in such a manner that the centers form the corners of an equilateral triangle. The contact surfaces of the monomers in the dimeric structure are formed by the N-terminal domains which interdigitate across the axis of symmetry and establish extensive contacts among the subunits[28-30]. Previous investigations of *Madsen et al.* had already shown that two cysteine side chains (108 and 142) are in or near the contact region, for carboxamidomethylation of these cysteins results in dissociation to monomers and inactivation. The remaining SH-groups become accessible to iodoacetamide only after irreversible denaturation of the protein[33-35]. Acylation with succinic-anhydride inactivates phosphorylase *b* and *a*. Inactivation is partly due to dissociation in inactive monomers[36][*].

1.3. Regulation

The pioneering work of *G. T.* and *C. F. Cori* (see [37]) established that glycogen phosphorylase of rabbit skeletal muscle can exist in two forms, *b* and *a*, of which the former is only active in the presence of 5′-AMP.

E. G. Krebs and *E. H. Fischer* subsequently elucidated the interconversion of both forms[38] (see also [39,40]). Phosphorylase *b* is transformed to *a* by phosphorylation of a seryl residue (serine-14) per subunit catalyzed by phosphorylase-kinase [EC 2.7.1.38], ATP and Mg^{2+}. Phosphorylase *a*, which is active without AMP, is dephosphorylated by an enzyme activity described first by *P. J. Keller* and *G. T. Cori*[41], which later proved to be a phosphorylase-phosphatase [EC 3.1.3.17][42]. Phosphorylase was the first enzyme whose activity was shown to be regulated both allosterically and by covalent modification. Phosphorylase *b′*, a tryptic degradation product of phosphorylase *b*, lacks the N-terminal sequence which is phosphorylated in the $b \rightarrow a$ transition. Phosphorylase *b′* can still be activated by AMP indicating that the site of phosphorylation differs from the site for AMP activation[43-45]. This is supported by recent ^{31}P-NMR measurements with native and succinylated phosphorylase *a* at different pH values: this work showed in agreement with recent results from X-ray crystallography that the thiophosphates (phosphates) of AMP-S, (AMP) and of the thiophosphoseryl-(phosphoseryl-) residues act cooperatively but on different sites of phosphorylase[36] (cf. Fig. 4).

Glycogen phosphorylases in muscle and liver are key enzymes whose activities are modulated in a very sophisticated manner in order to adjust them to the needs of cellular metabolism. They can be classed with the α-glucan phosphorylases. The α-glucan phosphorylases of plants and of procaryotes, however, are neither allosterically nor covalently controlled[6,46-48]. Glycogen phosphorylase from yeast is covalently, but not allosterically regulated[49]. Covalent modification ($b \leftrightarrow a$ interconversion) of phosphorylases is controlled by an enzyme cascade consisting of at least five separate enzymes each of which is again interconvertible, and of specific inhibitory proteins and modulator proteins for some of the enzymes. This has the advantage of large rate amplification and control at multiple sites in the cascade by different cellular messengers (Ca^{2+}, cAMP). *Philip Cohen* has contributed much in the last years to further our understanding of the phosphorylase kinase system, which has a key role in the regulation of the phosphorylase cascade[50]. The regulation of the phosphorylase interconversion cascade including hormonal regulation has been extensively reviewed in recent years[1,40,50-54].

2. Pyridoxal Phosphate in α-Glucan Phosphorylases

Baranowski, Illingworth, Brown, and *Cori*[55,56] reported in 1957, and *Kent, Krebs,* and *Fischer* in 1958[57], the presence of pyridoxal phosphate in rabbit skeletal muscle phosphorylase *a* in a stoichiometry of one mol per mol of subunit. Since then pyridoxal phosphate has been found, *inter alia,* in α-glucan phosphorylases from muscles of cat, rat, mouse, dogfish, man, frog, lobster and insects, in liver and brain, in yeast, potato tuber, corn, *Physarum polycephalum, Escherichia coli* and *Klebsiella pneumoniae*[1,6-8,24,37,46,49,53,58,59,102,157-163].

Muscle contains phosphorylase—and hence pyridoxal phosphate—in relatively high concentrations (3×10^{-6} M; about 30 mg per 100 ml of intercellular fluid); since muscle

[*] For the three dimensional structure of phosphorylase *a* and the related functions see *R. J. Fletterick, N. B. Madsen,* Ann. Rev. Biochem., in press.

tissue makes up about 40% of the body mass, more pyridoxal phosphate is present in muscle phosphorylase than in all other pyridoxal phosphate dependent enzymes together. This explains why vitamin B_6 deficiency causes a drastic decline in muscle phosphorylase activity[60,61].

A theory providing for the first time a comprehensive interpretation of the diverse pyridoxal phosphate dependent reactions was proposed by *Braunstein* and *Shemyakin*[62]. Independently, and at about the same time, a similar but more detailed proposal was published by *Metzler, Ikawa,* and *Snell*[63]. From *Snell*'s model studies of the non-enzymic reactions, a minimal structure, the 3-hydroxypyridine-4-carbaldehyde was derived. In the course of catalysis the formyl group forms a Schiffs base with the amino acid substrate which is stabilized by chelation with a metal ion. According to *Braunstein*[64] and *Snell*[65], all pyridoxal phosphate dependent reactions are explained by the special properties of the enzyme bound aldimine-ketimine intermediates [see Fig. 1].

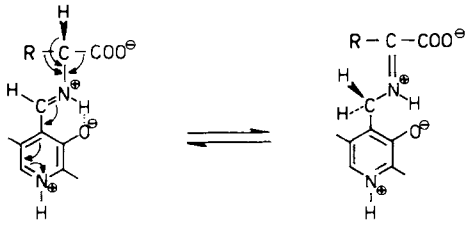


Fig. 1. Tautomerism in protonated Schiff bases of α-amino acids and derivatives of 3-hydroxypyridine-4-carbaldehyde. The arrows point to possible elimination steps.

The participation of an aldimine in catalysis is not restricted to pyridoxal phosphate dependent enzymes. In some enzymes, the formyl group of pyridoxal phosphate is substituted by a carbonyl group; in histidine decarboxylases from *Lactobacillus* and *Micrococcus* an N-terminal pyruvoyl-phenylalanyl residue carries out the function of the enzyme bound pyridoxal phosphate ε-aminolysyl residue[66]. In aldolases[67] and transaldolases[68], acetoacetate-decarboxylase[69], δ-aminolevulinic acid[70] and 2-keto-3-deoxy-L-arabinose dehydratase[71], a carbonyl group of the substrate forms an imine with an ε-aminolysyl side chain. The pivotal role of the Schiff base in catalysis is supported by inactivation following reduction with $NaBH_4$: the enzyme loses catalytic activity. However, one class of pyridoxal phosphate dependent enzymes, the α-glucan phosphorylases, is a remarkable exception. *Snell*[65] wrote: "Phosphorylase, the most plentiful pyridoxal phosphate dependent enzyme of mammals does not act *via* a Schiff base mechanism as shown by the fact that the borohydride reduced enzymes still show activity" (for reviews see [64,65]).

2.1. Chemical Structure of Pyridoxal Phosphate bound to Phosphorylase

C. F. Cori et al. first separated pyridoxal phosphate from crystalline rabbit skeletal muscle glycogen phosphorylases *a, b* and *b'* with $(NH_4)_2SO_4$ at pH 3—4, and obtained inactive crystalline pyridoxal phosphate-free apoenzymes[56]. Incidentally, *Otto Warburg* had already (1938) separated flavin-adenine-dinucleotide (FAD) in a similar manner from a flavin dependent dehydrogenase, the so called "gelbe Atmungsferment"[72]. A high yield of active holoenzyme on reconstitution of apoenzyme with pyridoxal phosphate is however only obtained with the procedure of *Fischer, Shaltiel,* and *Hedrick*[73-75]. According to this procedure, the structure of the phosphorylase *b* protein is first reversibly "deformed" with imidazole citrate.

The exposed Schiff base of pyridoxal phosphate can then be attacked stereospecifically with L-cysteine with formation of a thiazolidine. The cofactor can be removed under mild conditions at pH = 6.4 and 0 °C in about 35 min. This meth-

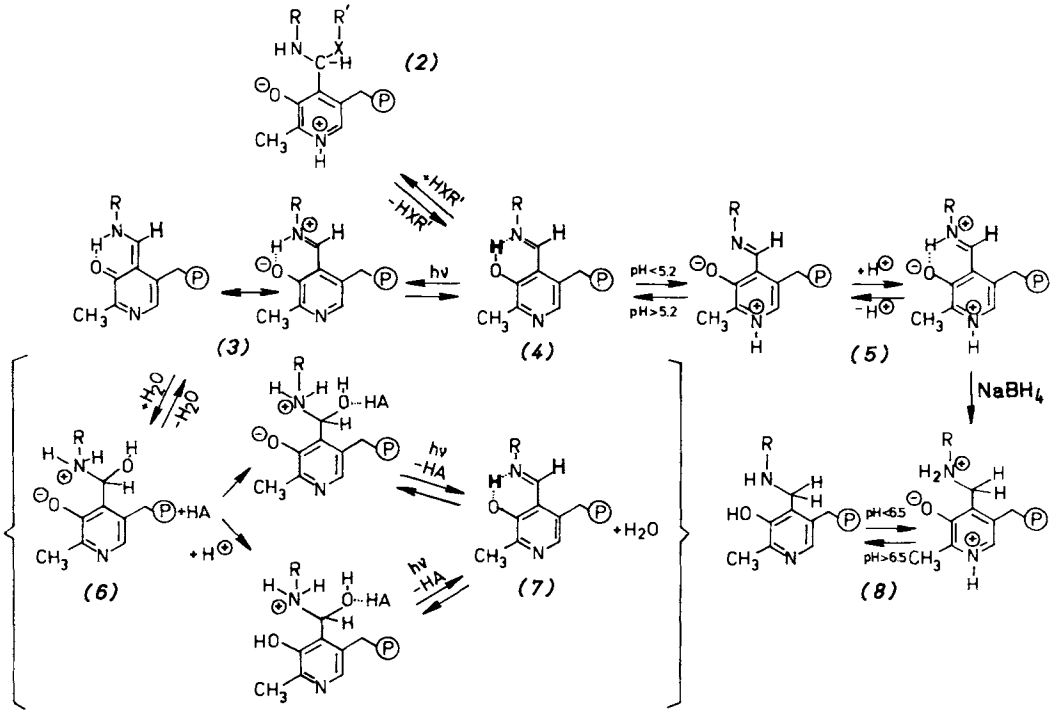


Fig. 2. Structures of phosphorylase bound pyridoxal phosphate (reproduced from [76]). *(2)—(8)*, see text.

od made possible the replacement of the natural cofactor pyridoxal phosphate by chemically modified analogues and the extensive study of the properties of the reconstituted phosphorylase derivatives.

Views on the binding mode of the cofactor to the phosphorylase protein were controversial until recently (see Fig. 2[76]). *Graves et al.*[77], *Shaltiel* and *Cortijo*[78,79] (see also [80,81]) assumed that the catalytically active form is a pyridoxal phosphate Schiff base *(4)*, which absorbs at 333 nm and forms tautomers *(3)*. However, according to *Kent et al.*[57] pyridoxal phosphate is bound in phosphorylase as a substituted aldimine *(2)* with the participation of an unknown nucleophilic group XR'. If this group were a hydroxyl group (*e.g.* of water), one would have an aminomethanol derivative, as was suggested by *Honikel* and *Madsen*[82]. Perturbations of the enzyme structure, for example by acidification, high concentrations of NaCl, exposure to cold, bring the cofactor in contact with the solvent. If the solvent is aqueous, an absorption at 415 nm arises which is characteristic for a Schiff base [*(3)* and *(5)*]. Only now, can the exposed azomethine linkage in *(5)* be reduced with $NaBH_4$[2] (see also [13,83,84]). In contrast, *Honikel* and *Madsen*[82] have proposed that the aminomethanols *(6)* lose water on photochemical excitation and form Schiff bases *(7)*. The different positions of the chelating protons of the hydroxyl group (bold print) in the structures *(4)* and *(7)* are due to different energy potentials[76,82,85]. The spectral properties are summarized in Table 1[76]. They emphasize how difficult it is to assign unequivocally the "abnormal" absorption at 333 nm of phosphorylase-bound pyridoxal phosphate by comparing it with the absorptions of Schiff bases of this cofactor and *n*-butylamine. For example, the 333 nm absorption can either be assigned to the phenolic form *(4)* or to the phenolates *(2)* and *(6)*. Although by comparison with the 3-*O*-methyl analogue of pyridoxal phosphate *(10)* (see Table 2) one can eliminate the phenolate form, but one cannot distinguish by UV spectroscopy alone between the sp^2 and sp^3 hybrids of the phenolic forms. For example, the sp^3 phenolic form of reduced phosphorylase has an absorption (290 nm) like the sp^2 phenolic form of the phosphorylase-bonded 3-*O*-methylpyridoxal phosphate *(10)* (297 nm). However, an unequivocal assignment was possible by comparing the NMR spectra of the proton at the C-atom bonded to the C-4 of pyridoxal phosphate with the UV-spectra: We found that the chemical shifts of the proton resonance of the Schiff base derivatives in dimethyl sulfoxide (DMSO) and D_2O were the same ($\delta = 8.9$). This shows that the phenolic forms of 3-*O*-methylpyridoxal phosphate, pyridoxal phosphate and pyridoxal can all form Schiff bases. The hypsochromic shift (333 nm→295 nm) of the 3-*O*-methylpyridoxal phosphate Schiff base is worth noting. This shift became apparent on comparing UV spectra in DMSO of the Schiff bases with *n*-butylamine and the phenolic forms of 3-*O*-methylpyridoxalphosphate on the one side and pyridoxal-P on the other. To sum up: These experiments prove the chemical structure of pyridoxal phosphate in muscle phosphorylase as a typical Schiff base in the phenolic form and support the assignment of *Johnson et al.*[77] and *Shaltiel* and *Cortijo*[78,79] who have argued that protonation of the 3-phenoxide group of a Schiff base in a hydrophobic environment is responsible for the unusual shift of the UV absorption (415 nm→333 nm) to shorter wavelength and for the fluorescence properties of pyridoxal phosphate bound to phosphorylase.

2.2. The Location of Pyridoxal Phosphate

The location of the catalytic center of phosphorylase was likewise in doubt until recently. The first X-ray structure analyses suggested that the active center of muscle phosphorylase is located in the N-terminal domain near the regulatory AMP-site. A location of the active center at or near the subunit contacts and the regulatory domain was attractive, because allosteric activity control is propagated *via* subunit interactions. Moreover, this location would have offered an explanation for our findings that phosphorylase monomers are inactive[25]. With the improvement in the resolution of the X-ray diffraction patterns down to 3 Å and finally to 2.5 Å[86,27] a second binding domain was found, where a second (weaker) binding site for the allosteric effector 5'-AMP and binding sites for glucose 1-phosphate, P_i and glucose, a competitive inhibitor for glucose 1-phosphate are located. Moreover, at higher resolution, pyridoxal phosphate could now be located: It was found in close proximity to the other sites in the second binding domain in the central core of the subunit.

Table 1. UV absorption maxima of pyridoxal phosphate derivatives (reproduced from [76]). The measurements were carried out in aqueous solutions, except where stated otherwise.

Cofactor	Reagents for the cofactor and products						
	L-Cysteine → thiazolidine	2-Mercapto-ethanol → hemi-mercaptal	H_2O → hydrate	Apo-phosphorylase *b* + $NaBH_4$ → reduced phosphorylase *b*	*n*-Butyl-amine → Schiff-base	Bovine serum albumin	Apo-phosphorylase *b* → native phosphorylase *b*
Pyridoxal phosphate phenoxide	325	322	325	333 [a]	415 [b]	415	415 [a]
Pyridoxal phosphate *(1)*	[148]	[149]	[150, 151]	[152]	[78, 153]	[154]	[57]
Pyridoxal phosphate *(1)*	297 [c]	288 [c]	295 [150]	290 [d]	333 [c], 335 [b] [78, 153]	332 [154]	333 [a] [57]
3-*O*-Methyl-pyridoxal phosphate *(10)*	278 [c]	277 [c]	278	—	295 [c]	300	297

[a] pH = 5—7. [b] In dioxane/water. [c] In dimethyl sulfoxide. [d] No solvent and pH data.

The active center of muscle phosphorylase is located at the bottom of a deep narrow crevasse near the center of the subunit where the three structural domains meet.

In this context, results of a recent ^{31}P-NMR study carried out by our group with succinylated rabbit skeletal muscle glycogen phosphorylases *b* and *a* are worth reporting, because they demonstrate quite impressively how NMR spectroscopy of the enzyme in solution can help to support or correct structural assignments made by X-ray diffraction methods. In this particular case, ^{31}P-NMR studies helped to clarify the location of pyridoxal phosphate in muscle phosphorylase[36]: We have compared the ionization of the phosphate group of pyridoxal phosphate in native and succinylated, partially dissociated (monomer:dimer ratio = 40:60) rabbit muscle phosphorylases *b* and *a* (Fig. 4[36]). It may be

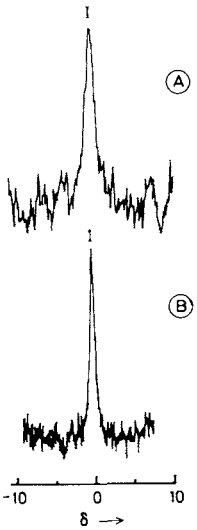


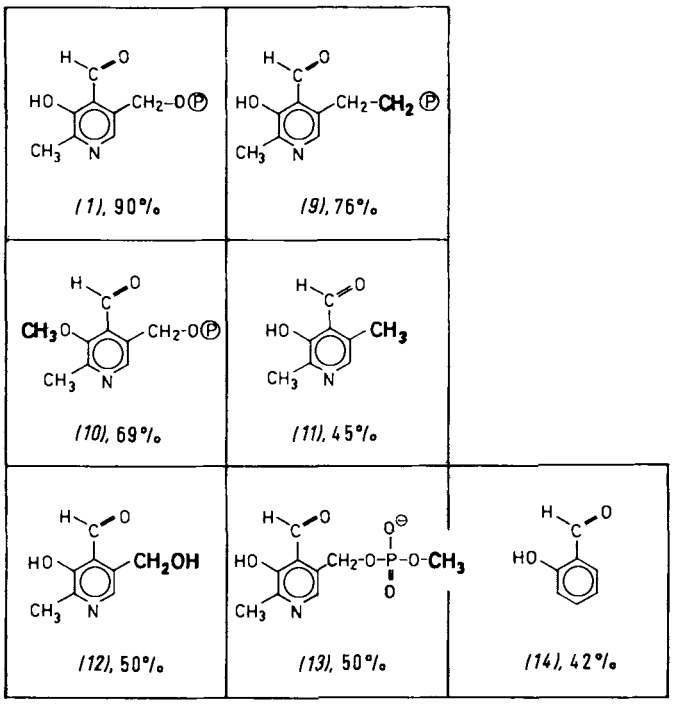
Fig. 3. ^{31}P-NMR spectra (72.86 MHz) of pyridoxal phosphate in (A) native rabbit skeletal muscle phosphorylase *b* and in (B) succinylated muscle phosphorylase *b*. (A) pH = 7.1, form I; (B) pH = 7.23, form I (reproduced from [36]).

noted that in the succinylated, partly dissociated enzyme the phosphate resonance of pyridoxal phosphate is at $\delta = -0.37$, and hence at the same location as the resonance of the protonated form I of the cofactor phosphate in the "inactive" conformation of native phosphorylase *b* ($\delta = -0.31$). At pH = 7.2, at which the experiment was performed, one would have anticipated more than 90% of the pyridoxal phosphate as dianion if dissociation to monomers had established contact of the cofactor with the aqueous solvent. This would have been expected if the active center were indeed situated on the contact-surfaces of the subunits in the dimer, as was originally assumed. But the results of our ^{31}P-NMR studies are only compatible with a location of the cofactor in a protected area in the monomer which is shielded from the solvent.

2.3. Catalytically Functional Groups of Pyridoxal Phosphate

Resolution of phosphorylase from pyridoxal phosphate results in dissociation of apophosphorylase into monomers. Crystalline apophosphorylase *b* is nearly completely monomeric at 35 °C[87] (see also [88,9]). This raised the question whether pyridoxal phosphate functions as a structural ligand in glycogen phosphorylase and whether it is required to stabilize the quaternary structure which is a prerequisite for activity and regulation. We have excluded this possibility[89]: Table 2 demonstrates convincingly that the chemical structure of the cofactor which is required for dimer formation

Table 2. Activity induction by aldehydes (reproduced from [89]). Substituents in bold type represent essential modications. The numbers signify the catalytic activity of a "dimer" of a native monomer and a monomer of apophosphorylase + aldehyde.



differs from the structure required for catalytic activity: In the experiments in Table 2, 50% activity implies that a monomeric subunit which carries a pyridoxal phosphate analogue which is *inactive* in the dimeric holoenzyme nevertheless can fully *elicit activity* on dimerization in a subunit carrying the original pyridoxal phosphate cofactor.

Many chemical analogues of pyridoxal phosphate[90-93] were tested for binding and reactivation of apophosphorylase. The results in Table 3 exclude, with exception of the nitrogen atom and the 5′-phosphate group, all other functional groups of pyridoxal phosphate for a role in catalysis of α-1,4-glucan phosphorylases (see also [53]). The nitrogen atom of the pyridine ring is however an anchor point like the formyl group; for example, if it is quaternated by a methyl group (No. 19), the cofactor can no longer bind to the apoenzyme[92]. The *N*-oxide analogue of the partially active 3-*O*-methylpyridoxal phosphate is bound, albeit weakly, but the reconstituted enzyme is inactive[94]. But participation of the nitrogen atom (pK = 8.7[95]) in catalysis seems unlikely. This view receives some support from the observations that drastic changes in the basicity of this group, for example by introduction of fluorine in position 6 or methylation of the 3-OH group still yield pyridoxal phosphate derivatives which form active phosphorylases[92,96]. This leaves the 5′-phosphate group of the cofactor: A direct participation of the phosphate group of pyridoxal phosphate as a reactant in phosphorolysis was already excluded by *Illingworth et al.*; there is no P_i-glucose 1-phosphate exchange with the 5′-phosphate group of the cofactor[88] (see also [37,56]). However, all modifications of the 5′-position of the cofactor yield inactive phosphorylases, when a) the 5′-phosphate group is miss-

Table 3. Pyridoxal phosphate analogues tested for reconstitution and reactivation of rabbit skeletal muscle phosphorylase (see: [53]). 22; [cf: 94]: 23; [cf: 155]; 24 and 25; [cf: 156]; 26; [cf: 97]; 27 and 28; [cf: 156].

No.	Cpd.	Changes at position						Activity [%]	Binding	Ref.
		1	2	3	4	5	6			
	Apoenzyme							0		
1	*(1)*							100	+	
2							CH_3	0	+	
3	*(12)*					CH_2OH		0	·	
4	*(11)*					CH_3		0	+	
5						CH_2CH_2COOH		0	+	
6						CH_2OSO_3H		0	+	
7						$CHOPO_3H_2$ CH_3		0	·	
8						$CH_2PO_3H_2$		4–8	·	
9	*(9)*					$CH_2CH_2PO_3H_2$		25	·	
10						$CH_2CH_2OPO_3H_2$		0	+	
11						$CH_2OPO_3HCH_2CH_2CN$		0	+	
12					$CH{=}CH_2$			100	+	
13					CH_2NH_2			0		
14					CH_2-Protein			60	+	
15					COOH			0	+	
16	*(10)*			OCH_3				25	+	
17			C_2H_5					0.5		
18			H					60	+	
19		CH_3						0		
20		→O						0		
21		→O		OCH_3				0	+	[94]
22						$CH_2OPO_2(OPO_3H$-Pyridoxal$)H$		0	+	[155]
23						CH_2SO_3H		0		[156]
24						$CH_2OPO_2(OPO_3H_2)H$		0	·	[156]
25	*(13)*					$CH_2OPO_2(OCH_3)H$		0	·	[97]
26						$CH_2OPO_2(OCH_2C_6H_5)H$		0	·	[156]
27						$CH_2OPO_2[OPO_2(OC_6H_5)H]H$		0	+	[156]

ing, b) the phosphate is replaced by another acidic group with a different pK, c) the sterical conformation of the 5′-phosphate has been altered, or d) the second protonatable group of the phosphate residue is blocked, as for example in the pyridoxal phosphate monomethyl ester *(13)* synthesized by us[94,97].

Graves et al.[98] made the remarkable observation that rabbit muscle phosphorylase *b* containing pyridoxal *(12)* has a few percent of the enzymic activity of the native enzyme in synthesis (and degradation) of glycogen when incubated in high phosphate concentrations (50 mM). The activity of pyridoxal phosphorylase *b* when compared with native pyridoxalphosphate phosphorylase *b* is about 6% with phosphate, 8% with phosphite and fluorophosphate and 3% with arsenate. All phosphate analogues which elicit activity have nearly identical tetrahedral structures. Thiophosphate, bicarbonate and pyrophosphate are strong inhibitors, sulfate and nitrate weak inhibitors. Pyrophosphate is bound stoichiometrically one mol per subunit, and blocks the binding site for phosphate, phosphite, fluorophosphate and glucose 1-phosphate. All anions which activate phosphorylase *b* reconstituted with pyridoxal seem to bind to the site normally occupied by the 5′-phosphate group of the natural cofactor. This assumption by *Parrish et al.*[98] is supported by experiments carried out by our group which demonstrated that high concentrations (100 mmol/l) of phosphate fail to activate phosphorylase reconstituted with pyridoxal phosphate monomethyl ester *(13)*, presumably because the inactive phosphoric acid ester blocks the phosphate site necessary for catalysis[98a]. Since fluorophosphate and phosphate bind equally tight to the enzyme, *Parrish et al.*[98] assumed that these phosphates are bound as dianions FPO_3^{2-} and $HOPO_3^{2-}$, respectively. This interpretation is in line with our ^{31}P-NMR measurements, which showed that the 5′-phosphate group of pyridoxal phosphate in native, enzymatically active phosphorylases is in the dianionic form[99,100,101][*].

2.4. The Role of Pyridoxal Phosphate in Allosteric Regulation

Monod et al.[103] classified phosphorylase *b* as an allosterically regulated enzyme of the "K" type which is either in the inactive T- or in the active R-conformation. The positive allosteric effector, 5′-AMP binds to the R-form. *Helmreich* and *Cori*[104] could demonstrate, with crystalline rabbit skeletal muscle phosphorylase *b* positively cooperative and reciprocal homo- and heterotropic interactions between substrates and AMP and thus found an explanation for the obligatory requirement of 5′-AMP for the activity of muscle phosphorylase *b*. In the meantime, several other nucleotides and nucleotide analogues have been tested as allosteric activators of phosphorylase *b*[105–108].

AMP and IMP generate different enzyme conformers which crystallize in different space groups. As a matter of fact, it was the IMP-phosphorylase *b* complex which permitted the successful exploration of its three dimensional structure by X-ray diffraction. Phosphorylase *b* forms tetragonal crystals in the presence of 2 mM IMP with a single subunit in the asymmetric unit[29]. The positive regulatory effector binding sites are all in the amino terminal part of the poly-

[*] The partial activation (8%) of the pyridoxal enzyme with fluorophosphate, which has a much lower pK value ($pK_{II}=4.8$) than phosphate ($pK_{II}=7.2$), is puzzling and needs to be explained, because the pK_{II} of fluorophosphate is too low to allow for a function as proton acceptor at a pH range where muscle phosphorylase is active. In that context, one should recall that the pH-activity-peak of yeast phosphorylase is at pH 5.8 [102]. Muscle phosphorylases have their maximal activities, dependent on buffer and conditions at around pH 6.2 [17].

peptide chain, whereas the catalytic sites are located in another ("heavy") segment (HS) of the chain. Both domains are loosely connected *via* a segment which is readily accessible to proteolytic enzymes. The molecular details of the conformational transitions resulting from the interactions of muscle phosphorylase *b* with the physiological activator, 5′-AMP, have not yet been worked out, but rapid progress may be anticipated in the near future once the structures of different conformers can be compared in the crystalline state (X-ray diffraction) and in solution (NMR-spectroscopy)[36] (see also [109, 110]).

In this context, allosteric regulation is of interest only insofar as the study of a possible structural role of pyridoxal phosphate in the regulation of muscle glycogen phosphorylases led one of us *(E. H.)* to consider a catalytic role for the cofactor. Some time ago, we studied[9, 10] the allosteric transitions of inactive apophosphorylase *b* and of the pyridoxal *(12)* and 5′-deoxypyridoxal *(11)* phosphorylase derivatives on binding of AMP. We could show that the inactive phosphorylase derivatives containing a cofactor without the 5′-phosphate group are still capable of binding 5′-AMP in a highly cooperative manner. These findings could be repeated more recently with nearly identical results by *Feldmann* using a new rate dialysis method and the inactive pyridoxal phosphate monomethyl ester *(13)* of phosphorylase *b* where the 5′-phosphate group of the cofactor is no longer protonatable at $pK = 6.2$[111]. Although these phosphorylase derivatives with or without a monoanionic 5′-phosphate group of the cofactor are not catalytically active, they nevertheless are allosterically regulated and still bind AMP positively cooperative with a Hill coefficient of about 2.0. Moreover these phosphorylase *b* derivatives sediment in the analytical ultracentrifuge like active, native pyridoxal phosphate containing phosphorylase *b*, whereas, apophosphorylase *b* sediments mainly as monomer[10, 97, 112]. Tritium-hydrogen exchange was used by *Weisshaar* and *Palm*[113, 114] in the Würzburg laboratory to compare the structures of the different phosphorylase derivatives. This approach is based on the observations of *Hvidt* and *Nielsen*[115] that different conformers of one and the same protein can be distinguished by the numbers and the rates of the exchanging hydrogens. The Tritium-hydrogen exchange rates of the pyridoxal phosphate monomethyl ester *(13)* reconstituted phosphorylase *b* derivative were very similar to those of the native phosphorylase *b*. It thus appears that this analogue is bound to apophosphorylase in a manner quite analogous to the natural cofactor pyridoxal phosphate[113, 114]. We could show, therefore, that at least in these special cases the 5′-phosphate group of the cofactor is not obligatorily required for the expression of allosteric control properties of oligomeric phosphorylases from mammalian muscle. Tritium-hydrogen exchange revealed that pyridoxal phosphate monomethyl ester *(13)* traps protons on binding to apophosphorylase as effectively as the natural cofactor which forms an active holoenzyme[113, 114]. Nevertheless, the enzymes containing a cofactor analogue with a modified 5′-phosphate group or lacking the 5′-phosphate are inactive. This provoked one of us [*E. H.*] already in 1968 to propose an additional, catalytic role for the 5′-phosphate group of pyridoxal phosphate[9]: "If one wishes to consider an additional role for the prosthetic group of phosphorylase, attention obviously centers on the 5′-phosphate, since the phosphate group is apparently essential for catalytic activity, whereas its role with respect to the allosteric properties of the enzyme protein is permissive." However, the observation of the phosphate of pyridoxal phosphate in its natural environment was made possible only once a superconducting wide-bore NMR-spectrometer with high resolving power allowed measurement in the Fourier-transform mode of the ^{31}P resonance of pyridoxal phosphate in the enzyme in solution.

2.5. Ionization Changes of the Phosphate Group of Pyridoxal Phosphate on Transition from Inactive to Active Phosphorylase

Feldmann and *Hull*[99] have shown by ^{31}P-NMR that 5′-AMP in cooperation with an anionic substrate triggers the deprotonation of the 5′-phosphate group of pyridoxal phosphate bound to rabbit skeletal muscle phosphorylase *b* (Fig. 4[99]). The weaker effect of AMP alone (without anionic substrate) is explained by the allosteric properties of phosphorylase *b*: The substrate strengthens the binding of the activator to muscle phosphorylase *b*, as was shown by *Helmreich* and *Cori*[104]. The activation constant (K_a) for 5′-AMP and phosphorylase *b* is 3×10^{-4}—5×10^{-4} M without and 4×10^{-5}—10×10^{-5} M with anionic substrate. Arsenate can replace phosphate. The tightening of the AMP-phosphorylase complex by arsenate shifts the ^{31}P-NMR signal of pyridoxal phosphate by about $\delta = -0.2$ to -3.6. A good separation of the ^{31}P-NMR signals of AMP and pyridoxal phosphate was achieved by substituting AMP by AMP-S, whose signal is shifted by about 40 ppm to lower field. Fortunately, AMP-S is even a more effective allosteric activator of phosphorylase *b* than AMP[116, 117]. On tightening the binding of the nucleotide, AMP-S to phosphorylase *b*, pyridoxal phosphate is

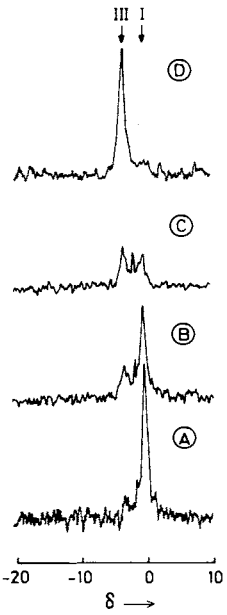


Fig. 4. Influence of AMP-S (adenosine 5′-monothiophosphate) on the ^{31}P-NMR spectrum (72.86 MHz) of pyridoxal phosphate in (D) native and (A—C) succinylated rabbit skeletal muscle phosphorylase *b* (reproduced from [36]). (A) no AMP-S, no arsenate, pH = 7.12; (B) 0.7 mM AMP-S, pH = 7.05; (C) 0.7 mM AMP-S and 30 mM arsenate, pH = 7.29; (D) 1.5 mM AMP-S and 36 mM arsenate, pH = 7.1; the resonance in (B) and (C) between forms I and III is most likely due to a phosphate containing impurity.

present almost exclusively as form III, the dianionic form ($\Delta\nu = 60$ Hz). K_d ($= k_{-1}/k_1$) is about 1×10^{-4} M for the AMP-S phosphorylase *b* complex with arsenate. These data are in good agreement with published values of K_a for AMP and phosphorylase *b* with phosphate or arsenate[104]. The ^{31}P-NMR signal of pyridoxal phosphate bound to phosphorylase *b* in the inactive state, *i.e.* in the absence of ligands, was assigned to form I, the protonated form. Addition of AMP or AMP-S in the presence of saturating concentrations of arsenate triggers the transition to the active conformation. This transition is accompanied by the transition of form I to form III of the cofactor phosphate.



Form I, inactive Form III, active

The chemical shift is compatible with the formation of the dianionic form III of the pyridoxal phosphate Schiff base. One can form with phosphorylase *b* kinase, Mg^{2+} and ATP-γ-S an active phosphorylase *a* derivative containing thiophosphoserine residues. The ^{31}P-NMR spectrum of this active phosphorylase *a* derivative recorded at pH = 7.7 was identical regarding chemical shift and linewidth ($\Delta\nu = 60$ Hz) with the phosphorylase *b*—AMP-S complex with 50 mM arsenate; the resonances were predominantly form III and a minor portion was form I resonance (Fig. 5A[99]). Binding of AMP-S (1 AMP-S per site) results in the transition of the residual form I into form III (Fig. 5B). One should recall here that muscle phosphorylase *a* is active without AMP whereas phosphorylase *b* is active only with AMP. Recently, we have repeated these experiments with partly dissociated succinylated phosphorylase *b* (Fig. 6[36]). As was expected transition of the inactive, protonated form I to the active, dianionic form III on binding of the nucleotide (AMP-S) is incomplete in the case of succinylated phosphorylase *b* and about one half as much form III is formed as in the case of native phosphorylase *b*. The transition from the inactive form I to the dianionic form III is likewise hindered in the case of succinylated phosphorylase *a*[36].

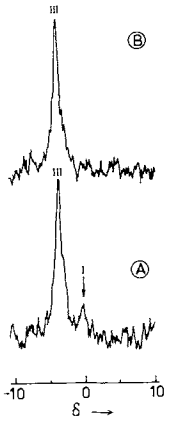


Fig. 5. ^{31}P-NMR spectra of pyridoxal-P (PLP) in native rabbit skeletal muscle phosphorylase *a* (reproduced from [99]). (A) no AMP-S; (B) 0.35 mM AMP-S, pH = 7.7.

The ^{31}P-NMR studies of *Feldmann* and *Hull*[99] with the regulated rabbit skeletal muscle phosphorylases *b* and *a* have shown that the transition from an inactive to an active conformation is accompanied by deprotonation of the cofactor phosphate. Another way to interpret these ionization changes implies that in aqueous solvent, the transition from form I to form III results in a lowering of the pK value of the phosphate group by at least three units. This shift to the acidic side is about equal to a change in free energy of about 3.9 kcal/mol, which is about the free energy required for formation and cleavage of α-glycosidic bonds or for hydrolysis of glucose 1-phosphate. Although this ionization change is compatible with a catalytic function of the phosphate group of pyridoxal phosphate in α-glucan phosphorylases, these experiments do not give us any information on how the phosphate dianion might participate in catalysis. But recent ^{31}P-NMR studies with the non-regulated *E. coli*[100] and potato[101] phosphorylases which we discuss now, have considerably extended our views on the catalytic role of the cofactor phosphate.

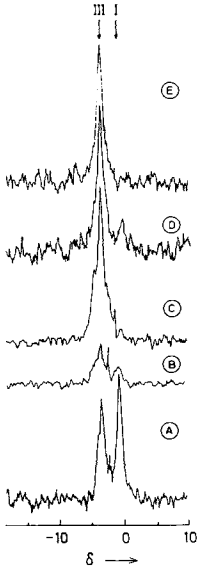


Fig. 6. ^{31}P-NMR spectroscopically observed differences in the ionization of pyridoxal phosphate in succinylated (A, B) and native (C—E) rabbit skeletal muscle phosphorylase *a* (after [36]). (A) residual activity 12%; pH = 7.35; (B) as in A, but with 1.17 mM AMP-S (3 mol/mol of monomer); (C) pH = 6.5; (D) pH = 7.67; (E) as in D, but with 0.35 mM AMP-S (1.3 mol/mol of monomer).

2.6 How Does the Phosphate Group of Pyridoxal Phosphate function in Catalysis?

The crystallographers have until now studied exclusively "inactive" conformers of the well-characterized crystalline rabbit skeletal muscle phosphorylases *b* and *a*[28,27]. We have recently initiated ^{31}P-NMR studies with phosphorylases whose activity is neither allosterically nor covalently controlled. These enzymes can be obtained in a pure state and crystallized and in the large quantities needed for NMR work[8,100,101]. The ^{31}P-NMR spectrum of native potato phosphorylase has a resonance line at $\delta = -4.5$ with a linewidth of $\Delta\nu = 35$ Hz (Fig. 7A[101]). Taking into account that potato- and muscle-phosphorylase have comparable molecular weights (103000 and 97412 respectively[4,6,7]), the linewidth of the pyridoxal phosphate signal of the potato phosphorylase ($\Delta\nu = 35$ Hz) is much narrower than the linewidth of the

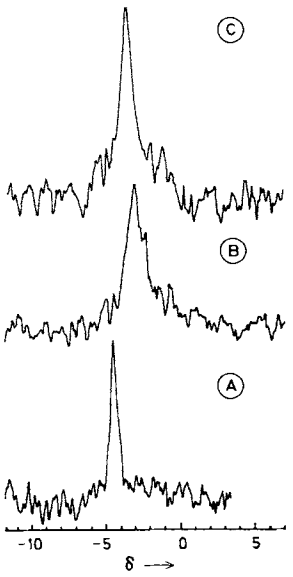


Fig. 7. ^{31}P-NMR spectra (72.86 MHz) of pyridoxal phosphate in potato-phosphorylase. In all experiments the pH was 6.5. (A) without ligands; (B) 90 mM glucose; (C) 90 mM glucose and 100 mM arsenate (after [101]).

phosphorus of the cofactor bound to muscle phosphorylase (35 Hz). One might speculate that the sharper resonance line results from a greater mobility of the 5′-phosphate group around the C—O bond. A comparably narrow linewidth ($\Delta\nu = 35$ Hz) was also observed with the *E. coli* maltodextrin phosphorylase, which has however a smaller molecular weight (83000 per subunit)[8]. The ^{31}P-NMR signal of potato phosphorylase was pH independent in the pH range 6.3 to 7.8. This indicates that the binding site is protected and shielded from the aqueous solvent. In analogy, with muscle phosphorylase we assign the signal at $\delta = -4.5$ to the dianionic form of the 5′-phosphate group. The corresponding signal of the muscle enzyme appears at $\delta = -3.76$ (Fig. 6C and 6D). This shift could be due to a distortion of the O—P—O angle resulting from electrostatic interactions with the protein and/or reflecting differences in the hydrophobic environment of the cofactor[118-120]. We will discuss that later. The substrate analogue, arsenate, but likewise other divalent anions which are not substrates, such as for example sulfate and methylphosphonate shift the ^{31}P-NMR signal of the cofactor on binding to potato phosphorylase to higher field in a small but reproducible and concentration dependent manner. In the presence of 30 mM arsenate, the signal is exchange-broadened with a linewidth of 50 Hz at $\delta = -3.98$. At saturating (60 mM) arsenate concentration, the signal is sharpened with a linewidth of 40 Hz and shifted upfield to $\delta = -3.75$[101]. At present, we cannot offer a mechanistic explanation for this effect of substrate and non-substrate/anions, except to speculate that high concentrations of arsenate may mobilize the 5′-phosphate group of the cofactor[99].

Of special interest are ionization changes of the 5′-phosphate group of the cofactor in potato phosphorylase on binding of glucose and oligosaccharides with or without arsenate. Glucose binds to rabbit skeletal muscle phosphorylase *a* either free or esterified with phosphate to the α-D-glucose 1-phosphate site[121]. Since glucose is also a competitive inhibitor with α-D-glucose 1-phosphate and potato phosphorylase, we have assumed that glucose binds likewise to the glucose 1-phosphate site in potato phosphorylase. The elucidation of the three dimensional structure of muscle phosphorylase *a* down to 2.5 Å resolution has allowed location of the anionic substrate sites of P_i, arsenate, glucose 1-phosphate and of the inhibitor glucose in the active center.

Substrates and inhibitor bind less than a few Å away from the 5′-phosphate of pyridoxal phosphate[27, 28, 86]. We admit however that the assumption that the structure of the catalytic centers in the muscle phosphorylases and the non-regulated potato and *E. coli* maltodextrin phosphorylases is nearly identical is at present only supported by sequence homologies of the pyridoxal phosphate sites in these enzymes (see Table 4 and [8]). The final proof requires comparative studies of the three dimensional structures of these enzymes by X-ray diffraction. Such efforts are presently being made[121a]. Experiments with glucose are also of interest, for rabbit skeletal muscle phosphorylase *a*, whose three dimensional structure is known in detail, has been studied by X-ray diffraction as glucose complex in the tetragonal, "T" (inactive) conformation[122]. Addition of 90 mM glucose shifts the ^{31}P-NMR signal of pyridoxal phosphate bound to potato phosphorylase upfield from $\delta = -4.5$ to $\delta = -3.0$. The signal is considerably broadened (see Fig. 7A and 7B)[101]. In contrast to muscle phosphorylase *A*, there is no evidence for glucose-induced conformational changes in potato phosphorylase. We have therefore neglected this possibility and interpret the upfield shift as indicating a drastic change in the pK of the 5′-phosphate group of the cofactor. With 90 mM glucose and 100 mM arsenate we observe a downfield shift ($\delta = -3.45$) and sharpening of the resonance line ($\Delta\nu = 65$ Hz; Fig. 7C). On the basis of the titration curve of the ^{31}P-NMR signal of a model Schiff base of pyridoxal phosphate and ε-amino caproic acid in aqueous solution (cf. Fig. 11) one could alternatively interpret that to mean that arsenate mobilizes and partially deprotonates the phosphate group of the cofactor protonated by glucose. It should be noted that in the presence of glucose (in contrast to its absence), deprotonation or shift in pK are specific. Neither sulfate nor methylphosphonate are effective. Sulfate, $pK_{II} = 1.9$, and methylphosphonate, $pK_{II} = 7.8$, do not function as substrates, but the latter is a competitive inhibitor for inorganic phosphate.

In the active, pyridoxal 5′-deoxymethylenephosphonate *(9)* containing rabbit skeletal muscle phosphorylase *a*, the situation is more difficult to interpret, because glucose induces a conformational transition which is reported by a partial

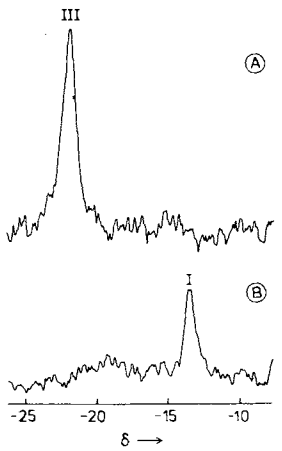


Fig. 8. ^{31}P-NMR spectra of pyridoxal 5′-deoxymethylenephosphonate *(9)* in rabbit skeletal muscle phosphorylase *a*. (A) pH = 7.07; no glucose; (B) as in A, but with 100 mM glucose (after [36]).

shift of the cofactor phosphate from the "active" dianionic form III (R-conformation) to the "inactive" protonated form I (T-conformation) (cf. Fig. 8[36,121]). As was expected, this allosteric transition is not observed with potato phosphorylase. However, both phosphorylases -the regulated skeletal muscle and the unregulated potato phosphorylase—have in common that in the presence of glucose the dianionic forms III of the phosphate of the cofactor are in rapid exchange with a mobile unknown form[*]. This is an interesting observation which needs to be studied in more detail.

Additional information was obtained with *E. coli* maltodextrin phosphorylase. The 5'-phosphate group of the cofactor can be titrated in this phosphorylase in the absence of substrates or substrate analogues in a pH dependent manner like a model Schiff base[100]. This is in striking contrast to the behavior of potato- and muscle phosphorylases. In fact, as we shall show later (cf. Fig. 11), the *E. coli* maltodextrin phosphorylase behaves in the absence of substrates like the "typical" pyridoxal phosphate dependent *E. coli* D-serine dehydratase[123]. However, if glucose is bound one also observes with *E. coli* phosphorylase the characteristic upfield shift, indicating that the 5'-phosphate group of the cofactor is protonated and becomes pH independent (Fig. 9A and 9B). In

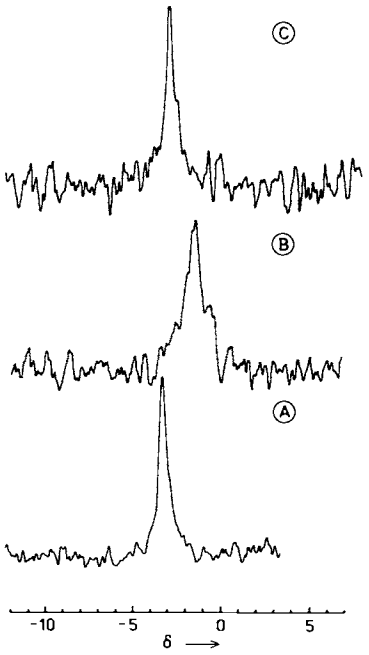


Fig. 9. ^{31}P-NMR spectra (72.86 MHz) of pyridoxal phosphate in *E. coli* maltodextrin phosphorylase. (A) pH = 6.92, no ligands; note that only without ligands and under these conditions the chemical shift is pH dependent (see Fig. 11). (B) pH = 6.59, 100 mM glucose; (C) pH = 7.05, 50 mM glucose and 100 mM arsenate (*H. W. Klein*, unpublished experiments).

the presence of arsenate and glucose, the ^{31}P-NMR spectra of the *E. coli* maltodextrin and the potato phosphorylases are at least qualitatively similar. Both spectra are indicative of an equilibrium between monoprotonated and dianionic forms (cf. Fig. 7C and 9C). But most important the ionization equilibria are now pH-independent also in the case of maltodextrin phosphorylase from *E. coli* in the range of pH 6.1—7.4 and in the range of 75—100% enzymatic activity[*].

α-Glucan phosphorylases, in contrast to sucrose phosphorylase, require an oligosaccharide as primer[124,125] (but see also [126,127]). Mammalian phosphorylases prefer α-1,6 branched α-1,4-polysaccharides, glycogen and amylopectin. Maltodextrin phosphorylases from *E. coli* and *Klebsiella pneumoniae* prefer maltodextrin and amylose[8,37,46,47]. Potato phosphorylase has no preference for branched or unbranched polysaccharides[6,7]. X-ray structure analyses[27-30,86] have shown an oligosaccharide binding site which is 33 Å—25 Å distant from the catalytic center of muscle phosphorylases *b* and *a*. *Kasvinsky et al.*[128] have therefore named this site the glycogen storage site, which is thought to be responsible for binding phosphorylase to glycogen in the living cell[129-131]. Since the glycogen storage site is located in muscle phosphorylases in the regulatory domain distant from the catalytic center, the participation of this site in glycogen activation which results in formation of active dimers and in heterotropic cooperativity with other substrate binding sites and the allosteric AMP activator site is plausible, whereas its participation in catalysis is unlikely, even when the presence of oligosaccharides or glycogen in the catalytic center has not yet been reported. *Kasvinsky et al.*[128] have recently presented a kinetic model which postulates that the glycogen storage site must be occupied before heptaamylose (or glycogen) can bind to the active center. Incidentally, a kind of "compulsory order of addition"for glycogen was invoked by *Michaelides* and *Helmreich* to explain the protection of muscle phosphorylase by the polysaccharide against inhibition by anti-phosphorylase Fab-fragments[132,133]. If glucose is replaced by heptaamylose, which has a much higher affinity to potato phosphorylase than glucose, one finds already with 1 mM

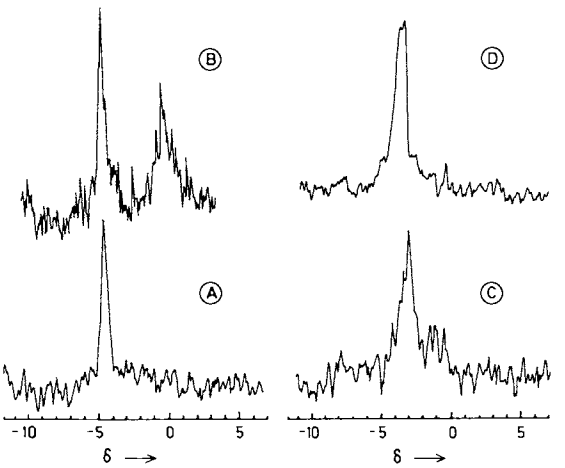


Fig. 10. ^{31}P-NMR spectra (72.86 MHz) of pyridoxal phosphate in potato phosphorylase. (A) no substrates; (B) 1 mM heptaamylose, (C) 15 mM heptaamylose; (D) 15 mM heptaamylose and 100 mM arsenate; all measurements at pH = 6.5 (after [101]).

[*] We have assigned the forms I and III in active pyridoxal 5'-deoxymethylenephosphonate *(9)* reconstituted phosphorylase *a* by analogy with the 5'-phosphate of pyridoxal phosphate *(1)* in native rabbit muscle phosphorylase *a*. On titration of a model Schiff base of *(1)* and ε-aminohexanoic acid in aqueous solvent (Fig. 11), the signals of the dianionic and the monoprotonated forms shift and in the opposite direction and less strongly than in the case of *(9)* in phosphorylase *a*. These differences warrant further investigation, because they point to a different geometry of the 5'-deoxymethylenephosphonate group of the cofactor in active muscle phosphorylase. Moreover, these results are of general interest regarding how the geometry of the phosphate group of the cofactor in the enzyme influences the chemical shifts.

[*] The pH activity profile of *E. coli* maltodextrin phosphorylase is dependent on the nature of the buffer and the direction of the reaction (synthesis or degradation). The information applies to synthesis in [4-(2-hydroxyethyl)piperazine]ethanesulfonic acid (HEPES) buffer.

heptamylose (1 mM = 1/90 of the glucose concentration) at pH = 6.5 together with the original signal a new signal which is shifted upfield by about 4 ppm (Fig. 10B)[101]). Linewidth and resolution show that both forms do not exchange or very slowly exchange. The broadened signal at higher field is, however, in exchange with a signal, which at higher oligosaccharide (15 mM heptaamylose) concentrations becomes the dominant signal (Fig. 10C). This resonance at $\delta = -3$ corresponds to the chemical shift induced by 90 mM glucose (Fig. 7B). 100 mM arsenate and 15 mM heptaamylose result in arsenolysis of the glycosidic bonds and in the formation of glucose and arsenate. Accordingly, a spectrum is obtained which resembles the spectrum in the presence of glucose and arsenate (cf. Fig. 7C and 10D).

We could demonstrate by ^{31}P-NMR spectroscopy that glucose in *E. coli* maltodextrin phosphorylase and glucose and oligosaccharide in potato phosphorylase change the p*K* of the 5′-phosphate group of pyridoxal phosphate. The pK changes may be interpreted as indicating protonation of the 5′-phosphate. Furthermore, we could show with potato phosphorylase that protonation is dependent on the oligosaccharide concentration. Control experiments carried out up to now, support the view that this effect is specific: Replacing glucose or oligosaccharide by 2-deoxy-D-glucose or D-glucal did not result in protonation. These findings and the finding that cyclodextrins which are bound and which are competitive inhibitors of potato phosphorylase with respect to glycogen and oligosaccharides but not substrates are ineffective, would seem to argue against "induced fit", *i. e.* structural rearrangements at the active site as the principal reasons for the ionization changes[134,135]. In the catalytic reaction with heptaamylose and arsenate or in the simulated reaction with the products glucose and arsenate, a rapid equilibrium between protonated and dianionic forms of the 5′-phosphate group of the cofactor is established (cf. Fig. 7 and 10). However, if one intends to interpret the protonation changes of the 5′-phosphate group of pyridoxal phosphate as proton-transfer in catalysis, one needs to know what role the 5′-phosphate group of the cofactor plays in catalysis by "classical" pyridoxal phosphate dependent enzymes.

2.7. Comparative ^{31}P-NMR Studies with Typical Pyridoxal Phosphate Dependent Enzymes

Martinez-Carrion[136] has recorded the ^{31}P-NMR spectrum of pyridoxal phosphate bound to aspartate aminotransferase from pig-heart cytosol (EC 2.6.1.1). The spectra were evaluated by comparison with unbound pyridoxal phosphate and interpreted to indicate that in the enzyme and in contrast to unbound pyridoxal phosphate the phosphate group of the bound cofactor is salt-bridged to a cationic amino acid residue at the catalytic site and inaccessible to aqueous solvent. This could explain the high stability of the coenzyme-apoenzyme complex compared with coenzyme-enzyme complexes lacking the 5′-phosphate group. Binding of substrates and substrate analogues did not change the ^{31}P-NMR signal; this would appear to rule out a catalytic role for the 5′-phosphate group of pyridoxal phosphate in this enzyme, which was postulated by *Furbish et al.*[137]. In aspartate aminotransferase the 5′-phosphate group is only an anchor point. The same applies to D-serine dehydratase of *E. coli* (EC 4.2.1.14) which is also a "classical" pyridoxal phosphate dependent enzyme. It was recently studied by *Schnackerz et al.*[123]. The ^{31}P-NMR resonance of pyridoxal phosphate bound to D-serine dehydratase in contrast to the cofactor bound to aspartate aminotransferase is pH dependent and behaves like an ε-aminohexanoic acid pyridoxal phosphate Schiff base in aqueous solution (see Fig. 11[100,123]). Binding of the substrate ana-

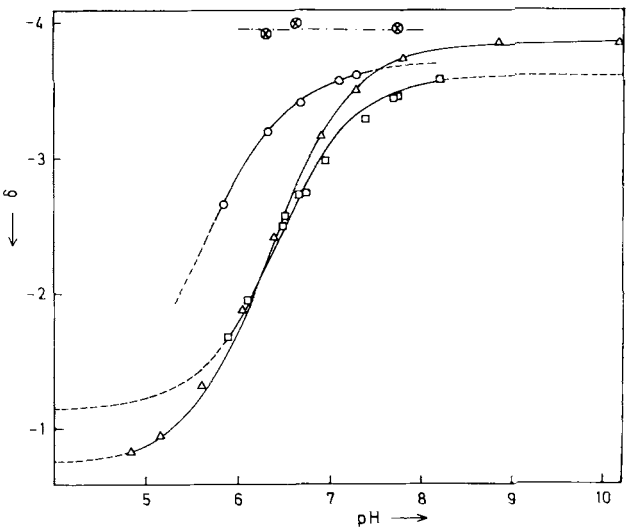


Fig. 11. Comparison of ^{31}P-NMR titration curves. ○—○: pyridoxal phosphate in *E. coli* maltodextrin phosphorylase; △—△: ε-amino hexanoic acid-pyridoxal phosphate Schiff base; □—□: pyridoxal phosphate in D-serine dehydratase; ⊗—⊗: pyridoxal phosphate in D-serine dehydratase with 25 mM isoserine (see [100, 123]).

logue isoserine shifts the ^{31}P-NMR signal downfield. It was thus assumed that the formation of the transaldimination complex required for catalysis is facilitated by immobilization of the 5′-phosphate group. When an azomethine complex between substrate and the formyl group of the pyridoxal phosphate bound to enzyme is formed, the dianionic 5′-phosphate group of the cofactor forms by electrostatic interactions a salt bridge with a cationic (arginyl) residue and removes the phosphate from the aqueous solvent. The phosphorus resonance becomes pH independent in the pH-stability range of the enzyme. Hence, also in D-serine dehydratase, the phosphate group of the cofactor serves only as a structural anchor point which helps to position and stabilize the transaldimination complex. In this respect, the role of the phosphate of the cofactor in D-serine dehydratase and in *E. coli* maltodextrin phosphorylase is different.

3. Interpretation and Synopsis

H. Neurath, E. H. Fischer et al. have recently summarized the evidence which supports a role of pyridoxal phosphate in the catalysis by α-1,4-glucan phosphorylases[4].

1) The amino acid sequence of the binding site of pyridoxal phosphate in muscle-[3 5], yeast-[49], potato-[138] and *E. coli* maltodextrin phosphorylase[8] has been highly conserved during evolution from procaryotes to eucaryotes (see Table 4[8]). This is in contrast to the N-terminal sequence which is phosphorylated and which is responsible for covalent and allosteric control. For example, the phosphory-

Table 4. Comparison of the amino acid sequences of the pyridoxal phosphate binding sites in several different phosphorylases: (A) rabbit skeletal muscle phosphorylase; (B) potato phosphorylase; (C) yeast phosphorylase; (D) *E. coli* maltodextrin phosphorylase [3-5, 138, 49, 8]. *P* Pxy indicates a singly bonded pyridoxal phosphate group (according to [8]).

	5	10	15	20
A	Glu - Ala - Ser - Gly - Thr - Gly - Asn - Met - Lys (*P* Pxy) - Phe	—— Met - Leu - Asn - Gly - Ala - Leu - Thr - Ile - Gly - Thr - Met - Asp - Gly		
B	Glu - Ala - Ser - Gly - Thr - Ser - Asn - Met - Lys (*P* Pxy) - Phe - Ala - Met	—— Asx - Gly - (Cys, Ile, Thr, Ile, Gly, Glx) - Leu - Asp - Gly		
C	Glu - Ala - Ser - Gly - Thr - Ser - Asn - Met - Lys (*P* Pxy) - Phe - Val - Met			
D	(Glu) - Ala - Ser - Gly - Thr - Gly - Asn - Met - Lys (*P* Pxy) - Leu - Ala	—— Leu - Asp - Gly - Ala - Leu - Thr - Val - Gly - Thr - Leu - Asp		

lated sequence of yeast phosphorylase[49] differs from the corresponding sequence of rabbit skeletal muscle phosphorylase. Moreover, the N-terminal sequences of rabbit skeletal muscle phosphorylase, of the plant phosphorylases, for example potato phosphorylase and of the bacterial maltodextrin phosphorylases differ from each other, although to a different degree[3, 4, 5, 48].

Up to now, phosphorylation and/or allosteric activation of plant and bacterial phosphorylases has not been reported.

2) The localization of the catalytic center in the three dimensional structure of skeletal muscle phosphorylases brought the pyridoxal phosphate site into close proximity of the sites for the two anionic substrates, phosphate (arsenate) and glucose 1-phosphate to which also glucose, a competitive inhibitor for glucose 1-phosphate, is bound. The van der Waals radii of the oxygen atoms of the phosphate group of pyridoxal phosphate and of the hydroxyl groups of the glucose moiety overlap, which makes a participation of the phosphate group of pyridoxal phosphate in catalysis feasible on structural grounds.
3) Our ^{31}P-NMR studies have shown that changes in the ionization of the phosphate group of pyridoxal phosphate signal the transition from inactive to active muscle phosphorylases *b* and *a*.

We now report on more recent ^{31}P-NMR investigations with the unregulated *E. coli* maltodextrin and potato phosphorylases which have shown that in the unregulated, *active* phosphorylases, as in the allosterically or covalently *activated* muscle phosphorylases, the phosphate group of pyridoxal phosphate is present as dianion. This explains our previous observation that phosphorylase derivatives containing a monoanionic pyridoxal 5′-phosphate monomethyl ester analogue are inactive in the pH range of catalysis[53] and as well the experiments of *Parrish et al.*[98] on partial reactivation of apophosphorylase with pyridoxal and phosphate. These findings taken as a whole support a role of the phosphate group of pyridoxal phosphate as a dianion in the catalysis of α-glucan phosphorylases.

A model for the participation of the phosphate group of pyridoxal phosphate in catalysis should consider the sucrose phosphorylase reaction [cf. [124, 139]]: Sucrose phosphorylase from *Pseudomonas saccharophilae* [EC 2.4.1.7] catalyzes the phosphorolysis of sucrose with retention of the α-configuration at the C-atom of glucose 1-phosphate:

Saccharose + $P_i \rightleftharpoons$ glucose 1-phosphate + fructose;

This reaction proceeds *via* a glucosyl-enzyme intermediate[124]. There is no report available that pyridoxal phosphate functions as a cofactor in sucrose phosphorylase. However, in contrast to α-glucan phosphorylases, sucrose phosphorylase neither requires a poly- or oligosaccharide as primer nor does it catalyze glucosyl transfer to poly- or oligosaccharides as acceptors. These differences between disaccharide and oligosaccharide phosphorylases make it attractive to speculate that pyridoxal phosphate with its 5′-phosphate group is required for the catalysis of α-glucan phosphorylases, because it has an essential function in glucosyl transfer from and to the oligo- or polysaccharide acceptors. If one considers for example that it is energetically more expensive to position and align for catalysis an oligo- or polysaccharide than a disaccharide in a narrow hydrophobic site, one could rationalize the need for a phosphate dianion instead of a monoanionic amino acid side chain in order to make catalysis effective in α-glucan phosphorylases. A requirement for a dianion would also be in line with the extremely hydrophobic environment of the catalytic site in glycogen phosphorylases pointed out first by *Shaltiel* et al.[78-81]. One would expect a hydrophobic environment to favor phosphorolysis over hydrolysis. The unusually strong hydrophobicity of the environment of the substituted pyridine ring system in phosphorylase can be deduced from the unusual spectral properties of the phosphorylase bound cofactor[76, 81]. However, UV and fluorescence studies cannot report on the environment of the 5′-phosphate group of pyridoxal phosphate in α-glucan phosphorylases. In order to obtain this information we have carried out ^{31}P-NMR experiments.

Protonation of the 5′-phosphate group of pyridoxal phosphate in the non-regulated α-glucan phosphorylases on binding of glucose and oligosaccharides may be interpreted as an increase of the p*K* value reporting increased hydrophobicity. One should recall that the catalytic site in *E. coli* maltodextrinphosphorylase becomes inaccessible to the aqueous medium on binding of glucose (see Fig. 9 and 11). An increased apparent p*K* value of the phosphate group of pyridoxal phosphate on changing the solvent from water to dioxane-water mixtures was noted by us before[97].

Consideration of the phosphate dianion of pyridoxalphosphate in *active* and *activated* forms of glycogen phosphorylases as proton acceptor in catalysis is more an additional rather than an alternative interpretation. It is so to speak, only the other side of the coin: We have presented evidence for a protonation-deprotonation equilibrium with participation of the 5′-phosphate of pyridoxal phosphate after the reaction reached equilibrium (see Fig. 7, 9, and 10). The ion-

ization equilibrium is pH independent in the range of pH = 6.1 to pH = 7.4 and in the range of 75 to 100% enzymatic activity. *Bender et al.*[164] obtained a 2500 fold rate acceleration of the hydrolysis of *endo*-5-[4′,(5′)-imidazolyl]bicyclo[2.2.1]hept-*endo*-2-yl cinnamate by addition of benzoate anions (0.5 M) in an aprotic solvent (H_2O:dioxane = 1:4 (mol/mol)). The rate acceleration was explained by deprotonation of the imidazole group by the benzoate anion followed by proton uptake by the imidazolyl group. Accordingly, a participation of the phosphate dianion of pyridoxal phosphate as a base and proton acceptor in catalysis is comprehensible. As acid, a glutamic acid residue might be considered which has been localized by *Sprang* and *Fletterick* by X-ray structure analysis at 2.5 Å resolution besides a histidine adjacent to the glucosyl residue of glucose 1-phosphate in the catalytic center of muscle phosphorylase *a*[27].

^{31}P-NMR spectra obtained with potato phosphorylase in the presence of arsenate and heptaamylose and arsenate and glucose resemble each other, at least qualitatively. This is to be expected since glucose 1-arsenate formed on arsenolysis of α-1,4-glycosidic bonds spontaneously decomposes to glucose and arsenate[141]. Judging from the chemical shift one estimates at equilibrium a 1:1 ratio of monoprotonated and dianionic forms of the 5′-phosphate group of pyridoxal phosphate. However these results raise an obvious question; namely, how can glucose and arsenate give the same chemical shift as glucose arising from heptaamylose and arsenate? Glucose, although it binds to the glucose 1-phosphate site which is in close proximity to the 5′-phosphate of pyridoxal phosphate, does not participate in catalysis. On the other hand, poly- and oligosaccharides, which are catalytically cleaved by arsenolysis forming glucose, bind to another, nonoverlapping site[27,28]. This dilemma is readily resolved when one postulates a transfer site which can either be filled with the "substrate glucosyl" of glucose 1-phosphate on the way to the poly- or oligosaccharide acceptor or with the "product glucosyl" before leaving the enzyme. The glucose, which is "sensed" by the phosphate of the cofactor, is bound to the common transfer site and would represent a "glucosyl analogue", which, however, in contrast to the "energized glucosyl" arising from glucose 1-phosphate cannot form a glucosyl-enzyme intermediate. This hypothesis seems worth testing:

The proton transfer during catalytic glucosyl transfer might be too fast to measure on the NMR time scale in the normal temperature range[143]. However, one might try to distinguish and compare the protonation-deprotonation state of the phosphate group of the cofactor after catalytic glucosyl transfer (see Fig. 7, 9, 10) and in the presence of cyclodextrin and glucose 1-phosphate when a glucosyl-enzyme intermediate might be formed. In the latter case, glucosyl transfer does not take place since the acceptor is missing. This experiment requires either a glucose 1-phosphate analogue which can form a glucosyl intermediate but which does not interfere with the ^{31}P-NMR detection of pyridoxal phosphate or a suitable "glucosyl transition state analogue". In addition, ^{13}C-NMR spectroscopy might have to be employed. Another but equally attractive approach would be to look for a glucosyl enzyme intermediate (see Fig. 12).

Gold and *Osber*[142] have searched without success for reversible cleavage of the phosphate-ester bond in ^{18}O-labeled glucose 1-phosphate with muscle phosphorylase. Such cleavage would have been anticipated when a ternary complex of phosphorylase, glucosyl residue and phosphate is formed with an enzyme bound orthophosphate, which can rotate freely. *Kokesh* and *Kakuda*[135] repeated this experiment with potato phosphorylase, which in contrast to muscle phosphorylase binds cyclodextrins which are competitive inhibitors with starch and glycogen, but which do not function as acceptors for glucosyl residues. Potato phosphorylase was indeed found to catalyze in the presence of cyclodextrin and glucose 1-phosphate labeled with ^{18}O in the ester position (like the glucose 1-phosphate in the experiment of *Gold* and *Osber*[142]) exchange between the ester oxygen of glucose 1-phosphate and the peripheral oxygens of the phosphate at a rate comparable with the rate of starch synthesis[135]:

Phosphorylase · glucose 1-phosphate · cyclodextrin ⇌
Phosphorylase · glucosyl · P_i · cyclodextrin

This experiment does not tell us the type of bond which links the glucosyl intermediate to potato phosphorylase. It is equally compatible with a covalently bound glucose or a bound glucose cation. The kinetic studies of *Firsov et al.*[144] (but see also [145]) with muscle phosphorylase *b* would seem to argue for a covalent intermediate, because no secondary isotope effect was found with C-1[^{3}H] and C-1[^{2}H] labeled glucose 1-phosphate, respectively. If a glucosyl cation were bound reversibly to the enzyme, a measurable secondary isotope effect would have been expected[144]. *Doudoroff*[139] had postulated a covalent glucosyl intermediate in the case of sucrose phosphorylase which was subsequently isolated by *De-Toma* and *Abeles*[146] and shown to be a β-glycosidically linked glucose, as to be expected in a double displacement reaction with retention of configuration (see Fig. 12[147]). We are making efforts to verify the existence of a covalent glucosyl intermediate in potato phosphorylase. For this purpose, the enzyme was incubated with α-cyclodextrin and ^{14}C-uniformly labeled glucose 1-phosphate[165]. The radioactive protein was subsequently separated from substrates by sepharose G 25 chromatography, denaturated with 5% trichloroacetic acid and exhaustively washed until radioactivity was no

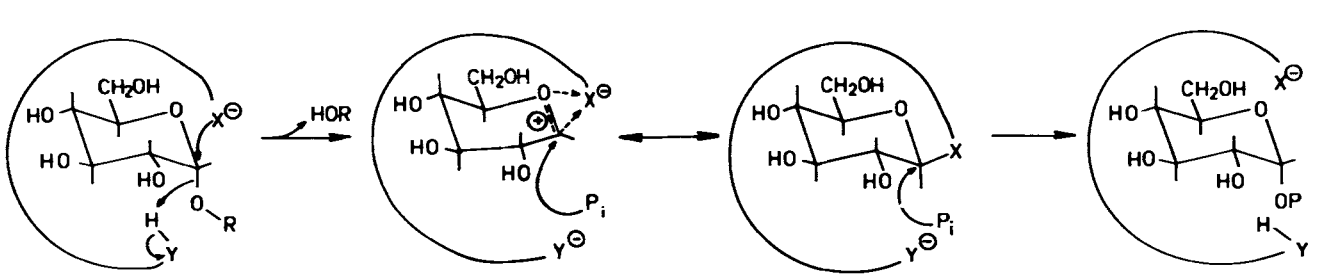


Fig. 12. Glucosyl enzyme intermediate, schematic. X: electron donor, nucleophile; HY: proton donor, electrophile; R: $(glucosyl)_n$; P_i: phosphate (after [147]).

longer detectable in the wash fluids. After chymotryptic digestion and electrophoretic separation ^{14}C-labeled peptides were found. No radioactivity in the peptides was found in control incubations of potato phosphorylase with ^{14}C-glucose or ^{14}C-glucose 6-phosphate or with ^{14}C-glucose 1-phosphate without α-cyclodextrin. Of course, unspecific binding can only be safely ruled out when the chemical structure of enzyme bound glucose has been elucidated and the glucose-enzyme intermediate located within the catalytic center.

Needless to say, the proposal that the dianionic phosphate group of pyridoxal phosphate functions as proton acceptor in the catalysis of α-glucan phosphorylases, although it is compatible with our ^{31}P-NMR data represents only one possibility. In fact, a role of the dianionic phosphate group of pyridoxal phosphate as a nucleophile has recently been proposed by *L. N. Johnson et al.*[140]. This proposal is the outcome of building models based on crystallographic data obtained with muscle phosphorylase *b* at 3 Å resolution. But whatever the answer may be, little doubt remains that the phosphate group of pyridoxal phosphate plays an obligatory role as dianion in the catalysis of α-glucan phosphorylases. It is to be hoped that further advances make it possible in the not too distant future to formulate a precise chemical mechanism of phosphorylase catalysis with the participation of the 5′-phosphate group of pyridoxal phosphate. It should then be possible to decide whether our prediction was correct that "nature may have found it advantageous to utilize in the case of glycogen phosphorylases protonatable groups of a vitamin rather than those of amino acid side chains to facilitate catalysis"[97].

Aside from the persons mentioned in our publications, the following colleagues at the University of Würzburg have greatly helped us in work on the role of pyridoxalphosphate in α-glucan phosphorylases: Priv.-Doz. Dr. Knut Feldmann, Professor Dieter Palm, Dr. George R. Philips, Dr. Klaus Schnackerz, Dr. Emil Schiltz and Dr. Manfred Bühner. We are grateful to Professors Louise N. Johnson, Oxford, Niels B. Madsen and Richard J. Fletterick, Edmonton, Donald J. Graves, Ames, Sh. Shaltiel and A. Kupfer, Rehovot, Henri Buc, Paris and T. Fukui, Osaka for making information available prior to publication. We are especially indebted to Dr. William H. Hull, Karlsruhe, Professor Edmond H. Fischer, Seattle, and Professor Esmond E. Snell, Austin, for criticism and valuable suggestions. Our work was supported in part by the Deutsche Forschungsgemeinschaft, by the Volkswagen foundation and by the Fonds der Chemischen Industrie.

Received: February 4, 1980 [A 320 IE]
German version: Angew. Chem. 92, 429 (1980)

[1] *E. Helmreich*, Compr. Biochem. *17*, 17 (1969).
[2] *E. H. Fischer, A. B. Kent, E. R. Snyder, E. G. Krebs*, J. Am. Chem. Soc. *80*, 2906 (1958).
[3] *K. Titani, A. Koide, J. Hermann, L. H. Ericsson, S. Kumar, R. D. Wade, K. A. Walsh, H. Neurath, E. H. Fischer*, Proc. Natl. Acad. Sci. USA *74*, 4762 (1977).
[4] *K. Titani, A. Koide, L. H. Ericsson, S. Kumar, J. Hermann, R. D. Wade, K. A. Walsh, H. Neurath, E. H. Fischer*, Biochemistry *17*, 5680 (1978).
[5] *A. Koide, K. Titani, L. H. Ericsson, S. Kumar, H. Neurath, K. Walsh*, Biochemistry *17*, 5657 (1978).
[6] *Y. P. Lee*, Biochim. Biophys. Acta *43*, 18 (1960).
[7] *A. Kamagawa, T. Fukui, Z. Nikumi*, J. Biochem. (Tokyo) *63*, 361 (1968).
[8] *K. H. Schächtele, B. Schiltz, D. Palm*, Eur. J. Biochem. *92*, 427 (1978).
[9] *L. L. Kastenschmidt, J. Kastenschmidt, E. Helmreich*, Biochemistry *7*, 3590 (1968).
[10] *L. L. Kastenschmidt, J. Kastenschmidt, E. Helmreich*, Biochemistry *7*, 4543 (1968).
[11] *E. G. Krebs, E. H. Fischer*, Adv. Enzymol. Relat. Subj. Biochem. *24*, 263 (1962).
[12] *N. B. Madsen*, Muscle Proc. Symp. *1965*, 122.
[13] *D. J. Graves, R. W. Sealock, J. H. Wang*, Biochemistry *4*, 290 (1965).
[14] *R. W. Sealock, D. J. Graves*, Biochemistry *6*, 201 (1967).
[15] *J. H. Wang, D. J. Graves*, J. Biol. Chem. *238*, 2386 (1963).
[16] *J. H. Wang, D. J. Graves*, Biochemistry *3*, 1437 (1964).
[17] *E. Helmreich, C. F. Cori*, Proc. Natl. Acad. Sci. USA *52*, 647 (1964).
[18] *C. Y. Huang, D. J. Graves*, Biochemistry *9*, 660 (1970).
[19] *J. H. Wang, M. L. Shonka, D. J. Graves*, Biochemistry *4*, 2296 (1965).
[20] *J. H. Wang, M. L. Shonka, D. J. Graves*, Biochem. Biophys. Res. Commun. *18*, 131 (1965).
[21] *E. Helmreich, M. C. Michaelides, C. F. Cori*, Biochemistry *6*, 3695 (1967).
[22] *S. G. Withers, B. D. Sykes, N. B. Madsen, P. J. Kasvinsky*, Biochemistry *18*, 5342 (1979).
[23] *B. E. Metzger, E. Helmreich, L. Glaser*, Proc. Natl. Acad. Sci. USA *57*, 994 (1967).
[24] *B. E. Metzger, L. Glaser, E. Helmreich*, Biochemistry *7*, 2021 (1968).
[25] *K. Feldmann, H. Zeisel, E. Helmreich*, Proc. Natl. Acad. Sci. USA *69*, 2278 (1972).
[26] *J.-I. Tu, D. J. Graves*, J. Biol. Chem. *248*, 4617 (1973).
[27] *S. Sprang, R. J. Fletterick*, J. Mol. Biol. *131*, 523 (1979).
[28] *I. T. Weber, L. N. Johnson, K. S. Wilson, D. G. R. Yeates, D. L. Wild, J. A. Jenkins*, Nature *274*, 433 (1978).
[29] *P. A. M. Eagles, M. Iqbal, L. N. Johnson, J. Mosley, K. S. Wilson*, J. Mol. Biol. *71*, 803 (1972).
[30] *R. J. Fletterick, J. Sygusch, N. Murray, N. B. Madsen, L. N. Johnson*, J. Mol. Biol. *103*, 1 (1976).
[31] *D. A. Chignell, W. B. Gratzer, R. C. Valentine*, Biochemistry *7*, 1082 (1968).
[32] *G. Puchwein, O. Kratky, C. F. Gölker, E. Helmreich*, Biochemistry *9*, 4691 (1970).
[33] *M. L. Battell, C. G. Zarkadas, L. B. Smillie, N. B. Madsen*, J. Biol. Chem. *243*, 6202 (1968).
[34] *M. L. Battell, L. B. Smillie, N. B. Madsen*, Can. J. Biochem. *46*, 609 (1968).
[35] *O. Avramovic-Zikic, L. B. Smillie, N. B. Madsen*, J. Biol. Chem. *245*, 1558 (1970).
[36] *M. Hörl, K. Feldmann, K. D. Schnackerz, E. J. M. Helmreich*, Biochemistry *18*, 2457 (1979).
[37] *D. H. Brown, C. F. Cori*, Enzymes *5B*, 207 (1961).
[38] *E. H. Fischer, E. G. Krebs*, J. Biol. Chem. *216*, 121 (1955).
[39] *E. W. Sutherland, Jr., W. D. Wosilait*, Nature *175*, 169 (1955).
[40] *E. G. Krebs, J. A. Beavo*, Annu. Rev. Biochem. *48*, 923 (1979).
[41] *P. J. Keller, G. T. Cori*, J. Biol. Chem. *214*, 127 (1955).
[42] *E. G. Krebs, A. B. Kent, E. H. Fischer*, J. Biol. Chem. *231*, 73 (1958).
[43] *G. T. Cori, C. F. Cori*, J. Biol. Chem. *158*, 321 (1945).
[44] *E. H. Fischer, D. J. Graves, E. R. Snyder Crittenden, E. G. Krebs*, J. Biol. Chem. *234*, 1698 (1959).
[45] *C. Nolan, W. B. Novoa, E. G. Krebs, E. H. Fischer*, Biochemistry *3*, 542 (1964).
[46] *D. Linder, G. Kurz, H. Bender, K. Wallenfels*, Eur. J. Biochem. *70*, 291 (1976).
[47] *M. Schwartz, M. Hofnung*, Eur. J. Biochem. *2*, 132 (1967).
[48] *E. Schiltz, D. Palm, H. W. Klein*, FEBS Lett. *109*, 59 (1980).
[49] *K. Lerch, E. H. Fischer*, Biochemistry *14*, 2009 (1975).
[50] *P. Cohen*, Curr. Top. Cell. Regul. *14*, 117 (1978).
[51] *E. H. Fischer, L. M. G. Heilmeyer, Jr., R. H. Haschke*, Curr. Top. Cell. Regul. *4*, 211 (1971).
[52] *C. Villar-Palasi, J. Larner*, Vitam. Horm. (New York) *26*, 65 (1969).
[53] *J. H. Wang, D. J. Graves*, Enzymes *7*, 435 (1976).
[54] *S. J. W. Busby, G. K. Radda*, Curr. Top. Cell. Regul. *10*, 89 (1976).
[55] *T. Baranowski, B. Illingworth, D. H. Brown, C. F. Cori*, Biochim. Biophys. Acta *25*, 16 (1957).
[56] *C. F. Cori, B. Illingworth*, Proc. Natl. Acad. Sci. USA *43*, 547 (1957).
[57] *A. B. Kent, B. G. Krebs, E. H. Fischer*, J. Biol. Chem. *232*, 549 (1958).
[58] *P. Cohen, T. Duewer, E. H. Fischer*, Biochemistry *10*, 2683 (1971).
[59] *E. H. Fischer, A. Pocker, J. C. Saari*, Essays Biochem. *6*, 23 (1970).
[60] *B. Illingworth, R. Kornfeld, D. H. Brown*, Biochim. Biophys. Acta *42*, 486 (1960).
[61] *E. H. Fischer, E. G. Krebs*, Vitam. Horm. (New York) *22*, 399 (1964).
[62] *A. E. Braunstein, M. M. Shemyakin*, Biokhimiya *18*, 393 (1953).
[63] *D. E. Metzler, M. Ikawa, E. E. Snell*, J. Am. Chem. Soc. *76*, 648 (1954).
[64] *A. E. Braunstein*, Enzymes *9*, 379 (1973).
[65] *E. E. Snell, S. J. Di Mari*, Enzymes *2*, 335 (1970).
[66] *P. Recsei, E. E. Snell*, Biochemistry *9*, 1492 (1970).
[67] *E. Grazi, T. Cheng, B. L. Horecker*, Biochem. Biophys. Res. Commun. *7*, 250 (1962).
[68] *B. L. Horecker, S. Pontremoli, C. Ricci, T. Cheng*, Proc. Natl. Acad. Sci. USA *47*, 1949 (1961).
[69] *W. Tagaki, P. H. Westheimer*, Biochemistry *7*, 901 (1968).
[70] *D. L. Nandi, D. Shemin*, J. Biol. Chem. *243*, 1236 (1968).

[71] *D. Portsmouth, A. C. Stoolmiller, R. H. Abeles,* J. Biol. Chem. *242*, 2751 (1967).
[72] *O. Warburg, W. Christian,* Biochem. Z. *298*, 368 (1938).
[73] *S. Shaltiel, J. L. Hedrick, E. H. Fischer,* Biochemistry *5*, 2108 (1966).
[74] *J. L. Hedrick, S. Shaltiel, E. H. Fischer,* Biochemistry *8*, 2422 (1969).
[75] *J. L. Hedrick, S. Shaltiel, E. H. Fischer,* Biochemistry *8*, 2429 (1969).
[76] *K. Feldmann, E. J. M. Helmreich,* Biochemistry *15*, 2394 (1976).
[77] *G. F. Johnson, J. I. Tu, M. L. S. Bartlett, D. J. Graves,* J. Biol. Chem. *245*, 5560 (1970).
[78] *S. Shaltiel, M. Cortijo,* Biochem. Biophys. Res. Commun. *41*, 594 (1970).
[79] *M. Cortijo, S. Shaltiel,* Biochem. Biophys. Res. Commun. *39*, 212 (1970).
[80] *M. Cortijo, I. Z. Steinberg, S. Shaltiel,* J. Biol. Chem. *246*, 933 (1971).
[81] *S. Veinberg, S. Shaltiel, I. Z. Steinberg,* Isr. J. Chem. *12*, 421 (1974).
[82] *K. O. Honikel, N. B. Madsen,* J. Biol. Chem. *247*, 1057 (1972).
[83] *E. H. Fischer, A. W. Forrey, J. L. Hedrick, R. C. Hughes, A. B. Kent, E. G. Krebs* in *E. E. Snell, P. M. Fasella, A. Braunstein, A. Rossi-Fanelli:* Chemical and Biological Aspects of Pyridoxal Catalysis. Pergamon Press, Oxford 1963, p. 543.
[84] *P. H. Strausbauch, A. B. Kent, J. L. Hedrick, E. H. Fischer,* Methods Enzymol. *11*, 671 (1967).
[85] *E. Daltrozzo, K. Fritz, G. Kollmannsberger,* Chimia *27*, 652 (1973).
[86] *J. Sygusch, N. B. Madsen, P. J. Kasvinsky, R. J. Fletterick,* Proc. Natl. Acad. Sci. USA *74*, 4757 (1977).
[87] *J. L. Hedrick, S. Shaltiel, E. H. Fischer,* Biochemistry *5*, 2117 (1966).
[88] *B. Illingworth, H. S. Jansz, D. H. Brown, C. F. Cori,* Proc. Natl. Acad. Sci. USA *44*, 1180 (1958).
[89] *K. Feldmann, H. Zeisel, E. J. M. Helmreich,* Eur. J. Biochem. *65*, 285 (1976).
[90] *S. Shaltiel, J. L. Hedrick, A. Pocker, E. H. Fischer,* Biochemistry *8*, 5189 (1969).
[91] *E. H. Fischer, A. W. Forrey, A. Pocker, J. C. Saari, C. L. Sevilla, J. Vidgoff,* Abstr. 8. Int. Congr. Biochem. Interlaken 1970, p. 102.
[92] *A. Pocker, E. H. Fischer,* Biochemistry *8*, 5181 (1969).
[93] *J. M. Vidgoff, A. Pocker, T. L. Hullar, E. H. Fischer,* Biochem. Biophys. Res. Commun. *57*, 1166 (1974).
[94] *Th. Pfeuffer, J. Ehrlich, E. Helmreich,* Biochemistry *11*, 2125 (1972).
[95] *M.-L. Ahrens, G. Maass, P. Schuster, H. Winkler,* J. Am. Chem. Soc. *92*, 6134 (1970).
[96] *D. J. Graves, R. F. Parrish, R. J. Uhing, W. Korytnyk* in *V. Essmann:* Regulatory Mechanisms of Carbohydrate Metabolism. Pergamon Press, Oxford 1978, p. 195.
[97] *Th. Pfeuffer, J. Ehrlich, E. Helmreich,* Biochemistry *11*, 2136 (1972).
[98] *R. F. Parrish, R. J. Uhing, D. J. Graves,* Biochemistry *16*, 4824 (1977).
[98a] *K. Feldmann,* unpublished.
[99] *K. Feldmann, W. E. Hull,* Proc. Natl. Acad. Sci. USA *74*, 856 (1977).
[100] *D. Palm, K. Schächtele, K. Feldmann, E. J. M. Helmreich,* FEBS Lett. *101*, 4031 (1979).
[101] *H. W. Klein, E. J. M. Helmreich,* FEBS Lett. *108*, 209 (1979).
[102] *M. Fosset, L. W. Muir, L. D. Nielsen, E. H. Fischer,* Biochemistry *10*, 4105 (1971).
[103] *J. Monod, J. Wyman, J.-P. Changeux,* J. Mol. Biol. *12*, 88 (1965).
[104] *E. Helmreich, C. F. Cori,* Proc. Natl. Acad. Sci. USA *51*, 131 (1964).
[105] *M. Morange, F. Garcia Blanco, B. Vandenbunder, H. Buc,* Eur. J. Biochem. *65*, 553 (1976).
[106] *D. Guènard, M. Morange, H. Buc,* Eur. J. Biochem. *76*, 447 (1977).
[107] *T. Okazaki, A. Nakazawa, O. Hayaishi,* J. Biol. Chem. *243*, 5266 (1968).
[108] *D. M. Mott, A. L. Bieber,* J. Biol. Chem. *245*, 4058 (1970).
[109] *P. J. Kasvinsky, N. B. Madsen, J. Sygusch, R. J. Fletterick,* J. Biol. Chem. *253*, 3343 (1978).
[110] *N. B. Madsen, P. J. Kasvinsky, R. J. Fletterick,* J. Biol. Chem. *253*, 9097 (1978).
[111] *K. Feldmann,* Anal. Biochem. *88*, 225 (1978).
[112] *J. L. Hedrick, S. Shaltiel, E. H. Fischer,* Biochemistry *5*, 2117 (1966).
[113] *D. Palm, H. D. Weisshaar* in: Internat. Symposium on Reaction-mechanisms and Control-properties of Phosphotransferases, Reinhardsbrunn. Akademie-Verlag, Berlin 1973, p. 297.
[114] *H. D. Weisshaar, D. Palm,* Biochemistry *11*, 2146 (1972).
[115] *A. Hvidt, S. O. Nielsen,* Adv. Protein Chem. *21*, 287 (1966).
[116] *A. W. Murray, M. R. Atkinson,* Biochemistry *7*, 4023 (1968).
[117] *D. Gratecos, E. H. Fischer,* Biochim. Biophys. Acta *58*, 960 (1974).
[118] *F. E. Evans, N. O. Kaplan,* FEBS Lett. *105*, 11 (1979).
[119] *D. G. Gorenstein, D. Kar,* Biochem. Biophys. Res. Commun. *65*, 1073 (1973).
[120] *J. Feeney, B. Birdsall, G. C. K. Roberts, A. S. V. Burgen* in *R. A. Dwek, I. D. Campbell, R. E. Richards, R. J. P. Williams:* NMR in Biology. Academic Press, London 1977, p. 111.
[121] *E. Helmreich, M. C. Michaelides, C. F. Cori,* Biochemistry *6*, 3695 (1967).
[121a] *M. Bühner,* unpublished.
[122] *R. J. Fletterick, J. Sygusch, H. Semple, N. B. Madsen,* J. Biol. Chem. *251*, 6142 (1976).
[123] *K. D. Schnackerz, K. Feldmann, W. H. Hull,* Biochemistry *18*, 1536 (1979).
[124] *J. J. Mieyal, R. H. Abeles,* Enzymes *7*, 515 (1972).
[125] *M. Abdullah, E. H. Fischer, M. Y. Qureshi, K. N. Slessor, W. J. Whelan,* Biochem. J. *97*, 9P (1965).
[126] *B. Illingworth, D. H. Brown, C. F. Cori,* Proc. Natl. Acad. Sci. USA *47*, 469 (1961).
[127] *B. Illingworth, D. H. Brown, C. F. Cori,* Proc. Natl. Acad. Sci. USA *47*, 479 (1961).
[128] *P. J. Kasvinsky, N. B. Madsen, R. J. Fletterick, J. Sygusch,* J. Biol. Chem. *253*, 1290 (1978).
[129] *F. Meyer, L. M. G. Heilmeyer, Jr., R. H. Haschke, E. H. Fischer,* J. Biol. Chem. *245*, 6642 (1970).
[130] *L. M. G. Heilmeyer, Jr., F. Meyer, R. H. Haschke, E. H. Fischer,* J. Biol. Chem. *245*, 6649 (1970).
[131] *R. H. Haschke, L. M. G. Heilmeyer, Jr., F. Meyer, E. H. Fischer,* J. Biol. Chem. *245*, 6657 (1970).
[132] *M. C. Michaelides, E. Helmreich,* Enzymol. Biol. Clin. *7*, 130 (1966).
[133] *M. C. Michaelides, R. Sherman, E. Helmreich,* J. Biol. Chem. *239*, 4171 (1964).
[134] *D. E. Koshland,* Proc. Natl. Acad. Sci. USA *44*, 98 (1958).
[135] *F. C. Kokesh, Y. Kakuda,* Biochemistry *16*, 2467 (1977).
[136] *M. Martinez-Carrion,* Eur. J. Biochem. *54*, 39 (1975).
[137] *F. S. Furbish, M. L. Fonda, D. E. Metzler,* Biochemistry *8*, 5169 (1969).
[138] *K. Nakano, S. Wakabayashi, T. Hase, H. Matsubara, T. Fukui,* J. Biochem. (Tokyo) *83*, 1085 (1978).
[139] *M. Doudoroff,* Enzymes *5*, 229 (1961).
[140] *L. N. Johnson, J. A. Jenkins, K. S. Wilson, G. Zanotti,* J. Mol. Biol., in press; *L. N. Johnson,* private communication.
[141] *J. Katz, W. Z. Hassid,* Arch. Biochem. Biophys. *30*, 272 (1950).
[142] *A. M. Gold, M. P. Osber,* Arch. Biochem. Biophys. *153*, 784 (1972).
[143] *M. Eigen, G. G. Hammes,* Adv. Enzymol. Relat. Subj. Biochem. *25*, 22 (1963), Table III therein.
[144] *L. M. Firsov, T. I. Bogacheva, S. E. Bresler,* Eur. J. Biochem. *42*, 605 (1974).
[145] *J.-I. Tu, G. R. Jacobson, D. J. Graves,* Biochemistry *10*, 1229 (1971).
[146] *F. De Toma, R. H. Abeles,* Fed. Am. Soc. Exp. Biol. *29*, 461 (Abst. 1214) (1970).
[147] *K. Feldmann, M. Hörl, H. W. Klein, E. J. M. Helmreich* in *V. Essmann:* Regulatory Mechanisms of Carbohydrate Metabolism. Pergamon Press, Oxford 1978, p. 205.
[148] *M. V. Buell, R. E. Hansen,* J. Am. Chem. Soc. *82*, 6042 (1960).
[149] *P. Schuster, H. Winkler,* Tetrahedron *26*, 2249 (1970).
[150] *Yu. V. Morozov, N. P. Bazhulina, L. P. Cherkashina, M. Ya. Karpeiskii,* Biofizika *12*, 773 (1967).
[151] *D. E. Metzler, C. M. Harris, R. J. Johnson, D. B. Siano, J. A. Thomson,* Biochemistry *12*, 5377 (1973).
[152] *K. Feldmann, B. J. M. Gaugler, H. Winkler, E. J. M. Helmreich,* Biochemistry *13*, 2222 (1974).
[153] *M. Arrio-Dupont,* Biochem. Biophys. Res. Commun. *44*, 653 (1971).
[154] *W. B. Dempsey, H. N. Christensen,* J. Biol. Chem. *237*, 1113 (1962).
[155] *S. Shimomura, N. Nakano, T. Fukui,* Biochem. Biophys. Res. Commun. *82*, 462 (1978).
[156] *S. Shimomura, T. Fukui,* Biochemistry *17*, 5359 (1978).
[157] *C. L. Sevilla, E. H. Fischer,* Biochemistry *8*, 2161 (1969).
[158] *A. A. Yunis, E. H. Fischer, E. G. Krebs,* J. Biol. Chem. *235*, 3163 (1960).
[159] *S. A. Assaf, D. J. Graves,* J. Biol. Chem. *244*, 5544 (1969).
[160] *C. C. Childress, B. Sacktor,* J. Biol. Chem. *245*, 2927 (1970).
[161] *B. Burr, O. E. Nelson,* Eur. J. Biochem. *56*, 539 (1975).
[162] *D. P. Wolf, E. H. Fischer, E. G. Krebs,* Biochemistry *9*, 1923 (1970).
[163] *W. Nader, J.-U. Becker,* Eur. J. Biochem. *102*, 345 (1979).
[164] *H. Komiyama, M. L. Bender, M. Utaka, A. Takeda,* Proc. Natl. Acad. Sci. USA *74*, 2634 (1977).
[165] *H. W. Klein, E. Schiltz, E. J. M. Helmreich,* unpublished.

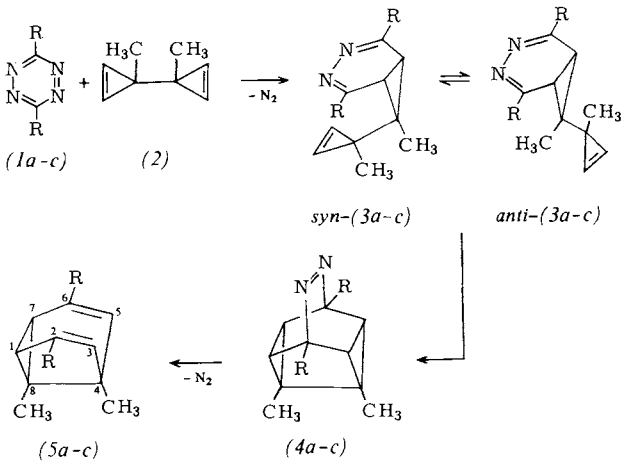
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

One-Pot Synthesis of Substituted Semibullvalenes

By *Dörte Paske, Richard Ringshandl, Ingeborg Sellner, Heinz Sichert,* and *Jürgen Sauer*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Ever since the first synthesis of a molecule having a "fluxional" structure was reported by *Doering* and *Roth*[1], these compounds have been the subject of numerous investigations[2]. We report here on a one-pot reaction for the synthesis of 2,4,6,8-tetra-substituted semibullvalenes *(5)* which proceeds *via* the diazasnoutenes *(4)*.



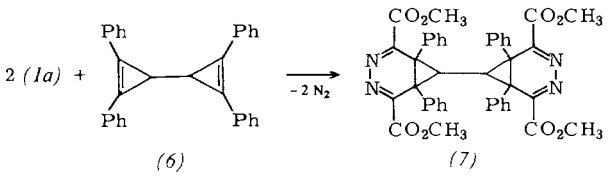
(1a-c) *(2)* *syn-(3a-c)* *anti-(3a-c)* *(5a-c)* *(4a-c)*

(a), R = CO_2CH_3; *(b)*, R = C_6H_5; *(c)*, R = CH_3

The high reactivity of 1,2,4,5-tetrazines in the addition to cyclopropenes makes 3,4-diazanorcaradienes of type *(3)* a readily accessible class of compounds[3]. We have been able to improve the yield of the synthesis of *(2)*[4] so that it is obtainable on a gram scale.

Semibullvalenes *(5)* are formed and can be isolated on allowing *(2)* to react with symmetrical tetrazines *(1)*. In the reaction of *(1b)* and *(1c)*, the diazanorcaradienes *(3)* can be detected by NMR spectroscopy; only on warming are they converted into the semibullvalenes *(5b)* and *(5c)*, respectively. Whether or not an equilibrium *syn-(3)* $\rightleftharpoons$ *anti-(3)* is involved is still uncertain. We have not been able to detect *(3a)* in the reaction of *(1a)* with *(2)*; apparently the intramolecular addition to give *(4a)* proceeds very rapidly. In no case could criteria be obtained evidencing measurable concentrations of *(4)*, since *(4)*, favored by the two *anti* cyclopropane rings, rapidly loses N_2 and forms *(5)* (cf. [2a]).

Attempts to carry out the analogous reaction with the cyclopropene derivative *(6)*[5] have failed so far. Even on using the dilution principle with *(1a)* we only obtained the 1:2 adduct *(7)*.



(6) *(7)*

The semibullvalenes *(5)* obtained by us already show the time-averaged spectra at room temperature with ^{1}H-NMR signals for the methyl protons between $\delta = 1$—2, for the ring protons between $\delta = 3.7$–4.8. The analogous ^{13}C-NMR average signals appear at $\delta = 15$ for the methyl C-atoms, at $\delta = 60$ for C-4/C-8 and at $\delta = 89$—94 for C-1, C-3, C-5, C-7 (see Table 1).

Received: April 3, 1980 [Z 465 IE]
German version: Angew. Chem. *92*, 464 (1980)

CAS Registry numbers:
(1a), 2166-14-5; *(1b)*, 6830-78-0; *(1c)*, 1558-23-2; *(2)*, 31707-64-9; *syn-(3a)*, 73712-28-4; *syn-(3b)*, 73712-29-5; *syn-(3c)*, 73712-30-8; *anti-(3a)*, 73745-78-5; *anti-(3b)*, 73745-79-6; *anti-(3c)*, 73745-80-9; *(4a)*, 73712-31-9; *(4b)*, 73712-32-0; *(4c)*, 73712-33-1; *(5a)*, 73712-34-2; *(5b)*, 32139-60-9; *(5c)*, 27031-42-1; *(6)*, 4919-54-4; *(7)*, 73712-35-3

[1] *W. v. E. Doering, W. R. Roth*, Tetrahedron *19*, 715 (1963).
[2] a) Abundant references are given, *e.g.* in *L. A. Paquette et al.*, J. Am. Chem. Soc. *96*, 7465, 7474 (1974); *97*, 2910 (1975); b) *R. Askani, R. Kirsten, B. Dugall*, Tetrahedron Lett. *1976*, 3891.
[3] *G. Heinrichs, H. Krapf, B. Schröder, A. Steigel, T. Troll, J. Sauer*, Tetrahedron Lett. *1970*, 1617; *H. D. Fühlhuber, J. Sauer, ibid. 1977*, 4393; *H. D. Fühlhuber, C. Gousetis, T. Troll, J. Sauer, ibid. 1978*, 3903.

Table 1. Some data of the semibullvalenes *(5)*.

Cpd.	Yield [%]	M.p. [°C] B.p. [°C/torr]	^{1}H-NMR [b] H-1,3,5,7	^{1}H-NMR [b] CH_3	^{13}C-NMR [b] C-1,3,5,7	^{13}C-NMR [b] C-4,8	^{13}C-NMR [b] C-2,6	^{13}C-NMR [b] CH_3
(5a)	48	99—100	4.79 (s)	1.13 (s)	93.7 (d)	60.6 (s)	127.2 (s)	14.9 (q)
(5b) [6]	45	180/0.01 [a]	4.36 (s)	1.13 (s)	88.7 (d)	58.5 (s)	133.3 or 137.3 (s)	15.8 (q)
(5c) [6]	38	40/0.01 [a]	3.74 (s)	0.98 (s)	90.9 (d)	59.0 (s)	128.4 (s)	15.8 or 16.3 (q)

[a] Bulb-bulb distillation. [b] In $CDCl_3$, TMS int., δ values; time-averaged spectra at room temperature.

[*] Prof. Dr. J. Sauer, D. Paske, R. Ringshandl, I. Sellner, Dipl.-Chem. H. Sichert
Institut für Chemie der Universität
Universitätsstr. 31, D-8400 Regensburg (Germany)

[4] *W. H. De Wolf, F. Bickelhaupt*, Recl. Trav. Chim. Pays-Bas *90*, 150 (1971); *W. H. De Wolf, W. Stol, I. J. Landheer, F. Bickelhaupt, ibid. 90*, 405 (1971); *W. H. De Wolf, I. J. Landheer, F. Bickelhaupt*, Tetrahedron Lett. *1975*, 179.
[5] *R. Weiss, H. Kölbl*, J. Am. Chem. Soc. *97*, 3222 (1975) and earlier work.

[6] *H. E. Zimmerman, H. Iwamura*, J. Am. Chem. Soc. *92*, 2015 (1970); *R. Askani*, Tetrahedron Lett. *1971*, 447.

Relation between Orbital Character and Reaction Product in the Reaction of Benzvalene and Homobenzvalene with Thiophenol[**]

By *Manfred Christl, Reinhard Lang, Rainer Herbert,* and *Gertrud Freitag*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Both olefins[1] as well as bicyclo[1.1.0]butanes[2] add thiols in radical chain reactions. In order to check which function is the more active partner for the thiol we treated benzvalene *(1)* and homobenzvalene *(8)*, which contain both these functions, with thiophenol. After 24 h at 20 °C the 1:2 mixture of *(1)* and thiophenol furnished four products: 3-phenylthiotricyclo[3.1.0.0^{2,6}]hexane *(2)*, *exo*- and *endo*-4-phenylthiobicyclo[3.1.0]hex-2-ene *(6)* (6:1), and 2-*exo*,5-*endo*-bis(phenylthio)bicyclo[2.1.1]hexane *(3)*. The constitution and the stereochemistry of these products follow from the NMR spectra (Table 1).

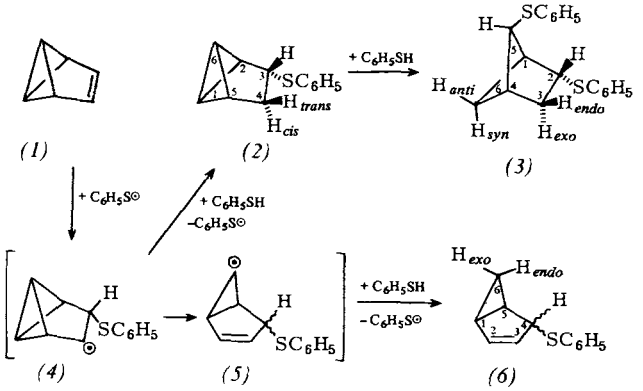


Table 1. NMR data of the new compounds (in $CDCl_3$, δ values, J in Hz).

(2): ^{1}H-NMR: 1.22 (dd, 4-H$_{cis}$, $J_{3,4}=3.1$, $J_{4,4}=11.7$), 1.83 (dd, 4-H$_{trans}$, $J_{3,4}=8.2$), 1.86—1.96 (m, 1-H, 5-H, 6-H), 2.19 (m, 2-H), 3.31 (dd, 3-H), 6.88—7.48 (m, C_6H_5); ^{13}C-NMR: 3.4 (d, C-1), 5.8 (d, C-6), 32.9 (d, C-5), 35.5 (t, C-4), 39.3 (d, C-2), 46.3 (d, C-3); C_6H_5: 125.4 (d), 128.6 (d), 129.3 (d), 137.5 (s)

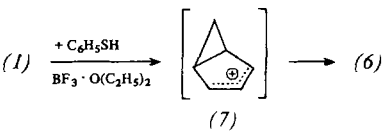
(3): ^{1}H-NMR: 1.42—1.66 (m, 6-H$_{anti}$, 3-H$_{exo}$), 1.58 (d, 6-H$_{syn}$, $J_{6,6}=7.6$), 2.50 (dd, 3-H$_{endo}$, $J_{2,3}=8.2$, $J_{3,3}=12.2$), 2.74 (m, 1-H, 4-H), 3.53 (q, 5-H, $J_{1,5}=J_{3\,exo,5}=J_{4,5}=2.4$), 3.96 (m, 2-H), 6.95—7.45 (m, C_6H_5)

exo-(6): ^{1}H-NMR [a]: −0.10 (q, 6-H$_{endo}$, $J_{1,6}=J_{5,6}=J_{6,6}=3.9$), 0.69 (dt, 6-H$_{exo}$, $J_{1,6}=J_{5,6}=7.6$), 1.40—2.10 (m, 1-H, 5-H), 4.00 (m, 4-H), 5.44 (m, 3-H, $J_{2,3}=5.5$), 6.10 (m, 2-H); C_6H_5: 7.15—7.50 (m, 3H) and 7.50—7.85 (m, 2H); ^{13}C-NMR: 19.5 (t, C-6), 23.4 (d) and 23.8 (d) (C-1 and C-5), 54.3 (d, C-4), 126.7 (d, C-3), 137.4 (d, C-2); C_6H_5: 126.3 (d), 128.5 (d), 131.2 (d), 135.1 (s)

(9): ^{1}H-NMR: 1.53 (d, 7-H$_{syn}$, $J_{7,7}=8.2$), 2.00 (dt, 7-H$_{anti}$, $J_{1,7}=J_{5,7}=5.4$), 2.15 and 2.75 (br. AB-System, 4-H$_{endo}$ and 4-H$_{exo}$, $J_{4,4}=18.3$), 2.65—2.90 (m, 1-H, 5-H), 3.76 (t, 6-H, $J_{1,6}=J_{5,6}=5.2$), 5.69 (m) and 6.08 (m) (2-H, 3-H, $J_{2,3}=9.0$), 6.90—7.50 (m, C_6H_5)

[a] In C_6D_6.

Mechanistic studies suggest a radical chain reaction in which the phenylthio radical, formed from thiophenol by oxidation with atmospheric oxygen, adds to the double bond in *(1)*. There are two routes open to the resulting radical *(4)*: hydrogen abstraction from thiophenol leads to *(2)*; preceding bond reorganization, in the sense of a cyclopropylmethyl-homoallyl radical rearrangement[3,4] to *(5)*, affords *(6)*. The addition of thiophenol to the central bicyclo[1.1.0]butane bond of *(2)* with formation of *(3)* follows known paths[2]; however, it proceeds considerably slower than the formation of *(2)* (see below).

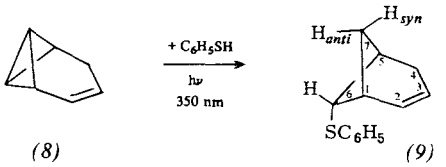


(6) could also be formed *via* the cation *(7)*[5]. We have enforced this ionic route by addition of boron trifluoride-ether and obtained pure *(6)*, b.p. 60—80 °C (bath)/0.01 torr, in 82% yield. Labeling experiments, however, rule out this route in the absence of boron trifluoride-ether.

Owing to the difference in molecularity the competing steps starting from the intermediate *(4)* require the dependence of the ratio *(2)*:*(6)* on the thiophenol concentration. This was indeed found:

Reaction of 6.40 mmol *(1)* and 27.2 mmol thiophenol in 13 ml ether for 20 min at 20 °C afforded 92% of a 96:4 mixture of *(2)* and *(6)*, b.p. 60 °C/0.01 torr. In contrast, on dropwise addition of 6.44 mmol of thiophenol in 50 ml ether over 7 h to 6.40 mmol of *(1)* in 13 ml ether, a 83% yield of a mixture of *(2)* and *(6)* in the ratio 12:88 was isolated.

As observed in the case of other tricyclo[3.1.0.0^{2,6}]hexane derivatives[6], UV irradiation also considerably promotes thiophenol addition to *(2)*. On irradiation of a mixture of 2.56 mmol *(1)* and 45.4 mmol of thiophenol in 5 ml ether for 18 h with 350-nm light we obtained 87% *(3)* as colorless crystals, m.p. 54—55 °C.



Homobenzvalene *(8)* reacts only slowly with thiophenol at room temperature. In contrast, on irradiation with 350-nm light the addition is complete within 2 h, giving 6-*endo*-phenylthiobicyclo[3.1.1]hept-2-ene *(9)* in 73% yield without formation of isomers. Together with results quoted in the literature, the structure, as confirmed by the ^{1}H-NMR spectrum (Table 1), and the reaction conditions suggest the radical

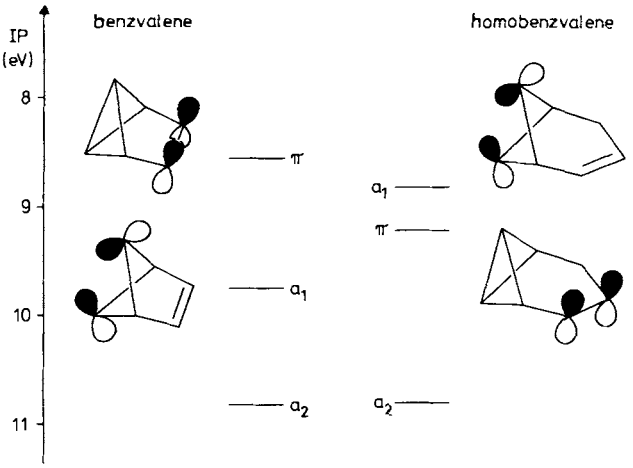


Fig. 1. Ionization potentials and orbitals of benzvalene *(1)* and homobenzvalene *(8)* according to [8].

[*] Prof. Dr. M. Christl, Dipl.-Chem. R. Lang, R. Herbert, G. Freitag
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

chain reaction already accepted in the case of other bicyclo[1.1.0]butanes[2].

Why does the phenylthio radical attack benzvalene *(1)* at the double bond but homobenzvalene *(8)* at the bicyclo[1.1.0]butane system? Since thio radicals have electrophilic character[7], the interaction with the HOMO of the substrate may play the decisive role in the transition state of the addition. As shown by the ionization potentials determined by photoelectron spectroscopy and assigned on the basis of MINDO/3 calculations[8], the HOMO in *(1)* is located in the double bond, in *(8)*, however, in the central bond of the bicyclo[1.1.0]butane system (Fig. 1).

Received: May 28, 1979 [Z 467a IE]
Publication delay at authors' request
German version: Angew. Chem. 92, 465 (1980)

CAS Registry numbers:
(1), 659-85-8; *(2)*, 73688-28-5; *(3)*, 73688-29-6; *(6) exo*, 73688-30-9; *(6) endo*, 73688-31-0; *(8)*, 35618-58-7; *(9)*, 73688-32-1; C_6H_5SH, 108-98-5

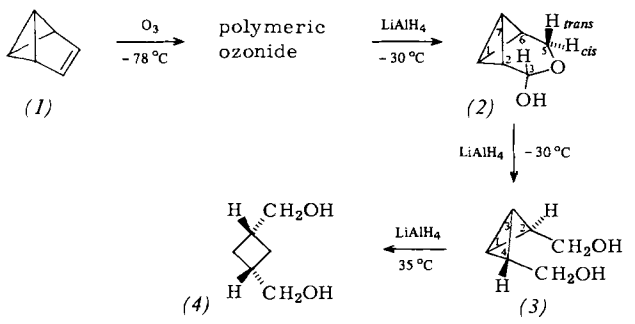
[1] Review: *K. Griesbaum*, Angew. Chem. *82*, 276 (1970); Angew. Chem. Int. Ed. Engl. *9*, 273 (1970).
[2] *G. Szeimies, A. Schloßer, F. Philipp, P. Dietz, W. Mickler*, Chem. Ber. *111*, 1922 (1978).
[3] Review: *J. W. Wilt* in *J. K. Kochi*: Free Radikals. Vol. 1. Wiley, New York 1973, p. 333.
[4] Further example of a bicyclobutylmethyl radical rearrangement: *J. Elzinga, H. Hogeveen*, J. Org. Chem. *44*, 2381 (1979).
[5] *L. Kaplan, D. J. Rausch, K. E. Wilzbach*, J. Am. Chem. Soc. *94*, 8638 (1972), and references cited therein; *J. A. Berson, N. M. Hasty, Jr., ibid. 93*, 1549 (1971); *T. J. Katz, E. J. Wang, N. Acton, ibid. 93*, 3782 (1971).
[6] *R. Herbert, M. Christl*, Chem. Ber. *112*, 2012 (1979).
[7] *C. Walling, D. Seymour, K. B. Wolfstirn*, J. Am. Chem. Soc. *70*, 2559 (1948).
[8] Benzvalene: *P. Bischof, R. Gleiter, E. Müller*, Tetrahedron *32*, 2769 (1976); *P. J. Harman, J. E. Kent, T. H. Gan, J. B. Peel, G. D. Willet*, J. Am. Chem. Soc. *99*, 943 (1977). Homobenzvalene: *P. Bischof, R. Gleiter, R. T. Taylor, A. R. Browne, L. A. Paquette*, J. Org. Chem. *43*, 2391 (1978).

Oxidation Reactions of Benzvalene: Ozonolysis, *cis*-Hydroxylation, Epoxidation, and Singlet Oxygen Addition[**]

By *Hartmut Leininger* and *Manfred Christl*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

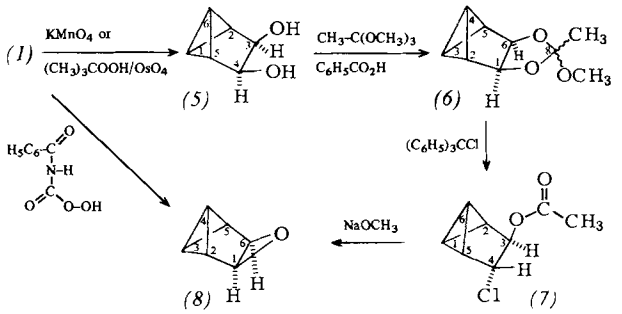
Ready accessibility and high reactivity predestine benzvalene *(1)* as a useful starting material for many bicyclo[1.1.0]butane derivatives and other small-ring polycycles[1,2]. By reaction of *(1)* with classical oxidizing agents, we have prepared some interesting synthetic building blocks containing the bicyclo[1.1.0]butane moiety.



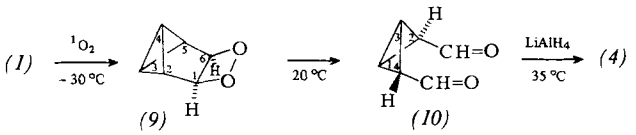
[*] Prof. Dr. M. Christl, Dipl.-Chem. H. Leininger
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

In our first investigation of the ozonolysis of *(1)* we surprisingly obtained the cyclobutane derivative *(4)* on reduction of the polymeric ozonide with $LiAlH_4$[3]. We have now found that the desired bicyclo[1.1.0]butane-2,4-*endo,endo*-dimethanol *(3)* is formed in 52% yield in tetrahydrofuran at $-30\,^{\circ}C$ if six equivalents of $LiAlH_4$ are used. If only three equivalents are employed, one obtains a 1:3 mixture of *(2)* and *(3)* which is separable by distillation. Reaction of *(2)* at $-30\,^{\circ}C$ and of *(3)* at $35\,^{\circ}C$ with $LiAlH_4$ in ether affords *(3)* and *(4)*, respectively, thus proving that *(4)* is formed *via* the alkoxides of *(2)* and *(3)*. The unexpected hydrogenation of a σ-bond in the reaction *(3)*→*(4)* is probably favored by the high p-character of the orbitals whose electrons form the (C-1)—(C-3) bond in *(3)*, and by the oxygen function, which may complex an Al—H species, so that H-transfer can take place intramolecularly.



The *cis*-hydroxylation of *(1)* in ether to give tricyclo[3.1.0.$0^{2,6}$]hexane-3,4-diol *(5)* can be performed under standard conditions with potassium permanganate or, with a better yield of 54%, with *tert*-butyl hydroperoxide/OsO_4 using the method of *Sharpless et al.*[4]. A new method[5] enabled us to convert *(5) via (6)* (two isomers in the ratio 7:3, 70% yield) and *(7)* (56%) into 7-oxatetracyclo[4.1.0.$0^{2,4}$.$0^{3,5}$]heptane *(8)*. Reaction of peracetic acid or *m*-chlorobenzoic acid with *(1)* does not give any *(8)*, even if trapping of the liberated acid is supposedly taken care of by a base or a buffer. On the other hand, the new epoxidizing agent benzoylperoxycarbaminic acid[6], which affords benzamide and carbon dioxide, leads to *(8)* in 54% yield.



As an olefin having a high energy HOMO[7], *(1)* also smoothly takes up singlet oxygen. On bubbling oxygen through an ethereal solution of *(1)* and tetraphenylporphine exposed to a sodium vapor lamp at $-30\,^{\circ}C$, *(1)* completely disappears within two days. The ^{1}H-NMR spectrum of the solution then shows, besides the CHO signal of *(10)* at $\delta = 9.15$, an intense broad singlet at $\delta = 5.20$, which could arise from 1-H and 6-H in the dioxetane *(9)*[8]. Further signals are superposed by ether bands. At room temperature, the singlet disappears within 6 h with concomitant growth of the band at $\delta = 9.15$, thus indicating the expected transformation[8] of *(9)* into *(10)*. After addition of C_6D_6 and removal of the ether, the ^{1}H-NMR spectrum showed all the signals of *(10)* (Table 1) gradually diminishing in intensity, besides slowly growing broad bands. The coupling constant $J_{1,2}$ (3.6 Hz) is of similar magnitude to that in *(3)* (4.0 Hz) and characteristic for the *exo* arrangement of 2-H, 4-H[9] in these compounds. The line separation of 1.5 Hz in the CHO-doublet of *(10)* resembles the value of 2.4 Hz in 1,3-*cis*-cyclobuta-

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-458 $ 02.50/0

nedicarboxaldehyde[10]. On treatment with $LiAlH_4$ in ether at 35 °C, *(10)* is reduced to *(4)*.

Table 1. Some physical data of the compounds *(2)*, *(3)*, *(5)*—*(8)* and *(10)* (NMR spectra in $CDCl_3$, in the case of *(10)* in C_6D_6, δ values).

(2), b.p. 40—50 °C (bath)/0.01 torr; ^{1}H-NMR: 2.05 (t, 1-H, 7-H, $J_{1,2} \approx J_{1,6} \approx J_{2,7} \approx J_{6,7} \approx 2.8$ Hz), 2.38—2.67 (m, 2-H, 6-H), 3.39 (dd, 5-H_{trans}, $J_{5,5} = 10.7$, $J_{5\,trans,6} = 3.0$ Hz), 3.75 (d, 5-H_{cis}), 3.94 (d, OH, $J_{OH,3} = 6.0$ Hz), 4.92 (dd, 3-H, $J_{2,3} = 2.7$ Hz); ^{13}C-NMR: 4.0 and 4.4 (in each case d 207 Hz, C-1 and C-7), 37.2 (d 156.6 Hz, C-6), 43.1 (d 158.9 Hz, C-2), 55.8 (t 144.9 Hz, C-5), 85.8 (d 165.5 Hz, C-3)

(3), b.p. 78 °C/0.05 torr; ^{1}H-NMR: 1.65 (t, 1-H, 3-H, $J_{1,2} = 4.0$ Hz), 2.91 (m, 2-H, 4-H), 3.58 (pseudo-t, CH_2, line sepn. *ca.* 5 Hz), 4.67 (t, OH, $J_{OH,CH_2} = 5.0$ Hz); ^{13}C-NMR: 11.4 (d 197.3 Hz, C-1, C-3), 55.8 (d 147.4 Hz, C-2, C-4), 63.3 (t, 142.7 Hz, CH_2)

(5), b.p. 72 °C/0.05 torr; ^{1}H-NMR: 1.90 (m, 1 H), 2.1—2.4 (m, 3 H), 3.87 (br. s, 3-H, 4-H), 4.12 (br. s, OH); ^{13}C-NMR: 0.1 and 2.4 (in each case d 215.5, 217.7 Hz, C-1, C-6), 37.9 (d 168.4 Hz, C-2, C-5), 70.7 (d 153.7 Hz, C-3, C-4)

(6), b.p. 25—35 °C (bath)/0.01 torr; ^{1}H-NMR: *(6a)* [a] 1.56 (s, CCH_3), 1.7—2.5 (m, 2-H, 5-H, 3-H, 4-H), 3.14 (s, OCH_3), 4.57 (br. s, 1-H, 6-H); *(6b)*: 1.37 (s, CCH_3), 1.7—2.5 (m, 2-H, 5-H, 3-H, 4-H), 3.38 (s, OCH_3), 4.45 (br. s, 1-H, 6-H); ^{13}C-NMR: *(6a)*: 2.8 (d 218.4 Hz, C-4), 6.3 (d 217.3 Hz, C-3), 23.6 (q 128.0 Hz, CCH_3), 37.9 (d 169.8 Hz, C-2, C-5); 48.9 (q 142.7 Hz, OCH_3), 83.2 (d 160.3 Hz, C-1, C-6), 126.2 (s, C-8); *(6b)*: 4.2 (d 219.1 Hz, C-4), 6.9 (d 217 Hz, C-3), 23.8 (q 128.0 Hz, CCH_3), 37.0 (d, 169.9 Hz, C-2, C-5), 50.1 (q 143.4 Hz, OCH_3), 81.6 (d 158.1 Hz, C-1, C-6), 126.6 (s, C-8)

(7), b.p. 45—50 °C (bath)/0.01 torr; ^{1}H-NMR: 2.06 (s, CH_3), 2.38 and 2.46 (in each case br. s, 1-H, 6-H, 2-H, 5-H), 3.84 (br. s, 4-H), 4.86 (br. s, 3-H); ^{13}C-NMR: 6.0 and 7.2 (in each case d 220.6 Hz, C-1, C-6), 20.9 (q, 129.4 Hz, CH_3), 35.6 (d 172.8 Hz, C-2), 39.7 (d 173.6 Hz, C-5), 65.0 (d 160.3 Hz, C-4), 85.2 (d 161.0 Hz, C-3), 170.4 (s, C=O)

(8), b.p. 40—60 °C (bath)/14 torr; ^{1}H-NMR: 2.19 (dt, 4-H, $J_{3,4} = 8.1$ Hz, $J_{2,4} = 2.6$ Hz), 2.33 (m, 2-H, 5-H), 2.98 (dt, 3-H, $J_{2,3} = 1.1$ Hz), 3.26 (s, 1-H, 6-H); ^{13}C-NMR: −1.1 (d 221.8 Hz, C-4), 26.5 (d 214.7 Hz, C-3), 37.0 (d 170.6 Hz, C-2, C-5), 56.9 (d 189.0 Hz, C-1, C-6)

(10), IR (ether): 1720 cm^{-1} (C=O); ^{1}H-NMR: 1.48 (t, 1-H, 3-H, $J_{1,2} = 3.6$ Hz), 2.81 (m, 2-H, 4-H), 9.15 (br. d, CH=O, line sepn. 2.4 Hz)

[a] *(6a)*: major amount isomer; *(6b)*: minor amount isomer.

The structures of *(2)*, *(3)*, *(5)*—*(8)*, and *(10)* are confirmed by NMR spectra (Table 1). Two phenomena warrant special comment: The value of 197.3 Hz for the direct CH coupling of C-1, C-3 in *(3)* is relatively small, but by comparison with known data[11] can possibly be explained in terms of the dihedral angle being enlarged by the two *endo* substituents. In *(8)* there is a large difference of 27.6 ppm between the chemical shifts of C-3 and C-4, indicating that the epoxide ring exerts a similar anisotropic effect as the cyclopropane[11,12] and aziridine[2] rings.

(3) and *(10)* are the first bicyclo[1.1.0]butanes containing no substituents other than two functional groups in the *endo* positions.

Received: April 3, 1980 [Z 467b IE]
German version: Angew. Chem. *92*, 466 (1980)

CAS Registry numbers:
(1), 659-85-8; *(2)*, 73688-07-0; *(3)*, 73688-08-1; *(5)*, 73688-09-2; *(6)*, isomer 1, 73688-10-5; *(6)*, isomer 2, 73744-67-9; *(7)*, 73688-11-6; *(8)*, 73688-12-7; *(9)*, 73688-13-8; *(10)*, 73688-14-9

[1] Review: *U. Burger*, Chimia *33*, 147 (1979); more recent works: *R. Aumann, H. Wörmann*, Chem. Ber. *112*, 1233 (1979); *R. J. Roth*, Synth. Commun. *9*, 751 (1979); *R. Herbert, M. Christl*, Chem. Ber. *112*, 2012 (1979).
[2] *M. Christl, H. Leininger*, Tetrahedron Lett. *1979*, 1553.
[3] *M. Christl, G. Brüntrup*, Chem. Ber. *107*, 3908 (1974); we now also carry out the ozonolysis in ether.
[4] *K. B. Sharpless, K. Akashi*, J. Am. Chem. Soc. *98*, 1986 (1976).
[5] *P. Dansette, D. M. Jerina*, J. Am. Chem. Soc. *96*, 1224 (1974); *M. S. Newman, C. H. Chen, ibid. 95*, 278 (1973).
[6] *J. Rebek, R. McCready, S. Wolf, A. Mossman*, J. Org. Chem. *44*, 1485 (1979).
[7] *P. Bischof, R. Gleiter, E. Müller*, Tetrahedron *32*, 2769 (1976); *P. J. Harman, J. E. Kent, T. H. Gan, J. B. Peel, G. D. Willet*, J. Am. Chem. Soc. *99*, 943 (1977).
[8] Review: *W. Adam*, Adv. Heterocycl. Chem. *21*, 437 (1977).
[9] Values for bicyclo[1.1.0]butane: $J_{1,2\,exo} = 2.9$ Hz and $J_{1,2\,endo} = 1.2$ Hz; *K. Wüthrich, S. Meiboom, L. C. Snyder*, J. Chem. Phys. *52*, 230 (1970).
[10] *H. Musso*, private communication; *W. Trautmann*, Dissertation, Universität Karlsruhe 1976.
[11] *M. Christl*, Chem. Ber. *108*, 2781 (1975).
[12] *M. Christl, R. Herbert*, Org. Magn. Reson. *12*, 150 (1979).

Indole Pigments from the Fruiting Bodies of the Slime Mold *Arcyria denudata*[**]

By *Wolfgang Steglich, Bert Steffan, Lothar Kopanski,* and *Gerd Eckhardt*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Slime molds constitute a class of very primitive organisms of uncertain systematic position which can be assigned neither to the plant nor the animal kingdom[1]. Their delicate fruiting bodies (Sporangia) often have bright colors, the chemical nature of which still remains virtually unknown[2].

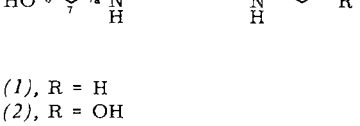
From 2 g of the red fruiting bodies of *Arcyria denudata* (L.) Wettstein, we obtained a red methanolic extract, which was separated by chromatography on Sephadex LH-20 (eluent methanol) into three red and two yellow main fractions (see Table 1).

Table 1. Pigments from *Arcyria denudata*, purified by re-chromatography. Empirical formulas were determined by high-resolution mass spectrometry [a].

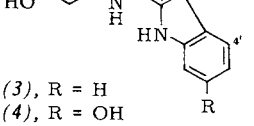
		R_f [b]	Color	Yield [%]	M.p. [°C]
Arcyriarubin B	*(1)*	0.33	red	0.4	154—155
Arcyriarubin C	*(2)* [c]	0.21	red	1.5	205—206
Arcyriaflavin B	*(3)*	0.33	pale yellow [d]	0.05	350
Arcyriaflavin C	*(4)*	0.21	pale yellow [d]	0.05	350
Arcyroxepin A	*(5)* [c]	0.42	red [e]	0.3	268—270

[a] *(1)*, $C_{20}H_{13}N_3O_3$; *(2)*, $C_{20}H_{13}N_3O_4$; *(3)*, $C_{20}H_{11}N_3O_3$; *(4)*, $C_{20}H_{11}N_3O_4$; *(5)*, $C_{20}H_{11}N_3O_3$. [b] Silica gel TLC plates, Merck 60 F_{254} (eluent: benzene/ethyl formate/formic acid 10:5:3). [c] Correct elemental analyses obtained. [d] Strong bright yellow fluorescence at 366 nm. [e] Reversible color change to violet over NH_3 vapor.

In its ^{1}H- and ^{13}C-NMR spectrum (Table 2) arcyriarubin C shows only half of the full set of signals and must therefore have a symmetrical structure. According to the IR bands at 1755 and 1705 cm^{-1} a maleimide moiety is present; this is confirmed by the ^{13}C-NMR signals at δ = 175.3 and 129.2[3]. From the splitting and position of the arene signals, and from the NH protons (coupled with 2-H) at $\delta = 10.42$ in the ^{1}H-NMR spectrum, it follows that the maleimide is substituted by two (5- or 6-hydroxy)indol-3-yl groups. The ^{13}C-NMR spectrum would favor *(2)*: the position of the C-7 signal at $\delta = 97.7$ can be reconciled only with the OH group being in a 6-position[4].



(1), R = H
(2), R = OH



(3), R = H
(4), R = OH

[*] Prof. Dr. W. Steglich, Dipl.-Chem. B. Steffan, Dipl.-Chem. L. Kopanski, Dr. G. Eckhardt
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

[**] Fungal Pigments, Part 36. This work was supported by the Deutsche Forschungsgemeinschaft. We thank Prof. Dr. *F. Oberwinkler*, Tübingen, and Dr. *H. Neubert*, Bühl/Baden, for identifying the species.—Part 35: *H. Besl, A. Bresinsky, L. Kopanski, W. Steglich*, Z. Naturforsch. *33c*, 820 (1978).

Table 2. Spectroscopic data of the *Arcyria* pigments.

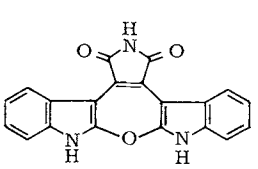
	UV [nm] in CH_3OH	IR [cm^{-1}] in KBr	^{1}H-NMR [a] in CD_3COCD_3	^{13}C-NMR [b] in CD_3OD
(1)	λ_{max} = 465 ($\log\varepsilon$ 3.77), 392 (sh, 3.57), 281 (3.93)	3440 br. s, 2960 m, 1760 m, 1715 s, 1630 w, 1538 s	6.24 (dd, J = 8.7 + 2.1 Hz, 5-H); 6.72 (d, 8.7 Hz, 4-H); 6.85 (d, 2.1 Hz, 7-H); 6.72—7.05 (m, 5',6',7'-H); 7.42 ("d", 8 Hz, 4'-H); 7.73 (d, 2.7 Hz, 2-H); 7.82 (d, 2.9 Hz, 2'-H); 9.63 (br. s, 10-NH); 10.52 (br. s, 1'-NH); 10.78 (br. s, 1-NH)	97.7 (C-7); 107.7 (C-3/3'); 110.8 (C-5); 112.3 (C-7'); 120.7 (CH); 120.9 (C-3a); 122.7 (CH); 123.0 (CH); 123.2 (C-4); 127.3 (C-3a'); 128.9 (C-2/8'); 129.7 (C-2'); 129.9 (C-8); 137.8 (C-7a'); 138.9 (C-7a); 154.5 (C-6); 175.3 (C-9/9')
(2)	λ_{max} = 474 ($\log\varepsilon$ 3.76), 283 (3.93)	3430 br. s, 1755 w, 1705 s, 1625 m, 1535 s	6.27 (dd, J = 8.4 + 2.2 Hz, 5,5'-H); 6.79 (d, 8.4 Hz, 4,4'-H); 6.85 (d, 2.2 Hz, 7,7'-H); 7.66 (d, 2.5 Hz, 2,2'-H); 9.51 (br. s, 10-NH); 10.42 (br. s, 1,1'-H)	97.7 (C-7); 107.8 (C-3); 110.9 (C-5); 121.0 (C-3a); 123.3 (C-4); 128.7 (J = 190 Hz, C-2); 129.2 (C-8); 138.8 (C-7a); 154.4 (C-6); 175.3 (C-9)
(3)	λ_{max} = 414 ($\log\varepsilon$ 3.19), 323 (4.11), 280 (3.75), 271 (3.70); 2.29 (4.07)	3420 br. s, 2955 s, 2880 m, 1750 w, 1705 s, 1620 br. m	6.93 (dd, J = 8.6 + 2.1 Hz, 5-H); 7.16 (d, 2.1 Hz, 7-H); 7.24—7.80 (m, 5',6',7'-H); 8.96 (d, 8.6 Hz, 4-H); 9.15 (broadened d, 7.9 Hz, 4'-H); 9.64 (br. s, 10-NH); 11.65 (br. s, 1,1'-NH)	
(4)	λ_{max} = 422 ($\log\varepsilon$ 3.34); 330.5 (4.29), 318 (sh, 4.09); 280 (3.70); 270 (3.66); 255 (sh, 3.77); 229 (4.14)	3420 br. s, 2960 s, 2880 m, 1740 w, 1710 s, 1635 br. s	6.89 (dd, J = 8.4 + 2.2 Hz, 5,5'-H); 7.13 (d, 2.2 Hz, 7,7'-H); 8.93 (d, 8.4 Hz, 4,4'-H); 9.56 (br. s, 10-NH); 11.92 (br. s, 1,1'-NH)	
(5)	λ_{max} = 471 ($\log\varepsilon$ 3.68); 362 (3.51), 283 (sh, 3.83), 273 (3.82), 226 (4.44)	3420 br. s, 1760 w, 1710 ss, 1625 w, 1510 m, 735 s	7.0—7.40 (m), 9.82 (br. s, 1,1'-NH); 11.22 (very br. s, 10-NH)	92* (C-3); 112.4 (CH); 116.1 (CH); 123*; 124.5*; 125.9 (CH); 133*, 143.2 (C-7a); 153.2* (C-2); 177.0 (C-9)

[a] 90-MHz; δ values, TMS (int.). [b] The signals marked with an asterisk are broadened by coalescence; assignment of the signals of coupled spectra by selective decoupling and increment calculation.

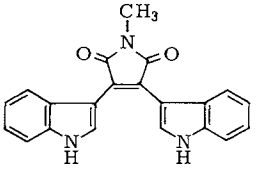
Arcyriarubin B has the structure and composition *(1)*, in agreement with all the spectroscopic data.

Like *(2)*, arcyriaflavin C is composed of two identical moieties. The absence of the 2,2' H-signals and the unusual downfield position of the 4,4' H-signal at δ = 8.93 are consistent only with structure *(4)*. The structure is confirmed by the transformation of *(2)* into *(4)*, which already occurs on gentle warming in conc. sulfuric acid. Arcyriaflavin B *(3)* has only one OH group, and an additional downfield signal is consequently observed in the ^{1}H-NMR spectrum at δ = 9.15.

Especially interesting is the third red pigment, $C_{20}H_{11}N_3O_3$, which shows a reversible color-change to violet on TLC plates over NH_3 vapor. According to the IR spectrum it contains the maleimide system and has a symmetrical structure. The absorption spectrum strongly resembles that of the reference compound *(6)*, which is readily accessible in 60% yield by condensation of indolylmagnesium iodide with 1-methyl-3,4-dibromomaleimide in benzene at 25 °C in the presence of a small amount of hexamethylphosphoric triamide[5]. In the 400-MHz ^{1}H-NMR spectrum of the pigment, three protons of the benzene ring are clearly recognizable [δ = 7.18 ("t", J = 8 Hz); 7.32 (br, "d", 8 Hz); 7.38 ("d", 8 Hz), while the shape and position of the fourth depends very strongly on the measuring conditions[6]. Since the indole NH-protons give rise to one singlet at δ = 9.82 and no signal is observed for the 2,2' H, the third oxygen atom can only link the two indole rings; hence the pigment called by us arcyroxepin A must have the formula *(5)*.



(5)



(6)

The arcyriaflavins are structurally related to staurosporin, an antibiotic and antihypertensive which has recently been isolated from *Streptomyces staurosporeus*[7]. In the platelet diffusion test, *(1)*, *(2)* and *(5)* exhibit medium inhibiting action against *Bacillus brevis* and *B. subtilis*[8].

Received: March 26, 1980 [Z 464 IE]
German version: Angew. Chem. 92, 463 (1980)

CAS Registry numbers:
(1), 73697-62-8; *(2)*, 73697-63-9; *(3)*, 73697-64-0; *(4)*, 73697-65-1; *(5)*, 73697-66-2

[1] Cf. *K. Mägdefrau* in *E. Strasburger:* Lehrbuch der Botanik. 31st Edit. Gustav Fischer, Stuttgart 1979, p. 596.
[2] Carotinoids in *Lycogala epidendron: S. Liaaen Jensen*, Phytochemistry *4*, 925 (1965).
[3] Cf. 3-methylmaleimide: δ(CO) = 173.2, δ(C-3) = 128.2; *M.-T. Chenon, R. J. Pugmire, D. M. Grant, R. P. Panzica, L. B. Townsend*, J. Heterocycl. Chem. *10*, 427 (1973).
[4] Cf. *e.g. M. Shamma, D. M. Hindenlang:* Carbon-13 NMR Shift Assignments of Amines and Alkaloids. Plenum Press, New York 1979.
[5] *(6)*: m.p. 276—278 °C; UV (CH_3OH): λ_{max} = 465 ($\log\varepsilon$ = 3.90), 371 (3.74), 284 (sh, 4.10), 276 (4.14), 248 (sh, 4.23); IR (KBr): 3460 m, 3320 m, 1760 w, 1690 vs, 1615 w, 1535 s, 755 vs, 745 vs; ^{1}H-NMR (CD_3COCD_3): δ = 3.10 (s, CH_3); 6.64 ("t", J = 8 Hz); 6.94 ("d", 8 Hz); 7.00 ("t", 8 Hz); 7.42 ("d", 8 Hz); 7.87 (d, 2.8 Hz), 10.80 (br. s); ^{13}C-NMR (CD_3OD): δ = 107.3 (C-3), 111.9 (C-7), 120.2 (CH), 122.2 (CH), 122.5 (CH), 126.6 (C-3a), 128.3 (C-8), 129.5 (C-2), 137.2 (C-7a), 173.6 (C-9).
[6] We thank Dr. *W. E. Hull*, Bruker, Karlsruhe, for recording the spectra.
[7] *A. Furusaki, N. Hashiba, T. Matsumoto, A. Hirano, Y. Iwai, S. Ōmura*, J. Chem. Soc. Chem. Commun. *1978*, 800.
[8] *T. Anke*, unpublished.

Sequence Analysis of Ergochrome-Biosynthesis by Competitive Incorporation[**]

By *Burchard Franck, Gerhard Bringmann,* and *Georg Flohr*[*]

Information about alternative intermediates is of cardinal importance for an understanding of natural product biosyntheses and for the development of biomimetic syntheses. By means of competitive incorporation[1] we have been able to detect alternative intermediates in the biosynthesis of mycotoxins of the ergochrome type[2], *e.g.* of secalonic acid D *(5)*, and to assign them to an informative sequence.

Ergochromes are formed by oxidative ring opening[2,3] of the anthraquinone emodin *(1)*, a key building block in the

[*] Prof. Dr. B. Franck, Dr. G. Bringmann
Organisch-chemisches Institut der Universität
Orléansring 23, D-4400 Münster (Germany)
Dr. G. Flohr
Unilever-Forschungslaboratorium
Behringstrasse 154, D-2000 Hamburg-Altona (Germany)

[**] Metabolites of Fungi, Part 30.—Part 29: *B. Franck, H. Backhaus, M. Rolf*, Tetrahedron Lett. *1980*, 1185.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-460 $ 02.50/0

biosynthesis of natural products[4]. In this reaction a hydroxy group has to be removed from C-6 and an additional one incorporated at C-4. Thus besides emodin *(1)*, the natural anthraquinones chrysophanol *(2)*, islandicin *(3)*, and catenarin *(4)*, whose hydroxy group arrangements resemble fully or partly that of a half-molecule of *(5)* (see box), are also of interest as intermediates in biosynthesis.

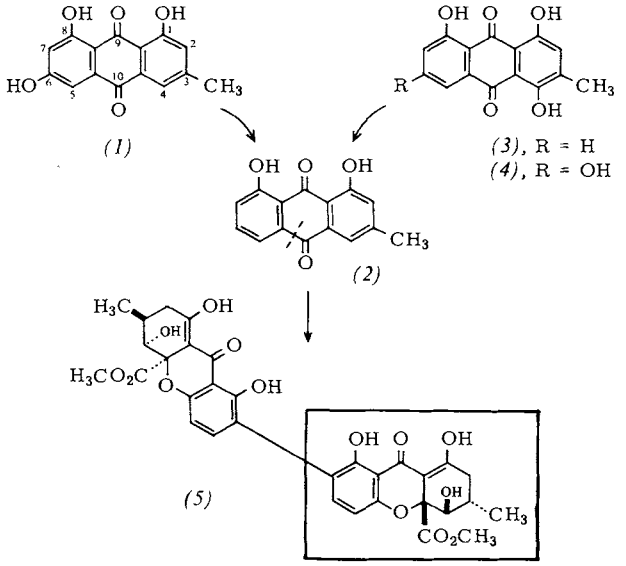


Table 1. Competitive incorporation of the radioactive anthraquinones *(1)*–*(4)* in secalonic acid D *(5)* by *Penicillium oxalicum* [a].

Expt.	Anthraquinone	Spec. incorp. [b] [%]	a/b
1	a) [U-^{14}C]emodin *(1)*	0.432	1.03
	b) [U-^{3}H]emodin *(1)*	0.418	
2	a) [U-^{14}C]chrysophanol *(2)*	3.42	3.56
	b) [U-^{3}H]emodin *(1)*	0.96	
3	a) [U-^{14}C]islandicin *(3)*	0.163	0.301
	b) [U-^{3}H]emodin *(1)*	0.541	
4	a) [U-^{14}C]catenarin *(4)*	0.008	0.022
	b) [U-^{3}H]emodin *(1)*	0.37	

[a] ATCC 10476. [b] Specific radioactivity of the isolated secalonic acid D *(5)* divided by that of the fed anthraquinone and by the number of anthraquinone molecules which can be incorporated in *(5)* × 100.

For the competitive incorporation, pairs composed of biosynthetically prepared uniformly labeled [U-^{3}H]emodin *(1)* and one of the [U-^{14}C]anthraquinones *(1)* to *(4)*[5] were fed to the mold *Penicillium oxalicum*[6]. After isolation and purification to constant radioactivity, the $^{3}H/^{14}C$ ratio in *(5)* was determined in a scintillation counter (Table 1).

As experiment 1 shows, [U-^{3}H]emodin loses only 3% or less of its tritium radioactivity (predominantly located in the methyl group) during conversion into *(5)* by the mold. It is therefore suitable as reference compound for competitive incorporation reactions. From the incorporation values (ratio a/b) referred to emodin *(1)* of the other experiments it significantly follows, irrespective of deviations of the enzyme activity of various components, that chrysophanol *(2)* (Experiment 2) is incorporated into *(5)* 3.6 times better than *(1)* and 11.8 times better than *(3)* (Experiment 3). In contrast, *(4)* can be ruled out as a biosynthetic precursor[7].

From these findings it can be concluded that emodin *(1)* and islandicin *(3)* are converted into the ergochromes, *e.g. (5)*, *via* chrysophanol *(2)*. The hydroxy group on C-4 is thus incorporated after oxidative ring opening which precedes the dimerization[3,8]. The preferred suitability of *(2)* for preparatively useful biomimetic ring-opening reactions is already well known[9].

Received: March 20, 1980 [Z 466a IE]
German version: Angew. Chem. *92*, 483 (1980)

CAS Registry numbers:
(1), 518-82-1; *(2)*, 481-74-3; *(3)*, 476-56-2; *(4)*, 476-46-0; *(5)*, 35287-69-5

[1] *B. Franck, G. Fels, G. Ufer*, Angew. Chem. *89*, 677 (1977); Angew. Chem. Int. Ed. Engl. *16*, 652 (1977).
[2] *B. Franck, H. Flasch*, Fortschr. Chem. Org. Naturst. *30*, 151 (1973).
[3] *B. Franck* in *P. S. Steyn:* The Biosynthesis of Mycotoxins. Academic Press, New York, in press.
[4] *B. Franck*, Angew. Chem. *91*, 453 (1979); Angew. Chem. Int. Ed. Engl. *18*, 429 (1979).
[5] [U-^{14}C]islandicin *(3)* and [U-^{14}C]catenarin *(4)* were obtained directly from [2-^{14}C]acetate with *Penicillium islandicum* (ATCC 10127) and *Helminthosporium catenarium* (CBS 191.29), respectively. [U-^{3}H]- and [U-^{14}C]emodin *(1)* and [U-^{14}C]chrysophanol *(2)* were obtained from [2-$^{3}H_3$]acetate and [2-^{14}C]acetate respectively with *Penicillium islandicum* (CBS 338.48) and *Talaromyces wortmannii* (ATCC 10517) by reductive and alkaline cleavage of the initially formed bisanthraquinonyls skyrin and rugulosin (ATCC: American Type Culture Collection; CBS: Centralbureau voor Schimmelcultures, Baarn, Holland).
[6] *P. S. Steyn*, Tetrahedron *26*, 51 (1970).
[7] Since none of the anthraquinones *(1)* to *(4)* have previously been found in cultures of *Penicillium oxalicum* the incorporation values might not be essentially determined by different pool sizes.
[8] *I. Kurobane, L. C. Vining*, Tetrahedron Lett. *1978*, 1379.
[9] *B. Franck, B. Berger-Lohr*, Angew. Chem. *87*, 845 (1975); Angew. Chem. Int. Ed. Engl. *14*, 818 (1975).

Citreoviridins from *Aspergillus terreus*[**]

By *Burchard Franck* and *Henning-Peter Gehrken*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

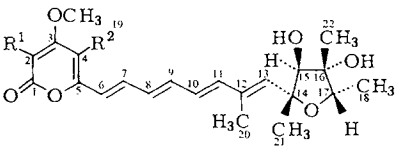
The potent neurotoxic mycotoxin citreoviridin *(1a)* is responsible for the epidemic-like occurrence of *cardiac beriberi*[1] in East Asia. Its acute toxicity, comparable to that of the aflatoxins, is caused by inhibition of the mitochondrial ATP synthetases[2]. *(1a)* was previously found in moldy rice and in *Penicillium citreoviride* and related *Penicillium* species[3]. We isolated citreoviridin *(1a)* and further previously unknown derivatives of similar structure from the mold *Aspergillus terreus*, one of the commonest organisms occurring in soil, on various types of grain and sugar-containing nutrients and which is used biotechnologically[4]. It deserves special mention that the occurrence of citreoviridin, which belongs to the most dangerous mycotoxins, is not restricted to East Asian mold fungi, and that the citreoviridin production by strains of *Aspergillus terreus* is extremely high—up to 2% of the dried mycelium. This made possible a thorough biogenetic analysis of the mycotoxin.

On closer examination of *Aspergillus terreus* for active substances, we discovered in the case of 5 of 13 strains[5] brilliant yellow metabolites showing typical polyene UV/VIS spectra. The main metabolite (deep-yellow needles, m.p. 109–110 °C, from MeOH, $\lambda_{max} = 237, 287, 295, 388$ nm) proved to be identical to citreoviridin *(1a)*[6]; in addition we found

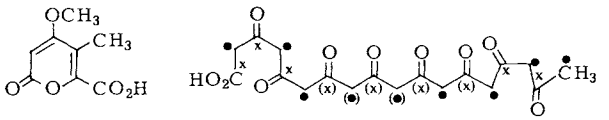
[*] Prof. Dr. B. Franck, Dr. H.-P. Gehrken
Organisch-chemisches Institut der Universität
Orléansring 23, D-4400 Münster (Germany)

[**] Metabolites of Fungi, Part 31.—Part 30: *B. Franck, G. Bringmann, G. Flohr*, Angew. Chem. *92*, 483 (1980); Angew. Chem. Int. Ed. Engl. *19*, 460 (1980).

small amounts of five very similar metabolites. We therefore give the citreoviridin *(1a)* the suffix "A" and the other components in order of their R_s values (1.44, 1.35, 1.24, 0.72, 0.62; ethyl acetate on TLC strips SI F-Riedel de Haen) referred to *(1a)* = 1.00 as B, C, D, E, and F. The components C and D could be assigned the structures *(1b)* and *(1c)* from spectroscopic data. Fragments formed in the mass spectrometer by cleavage of the C-5/C-6 bond indicated that *(1a)*, *(1b)*, and *(1c)* differ only by methyl groups on C-2 and C-4. Accordingly, only the signals of C-2 and C-4 showed significant differences in the ^{13}C-NMR spectra ([D$_6$]acetone).



(1a), R^1 = H, R^2 = CH_3; *(1b)*, R^1 = CH_3, R^2 = H; *(1c)*, R^1, R^2 = CH_3



(2) *(3)*

x, ●: labeling with [1-^{13}C]- and [2-^{13}C]acetate, resp.

Table 1. ^{13}C-NMR data and ^{13}C-enrichment of the isotopomeric citreoviridins A *(1a)*, which were obtained after feeding [1-^{13}C]- and [2-^{13}C]acetate on *Aspergillus* terreus (CBS 503.65) (measured in [D$_6$]acetone, values of the enrichment in multiples of the natural abundance [7]).

C atom	δ and multiplicity	^{13}C-enrichment *(1a)* from [1-^{13}C]acetate	*(1a)* from [2-^{13}C]acetate
C-1	163.5 s	10.32	—
C-2	88.9 d	—	26.2
C-3	171.2 s	9.44	—
C-4	108.3 s	—	17.0
C-5	155.0 s	9.58	—
C-6	119.6 d	—	21.4
C-7 [a]	136.3 d	19.4	—
C-8 [b]	127.0 d	—	23.7
C-9 [a]	139.4 d	14.9	—
C-10 [b]	131.5 d	—	21.2
C-11 [a]	142.2 d	17.8	—
C-12	132.9 s	—	18.9
C-13 [a]	144.5 d	16.4	—
C-14	84.8 s	—	17.4
C-15	86.5 d	13.6	—
C-16	80.8 s	—	18.8
C-17	78.5 d	18.0	—
C-18	13.0 q	—	24.6
C-19	8.94 q	—	—
C-20	21.8 q	—	—
C-21	19.3 q	—	—
C-22	13.5 q	—	—
OCH_3	56.8 q	—	—

[a, b] These assignments can be interchanged.

The structure of citreoviridin A *(1a)* suggests a biosynthesis from nine acetate moieties *via* acetyl- and malonylcoenzyme A and the C_{18} polyketide *(3)*, and its *C*-methylation at four positions (C-4, C-12, C-14, C-16). This is consistent with previous incorporation experiments[3b] with acetate and methionine, in which, however, only few positions of incorporation could be determined by chemical degradation because of labeling with ^{14}C. Application of [1-^{13}C]- and [2-^{13}C]acetate (90% ^{13}C-enrichment; 200 mg/100 ml nutrient) to *Aspergillus terreus* (CBS 503.65)[4] gave isotopomeric citreoviridins A *(1a)*. Their unusually high incorporation of 17.6 and 25.7%, respectively[7], enabled accurate determination of ^{13}C-positions by ^{13}C-NMR spectra (Table 1). It follows from the spectra that all odd C-atoms (×) of polyketide chain *(3)* of *(1a)* originate from the carboxy groups of the acetate building block and the even C-atoms (●) of *(3)* from the methyl groups. The C-atoms of the methoxy and of the C-methyl groups, like the unlabeled C-atoms of the C_{18} chain, showed no significant signals consistent with their origin from the C_1 pool of the organism.

As an advanced intermediate of the citreoviridin biosynthesis from acetate moieties, attention was directed to oleic acid. It contains as many C-atoms as the polyketide *(3)* and is a key building block[8] for the biosynthesis of many polydehydrocarboxylic acids[9]. The radioactivity of citreoviridin *(1a)* isolated after the feeding of *Aspergillus terreus* with [1-^{14}C]oleic acid corresponded to a small incorporation of only 0.00093%. $KMnO_4$-oxidation of this citreoviridin *(1a)* afforded a cumalic acid derivative *(2)*, which contained only 36% of the radioactivity to be expected on direct incorporation. The low incorporation of the [1-C^{14}]oleic acid might therefore be best explained in terms of a degradation to ^{14}C-acetate.

Procedure

Isolation of *(1a)*: 200 surface cultures of *Aspergillus terreus* (CBS 503.65) on 350 ml batches of Czapek-Dox nutrient[11] in 1 l Erlenmayer flasks, which were grown for 21 d at 26 °C, gave 750 g of freeze-dried mycelium. This was washed consecutively, five times with 3.5 l petroleum ether (126 g residue) and acetone (65.2 g residue). The acetone residue was taken up in ethyl acetate, the insoluble material removed by filtration and the filtrate chromatographed several times with ethyl acetate on columns of silica gel (Merck, particle size 0.063—0.2 mm). The residue obtained on evaporation of the combined eluates was recrystallized from methanol; yield 15.1 g (2.01% of the dry mycelium) *(1a)*, m.p. 108—110 °C.

Received: March 20, 1980 [Z 466b IE]
German version: Angew. Chem. *92*, 484 (1980)

CAS Registry number:
(1a), 25425-12-1

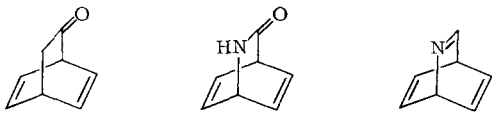
[1] *Y. Ueno* in *I. F. H. Purchase:* Mycotoxins. Elsevier, New York 1974, p. 283.
[2] *P. E. Linnett, A. D. Mitchell, M. D. Osselton, L. J. Mulheirn, R. B. Beechey,* Biochem. J. *170*, 503 (1978).
[3] a) *D. W. Nagel, P. S. Steyn, D. B. Scott,* Phytochemistry *11*, 627 (1972); b) *D. W. Nagel, P. S. Steyn, N. P. Ferreira,* Phytochemistry *11*, 3215 (1972).
[4] *K. B. Raper, D. I. Fennell:* The Genus Aspergillus. Williams and Wilkins, Baltimore 1965.
[5] The citreoviridin-forming strains of *Aspergillus terreus* have the designations: CBS (Centraalbureau voor Schimmelcultures, Baarn, Holland) 503.65, 594.65, 130.55; ATCC (American Type Culture Collection) 16.792; CMI Commonwealth Mycological Institute 61.457. Of these, the first mentioned shows the highest hitherto known formation of citreoviridin *(1a)*.
[6] *N. Sakabe, T. Goto, Y. Hirata,* Tetrahedron Lett. *27*, 1825 (1964).
[7] The incorporation was determined mass spectrometrically. For calculation of the ^{13}C enrichment in the labeled positions of the citreoviridin *(1a)* obtained after feeding [1-^{13}C]- and [2-^{13}C]acetate, the intensities of their ^{13}C-NMR signals are divided by the corresponding intensities of unlabeled *(1a)*. The reduced intensities I_r thus obtained are multiplied by the quotients $\bar{A}_m/\bar{I}_r$ ($\bar{A}_m$ = mass spectrometrically determined, average ^{13}C enrichment at the labeled positions in multiples of the natural ^{13}C abundance).
[8] *B. Franck,* Angew. Chem. *91*, 453 (1979); Angew. Chem. Int. Ed. Engl. *18*, 429 (1979).
[9] *F. Bohlmann,* Fortschr. Chem. Org. Naturst. *25*, 1 (1967); *E. D. Korn,* J. Biol. Chem. *239*, 396 (1964).
[10] *O. W. Thiele:* Lipide, Isoprenoide mit Steroiden. Thieme, Stuttgart 1979, p. 58.
[11] As described by S. Gatenbeck, Acta Chem. Scand. *23*, 3493 (1969).

2-Azabarrelenone and 3-Methoxy-2-azabarrelene[**]

By *Rudolf Gompper* and *Axel Schmidt*[*]

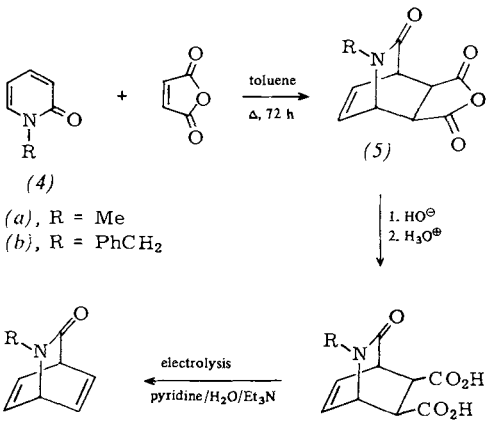
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Barrelene is to be classed among the antibicycloaromatic compounds[1]. In the case of the anions of the barrelenone *(1)*[2a] and other bicyclo[2.2.2]octenones the antibicycloaromaticity or antihomoaromaticity has its effect on the polarity of the enol systems and hence on the course of methylation in accordance with the allopolarization principle[2b] (*O- vs. C*-methylation). Besides *(1)* and methylenebarrelene[2c], 2-azabarrelenone *(2)* is a further interesting species for the study of homoallylic interactions. Moreover, *(2)* can be used as starting material for the synthesis of the hitherto unknown 2-azabarrelenes (cf. [3]). According to STO-3G calculations, 2-azabarrelene *(3)* and barrelene have similar stabilities[4]; 2-methoxycarbonyl-2-azabicyclo[2.2.2]octa-5,7-diene already decomposes at room temperature[5].



(1) *(2)* *(3)*

C,N-Substituted derivatives of *(2)* have been prepared by reaction of *N*-substituted α-pyridones with dehydrobenzene[6a] or acetylenedicarboxylates[6b]. For the synthesis of *(2)* and *C*-unsubstituted derivatives of *(2)* we have used the 2-aza-3-oxobicyclo[2.2.2]octa-7-ene-5,6-dicarboxylic acids *(7)* as starting compounds; *(7b)* (yield 97%, m.p. 170 °C) (see Table 1) was obtained analogously to *(7a)*[7] from *(4b)* and maleic anhydride *via* the anhydride *(5b)* (yield 31%, m.p. 161 °C (from ethyl acetate)). The electrolytic bisdecarboxylation (cf. [2a,c,8]) of *(7)* affords the 2-azabicyclo[2.2.2]octa-5,7-dien-3-ones *(6)* (see Table 1) in yields of up to 45% (the yields vary owing to the difficulty in accurately reproducing the experimental conditions).

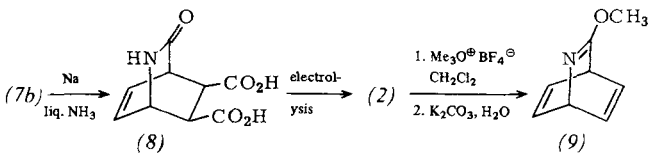


(4) *(5)* *(6)* *(7)*

(a), R = Me
(b), R = $PhCH_2$

The IR carbonyl bands of *(6a)* and *(6b)* (1673 and 1670 cm^{-1}, respectively ($CDCl_3$)) appear at higher wave numbers than is found in the case of the tetrahydro derivatives of *(6)* (1658 (CCl_4) and 1645 cm^{-1} ($CHCl_3$)[9a]); this can be attributed to a relatively large contribution of the polar resonance structure (cf. also 7-azabicyclo[4.2.2]deca-2,4,9-trien-8-one: $\nu_{C=O}$ 1667 cm^{-1}[9b]). Also in agreement with this assumption is the position of the N—CH_3 signal at $\delta = 2.83$ in the ^{1}H-NMR spectrum of *(6a)*; for comparison: the N—CH_3 signals of 1-methyl-4-(*p*-methoxyphenyl)-2-azabicyclo-[2.2.2]octane and 1-methyl-2-azabicyclo[2.2.2]octan-6-ol appear at $\delta = 3.02$[9c] and 3.06[9d], respectively.

The benzyl group of *(7b)* can be cleaved with sodium in liquid ammonia to give the dicarboxylic acid *(8)* (yield 88%, m.p. 176 °C, from water) (see Table 1). Electrolysis of *(8)* affords the desired 2-azabicyclo[2.2.2]octa-5,7-dien-3-one (2-azabarrelenone) *(2)* in moderate yield (6—8%, colorless fine crystals, m.p. 151 °C (sublimation at 80 °C/0.01 mbar)) (see Table 1)—the reaction solution was evaporated down in a vacuum, the brown-red semi-solid residue digested several times with ethyl acetate, the resulting solution evaporated in a vacuum and the residue chromatographed with chloroform/ethyl acetate (1:1) on silica gel; the middle fraction gave, after removal of the solvent by distillation, colorless crystals in a yellowish oil, which could be removed with CCl_4 (see Table 1).



(7b) *(8)* *(2)* *(9)*

Table 1. Some physical data of the compounds *(2)*, *(6a)*, *(6b)*, *(7b)*, *(8)*, and *(9)*.

(2): IR ($CHCl_3$): 3445, 2993, 1685 (C=O), 1623 cm^{-1} (C=C); ^{1}H-NMR ($CDCl_3$): $\delta = 4.10$—4.60 (m; 1H, H-4), 4.83—5.32 (m; 1H, H-1), 6.63—7.22 (m; 4H, H-5, 6, 7, 8), 7.47—8.75 (m; 1H, NH); ^{13}C-NMR ($CDCl_3$): $\delta = 177.19$ (C-3), 137.12 and 136.72 (C-5, 6, 7, 8), 54.31 (C-4), 52.82 (C-1); MS (70 eV, 100 °C): $m/e = 121$ (1%, M^+), 78 (100%, M − HNCO), 43 (18%, $M - C_6H_6$))

(6a): colorless leaflets, m.p. 58 °C (from ether/pentane), b.p. 100 °C/0.1 mbar (bulb tube); IR (KBr): 1650, 1582 cm^{-1}; IR ($CDCl_3$): 1673 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): $\delta = 2.83$ (s; 3H, CH_3), 4.36 (mc; 1H, H-4), 4.83 (mc; 1H, H-1), 6.83 (mc; 4H, H-5, 6, 7, 8); ^{13}C-NMR ($CDCl_3$): $\delta = 172.89$ (C-3), 136.53 and 135.42 (C-5, 6, 7, 8), 59.83 (C-4), 54.22 (C-1), 33.33 (CH_3)

(6b): colorless, broad needles, m.p. 56 °C (from ether/pentane), b.p. 150 °C/0.1 mbar (bulb tube); IR (KBr): 1675, 1658 cm^{-1}; IR ($CDCl_3$): 1670 cm^{-1} (C=O)

(7b) IR (KBr): 1730, 1625 cm^{-1}; ^{1}H-NMR ([D_6]DMSO): $\delta = 3.26$ (mc; 2H, H-5, 6), 3.60 (mc; 1H, H-4), 4.0—4.8 (m; 3H (H-1, CH_2), 6.46 (mc; 2H, H-7, 8), 7.33 (mc; 5H, aromatic-H, 12.26 (mc; 2H, CO_2H)

(8): ^{1}H-NMR ([D_6]DMSO): $\delta = 3.26$ (m; 3H, H-4, 5, 6), 4.30 (mc; 1H, H-1), 6.40 (mc; 2H, H-7, 8), 8.13 (mc; 1H, NH), 10.26 (mc; 2H, CO_2H)

(9): IR (film): 1656, 1625 cm^{-1}; IR ($CHCl_3$): 1647 (C=N), 1615 cm^{-1} (C=C); ^{1}H-NMR ($CDCl_3$): $\delta = 3.62$ (s; 3H, OCH_3), 4.33—4.73 (m; 1H, H-4), 5.53—5.90 (m; 1H, H-1), 6.43—6.97 (m; 4H, H-5, 6, 7, 8); ^{13}C-NMR ($CDCl_3$): $\delta = 181.61$ (C-3), 140.57 and 134.88 (C-5, 6, 7, 8), 63.46 (C-4), 55.40 (OCH_3), 49.95 (C-1); MS (70 eV): $m/e = 135$ (48%, M^+), 134 (81%, M − H), 105 (71%, $M - CH_2O$), 104 (67%, $M - CH_3O$), 78 (100%, $M - CH_3OCN$), 57 (14%, $M - C_6H_6$))

The conversion of *(2)* into 3-methoxy-2-azabicyclo-[2.2.2]octa-2,5,7-triene (3-methoxy-2-azabarrelene) *(9)* (yield 75%, colorless oil with a pleasant eucalyptus-like aromatic odor, b.p. 80 °C/0.01 mbar) (see Table 1) was achieved by reaction with trimethyloxonium tetrafluoroborate according to known methods (cf.[9b]). *(9)* slowly decomposes at room temperature; however, the decomposition is minimal during distillation (80 °C). *(9)* is thermally less stable than *(6a)*; this can be ascribed to an antiaromatic effect.

Received: February 25, 1980 [Z 469 IE]
German version: Angew. Chem. 92, 468 (1980)

[*] Prof. Dr. R. Gompper, Dipl.-Chem. A. Schmidt
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

CAS Registry numbers:
(2), 53173-29-8; *(4b)*, 1753-62-4; *(5b)*, 73697-67-3; *(6a)*, 73697-68-4; *(6b)*, 73697-69-5; *(7a)*, 53991-09-6; *(7b)*, 73697-70-8; *(8)*, 73697-71-9; *(9)*, 73697-72-0; maleic anhydride, 108-31-6

[1] *M. J. Goldstein, R. Hoffmann*, J. Am. Chem. Soc. *93*, 6193 (1971).
[2] a) *R. Gompper, K.-H. Etzbach*, Angew. Chem. *90*, 630 (1978); Angew. Chem. Int. Ed. Engl. *17*, 603 (1978); b) *R. Gompper, H.-U. Wagner, ibid. 88*, 389 (1976) and *15*, 321 (1976); c) *R. Gompper, K.-H. Etzbach, ibid. 91*, 500 (1979) and *18*, 470 (1979).
[3] *S. Kikkawa, R. L. Bartosiewics, S. I. Miller*, J. Org. Chem. *27*, 320 (1962).
[4] *G. Leroy, D. Peeters, J.-L. Ruelle*, J. Chim. Phys. *71*, 475 (1974).
[5] *H. Sliwa, Y. Le Bot*, Tetrahedron Lett. *1977*, 4129.
[6] a) *E. B. Sheinin, G. E. Wright, C. L. Bell, L. Bauer*, J. Heterocycl. Chem. *5*, 859 (1968); *P. S. Mariano, P. L. Huesman, R. L. Beamer, D. Dunaway-Mariano*, Tetrahedron *34*, 2617 (1978); b) *U. Heep, ibid. 31*, 77 (1975).
[7] *H. Tomisawa, H. Hongo*, Chem. Pharm. Bull. *18*, 925 (1970).
[8] *H. H. Westberg, H. J. Dauben*, Tetrahedron Lett. *1968*, 5123; *P. Radlick, R. Klem, S. Spurlock, J. J. Sims, E. E. van Tamelen, T. Whitesides, ibid. 1968*, 5117.
[9] a) *W. Schneider, P. Dillmann*, Chem. Ber. *96*, 2377 (1963); b) *L. A. Paquette, J. R. Malpass, T. J. Barton*, J. Am. Chem. Soc. *91*, 4714 (1969); c) *M. Takeda, M. Kawamori, H. Inoue, K. Noguchi, S. Nurimoto*, Chem. Pharm. Bull. *25*, 775 (1977); d) *R. Borne, C. R. Clark, J. M. Holbrook*, J. Med. Chem. *16*, 853 (1973).

Brominations with *N*-Bromosuccinimide: Solvent and Selectivity[**]

By *Werner Offermann* and *Fritz Vögtle*[*]

We have found that brominations with *N*-bromosuccinimide (NBS) lead all the more selectively to the benzyl bromide derivative the lower the refractive index of the solvent. Since the reactivity-selectivity principle[2] would appear valid one can select a solvent as reactive as necessary and as selective as possible. In the traditional solvent tetrachloromethane[3] the selectivity is very low. Very "selective solvents" such as methyl formate direct bromine into the ring of electron-rich arenes; this can be exploited preparatively for the bromination of benzo[15]crown-5.

By ^{1}H-NMR integrative evaluation of competitive experiments[1] we have determined the selectivity κ for NBS bromination in eleven solvents (Table 1).

$$\kappa = k_1/k_2 \quad (1)$$

$$\text{Aryl-CH}_3 \xrightarrow{k_1} \text{Aryl-CH}_2\text{Br} \xrightarrow{k_2} \text{Aryl-CHBr}_2 \quad (2)$$

Model substrates were *p-tert*-butyltoluene, 4-methylbiphenyl (*p*-phenyltoluene), and *p*-nitrotoluene; the solvents were chosen on the basis of two criteria: dielectric constant less than 10, so as to avoid ring bromination, availability from the standpoint of preparative use.

The selectivities κ determined at the boiling points were corrected[4] *via* the isoselective temperature[2] to 20 °C. From these values and the σ^+ constants of the toluene substituents (NO_2, Ph, *t*Bu) the following structure-selectivity (σ^+/κ) relationships (3) to (9) (valid at 20 °C) could be estimated.

methyl formate:	$\log\kappa = 1.57 - 0.47\,\sigma^+$	(3)
methyl acetate:	$\log\kappa = 1.52 - 0.48\,\sigma^+$	(4)
dichloromethane:	$\log\kappa = 1.41 - 0.57\,\sigma^+$	(5)
trichloromethane:	$\log\kappa = 1.38 - 0.62\,\sigma^+$	(6)
tetrachloromethane[1]:	$\log\kappa = 1.09 - 0.62\,\sigma^+$	(7)
benzene:	$\log\kappa = 1.38 - 0.69\,\sigma^+$	(8)
carbon disulfide:	$\log\kappa = 1.04 - 0.71\,\sigma^+$	(9)

Table 1. Selectivity κ and maximum yield Y_{max} for NBS bromination of three substrated toluenes in eleven solvents; at the boiling points (above), and corrected to 20 °C (below).

Solvent	n_D^{20} [5a]	*p*-Nitrotoluene		4-Methylbiphenyl		*p-tert*-Butyltoluene	
		κ	Y_{max}	κ	Y_{max}	κ	Y_{max}
HCO_2Me	1.3433	13.94	0.82	40.14	0.91	38.76	0.91
		15.86	0.83	48.26	0.92	46.43	0.92
CCl_2FCClF_2	1.3557	1.05	0.38	21.66	0.86	21.34	0.86
		1.05	0.38	31.45	0.89	30.88	0.89
$MeCO_2Me$	1.3593	9.53	0.77	25.77	0.88	24.31	0.87
		13.71	0.81	43.79	0.92	40.94	0.91
$tBuCO_2Me$	1.388	—	—	18.58	0.85	19.65	0.85
		—	—	55.17	0.93	59.55	0.93
CH_2Cl_2	1.4242	7.76	0.74	23.34	0.87	28.71	0.89
		9.25	0.76	30.66	0.89	38.43	0.91
$CHCl_3$	1.4459	5.70	0.69	18.81	0.85	19.52	0.85
		7.81	0.74	32.27	0.90	33.81	0.90
CCl_4 (pure)	1.4601	3.37	0.60	10.98	0.79	8.73	0.76
		4.52	0.65	20.11	0.86	15.04	0.82
CCl_4 (Uvasol)	1.4601	4.37	0.65	12.56	0.80	11.29	0.79
		6.28	0.71	23.80	0.87	20.82	0.86
CCl_4 (P_2O_5)	1.4601	4.31	0.64	17.67	0.84	9.99	0.77
		6.17	0.70	36.57	0.90	17.85	0.84
CCl_4 (KOH)	1.4601	4.49	0.65	12.19	0.80	8.19	0.75
		6.50	0.71	22.92	0.86	13.87	0.82
C_2HCl_3	1.4773	2.63	0.55	12.47	0.80	—	—
		3.47	0.60	26.76	0.88	—	—
C_6H_6	1.5011	4.62	0.66	14.73	0.82	17.55	0.84
		6.93	0.72	30.43	0.89	38.05	0.91
C_6H_5Cl	1.5248	4.28	0.64	—	—	—	—
		9.06	0.76	—	—	—	—
CS_2	1.6280	2.67	0.56	13.00	0.81	10.78	0.78
		2.97	0.58	17.41	0.84	14.14	0.82

Solvent effects on radical reactions have rarely been described quantitatively. Of the solvent parameters n_D^{20}[5a] $(M/\varrho)\cdot(n-1)$[5b], $(M/\varrho)\cdot(n^2-1)/(n+0.4)$[5b], $(n^2-1)/(n+0.4)$, $(M/\varrho)\cdot(n^2-1)/(n^2+2)$[5b], $(n^2-1)/(n^2+2)$, $(1-1/n^2)$[5c], $(1/n^2-1\,D)$[5c], $(\varrho/M)\cdot(D-1)/(2D+1)$[5d], $(D-1)/(2D+1)$[5d],

[*] Prof. Dr. F. Vögtle, Dr. W. Offermann
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn 1 (Germany)

[**] NBS bromination selectivity Part 6. This work was supported by the Fonds der Chemischen Industrie. We thank Dipl.-Chem. *B. Jansen* for carrying out the experiments with benzo[15]crown-5. Part 5: [1].

E_T[5e] and δ[5f,6] the refractive index n and its functions yield the best correlations, saving the tetrachloromethane values. With $(1-1/n^2)$, the solvent-dependent term of an energy parameter[5c], one obtains the relationships (10) to (12) (valid at 20 °C):

p-tert-butyltoluene:	$\log\kappa = 0.315 + 2.50/n^2 \; (r^2 = 0.76)$	(10)
4-methylbiphenyl:	$\log\kappa = 0.392 + 2.32/n^2 \; (r^2 = 0.94)$	(11)
p-nitrotoluene:	$\log\kappa = -0.972 + 3.93/n^2 \; (r^2 = 0.98)$	(12)

Figure 1 illustrates the exceptional behavior of tetrachloromethane. Though the selectivity in specially purified tetrachloromethane (Table 1) is higher, even these values do not fit into the relations *(10)* to *(12)*.

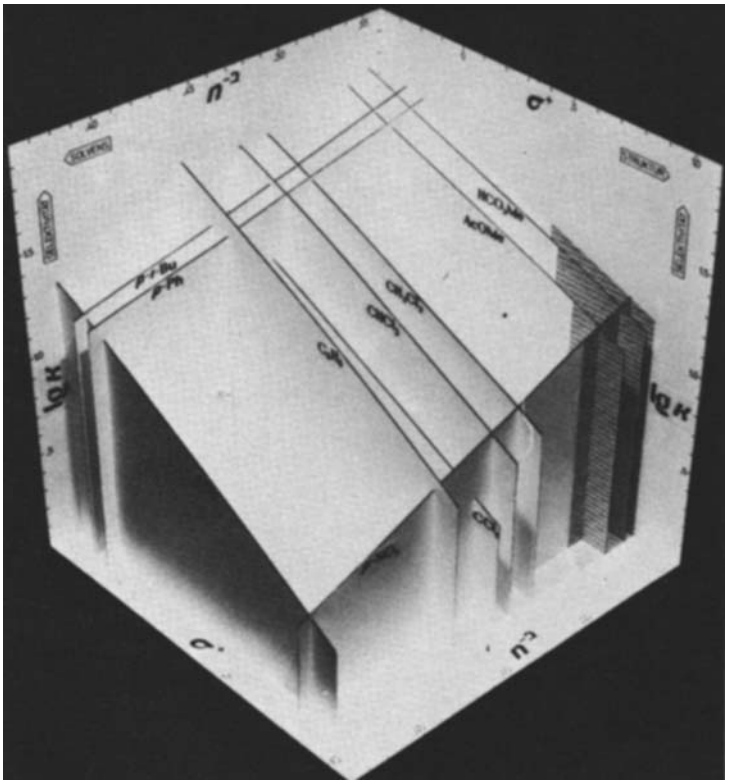


Fig. 1. Influence of solvent and substrate on the selectivity (at 20 °C).

Thus, the most promising solvents for NBS brominations would appear to be methyl formate and dichloromethane, which combine two properties promoting selectivity: low refractive index and low reaction temperature[4]. In certain cases the yields can be doubled with these solvents[7]. In methyl formate very weakly reactive substrates are no longer converted to the predicted extent Y_{max}[1], even by an excess of NBS (Fig. 1). On increasing the refractive index stepwise the solvent is adapted to inert substrates. The "ideal" solvent just meets the "reactivity requirements" of the substrate. This accommodation is all the more important since unreactive substrates obeying the inverse reactivity-selectivity principle also react unselectively[1].

Table 2. Ring bromination of benzo[15]crown-5 by NBS at the boiling points.

Solvent	Catalyst [mol $AlCl_3$/mol educt]	Yield [%]
CCl_4	—	57 [8]
CCl_4	1	85
HCO_2Me	—	80
HCO_2Me	1	63
HCO_2Me	2	59

In NBS brominations of electron rich substrates "selective" media promote formation of ring-brominated products. Thus the ring bromination of benzo[15]crown-5[8] can be improved (Table 2).

In bromine solvate complex, methyl formate acts like a Lewis acid on bromine. This type of solvation also increases the selectivity in radical reactions. In contrast, in chlorinations the selectivity increases in basic medium[9].

Received: December 12, 1979 [Z 470 IE]
German version: Angew. Chem. *92*, 471 (1980)

CAS Registry numbers:
Benzo[15]crown-5, 14098-44-3; *p-tert*-butyltoluene, 98-51-1; 4-methylbiphenyl, 644-08-6; p-nitrotoluene, 99-99-0; HCO_2Me, 107-31-3; CCl_2FCClF_2, 76-13-1; $MeCO_2Me$, 79-20-9; *t*-$BuCO_2Me$, 598-98-1; CH_2Cl_2, 75-09-2; $CHCl_3$, 67-66-3; CCl_4, 56-23-5; C_2HCl_3, 79-01-6; C_6H_6, 71-43-2; C_6H_5Cl, 108-90-7; CS_2, 75-15-0; $AlCl_3$, 7446-70-0; NBS, 128-08-5

[1] *W. Offermann, F. Vögtle*, J. Org. Chem. *44*, 710 (1979).
[2] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).
[3] *P. S. Skell, J. C. Day*, Acc. Chem. Res. *11*, 381 (1978); *L. Horner, E. H. Winkelmann*, Angew. Chem. *71*, 349 (1959); *A. Roedig* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Vol. IV/4. Thieme, Stuttgart 1960, p. 391; *C. Djerassi*, Chem. Rev. *43*, 271 (1948).
[4] *W. Offermann*, Dissertation, Universität Bonn 1979.
[5] a) *J. A. Riddick, W. B. Bunger:* Organic Solvents. Wiley, New York 1970; b) Identities of molar refraction: *F. Klages:* Lehrbuch der Organischen Chemie II. de Gruyter, Berlin 1957; c) *E. S. Amis:* Solvent Effects on Reaction Rates and Mechanisms. Academic Press, New York 1966; d) *J. A. Howard, K. U. Ingold*, Can. J. Chem. *42*, 1044 (1964); e) *C. Reichardt*, Angew. Chem. *91*, 119 (1979); Angew. Chem. Int. Ed. Engl. *18*, 98 (1979); f) *M. H. Abrahams*, Prog. Phys. Org. Chem. *11*, 1 (1974).
[6] M = molecular weight, ϱ = density, D = dielectric constant.
[7] Cf. *W. Offermann, F. Vögtle*, Synthesis *1977*, 272.
[8] *R. Ungaro, B. El Hadj, J. Smid*, J. Am. Chem. Soc. *98*, 5198 (1976).
[9] *G. A. Russell*, J. Am. Chem. Soc. *80*, 4987 (1958).

Thermal Decarboxylation of β-Lactones: Steric Hindrance of Mesomerism as Indication of a Zwitterionic Intermediate

By *Johann Mulzer, Matthias Zippel*, and *Gisela Brüntrup*[*]

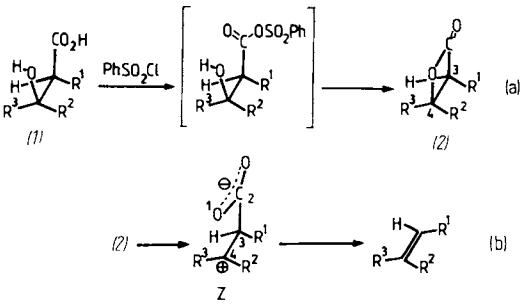
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The thermal decarboxylation of β-lactones (2-oxetanones) has repeatedly been employed in the stereospecific synthesis of olefins[1]. The reaction belongs to the rare type of [2+2]-cycloreversions proceeding with retention of configuration and is thus of special interest from the mechanistic viewpoint[2]. It was unclear so far whether the reaction proceeds in a concerted manner or *via* an intermediate (Z). We report here on kinetic experiments giving clear evidence for the participation of Z.

The β-lactones *(2)* (see Table 1) were prepared in a conventional way[1d,e,h] from the 3-hydroxycarboxylic acids *(1)* [eq. (a)]; remarkably, the *threo* acids always gave the *trans*-lactone, the *erythro* acids the *cis*-lactone.

The kinetics of the decarboxylation of *(2)* was monitored by ^{1}H-NMR spectroscopy. Particularly informative from the mechanistic point of view is the comparison of the rate constants of analogously substituted *cis*- and *trans*-β-lactone isomers (Table 1). For a concerted process one would expect *k (cis)* to be greater than *k (trans)* since the substituents move

[*] Dr. J. Mulzer, Dipl.-Chem. M. Zippel, G. Brüntrup
Institut für Organische Chemie der Universität
Karlstr. 23, D-8000 München 2 (Germany)



contrast, fully benefits from the anisyl resonance stabilization. Hence Q is especially large.

That, despite the acyclic intermediate Z, the decarboxylation proceeds with retention of configuration is astonishing, but easily explainable. Z can be regarded as a heterotetramethylene; therefore we may expect in Z similarly high rotation barriers as those which have been calculated[4] and experimentally confirmed[5] for 1,4-butanediyls, the parent all-carbon systems.

Received: November 22, 1979 [Z 468a IE]
German version: Angew. Chem. 92, 469 (1980)

Table 1. Reaction rate constants for the thermal decarboxylation of *(2)* in 1,2-dichlorobenzene [a].

Lactone	R^1	R^2	R^3	Config.	$k \times 10^5$ [s^{-1}] (bei [°C])	$Q = k$ *(trans-2)*/ k *(cis-2)* [b]
(2a)	*t*-Bu	Ph	H	*cis*	1.14 (140.0)	250
(2b)	*t*-Bu	H	Ph	*trans*	4.36 (100.0)	
(2c)	Ph	*t*-Bu	H	*cis*	1.42 (140.0)	2.7
(2d)	Ph	H	*t*-Bu	*trans*	3.76 (140.0)	
(2e)	CH_3	Ph	H	*cis*	68.6 (140.0)	26
(2f)	CH_3	H	Ph	*trans*	32.5 (100.0)	
(2g)	*t*-Bu	2,6-$Cl_2C_6H_3$	H	*cis*	0.391 (175.0)	390
(2h)	*t*-Bu	H	2,6-$Cl_2C_6H_3$	*trans*	3.40 (140.0)	
(2i)	*t*-Bu	4-$CH_3OC_6H_4$	H	*cis*	9.80 (100.0)	1100
(2j)	*t*-Bu	H	4-$CH_3OC_6H_4$	*trans*	37.3 (50.0)	

[a] All β-lactones *(2)* (yield 82—93%) were characterized spectroscopically and by elemental analysis. As examples the IR and ^{1}H-NMR data ($CDCl_3$, TMS, 60 MHz) of *(2a—d)* are given: *(2a)*: m.p. 88—89 °C; IR (KBr): 1810 (C=O), 1130 (C—O) cm^{-1}; ^{1}H-NMR: $\delta = 0.85$ (s, 9H, *t*Bu), 3.90 (d, $J = 6.5$ Hz, 1H, C*H*—*t*Bu), 5.70 (d, $J = 6.5$ Hz, 1H, C*H*—O), 7.42 (s, 5H, phenyl-H); *(2b)*: m.p. 38—39 °C; IR (KBr): 1835 (C=O), 1115 (C—O) cm^{-1}; ^{1}H-NMR: $\delta = 1.13$ (s, 9H, *t*Bu), 3.38 (d, $J = 4$ Hz, 1H, C*H*tBu), 5.35 (d, $J = 4$ Hz, 1H, C*H*—O), 7.42 (s, 5H, phenyl-H); *(2c)*: m.p. 86.5—87 °C; IR (KBr): 1810 (C=O), 1110 (C—O) cm^{-1}; ^{1}H-NMR: $\delta = 0.80$ (s, 9H, *t*Bu), AB-system ($\delta_A = 4.33$, $\delta_B = 4.96$, $J = 7$ Hz), 7.18 (s, 5H, phenyl-H); *(2d)*: m.p. 39.0—39.5 °C; IR (neat): 1820 (C=O), 1120 (C—O) cm^{-1}; ^{1}H-NMR: $\delta = 1.05$ (s, 9H, *t*Bu), AB-system ($\delta_A = 4.25$, $\delta_B = 4.52$, $J_{AB} = 4$ Hz), 7.30 (s, 5H, phenyl-H). [b] For comparison of the *cis-trans* reactivities at different temperatures the k (*cis*-2) value was in each case extrapolated with the aid of the activation parameters to the lower temperature of the k (*trans*-2) value.

apart from one another on going from the β-lactone to the olefin and, thus, the strain relief in the *cis* compound should be greater than in the *trans* isomer. However, as shown in Table 1, the *trans*-lactone generally decarboxylates far more quickly. This is consistent not with a synchronous mechanism, but rather with a reaction *via* Z [eq. (b)].

A decisive factor is the stabilization of the unsaturated center at C-4 of Z. In *(2b)* the 4-phenyl group can rotate in the plane of the resulting sp^2 carbon atom. In *(2a)* it cannot, because it is forced into a twisted conformation by the bulky 3-*tert*-butyl substituent. The result is a rate quotient (Q) (k *(2b)*/k *(2a)*) of 250! On the other hand, in the case of *(2c)*/*(2d)*, where only a weakly stabilizing *tert*-butyl group is present at C-4, Q is *ca.* 10^2 smaller. Similarly, a comparison of the rate constants of the four isomers *(2a)—(2d)* also clearly indicates the participation of Z: *(2b)*, whose Z has by far the most effective C-4 stabilization, decomposes 100 to 350 times more rapidly than *(2a)*, *(2c)* and *(2d)*, which differ only slightly in their reactivity.

A high value for Q in the thermolysis of *cis-trans* isomeric lactones is thus inevitably connected with the presence of a highly twisted 4-aryl group in Z. This is again confirmed by the pairs *(2e)*/*(2f)* ($R^1 = CH_3$, therefore only slight twisting) and *(2g)*/*(2h)* (bulky groups at C-3 and C-4), therefore strong twisting): compared to the pair *(2a)*/*(2b)*, Q decreases by a factor of 10 and increases by a factor of 1.6, respectively.

Is Z a zwitterion or a diradical? A Hammett diagram for the aryl analogues of *(2b)* clearly answers this question in favor of the zwitterion (*p*-substituents: NO_2, CN, Cl, CH_3OCH_3, σ^+ correlation[3], $\rho = -3.4$ with $r = 0.992$). The last pair *(2i)*/*(2j)* in Table 1 may be seen as a summary of the results we have presented so far: in *(2i)* the aryl group of Z is twisted; the carbenium center at C-4 profits very little from the +M effect of the *p*-CH_3O substituent. The Z of *(2i)*, by

CAS Registry numbers:
(1a), 58113-93-2; *(1b)*, 58113-94-3; *(1c)*, 34296-63-4; *(1d)*, 33398-52-6; *(1e)*, 14366-87-1; *(1f)*, 14366-86-0; *(1g)*, 73697-84-4; *(1h)*, 73697-85-5; *(1i)*, 73697-86-6; *(1j)*, 73697-87-7; *(2a)*, 73378-20-8; *(2b)*, 73378-21-9; *(2c)*, 71647-84-2; *(2d)*, 69974-12-5; *(2e)*, 73318-17-3; *(4)*, 71155-82-3; *(2g)*, 73697-88-8; *(2h)*, 73697-89-9; *(2i)*, 73697-90-2; *(2j)*, 73697-91-3

[1] a) Reviews: *J. Faulkner*, Synthesis *1971*, 175; *A. S. Arora, I. K. Ugi* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Vol. V/1b. Thieme, Stuttgart 1972; b) *D. S. Noyce, E. H. Banitt*, J. Org. Chem. *31*, 4043 (1966); c) *O. L. Chapman, W. R. Adams, J. Am. Chem. Soc. 90*, 2333 (1968); d) *W. Adam, J. Baeza, J.-C. Liu, ibid. 94*, 2000 (1972); e) *S. Mageswaran, M. U. S. Sultanbawa*, J. Chem. Soc. Perkin Trans. I *1976*, 884; f) *L. A. Marshall, H. Fauble*, J. Am. Chem. Soc. *92*, 948 (1970); g) *J. A. Marshall, L. Karas, ibid. 100*, 3615 (1978); h) *J. Mulzer, A. Pointner, A. Chucholowski, G. Brüntrup*, J. Chem. Soc. Chem. Commun. *1979*, 52.

[2] Only very few kinetic data are available: *T. Imai, S. Nishida*, J. Org. Chem. *44*, 3594 (1979); *H. O. Krabbenhoft, ibid. 43*, 1305 (1978).

[3] *H. C. Brown, J. Okamoto*, J. Am. Chem. Soc. *79*, 1913 (1957); *80*, 4979 (1958).

[4] *R. Gleiter, W. D. Stohrer, R. Hoffmann*, Helv. Chim. Acta *55*, 893 (1972); *G. A. Segal*, J. Am. Chem. Soc. *96*, 7892 (1974); *R. Gleiter*, Angew. Chem. *86*, 770 (1974); Angew. Chem. Int. Ed. Engl. *13*, 696 (1974); *P. Hofmann, R. Gleiter*, Tetrahedron Lett. *1974*, 159.

[5] *R. Huisgen, G. Steiner*, J. Am. Chem. Soc. *95*, 5094 (1973).

2-Thietanimines from α-Deprotonated β-Lactones and Phenyl Isothiocyanate—A Novel Four-Membered Ring/Four-Membered Ring Recyclization

By *Johann Mulzer* and *Thomas Kerkmann*[*]

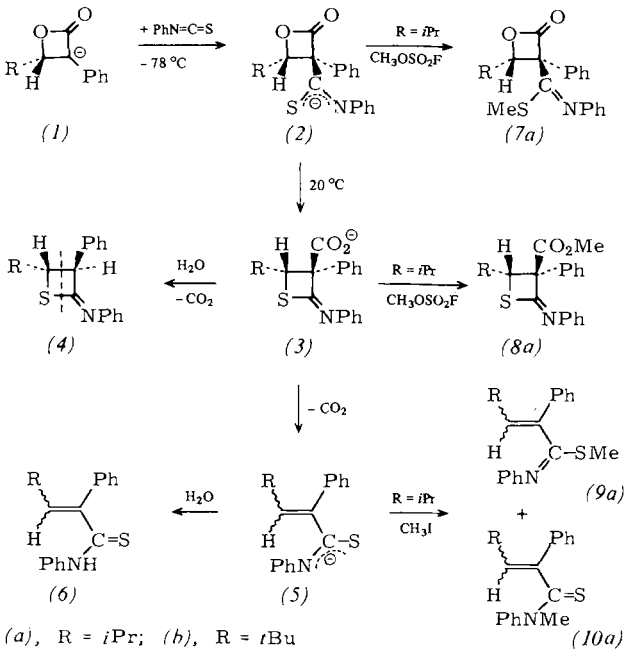
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

2-Thietanimines are a rare class of substances for which only two examples have so far been described[1]. We have

[*] Dr. J. Mulzer, T. Kerkmann
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-466 $ 02.50/0

now found a novel entry to this class of compounds. If β-lactones (2-oxetanones) are deprotonated with lithium diisopropylamide (LDA) and the resulting anion *(1)*[2] is allowed to react with phenyl isothiocyanate one obtains after hydrolysis the *N*-phenylthietanimine *(4)*[3] and the thioamide *(6)*, which can be separated by TLC. Thus, in the overall reaction CO_2 is exchanged for PhNCS. In the case of the isopropyl derivatives, the anionic intermediates *(2)*, *(3)* and *(5)* can be trapped by methylation.



to the isopropyl group; hence, 3,3,4-trisubstituted compounds *(4)* can also be prepared in sterically pure form, *e.g. c*-4-isopropyl-3-methyl-*r*-3-phenyl-2-thietan-*N*-phenylimine.

When heated to 120 °C *(4a)* completely rearranges to *(6a)*; in contrast to β-lactones, *(4)* does not yield an olefin on thermolysis.

Procedure

4-Isopropyl-3-phenyl-2-oxetanone (500 mg, 2.63 mmol) is deprotonated in anhydrous THF (2 ml) at −78 °C with 2.63 mmol of LDA. After 10 min the solution is treated with 2.63 mmol of phenyl isothiocyanate, allowed to warm up for 30 min and, after addition of water, extracted with ether. The crude product mixture consists of *(4a)* and *(6a)* (70:30) and is separated by TLC on silica gel with pentane/ether (95:5); yield 305 mg (41%) *(4a)* and 270 mg (36%) *(6a)*. Analogously 405 mg (52%) *(4b)* and 310 mg (40%) *(6b)* were obtained from the appropriate educts.

Trapping experiments: (2a): Immediately after addition of the phenyl isothiocyanate the mixture is treated at −78 °C with 1.25 mol. equiv. of methyl fluorosulfate; yield after workup with H_2O/Et_2O, 185 mg (21%) *(7a).—(3a):* After addition of the phenyl isothiocyanate the mixture is allowed to warm up for 10 min and is then treated with 1.25 mol. equiv. of methyl fluorosulfate; hydrolytic workup yields 280 mg (32%) *(8a).—(5a):* The same procedure is used as in the preparation of *(4a)/(6a)* except that methyl iodide is added in the molar ratio 1:8. Usual workup affords 880 mg (56%) of a mixture of *(9a)* and *(10a)* (63:37).

Received: February 28, 1980 [Z 468b IE]
German version: Angew. Chem. 92, 470 (1980)

CAS Registry numbers:
(4a), 73688-15-0; *(4b)*, 73688-16-1; *(6a)*, 73688-17-2; *(6b)*, 73688-18-3; *(7a)*, 73688-19-4; *(8a)*, 73688-20-7; *(9a)*, 73688-21-8; *(10a)*, 73688-22-9; 4-isopropyl-3-phenyl-2-oxetanone, 73688-23-0; 4-*tert*-butyl-3-phenyl-2-oxetanone, 57015-12-0; phenyl isothiocyanate, 103-72-0

Table 1. Some data of the prepared compounds. Correct CHNS analyses obtained. *(a):* R = *i*Pr, *(b):* R = *t*Bu.

	^{1}H-NMR ($CDCl_3$, 60 MHz, TMS int., δ value)	IR [cm^{-1}]
(4a) yellow oil	0.99 (d, J = 6.5 Hz, 6H, CH_3), 1.8—2.5 (m, 1H, C*H*Me$_2$), 3.48 (dd, J = 4.5 and 8.5 Hz, 4-H), 4.78 (d, J = 4.5 Hz, 3-H), 6.82—7.60 (m, 10 phenyl-H)	(film): 2960 (CH), 1659 (C=N), 1593, 1490, 693
(6a) yellow crystl., m.p. 92—93 °C	1.02 (d, J = 6 Hz, 6H, CH_3), 2.0—2.7 (m, 1H, CHMe$_2$), 7.1—7.6 (m, 12H, phenyl-H + 3-H + NH)	(KBr): 3310 (NH), 2970 (CH), 1632 (C=C), 1512, 1352 (Amide I and II)
(4b) yellow oil	1.03 (s, *t*Bu), 3.67 (d, J = 4.5 Hz, 4-H), 4.84 (d, J = 4.5 Hz, 3-H), 6.9—7.7 (m, 10 phenyl-H)	(film): 2960 (CH), 1662 (C=N), 695
(6b) yellow cryst., m.p. 75.5—76.5 °C	0.93 (s, *t*Bu), 7.15—7.5 (m, 10 phenyl-H), 7.63 (s, 3H), 8.40 (br. s, NH)	(KBr): 3330 (NH), 2965 (CH), 1625 (C=C), 1536, 1352 (Amide I and II)
(7a) colorless cryst., m.p. 129.5—130 °C	0.62 and 0.98 (2 d, J = 6 Hz, 6H, diast. CH_2), 1.2—1.9 (m, 1H, C*H*Me$_2$), 2.00 (s, S—CH_3), 5.38 (d, J = 10 Hz, 4-H), 6.8—7.6 (m, 10 phenyl-H)	(KBr): 1980 (CH), 1820 (C=O), 1126 (C=O), 703
(8a) bright yellow cubes, m.p. 74—75.5 °C	0.70 and 0.80 (2 d, J = 6 Hz, 6H, diast. CH_3), 1.2—2.0 (m, 1H, C*H*Me$_2$), 3.85 (s, OCH_3), 4.44 (d, J = 9.5 Hz, 4-H), 6.9—7.6 (m, 10 phenyl-H)	(KBr): 2960 (CH), 1734 (C=O), 1662 (C=N), 1230 (C—O), 698
(9a)/(10a) 63:37 mixture cf. m.p. 63—65 °C	*(9a):* 0.93 (d, J = 6.5 Hz, 6H, CH(C*H*$_3$)$_2$), 2.4—3.0 (m, 1H, C*H*Me$_2$), 2.53 (s, S—CH_3), 5.66 (d, J = 10.5 Hz, 3-H), 6.5—7.7 (m, 10 phenyl-H) *(10a):* 1.18 (d, J = 6.5 Hz, 6H, CH(C*H*$_3$)$_2$), 2.11 (s, N—CH_3), 2.4—3.0 (m, 1H, C*H*Me$_2$), 6.05 (d, J = 10 Hz, 3-H), 6.5—7.7 (m, 10 phenyl-H)	*(9a)/(10a)* (KBr): 2960 (CH), 1628 (C=N), 1046 (C—S)

The key step of this remarkable synthesis is the four-membered ring recyclization *(2)*→*(3)*, which proceeds—as the structure of the trapping product shows[4]—with inversion at C-4, at least in the case of the isopropyl derivatives. Equally surprising is the ring opening *(3)*→*(5)*, which corresponds to a fragmentation.

(4a) can be smoothly deprotonated with LDA at −78 °C in tetrahydrofuran, and reacted with methyl iodide; as in the reaction *(1)*→*(2)*, the electrophile attacks at the position *trans*

[1] *V. Bertolasi, G. Gilli*, Acta Crystallogr. *B 34*, 3403 (1978); *A. Dondoni, A. Battaglia, P. Giorgianni, G. Gilli, M. Sacerdoti*, J. Chem. Soc. Chem. Commun. *1977*, 43.

[2] *J. Mulzer, Th. Kerkmann*, J. Am. Chem. Soc., in press.

[3] The *trans* configuration of *(4a)* and *(4b)* follows from the ^{1}H-NMR coupling constant $J_{3,4}$ = 4.5 Hz; the same value was found in the case of *trans*-3,4-di-

substituted β-lactones. That compounds *(4)* are thietanimines and not the isomeric β-thiolactams [attack at nitrogen in the reaction step *(2)*→*(3)*] follows from the mass spectra of *(4)*. The indicated fragmentation leads to a signal $m/e = 193$ (Ph—CH=C=NPh); no signals appears at $m/e = 134$ (Ph—CH=C=S). The IR band at *ca.* 1660 cm^{-1} is also characteristic (cf. [1]).

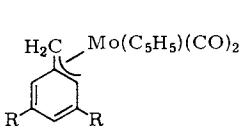
[4] Assignment of the configuration of *(7a)* and *(8a)* is supported by the anisotropy of the isopropyl-CH_3 in the ^{1}H-NMR spectrum (cf. Table 1); this would indicate a vicinal phenyl group *cis* to the isopropyl group. In *(4a)* these groups are *trans*; no anisotropy is observed.

(1,2,5,6-η-1,5-Cyclooctadiene)-(1,2,7-η-7-methylbenzyl)(7,8-η-styrene)rhodium(I)—Antarafacial Fluctuation of the Benzyl Ligand and Temperature-Dependent Coordination of Styrene

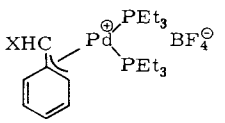
By *Hans-Otto Stühler*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

Fluctuating η^3-benzyl ligands represent an unusual type of coordination in transition metal compounds. Since the discovery of this type of bonding in (η^3-benzyl)(η^5-cyclopentadienyl)dicarbonylmolybdenum[1], NMR spectroscopic investigations on complexes *(1)* and *(2)*, for example, have shown that the fluctuation of the benzyl ligand proceeds through all four positions (side and edge combinations) α-δ (Fig. 1)[2,3], thus requiring both supra- and antarafacial rearrangements.



(1)



(2), X = H
(2a), X = D

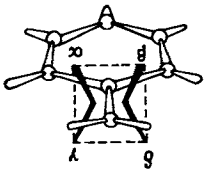


Fig. 1. Positions of possible coordination to η^3-benzyl ligands.

On the NMR time-scale this leads to equivalence, both of the two benzyl protons as well as of the *ortho* protons of the benzyl ligand. At low temperature the metal atom can be fixed in one of the four positions. In the case of *(2a)* it was shown[3] that the fluctuation of the benzyl ligand is to be understood in the sense of the known η^3,η^1,η^3-allyl rearrangement[4].

We have now synthesized and investigated the rhodium compound *(3)* (see Procedure). The ^{1}H-NMR spectroscopic findings indicate that a temperature-dependent equilibrium exists between *(3a)*, *(3b)*, and *(3c)* in solution, and that the benzyl ligand fluctuates above −40 °C (Fig. 2).

At room temperature the ^{1}H-NMR spectrum ([D_{10}]diethyl ether) shows the signals of free styrene. On cooling, the signals of the vinylic protons are strongly shifted upfield until at −50 °C they overlap the signals of the olefinic protons of the coordinated cyclooctadiene at $\delta \approx 3.90$, *i.e.* coordination of the styrene *via* the exocyclic double bond increases with decreasing temperature. The η^3-bonded part of the benzyl ligand gives rise to three signals at room temperature: a sharp

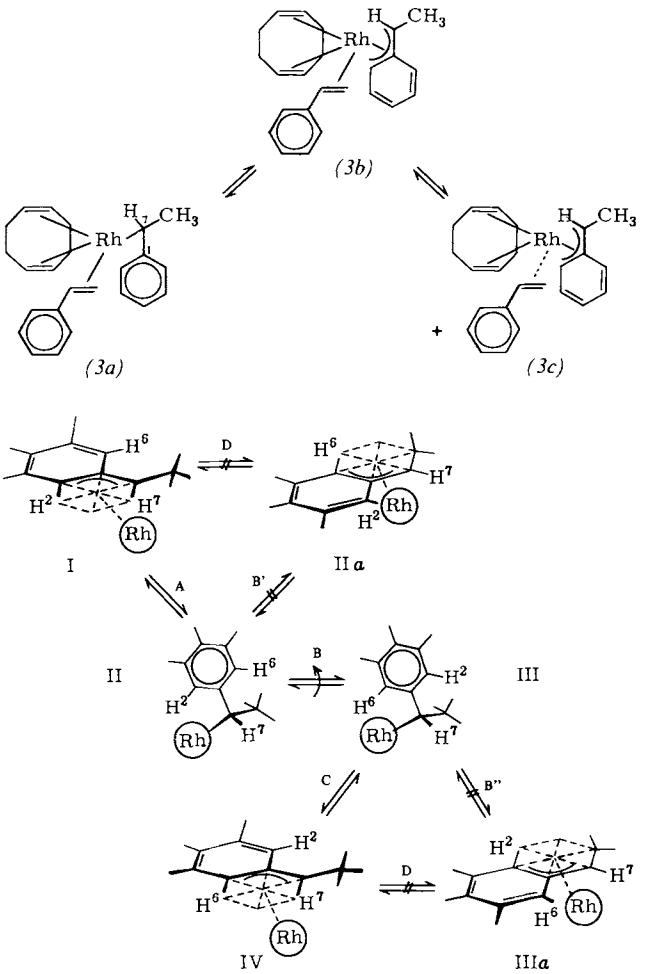


Fig. 2. Mechanism of fluctuation of the η^3-7-methylbenzyl ligand.

doublet of a *syn*-methyl group[5] at δ = 1.50, the quartet of an *anti* proton at δ = 2.20, and a broad signal (δ = 5.80) of the two *ortho* protons. On warming to +50 °C this signal becomes sharper; on cooling it broadens and almost disappears into the background at −30 °C. At the same time, it is shifted downfield; the signals of the methyl group and of the *anti* proton H^7 are correspondingly shifted upfield. Both signals, however, remain sharp from +50 to −70 °C; despite the rapid rearrangement of the benzyl ligand, which leads to equivalence of the two *ortho* protons, the *steric environment at the benzyl carbon does not alter.* This requires existence in the transition state[3] of the short-lived σ-alkyl compound II, from which IV is formed after rotation about the C^1—C^7 axis through 180° (to III) (reaction sequence A, B, C in Fig. 2). The overall reaction is an antarafacial rearrangement, *i.e.* the two *ortho* protons H^2 and H^6 change places relative to the substituent on C-7.

An antarafacial rearrangement by rotation of the η^3-benzyl group through 180°, on the other hand, would give the enantiomorphic form of I, but would not lead to exchange of the *ortho* protons H^2 and H^6. Suprafacial shifts[6] (reaction paths A,B′; C,B″; D = [1,5]-shift) lead to the *anti*-isomers IIa and IIIa, which however are not observed. The steric reasons for this may be the same as those which led exclusively to formation of the *syn*-isomers in the complexes (diene)Rh(subst. allyl)[5].

At low temperature the fluctuation comes to a standstill. At −40 °C two broad signals of the non-equivalent *ortho* protons are observed at δ = 7.0 and 6.2; the first of these sig-

[*] Dr. H.-O. Stühler
Institut für Anorganische und Analytische Chemie
der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

nals disappears under the signals of the aromatic protons at $-50\,^{\circ}C$, the last only at *ca.* $-100\,^{\circ}C$. This can be interpreted in the sense of a successive transition from *(3b)* to *(3a)*. The presence of the η^1-bonded benzyl ligand in the low-temperature form *(3a)* can be regarded as a further indication that the fluctuation of the η^3-benzyl ligand takes place at higher temperature *via* this σ-form. The signals of the rigid cyclooctadiene ligand also show temperature-dependent changes.—*(3a)* and *(3c)* formally contain 16 valence electrons. In the case of complexes of the type (diene)Rh(allyl) several such systems are known[5, 7].

A selective antarafacial rearrangement of an η^3-benzyl ligand has to our knowledge hitherto not been reported. This rearrangement at the same time proves that an η^1-bonded benzyl moiety must be present in its transition state.

Procedure

All operations must be carried out under an inert gas. A solution of styrene (3 ml) in ether (10 ml) is added to a solution of di-μ-chlorobis(1,5-cyclooctadiene)dirhodium[8] (0.98 g, 2 mmol) in ether (20 ml) at $-78\,^{\circ}C$ and the stirred mixture treated with a Grignard solution prepared from 0.19 g (8 mmol) Mg and 1 ml i-C_3H_7Br. The mixture is allowed to warm within 3 h to $0\,^{\circ}C$ and the solvent and excess ligand are then removed in a high vacuum. After elution with 200 ml of pentane and filtration on Al_2O_3 (7% H_2O) (frit and receiver cooled to $-78\,^{\circ}C$), analytically pure orange-red *(3)* crystallizes at $-78\,^{\circ}C$; yield 1.498 g (3.75 mmol; 89%), m.p. $-9\,^{\circ}C$.

Received: October 8, 1979 [Z 476 IE]
German version: Angew. Chem. *92*, 475 (1980)

CAS Registry numbers:
(3), 73758-13-1; di-μ-chlorobis(1,5-cyclooctadiene)dirhodium, 12092-47-6; styrene, 100-42-5; i-C_3H_7Br, 75-26-3

[1] *R. B. King, A. Fronzaglia*, J. Am. Chem. Soc. *88*, 709 (1966).
[2] *F. A. Cotton, T. J. Marks*, J. Am. Chem. Soc. *91*, 1339 (1969).
[3] *Y. Becker, J. K. Stille*, J. Am. Chem. Soc. *100*, 845 (1978).
[4] *F. A. Cotton, G. Wilkinson:* Anorganische Chemie, 3. Aufl. Verlag Chemie, Weinheim 1974, Kap. 23; Advanced Inorganic Chemistry. 3rd Ed. Wiley-Interscience, New York 1972, Chapt. 23.
[5] *H.-O. Stühler, J. Müller*, Chem. Ber. *112*, 1359 (1979).
[6] Cf. *B. E. Mann, A. Keasey, A. Sonoda, P. M. Maitlis*, J. Chem. Soc. Dalton Trans. *1979*, 338.
[7] *J. Müller, H.-O. Stühler, W. Goll*, Chem. Ber. *108*, 1074 (1975).
[8] *J. Chatt, L. M. Venanzi*, J. Chem. Soc. *1957*, 4735.

Liquid Chromatography of Enantiomers: Determination of Enantiomeric Purity in Spite of Extensive Peak Overlap[**]

By *Albrecht Mannschreck, Mladen Mintas, Georg Becher,* and *Georgine Stühler*[*]

Several methods have been used for determining the enantiomeric purity P of a chiral substrate[2]; however, none of them seems to be universally applicable.

[*] Prof. Dr. A. Mannschreck, Dr. M. Mintas, Dr. G. Becher, and G. Stühler
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

[**] Liquid Chromatography on Triacetylcellulose, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie. The samples of (±)-*(1)* and (−)-*(1)* were provided by Professor Dr. *K. H. Büchel* and Dr. *G. Jäger*, Bayer AG, Leverkusen, who have also kindly checked the manuscript. We are grateful to Dr. *M. Holík* and Dipl.-Phys. *R. Küspert*, Regensburg, for helpful suggestions.—Part 1: [1a]. Part 2: [1b].

As far as the measurement of P by chromatography is concerned, conversion of the enantiomers to diastereoisomers by a reagent and subsequent analysis on an *achiral* sorbent represent an established procedure. It relies on the absence of racemization and on a knowledge of P of the reagent[2]. Chromatography on an *optically active* stationary phase does not need a standard for P and is therefore one of the few *absolute*[2] methods. In this respect, gas chromatography has advanced considerably, *i.e.* baseline separations of enantiomers have been achieved in many cases. The areas under their peaks permit the direct calculation of P. Gas chromatography usually requires elevated temperatures, whereas liquid chromatography (LC) can be performed at room temperature, thus reducing the rates of possible decompositions or racemizations. However, this technique has not been widely used for P determinations, mainly because enantiomers frequently give overlapped or even fused peaks[1a, 3]. Therefore, a method applicable *in spite of peak overlap or fusion* (Fig. 1a), would clearly extend the analytical possibilities.

$$P = \frac{\varepsilon b \int \alpha \, dv}{[\alpha] l \int A \, dv} = \frac{\int \alpha \, dv}{C_+ \int A \, dv} \qquad (1)$$

In eq. (1)[4] v is the actual eluate volume, $\alpha(v)$ the angle of rotation and $A(v)$ the absorbance (see *e.g.* Fig. 1). The factor[4] $C_+ = \alpha_+ / A_+$ relates the rotation angle and absorbance of the predominant, dextrorotatory enantiomer. If this enantiomer appears at higher v, the eluate *cannot contain a relevant amount of the less abundant enantiomer* in the Δv region of Fig. 1. Therefore, in this region, α equals α_+ and A equals

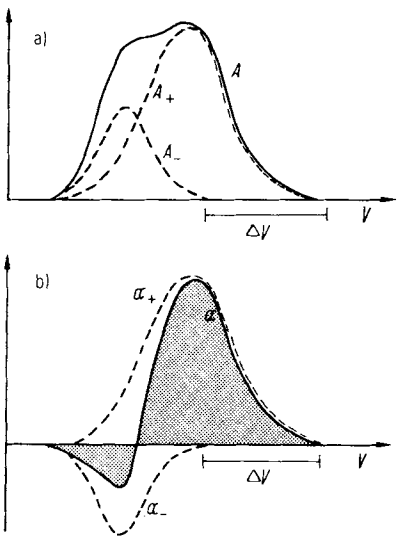


Fig. 1. Schematic chromatograms a) $A(v)$ and b) $\alpha(v)$ for a mixture of enantiomers (+ prevailing) after passage through an optically active sorbent. v: Actual volume of eluate. Δv: Region of v, where the eluate does not contain a relevant amount of the less abundant enantiomer. A: Absorbance of eluate. A_+ and A_-: Absorbances of the enantiomers ($A_+ + A_- = A$). α: Rotation angle of eluate. α_+ and α_-: Rotation angles of the enantiomers ($\alpha_+ + \alpha_- = \alpha$). The derivation [4] of eq. (1) does not depend upon the particular shapes (e.g. symmetry) of the component peaks (-----) chosen for demonstration.

A_+, *i.e.* $\alpha_+ / A_+ = C_+$ can be measured from a plot of α *versus* A (cf. Fig. 2b) by determining its slope at high volumes. $\int \alpha \, dv$, consisting of a positive and a negative area, and $\int A \, dv$ are also accessible, *e.g.* by the cut-and-weigh procedure, from the same experiment. In a preliminary test, LC (Fig. 2) of (+)-1-phenylethanol ($P = 52\%$, calculated from the specific rotation) resulted in $P = 54\%$ *via* eq. (1).

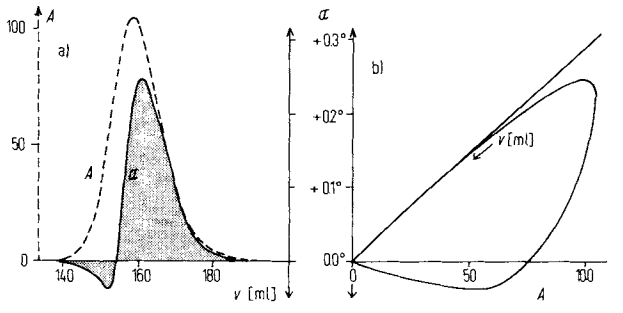
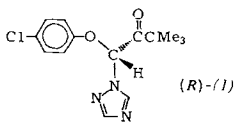


Fig. 2. a) Chromatograms $A(v)$ and $\alpha(v)$ and b) diagram $\alpha(A)$ of (+)-1-phenylethanol ($P = 52\%$) in ethanol/H_2O (96:4) after passage (flow rate 3.1 ml/min) through a column of triacetylcellulose. v: Actual volume of eluate; injection at $v = 0$. A: Absorbance at 254 nm, measured in "units" *i.e.* mV; α: Rotation angle at 365 nm. The straight line in b) has a slope of $C_+ = 0.0031°$/unit. We have used microcrystalline, swollen triacetylcellulose [1, 3b, 5] (particle sizes 0.03 to 0.06 mm, column 30 cm × 2.5 cm). Further details are: Eluent ethanol/water (96:4); temperature 22 °C; pressure ~11 bar; flow rate 2.1 ml/min, except for Fig. 2. The eluate was passed through one compartment (path length 2.0 mm, volume 0.08 ml) of the photometer double-cell, then through the polarimeter cell (path length 100 mm, volume 1 ml), and back through the photometer, in order to simulate the simultaneity of the detections which seems to be important for the measurement of C_+ (or C_-). A x-y recorder was used for the diagrams $\alpha(A)$, a two-pen recorder for $A(v)$ and $\alpha(v)$.

Our procedure was checked by 25 mg samples[6] of (−)-*(1)* (Table 1), the P-values of which were known (for experimental details see legend of Fig. 2; flow rate 2.1 ml/min). The 67.6% sample gave recordings very similar to Figure 2. For all measurements, $C_- = 0.0045$ to $0.0051°$/unit in the linear $\alpha(A)$ region. The agreement (Table 1) between the initial P-values and the ones obtained *via* eq. (1) is satisfactory. The determination of errors must be deferred until more results are available.

Further support for our method is derived from samples of (+)- and (−)-1,2-diphenylcyclopropane, separated[5] by LC on triacetylcellulose. Application of eq. (1) yields $P = 86\%$ and 100%, respectively. As the overlap of the (+)- and (−)-peaks is weak, the areas under the $\alpha(v)$ curve must represent good approximations for the relative concentrations. As expected, the results $P = 84\%$ and 100% are close to the above findings[5].

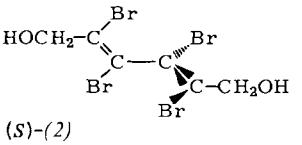
Table 1. Enantiomeric purity P of (−)-*(1)* samples.

	P [%] [a]	P [%] [b]
 (*R*)-*(1)*	4.9	6
	10.1	10
	48.9	49
	67.6	68
	88.3	87

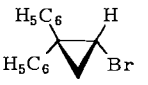
[a] Weighed amounts of (±)-*(1)*, Triadimefon (Bayleton®, Bayer AG), and of a sample of (−)-*(1)* were mixed. For the latter, $P = 99.8\%$ had been measured using calorimetry [7] by Dr. *H. Doerr*, Bayer AG, Leverkusen. The error of the above initial P-values is estimated to amount to ±0.2%. [b] For these mixtures, P was determined *via* eq. (1) (see text).

As a first application we have analyzed a sample of (−)-*(2)*, obtained by LC on triacetylcellulose ($[\alpha]_{589}^{20} = -29°$, 2.48 mg/ml, acetone; m.p. 99—100 °C), in order to obtain the hitherto unknown specific rotation of the pure enantiomer. Similarly to Figure 2 and to the diagrams of (−)-*(1)*, the $A(v)$ curve showed no sign of a splitting, *i.e.* the peaks of (+)- and (−)-*(2)* were fused. Application of eq. (1), using a 35 mg sample[6], resulted in $P = 29\%$, which means $[\alpha]_{589}^{20} = -100°$ for pure (−)-*(2)*. From this figure, the unknown P of an earlier preparation[8] of (−)-*(2)* *via* crystallization of diastereoisomers has now been calculated to 14%.

As application of our method to an enantioselective synthesis, we investigated 6 mg[6] (−)-*(3)* ($[\alpha]_{365}^{31} = -584°$, 1.07 mg/ml, ethanol), which were likewise obtained by LC on triacetylcellulose. We found $P = 71\%$, *i.e.* $[\alpha]_{365}^{31} = -826°$ for pure (−)-(*R*)-*(3)*, from which the unknown optical yields of (+)- and (−)-*(3)* samples[9] obtained cathodically (in presence of alkaloids) can be calculated.



(*S*)-*(2)*



(*R*)-*(3)*

The present determination of P depends neither upon the symmetry of each peak nor upon equal widths of the peaks. It does, however, depend upon *some* separation by the sorbent (generating an $\alpha(v)$ detection), though a separation yielding a *split* $A(v)$ chromatogram is not needed. Our method may be improved by avoiding manual area determination. Finally, eq. (7)[4] suggests the calculation of $[\alpha]$, the specific rotation of a pure enantiomer, from the measurement of C_+ (or C_-) by using *exclusively* the racemate. A preliminary trial showed that this suggestion is realistic.

Received: September 18, 1979
revised: April 3, 1980
German version: Angew. Chem. *92*, 490 (1980)

CAS Registry numbers:
(*R*)-*(1)*, 73804-20-3; (*S*)-*(2)*, 53152-83-3; (*R*)-*(3)*, 71808-83-8

[1] a) *H. Häkli, M. Mintas, A. Mannschreck*, Chem. Ber. *112*, 2028 (1979); b) *K. R. Lindner, A. Mannschreck*, J. Chromatogr. *193*, 308 (1980).
[2] Review: *M. Raban, K. Mislow*, Top. Stereochem. *2*, 199 (1967).
[3] a) See *e.g. F. Mikeš, G. Boshart*, J. Chromatogr. *149*, 455 (1978), and earlier papers; *I. S. Krull*, Adv. Chromatogr. *16*, 175 (1978); b) *G. Hesse, R. Hagel*, Justus Liebigs Ann. Chem. *1976*, 996, and earlier papers.
[4] If a mixture contains n_+ and n_- moles of the enantiomers ($n_+ > n_-$), P is given [2] by

$$P \equiv (n_+ - n_-)/(n_+ + n_-) = \int (c_+ - c_-)\,dv / \int (c_+ + c_-)\,dv \qquad (2)$$

where n_+ and n_- have been replaced by $\int c_+\,dv$ and $\int c_-\,dv$, respectively, *i.e.* the injected n_+ moles are distributed (actual concentration c_+) in the eluate volume v. The absorbances A_+ and A_- (Fig. 1a) are expressed by Beer's law, the rotation angles α_+ and α_- (Fig. 1b) by Biot's law:

$$\varepsilon b c_+ = A_+ \qquad (3)$$
$$\varepsilon b c_- = A_-$$
$$\varepsilon b (c_+ + c_-) = A_+ + A_- \equiv A \qquad (4)$$

$$+[\alpha] l c_+ = \alpha_+ \qquad (5)$$
$$-[\alpha] l c_- = \alpha_-$$
$$[\alpha] l (c_+ - c_-) = \alpha_+ + \alpha \equiv \alpha \qquad (6)$$

$A(v)$ and $\alpha(v)$ represent chromatograms (*e.g.* Fig. 1) of passage through an optically active sorbent, whereby partial separation of the enantiomers, *i.e.* overlap or fusion of their peaks, has occurred. Introduction of eq. (4) and (6) transforms eq. (2) into eq. (1); then

$$C_+ \equiv [\alpha] l \varepsilon^{-1} b^{-1} \qquad (7)$$

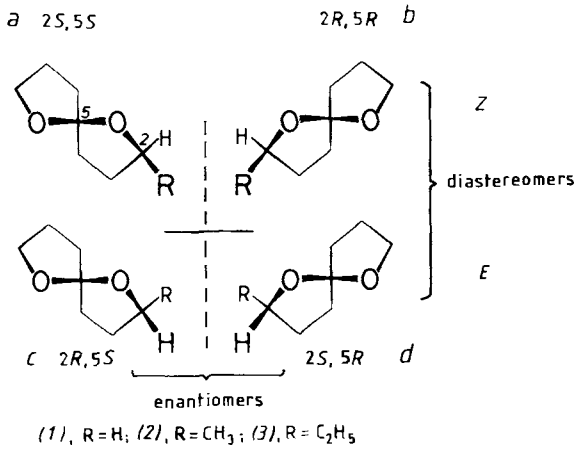
Using eq. (3) and (5) we get $C_+ = \alpha_+ / A_+$.
[5] *M. Mintas, A. Mannschreck, M. P. Schneider*, J. Chem. Soc. Chem. Commun. *1979*, 602.
[6] The diagrams obtained suggest that *lower* amounts of sample (about one half of the amounts used) would have resulted in similar accuracy.
[7] *S. Wilen, A. Collet, J. Jacques*, Tetrahedron *33*, 2725 (1977), and earlier papers; *R. Luckenbach, L. Horner*, Thermochim. Acta *11*, 216 (1975).
[8] *M. Rösner, G. Köbrich*, Angew. Chem. *86*, 775 (1974); Angew. Chem. Int. Ed. Engl. *13*, 741 (1974).
[9] *R. Hazard, S. Jaouannet, A. Tallec*, Tetrahedron Lett. *1979*, 1105, and unpublished results.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-470 $ 02.50/0

Quantitative Separation of the Enantiomeric Pairs of the Pheromone 2-Ethyl-1,6-dioxaspiro[4.4]nonane by Complexation Chromatography on an Optically Active Metal Complex[**]

By *Bernhard Koppenhoefer, Klaus Hintzer, Roland Weber,* and *Volker Schurig*[*]

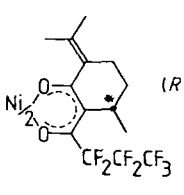
Spiroketals are widespread in Nature, yet little is known about their chiroptical properties. 2-Ethyl-1,6-dioxaspiro[4.4]nonane (Chalcogran) *(3)*, the main component in the aggregation pheromone of the forest pest *Pityogenes chalcographus (L.)* ("Kupferstecher"), has recently been identified and synthesized[1]. *(3)* contains two asymmetric centers; therefore, four configurational isomers can exist.



(1), R = H; *(2)*, R = CH_3; *(3)*, R = C_2H_5

The influence of the stereochemistry of chiral pheromones on their biological activity has been demonstrated[2]. A method for the quantitative determination of the stereochemical composition of naturally occurring (and biologically active) spiroketals is of interest with regard to the directed application of synthetic attractants in biological field trials, the investigation of the biosynthesis from chiral precursors, and the search for genetic relationships between species and genuses.

So far, only the gas chromatographic separation of the racemic *Z*- and *E*-diastereomers of *(3)* has been described[1a], but not their further separation into the enantiomeric pairs. The quantitative analytical separation of the four configurational isomers of *(3)* has now been accomplished by complexation gas chromatography, exploiting the diastereo- and enantiospecific coordinative interaction of *(3)* with the optically active metal chelate nickel(II) bis(6-heptafluorobutyryl)-(*R*)-pulegonate (*R*)-*(4)*.



(*R*) - *(4)*

[*] Prof. Dr. V. Schurig, Dipl.-Chem. B. Koppenhoefer, Dipl.-Chem. K. Hintzer, Dipl.-Chem. R. Weber
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

[**] Based on a lecture delivered at the conference "Chiral Structures" on May 23, 1979, in Milly la Forêt (France) *(V. S.)*. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Haarmann and Reimer, Holzminden (Germany), for generously supplying us with a sample of (*R*)-pulegone.

The novel optically active stationary phase (*R*)-*(4)* combines the advantage of considerable enantiomeric differentiation with short retention times and is thus suited for the enantiomeric resolution of substrates which are volatile only at elevated temperatures. By means of a nickel capillary column coated with a solution of (*R*)-*(4)* in squalane (0.09 m), the unsubstituted spiroketal *(1)* (also known as oxetone) can be resolved into the antipodes within 150 min at 50 °C. Following proof of the configurational stability of the spiro carbon atom of *(1)* during the separation by the occurrence of sharply separated peaks, we synthesized the homologs *(2)* and *(3)* (Chalcogran) according to procedures given in the literature[1a,c] and chromatographed the spectroscopically characterized compounds on 0.12 m (*R*)-*(4)* in squalane (Fig. 1, above).

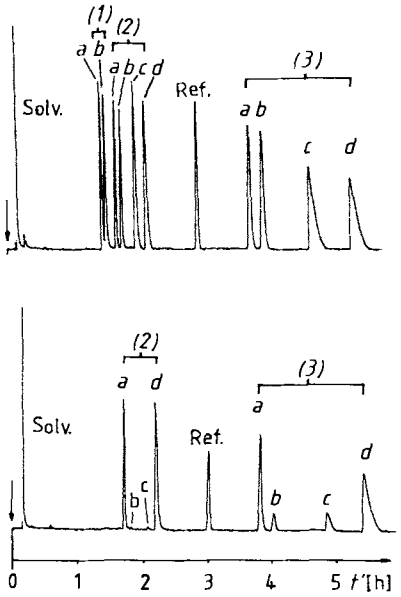


Fig. 1. Separation of enantiomers and diastereomers of chiral spiroketals by complexation chromatography on (*R*)-*(4)* (0.12 m in squalane) at 60 °C. Top: Separation of the racemic enantiomeric pairs *(1a, b)*, $\alpha = 1.04$; *(2a, b)*, $\alpha = 1.05$; *(2c, d)*, $\alpha = 1.09$; *(3a, b)*, $\alpha = 1.06$; *(3c, d)*, $\alpha = 1.15$. Bottom: Analysis of enantiomer-enriched (2*S*,5*R*/*S*)-*(2)* and (2*S*,5*R*/*S*)-*(3)*. Reference standard: *n*-decane; solvent: ethyl acetate; column: 100 m × 0.5 mm nickel capillary, carrier gas: 2.8 ml/min N_2; split 1:50.

As follows from Figure 1 the *Z*- and *E*-diastereomers of *(2)* and *(3)*, which are present in different concentrations, are each resolved into two enantiomeric pairs (*a, b* and *c, d*). The separation of the four configurational isomers was confirmed by the identity of the mass spectra for all four peak eluates *(a—d)* and their agreement with authentic *(2)*, and *(3)*, respectively[3].

Enantiomer-enriched Chalcogran (2*S*,5*R*/*S*)-*(3)* was obtained from (*S*)-1,2-epoxybutane (enantiomeric excess 69 ± 0.5%[4]), which was prepared racemization-free from technical (*R*)-2-amino-1-butanol (ee 69 ± 0.5%[5]) *via* the trimethylammonium hydroxide by Hofmann elimination; (2*S*,5*R*/*S*)-*(2)* was synthesized from (*S*)-epoxypropane[4] (ee 96.4 ± 0.2%[4]) according to the method of *Mori et al.*[1c]. The chromatogram is shown in Figure 1.

The appearance of pairwise unequal peak areas ($a/b = d/c$) in Figure 1 proves the separation into two enantiomeric pairs. Furthermore, the enantiomeric excess determined by integration for (2*S*)-configurated *(3)* (69 ± 0.5%) and *(2)* (96.3 ± 0.2%) confirms the racemization-free synthesis[1c]. The two (2*S*)-configurated isomers of *(2)* and of *(3)* both exhibit the weakest and the strongest coordinative interaction

with *(R)-(4)*. It follows therefore that the chiral discrimination of the enantiomeric pairs (*a*, *b* and *c*, *d*) is determined by the absolute configuration at the chiral spiro center C-5. Assuming[1b] that the *E* isomers of *(2)* and *(3)* undergo the stronger interaction with *(R)-(4)* on steric grounds, the assignment of the peaks can be given as follows: $a = 2S,5S$, $b = 2R,5R$, $c = 2R,5S$ and $d = 2S,5R$. The splitting patterns of *(2)* and *(3)* on *(R)-(4)* are identical (Fig. 1, bottom). Therefore, a rule developed earlier[4] for homologous oxiranes for correlation of the absolute configuration with the retention behavior on an optically active metal complex is also valid for spiroketals and can thus be used for determining the configuration at C-2.

To our knowledge this is the first direct gas chromatographic resolution of enantiomers of a chiral pheromone. Complexation chromatography surpasses other methods[6], since purification and derivatization are unnecessary and only a small sample size is required.

Received: December 4, 1979 [Z 472 IE]
German version: Angew. Chem. *92*, 473 (1980)

CAS Registry numbers:
(R,R)-(3), 69744-44-1; *(R,S)-(3)*, 70427-57-5; *(S,R)-(3)*, 69744-43-0; *(S,S)-(3)*, 70427-58-6

[1] a) *W. Francke, V. Heemann, B. Gerken, J. A. A. Renwick, J. P. Vité*, Naturwissenschaften *64*, 590 (1977); b) *L. R. Smith, H. J. Williams, R. M. Silverstein*, Tetrahedron Lett. *1978*, 3231; c) *K. Mori, M. Sasaki, S. Tamada, T. Suguro, S. Masuda*, Tetrahedron *35*, 1601 (1979).

[2] a) *R. Rossi*, Synthesis *1978*, 413, and references cited therein; b) *J. P. Vité, J. A. A. Renwick*, Z. Angew. Entomol. *82*, 112 (1976).

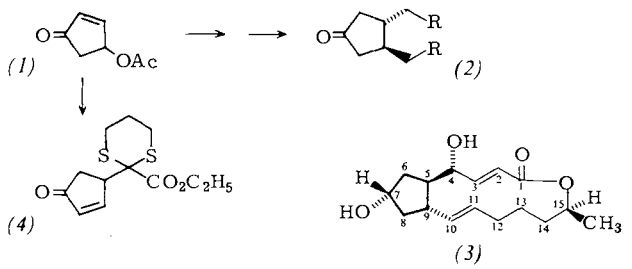
[3] Varian MAT 111, coupled GC-MS, *m/e* (*M*$^+$): 128 *(1)*, 142 *(2)*, 156 *(3)*.

[4] *V. Schurig, B. Koppenhoefer, W. Bürkle*, Angew. Chem. *90*, 993 (1978); Angew. Chem. Int. Ed. Engl. *17*, 937 (1978).

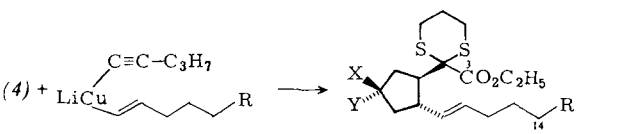
[5] Determined as trifluoroacetic acid derivative on Chirasil-Val: *H. Frank, G. J. Nicholson, E. Bayer*, Angew. Chem. *90*, 396 (1978); Angew. Chem. Int. Ed. Engl. *17*, 363 (1978).

[6] In the case of pheromones, the use of chiral NMR shift reagents [7a] is limited by purity criteria, amount of substance required, and complexity of the spectra. The indirect gas chromatographic method using diastereomers [7b] requires the presence of functional groups which are derivatized free of racemization.

[7] a) *T. E. Stewart, E. L. Plummer, L. L. McCandless, J. R. West, R. M. Silverstein*, J. Chem. Ecol. *3*, 27 (1977); b) *K. Kruse, W. Francke, W. A. König*, J. Chromatogr. *170*, 423 (1979).

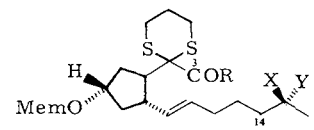


ous steps[4d], is possible. We first prepared the intermediates *(6a)* and *(6b)* from the oxo esters *(4)*[1b] by Michael addition of the cuprates *(5a)* and *(5b)* (see Table 1).



(6), X, Y = O;
(7), X = OH, Y = H;
(5-9a), R = Cl; *(5-9b)*, R =
(8), X = H, Y = OH;
(9), X = H, Y = OMem;
(9c), X = H, Y = OMem, R = C≡N

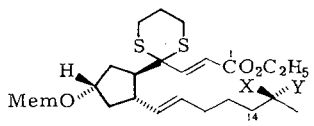
The alcohols *(7)* were obtained with high stereoselectivity by selectride reduction[6] of *(6)*, the epimers *(8)* by Walden inversion[7] of *(7)*. Both alcohols can be converted in the usual way into the mem-ethers *(9)*[8]. Lengthening of the side chain of *(9a)* affords *(9c)*, which on reaction with methyl lithium and subsequent hydrolysis of the imine gives the ketone *(10)*. Compound *(10)* can also be obtained by hydrolysis of the ketal *(9b)*.



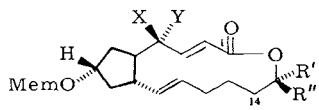
(10), X, Y = O, R = OC_2H_5
(11), R = OC_2H_5
(12), R = H

(11, 12a), X = H, Y = O–Si$(CH_3)_2$–C$(CH_3)_3$
(11, 12b), X = O–Si$(CH_3)_2$–C$(CH_3)_3$, Y = H

With other organometallic compounds, various other groups could be incorporated at C-15; in principle there is also the possibility of preparing the corresponding lactam *via* the imine (direct reduction!). After protection of the hydroxy groups, reduction of the carbonyl groups in the side chain of *(10)* affords a mixture of the epimeric silyl ethers *(11a)* and *(11b)*.



(13a), X = H, Y = O–Si–
(13b), X = O–Si–, Y = H
(14a), X = H, Y = OH
(14b), X = OH, Y = H
(15), X–Y = –S$(CH_2)_3$S–
(16), X, Y = O
(17a), X = H, Y = OH
(17b), X = OH, Y = H



(15-17a), R' = H, R'' = CH_3; *(15-17b)*, R' = CH_3, R'' = H

Stereoselectivity was not considered an aim at this juncture, since *Corey*[4a] had already described a markedly higher

A Novel Entry to Brefeldin A[**]

By *Yetkin Köksal, Peter Raddatz*, and *Ekkehard Winterfeldt*[*]

In order to exploit the synthetic potential of 4-oxo-2-cyclopentenyl acetate *(1)* for the synthesis of *trans*-disubstituted cyclopentanones by successive Michael addition [*(1)*→*(2)*] we chose as synthesis target the macrolide antibiotic brefeldin *(3)*[2], previously isolated from *Penicillium Brefeldianum*. *(3)* displays antifungal and cytostatic activity. Its structure and composition were first elucidated in 1964[3]; a few total syntheses and special reactions of this lactone have already been described[4].

Since *(1)* is available as optically active compound[5], in principle, an enantioselective synthesis of *(3)*, which hitherto could only be achieved *via* a tedious route involving numer-

[*] Prof. Dr. E. Winterfeldt, Dipl.-Chem. Y. Köksal, Dipl.-Chem. P. Raddatz
Institut für Organische Chemie der Universität Hannover
Schneiderberg 1B, D-3000 Hannover (Germany)

[**] Cyclopentenones, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *A. von Wartburg* and Dr. *H. Hauth*, Sandoz AG, Basel (Switzerland) for supplying us with natural brefeldin A.—Parts 1 and 2, see [1a] and [1b].

rate of formation of the lactone derivative with a natural configuration on C-15, so it appeared possible to exploit this effect for the separation of the epimers. For completion of the other chains the mixture of the aldehydes *(12a)* and *(12b)* is first prepared by reduction of *(11a)* and *(11b)* with $LiAlH_4$ followed by reoxidation; subsequent Wittig olefination affords the unsaturated esters *(13)*.

We removed the silyl ether groups in *(13)* with fluoride ions to give a mixture of the alcohols *(14)*, without separation of the epimers. The hydroxy acids obtained on hydrolysis could be cyclized with α-chloro-*N*-methylpyridinium iodide according to the method of *Mukaiyama*[9] to give a mixture of the lactones *(15)*, which is converted by cleavage of thioketal into the ketones *(16)* (see Table 1).

Table 1. Some physical data of the compounds *(6a)*, *(6b)*, *(15a)* + *(15b)*, and *(16a)* + *(16b)*; $M^{\oplus}$ determined mass spectrometrically.

(6a), IR ($CHCl_3$): 3040, 1600, 1740, 1720 cm^{-1}; ^1H-NMR ($CDCl_3$): $\delta = 5.4$ (2) m, 4.32 (2) q ($J = 7$ Hz), 3.53 (2) t ($J = 6$ Hz), 2.33—3.8 (6) m, 1.5—2.3 (10) m, 1.35 (3) t ($J = 7$ Hz); MS (80 °C): $m/e = 376$ (15%, $M^{\oplus}$), 329 (5), 303 (43), 191 (58), 145 (100); $M^{\oplus}$ (^{35}Cl and ^{37}Cl): calc. 376.0934, obs. 376.0935 and calc. 378.0904, obs. 378.0910

(6b), IR (CCl_4): 1750, 1730, 1070 cm^{-1}; ^1H-NMR ($CDCl_3$): $\delta = 5.35$ (2) m, 4.21 (2) q ($J = 7$ Hz), 3.97 (4) s, 2.35—3.6 (8) m, 1.44—2.3 (10) m, 1.23 (3) t ($J = 7$ Hz), 1.2 (3) s; MS (200 °C): $m/e = 428$ (5%, $M^{\oplus}$), 413 (5), 355 (19.5), 191 (73.5), 163 (23), 145 (100), 87 (96.5)

(15a) + *(15b)*: IR (CCl_4): 1712, 1630 cm^{-1}; ^1H-NMR (CCl_4): $\delta = 6.96$, 6.54 (1) d ($J = 15.5$ Hz), 5.99, 5.96 (1) d ($J = 15.5$ Hz), 5.2 (2) m, 4.9 (1) m (H-15), 4.6 (2) s (OCH_2O), 4.08 (1) m (H-7), 3.5 (4) m (OC_2H_4O), 3.3 (3) s (OCH_3), 2.5—3.2 (4) m, 1.2—2.5 (12) m, 1.26, 1.22 (3) d ($J = 6$ Hz, C—CH_3); MS (160 °C): $m/e = 455$ (4%, $M^{\oplus}$), 427 (2), 412 (1), 380 (7), 367 (14), 350 (11), 89 (100); $M^{\oplus}$ calc. 456.2004, obs. 456.2004

(16a) + *(16b)*: IR (CCl_4): 1728, 1702, 1630 cm^{-1}; ^1H-NMR (CCl_4): $\delta = 7.69$, 7.32 (1) d ($J = 16$ Hz), 6.31, 6.30 (1) d, 5.5 (2) m, 5.2, 4.6 (1) m (H-15), 4.6 (2) s (OCH_2O), 4.1 (1) m (H-7), 3.5 (4) m (OC_2H_4O), 3.29 (3) s (OCH_3), 1.2—2.3 (12), 1.3, 1.21 (3) d ($J = 6$ Hz, C—CH_3); MS (380 °C): $m/e = 366$ (2%, $M^{\oplus}$), 290 (7.5), 261 (10), 89 (100); $M^{\oplus}$ calc. 366.2042, obs. 366.2040

Also in our lactonization technique, no differences attributable to alternative configurations at C-15 could be observed; however, we could confirm the high stereospecificity of the reduction of the oxo group on C-4 in *(16)* described by *Bartlett*[4c].

On reduction with $NaBH_4$ (−78 °C), the mixture of the C-15 epimeric ketones *(16)* furnished only two easily separable alcohols, namely *(17a)* and *(17b)*, of which *(17a)* could be resolved with $TiCl_4$ into sterically pure brefeldin A *(3)*, whose IR, NMR and mass spectra as well as TLC behavior were identical with those of an authentic sample of the natural product.

Experimental

(6a): A solution of 5-chloro-1-iodo-1-pentane (6.5 g, 28 mmol) in anhydrous ether (80 ml) was added at −78 °C to a solution of 1.6 N butyllithium (17.5 ml, 28 mmol) in hexane and the mixture stirred for 1 h at −78 °C. A mixture of copper(I) 1-pentyn-1-ide (3.67 g, 28 mmol) and tris(dimethylamino)phosphane (9.2 g, 56 mmol) in anhydrous ether (50 ml) was prepared in a separate flask and stirred for 0.5 h at room temperature (yellow-brown solution). This mixture was then poured slowly at −78 °C into the solution of the organolithium reagent and the resulting mixture stirred for a further 0.5 h and then treated with a solution of *(4)* (7 mmol) in anhydrous ether (40 ml). After 1 h the reaction mixture was poured into 0.5 N HCl, extracted with ether, washed with 2 N HCl and saturated $NaHCO_3$ solution, dried over $MgSO_4$ and, after removal of the ether, chromatographed on silica gel (ether/petroleum ether 7:4); yield 2 g (76%).

(6b) was prepared analogously; yield 1.55 g (75%).

(15a) + *(15b)*: A solution of the seco acid mixture *(14a)* + *(14b)*, H instead of C_2H_5, in anhydrous acetonitrile was treated with 250 mg (2.5 mmol) of triethylamine and then syringed into a refluxing solution of α-chloro-N-methylpyridinium iodide (400 mg, 1.5 mmol) in acetonitrile. The mixture was allowed to boil for 1 h, the solvent removed *in vacuo*, and the residue taken up in ether, washed with 2 N HCl and saturated NaCl solution, dried over $MgSO_4$ and chromatographed after removal of solvent with ether/petroleum ether (7:4); yield 63 mg (68%).

(16a) + *(16b)*: A solution of $AgNO_3$ (70 mg, 0.4 mmol) and *N*-chlorosuccinimide (70 mg, 0.5 mmol) in acetonitrile (2 ml, 20% H_2O) was treated with 6 drops of lutidine and the mixture immediately poured into a solution of the mixture of *(15a)* + *(15b)* (16 mg, 0.035 mmol) in acetonitrile (1 ml). After 1.5 minute's stirring at room temperature a saturated solution of $NaHSO_3$ and NaCl was added and the reaction mixture extracted with CH_2Cl_2. The organic phase was washed with 2 N HCl and saturated $NaHCO_3$ solution, dried over $MgSO_4$ and, after removal of the solvent in a vacuum, chromatographed on silica gel (ether); yield 11 mg (83%).

Received: January 10, 1980 [Z 473 IE]
German version: Angew. Chem. 92, 486 (1980)

CAS Registry numbers:
(1), 768-48-9; *(3)*, 20350-15-6; *(4)*, 72103-46-9; *(5a)*, 73816-16-7; *(5b)*, 73816-17-8; *(6a)*, 73805-63-7; *(6b)*, 73805-64-8; *(7a)*, 73805-65-9; *(7b)*, 73805-66-0; *(8a)*, 73836-96-1; *(8b)*, 73836-97-2; *(9a)*, 73805-67-1; *(9b)*, 73805-68-2; *(9c)*, 73805-69-3; *(10)*, 73805-70-6; *(11a)*, 73805-71-7; *(11b)*, 73836-98-3; *(12a)*, 73805-72-8; *(12b)*, 73836-99-4; *(13a)*, 73805-73-9; *(13b)*, 73837-00-0; *(14a)*, 73805-74-0; *(14b)*, 73837-01-1; *(15a)*, 73805-75-1; *(15b)*, 73837-02-2; *(16a)*, 73805-76-2; *(16b)*, 73837-03-3; *(17a)*, 73805-77-3; *(17b)*, 73837-04-4

[1] a) *V. Osterthun, E. Winterfeldt*, Chem. Ber. *110*, 146 (1977); b) *Y. Köksal, V. Osterthun, E. Winterfeldt*, Justus Liebigs Ann. Chem. *1979*, 1300.
[2] *E. Härri, W. Loeffler, H. P. Sigg, H. Stähelin, Ch. Tamm*, Helv. Chim. Acta *46*, 1235 (1963).
[3] *H. P. Sigg*, Helv. Chim. Acta *47*, 1401 (1964).
[4] a) *E. J. Corey, R. H. Wollenberg*, Tetrahedron Lett. *1976*, 4701; b) *E. J. Corey, R. H. Wollenberg, D. R. Williams, ibid. 1977*, 2243; *R. Baudony, P. Crabbé, A. E. Greene, C. LeDrian, A. F. Orr, ibid. 1977*, 2973; *D. P. Curran, D. Scholz*, Monatsh. Chem. *108*, 1401 (1977); c) *P. A. Bartlett, F. R. Green*, J. Am. Chem. Soc. *100*, 4858 (1978); d) *T. Kitahara, K. Mori, M. Matsui*, Tetrahedron Lett. *1979*, 3021.
[5] *M. Grill, R. W. Rickards*, Tetrahedron Lett. *1979*, 1539.
[6] Selectride = Li[(*sec*-C_4H_9)$_3$BH].
[7] *A. K. Bose, B. Lal, W. A. Hoffman, M. S. Manhas*, Tetrahedron Lett. *1973*, 1619.
[8] *E. J. Corey, J.-L. Gras, P. L. Ulrich*, Tetrahedron Lett. *1975*, 617; Mem = methoxy-ethoxymethyl($CH_3OC_2H_4OCH_2$—).
[9] *T. Mukaiyama, M. Usui, K. Saigo*, Chem. Lett. *1976*, 49.

Euglenapterin—An Unusual New Natural Pteridine Derivative from *Euglena gracilis*

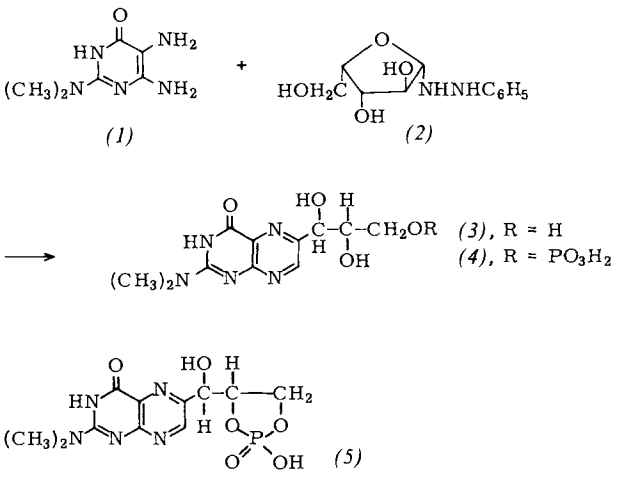
By *Manfred Böhme, Wolfgang Pfleiderer, Erich F. Elstner,* and *Wilhelm J. Richter*[*]

The phytoflagellate *Euglena gracilis* shows both animal and plant metabolic characteristics. During studies on the constituents[1] of this organism, three components showing

[*] Prof. Dr. W. Pfleiderer, Dipl.-Chem. M. Böhme
Fakultät für Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)
Prof. Dr. E. F. Elstner
Institut für Botanik und Mikrobiologie der Technischen Universität
München (Germany)
Dr. W. J. Richter
Zentrale Funktion Forschung, Ciba-Geigy AG
Basel (Switzerland)

yellowish fluorescence were obtained after treatment of the natural material with MnO_2 in acetic acid solution; they were regarded as possible unconjugated pteridines. However, since none of these products could be identified by chromatographic or spectroscopic methods as one of the natural pterins we have re-investigated them. First of all, the component showing the greatest migration on chromatography on cellulose with *n*-propanol/1% ammonia (2/1) ($R_f = 0.48$) was enriched chromatographically and then purified by HPLC on RP-8 carrier material.

The field desorption mass spectrum (FD-MS) of the isolated material gave a $M^{\oplus\ominus}/MH^{\oplus}$ double signal ($m/e = 281/282$) corresponding to the molecular formula $C_{11}H_{15}N_5O_4$, which was confirmed by the high resolution electron impact mass spectrum (EI-MS) of the tetrakis(trimethylsilyl) derivative obtained by reaction with bis(trimethylsilyl)acetamide in pyridine at 60 °C ($M^{\oplus\ominus}$ at $m/e = 569$, $C_{23}H_{47}N_5O_4Si_4$). The possible structure of a 2-dimethylamino-6-trihydroxypropyl-4-oxo-3,4-dihydropteridine could be deduced from the presence of four silylatable (acidic) H atoms, the characteristic mass spectrometric fragments, and UV spectra of the various forms of the molecule, which show a slight bathochromic shift relative to the pterins. This structure could be confirmed, and the stereochemistry of the trihydroxypropyl side chain established, by chemical synthesis of all four stereoisomers from 5,6-diamino-2-dimethylamino-4-oxo-3,4-dihydroxypyrimidine *(1)* and the phenylhydrazones of D- and L-arabinose and D- and L-xylose *(2)* by conventional methods of pterin chemistry[2].



(1) *(2)* *(3)*, R = H; *(4)*, R = PO_3H_2 *(5)*

Comparison of the CD spectra of the four synthetic products with that of the natural material reveals the side chain to have the L-*threo* configuration *(3)*, and that a structural analogy exists with ciliapterin which was isolated from *Tetrahymen pyriformis*[3].

Once the constitution of euglenapterin *(3)* had been established, the structures of the other two yellow-fluorescing constituents, which had already been recognized as phosphates[1], could be assigned as the 3′-phosphate *(4)* (FD-MS: $MH^{\oplus}$ at $m/e = 362$; EI-MS after trimethylsilylation: $M^{\oplus\ominus}$ of the expected pentakis(trimethylsilyl) derivative at $m/e = 721$ and characteristic fragmentation) and as the 2′,3′-cyclophosphate *(5)* (FD-MS: $MH^{\oplus}$ at $m/e = 344$, $MNa^{\oplus}$ at $m/e = 366$; EI-MS after trimethylsilylation: $M^{\oplus\ominus}$ of the tris(trimethylsilyl) derivative at $m/e = 559$). Phosphorylation of *(3)* with $POCl_3$ in trimethyl phosphate by the Yoshikawa method[4], which preferentially attacks the primary OH function, leads to good yields of *(4)* or *(5)*, depending upon the conditions of work-up. Both substances (isolated as barium salts) are chromatographically and spectrometrically identical with the natural products.

Euglenapterin is thus the first example of a novel natural type of pterin. It remains to be seen whether the structural modification of the 2-amino group of the pterin system[5] is of general biological and physiological relevance.

Received: January 14, 1980 [Z 474 IE]
German version: Angew. Chem. *92*, 474 (1980)

CAS Registry numbers:
(1), 61693-31-0; L-threo-*(3)*, 73789-39-6; D-threo-*(3)*, 73789-40-9; L-erythro-*(3)*, 73789-41-0; D-erythro-*(3)*, 73804-21-4; L-threo-*(3)*, 4-TMS, 73789-42-1; *(4)*, 73789-43-2; *(4)*, 5-TMS, 73789-44-3; *(5)*, 73789-45-4; *(5)*, 3-TMS, 73789-46-5; D-xylose phenylhydrazone, 14685-87-1; L-xylose phenylhydrazone, 28640-06-4; D-arabinose phenylhydrazone, 28767-74-0; L-arabinose phenylhydrazone, 622-12-8

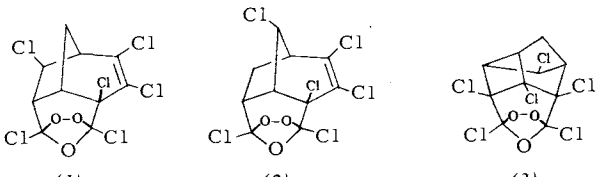
[1] *E. F. Elstner, A. Heupel*, Arch. Biochem. Biophys. *173*, 614 (1976).
[2] *M. Viscontini, R. Provenzale, S. Ohlgart, J. Mallevialle*, Helv. Chim. Acta *53*, 1202 (1970).
[3] *G. W. Kidder, V. C. Dewey*, J. Biol. Chem. *243*, 826 (1968).
[4] *M. Yoshikawa, T. Kato, T. Takenishi*, Bull. Chem. Soc. Jpn. *42*, 3505 (1969).
[5] *W. Pfleiderer*, Angew. Chem. *75*, 993 (1963); Angew. Chem. Int. Ed. Engl. *3*, 114 (1964).

Ozonolysis of 1,2-Dichloroacenaphthylene

By *Helmut Seltzer, Siegmar Gäb*, and *Friedhelm Korte*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In the ozonolysis of olefins, monomeric normal ozonides (1,2,4-trioxolanes) are obtained if the cycloaddition of the carbonyl oxide ($>C=\overset{\oplus}{O}-O^{\ominus}$) to the carbonyl compound can successfully compete with other stabilizing reactions. The activity of the carbonyl function and the lifetime of the carbonyl oxide play a decisive role[1]. If both groups are in one molecule, then intramolecular cycloaddition is preferred, particularly if the two groups cannot be removed far from each other spatially after the cycloreversion of the primary ozonide (1,2,3-trioxolane). In agreement with this, the chlorine-containing ozonides *(1)*, *(2)*, and *(3)* are formed in high yields from the corresponding chloroolefins[2], while the ozonization of *trans*-2,3-dichloro-2-butene affords only small amounts of products ascribable to a 3,5-dichloro-1,2,4-trioxolane[3].

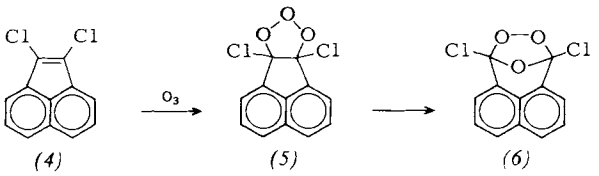


(1) *(2)* *(3)*

The formation of a monomeric ozonide should also be favored on steric grounds in the case of 1,2-dichloroacenaphthylene *(4)*. When *(4)* is ozonized at 0 °C in inert solvents, two stable O_3-addition compounds can be isolated from the reaction mixture by chromatography on silica gel. On the basis of analytical data the structures *(5)* and *(6)* are proposed for the colorless crystalline substances[4].

[*] Prof. Dr. F. Korte, Dr. H. Seltzer, Dr. S. Gäb
Institut für Ökologische Chemie der
Gesellschaft für Strahlen- und Umweltforschung mbH München
D-8050 Freising-Attaching (Germany)
and Lehrstuhl für Ökologische Chemie, Institut für Chemie
der Technischen Universität München
D-8050 Freising-Weihenstephan (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0606-474 $ 02.50/0



(4) (5) (6)

According to molecular weight (268, cryoscopically in benzene) and spectroscopic data, compound *(6)* (1,4-dichloro-1,4-epoxy-1*H*,4*H*-naphtho[1,8-*de*][1,2]dioxepin) is a monomeric ozonide. The EI mass spectrum shows the molecular ion with characteristic isotope distribution for two Cl atoms at $m/e = 268$. In the IR spectrum bands appear at 1040 and 1090 cm^{-1}, which are typical for the C—O stretching vibrations of 1,2,4-trioxolanes[5]. The total of seven ^{13}C-NMR signals between $\delta = 120.42$ and 133.40 ([D_6]acetone, TMS) is consistent with the molecule having a symmetrical structure.

The ^{13}C-NMR spectrum of *(5)* shows the same number of lines between $\delta = 116.39$ and 136.97 ($CDCl_3$, TMS). The observed upfield shift of the trioxolane carbon in *(5)* ($\delta = 116.39$) compared with in *(6)* ($\delta = 120.42$) is analogously found with trioxolane protons in the primary and normal ozonides of *cis*- and *trans*-alkenes[6]. Both the molecular weight (266, cryoscopically in benzene) and the FD mass spectrum ($m/e = 268$, 2 Cl, M^+) of *(5)* indicate a monomeric ozonide.

For further differentiation between primary ozonide and normal ozonide, either the larger thermal stability of *(6)*, or the difference in behavior of *(5)* and *(6)* towards tetracyanoethylene (TCNE) can be consulted[7]. While *(5)* is no longer detectable after a short while in the presence of TCNE, *(6)* remains unchanged[8]. The reaction sequence *(5)*→*(6)* (TLC detection) under the conditions of ozonolysis is important for the assignment.

The ozonide *(6)* decomposes slowly under our reaction conditions into 1,8-naphthalenedicarboxylic anhydride[9], which, after ozonolysis of *(4)*, can be isolated from the reaction mixture in over 70% yield.

Procedure

A solution of *(4)* (2.2 g) in dichloromethane (150 ml) is treated at 0 °C with ozone until the yellow color disappears. After distillation of the solvent in a vacuum the colorless, crystalline residue is separated by column chromatography at −7 °C on silica gel (eluent: *n*-hexane/benzene 1:1). The purity of the fractions is monitored by thin-layer chromatography (TLC plates Kieselgel 60, Merck; eluent: *n*-hexane/benzene 1:1; on spraying with diphenylamine the spots of *(5)*, $R_f = 0.27$, and *(6)*, $R_f = 0.51$, turn dark grey. One obtains 180 mg (6.7%) of *(5)* and 260 mg (9.7%) of *(6)*.

Received: January 23, 1980 [Z 475 IE]
German version: Angew. Chem. 92, 483 (1980)

CAS Registry numbers:
(4), 18105-08-3; *(5)*, 73747-05-4; *(6)*, 73747-06-5; ozone, 10028-15-6

[1] *R. Criegee*, Angew. Chem. *87*, 765 (1975); Angew. Chem. Int. Ed. Engl. *14*, 745 (1975), and references cited therein.

[2] *S. Gäb, S. Nitz, H. Parlar, F. Korte*, Angew. Chem. *88*, 479 (1976); Angew. Chem. Int. Ed. Engl. *15*, 433 (1976); Chem. Ber. *111*, 1440 (1978); Compound *(3)* is obtained in 65% yield on ozonolysis of 3a,4,5,5a,5b,6-hexachloro-1a,2,3,3a,5a,5b-hexahydro-1,3-methano-1*H*-cyclobuta[*gh*]pentalene; m.p. 126–128 °C. ^{13}C-NMR ([D_6]acetone): $\delta = 120.19$, 122.01 (trioxolane-C atoms).

[4] The elemental analyses gave satisfactory values.

[5] *P. S. Bailey*: Ozonation in Organic Chemistry. Vol. I. Academic Press, New York 1978, and references cited therein.

[6] *L. J. Durham, F. L. Greenwood*, J. Org. Chem. *33*, 1629 (1968).

[7] *R. Criegee, P. Günther*, Chem. Ber. *96*, 1564 (1963).

[8] The finding that *(6)* is formed on ozonolysis of *(4)* in the presence of TCNE, but not in the reaction of *(5)* with TCNE can be explained in terms of different reaction paths.

[9] 2,3,4,6-Tetrachlorobicyclo[3.2.1]oct-3-ene-2,7-dicarboxylic anhydride (m.p. 198—200 °C) is formed in good yields on photolysis ($\lambda > 290$ nm) of the stable ozonide *(1)* in CCl_4.

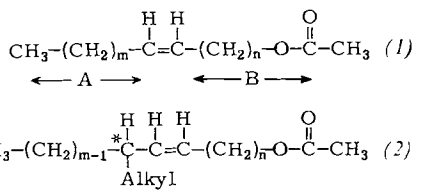
Differentiation between Chiral Pheromone Analogues by Chemoreceptors[**]

By *Hans Jürgen Bestmann, Hans Ludwig Hirsch, Hans Platz, Marlies Rheinwald,* and *Otto Vostrowsky*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

On the basis of structure-activity studies on pheromones and their analogues[1], we recently proposed a dynamic model for the interaction between pheromone molecule and the receptor region on the dendritic membrane of the sensilla of Lepidoptera[2]: the signal molecule is considered to be flexibly incorporated into the entire receptor region[3].

Presumably the receptor region contains several chirality elements, and the sections of the multiply prochiral pheromone molecule [*e.g.* A or B in *(1)*] will only fit into one of the two enantiotopic sides of the respective prochirality centers. This means that the signal molecule is incorporated in a definite conformation. Changes in the receptor region are also to be expected during this process. If these model concepts are correct, then receptors showing a maximum response to achiral pheromone molecules of type *(1)* should be able to distinguish between the enantiomers of chiral pheromone analogues *(2)* because additional diastereoisomeric interactions occur and only one of the two enantiomers can extensively adopt the conformation of section A of the signal molecule as required by the receptor region.



(1)

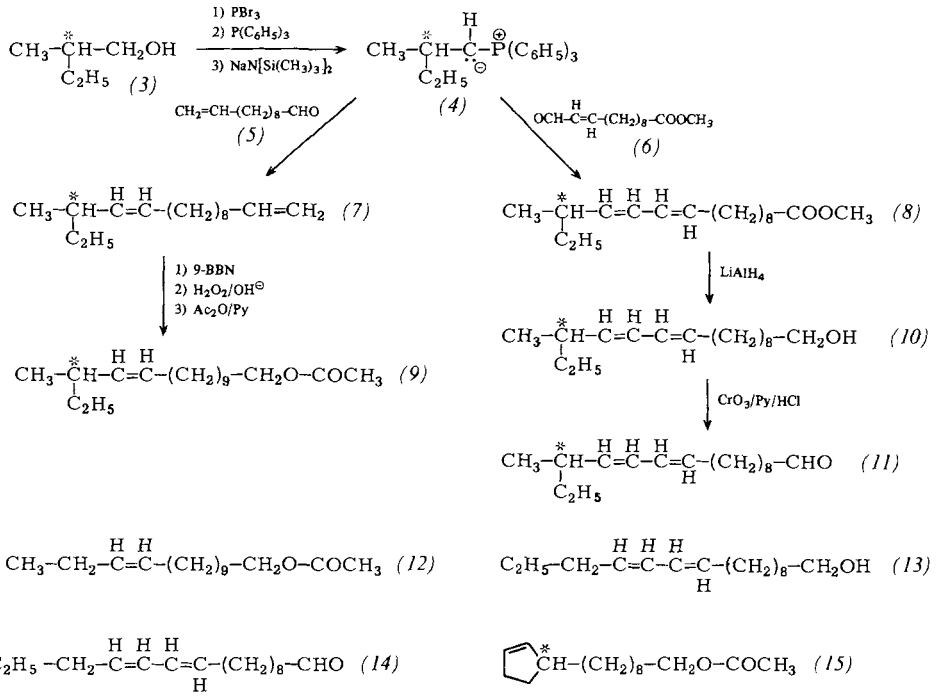
(2)

We have prepared the optically active pheromone analogues *(9)*, *(10)*, and *(11)* in order to test this postulate.

The synthon for the chiral moiety was 2-methyl-1-butanol *(3)*, whose (*S*)-(−)-enantiomer is commercially available. Attempts to obtain the (*R*)-(+) antipode by conventional resolution of (*R,S*)-*(3)* were unsuccessful. However, we were able to resolve racemic 2-methylbutyric acid with (−)-α-phenylethylamine to give the (*R*)-(−) enantiomer ($[\alpha]_D^{20} = -15.70°$ (100%), 90% optical purity). Its reduction to (*R*)-(+)-*(3)* with $LiAlH_4$ can be accomplished without racemization ($[\alpha]_D^{20} = 4.060°$ (100%), 90% optical purity). The enantiomers of *(3)* are transformed into the bromides and thence,

[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. H. L. Hirsch, Dipl.-Chem. H. Platz, M. Rheinwald, Dr. O. Vostrowsky
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)

[**] Pheromones, Part 31. We wish to thank Hoechst AG for supplying *O. nubilalis*, Prof. Dr. *K. E. Kaissling* for *B. mori*, and Prof. Dr. *W. L. Roelofs* and Dr. *H. F. Goonewardene* for *A. velutinana*, as well as Prof. Dr. *O. L. Chapman* and Dr. *J. A. Klun* for the test compound *(15)*.—Part 30: *H. J. Bestmann, T. Brosche, K. H. Koschatzky, K. Michaelis, H. Platz, O. Vostrowsky, W. Knauf*, Tetrahedron Lett. *1980*, 747.



by treatment with triphenylphosphane into the phosphonium bromides, from which the corresponding ylides *(4)* are generated on reaction with sodium bis(trimethylsilyl)-amide[4]. Their reaction with 10-undecenal *(5)* affords diolefins *(7)*, which can be converted by hydroboration with 9-borabicyclo[3.3.1]nonane (9-BNN), oxidation, and subsequent acetylation into the pheromone analogues *(9)* (cf. Table 1).

Z-Stereoselective Wittig reaction of *(4)* with the formyl ester *(6)* leads to the hexadecadiene esters *(8)*, whose reduction with $LiAlH_4$ gives the 14-methylbombykols *(10)*. Oxidation of *(10)* affords the 14-methylbombykals *(11)*.

Table 1. Yields, boiling points, and rotations of the compounds synthesized [*(9)*, in ethanol; *(10)*, neat; *(11)*, in chloroform].

Cpd.	Yield [%]	B.p. [°C/torr] [a]	$[\alpha]_D^{20}$	*c* [g/100 ml]
(R)-(−)-*(9)*	80	100/0.05	− 6.067°	2.65
(S)-(+)-*(9)*	94	100—110/0.05	+ 6.454°	2.82
(R)-(−)-*(10)*	88	120/0.05	−10.825°	
(S)-(+)-*(10)*	94	120—125/0.05	+11.660°	
(R)-(−)-*(11)*	60	110/0.05	− 9.564°	2.98
(S)-(+)-*(11)*	77	105—110/0.05	+10.419°	2.86

[a] Bulb-to-bulb distillation, bath temperature.

We have measured the electrophysiological activity of the two enantiomers and of the racemate of *(9)* in an electroantennogram (EAG) test[5] on *Ostrinia nubilalis* and *Argyrotaenia velutinana*. Both species use (*Z*)-11-tetradecenyl acetate *(12)*[6] as the principal pheromone component; *i.e. (9)* is a 13-ethyl derivative of the species-specific pheromone. *(10)* and *(11)* were tested on *Bombyx mori*, which contains the pheromones bombykol *(13)*[7] and bombykal *(14)*[8] (Table 2).

Table 2. Relative EAG activities [1b] of the compounds *(9)*—*(15)*. Activity of the species-specific pheromone ≙ 100.

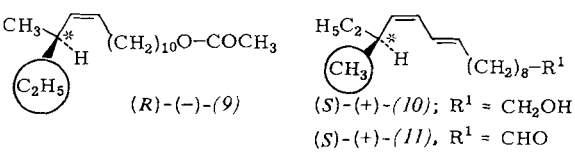
Cpd.	*O. nubilalis*	*A. velutinana*	Cpd.	*Bombyx mori*
(12)	100	100	*(13)*	100
(R)-(−)-*(9)*	10	10	*(S)*-(+)-*(10)*	10
(R,S)-*(9)*	1	1	*(R,S)*-*(10)*	3—10
(S)-(+)-*(9)*	0.1	0.1	*(R)*-(−)-*(10)*	3
(S)-(−)-*(15)*	0.3	0.1	*(14)*	100
(R,S)-*(15)*	0.03	0.03	*(S)*-(+)-*(11)*	10
(R)-(+)-*(15)*	0.01	0.01	*(R,S)*-*(11)*	3—10
			(R)-(−)-*(11)*	3

We have included the enantiomers synthesized by *Chapman et al.*[9] and the racemate of *(15)* in our measurements. In contrast to *(9)*, compound *(15)* is not free to adopt any conformation in part A of the molecule because it is fixed by the ring. In *(15)* the chirality center is located in part B.

The relative EAG activities listed in Table 2 show that the receptors are able to distinguish between the enantiomers in all cases. In the case of *Ostrinia* and *Agyrotaenia*, which use the same pheromone molecule although they belong to different families, *(R)*-*(9)* is one hundred times as effective as the (*S*) enantiomer. The enantiomers of *(15)* are also distinguished by the two species (factor of 10—30). The activity of the racemate lies between those of the enantiomers in all cases examined by the present statistical method[1b]. In a behavioral test the racemate of *(15)* was more effective than the antipodes for *Agyrotaenia velutinana*[9], but not in the EAG test.

Table 2 also shows that the activities of the mobile *(R)*-*(9)* and of the rigid *(S)*-*(15)* differ by a factor of 30 and 100, respectively, in the two species. Compared with the species-specific pheromone the activity of *(R)*-*(9)* is diminished only tenfold, but that of *(S)*-*(15)* 300- or 1000-fold.

Bombyx mori also distinguishes between the (*R*)- and the (*S*)-form of *(10)* and *(11)*. However, the (*S*)-enantiomer is only three times as active as the (*R*)-form, and the racemate lies between the two.



All these results support the above ideas concerning the dynamics of the interaction between pheromone molecule

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0606-476 $ 02.50/0

and chiral acceptor region. We consider it remarkable that the position of the additional side chain (circled) at the asymmetric C atom in the preferred enantiomers is the same. This applies to all the species examined so far, even when they belong to different families.

Received: January 2, 1980 [Z 477 IE]
German version: Angew. Chem. 92, 492 (1980)

CAS Registry numbers:
(R)-(3), 616-16-0; *(S)-(3)*, 1565-80-6; *(R)-(4)*, 73789-47-6; *(S)-(4)*, 54526-11-3; *(5)*, 112-45-8; *(6)*, 63024-87-3; *(R)-(7)*, 73789-48-7; *(S)-(7)*, 73789-49-8; *(R)-(8)*, 73789-50-1; *(S)-(8)*, 73789-51-2; *(R)-(9)*, 73804-22-5; *(S)-(9)*, 73804-23-6; *(R,S)-(9)*, 65340-57-0; *(R)-(10)*, 73789-52-3; *(S)-(10)*, 73789-53-4; *(R,S)-(10)*, 73804-24-7; *(R)-(11)*, 73789-54-5; *(S)-(11)*, 73789-55-6; *(R,S)-(11)*, 73804-25-8; *(12)*, 20711-10-8; *(13)*, 63024-96-4; *(14)*, 63024-98-6; *(R)-(15)*, 67920-76-7; *(S)-(15)*, 67920-79-0; *(R,S)-(15)*, 67886-20-8

[1] a) *O. Vostrowsky, H. J. Bestmann, E. Priesner*, Nachr. Chem. Tech. *21*, 501 (1973); b) *E. Priesner, M. Jacobson, H. J. Bestmann*, Z. Naturforsch. *C 30*, 283 (1975); c) *E. Priesner, H. J. Bestmann, O. Vostrowsky, P. Rösel, ibid. 32*, 979 (1977); *H. J. Bestmann*, Z. Angew. Entomol. *82*, 110 (1976).
[2] *H. J. Bestmann, P. Rösel, O. Vostrowsky*, Justus Liebigs Ann. Chem. *1979*, 1189; *H. J. Bestmann, O. Vostrowsky*, Seifen-Öle-Fette-Wachse *105*, 443 (1979).
[3] Cf. also the general proposals made by *A. S. V. Burgen, G. C. K. Roberts, J. Feeney*, Nature *253*, 753 (1975).
[4] *H. J. Bestmann, W. Stransky, O. Vostrowsky*, Chem. Ber. *109*, 1964 (1976).
[5] *D. Schneider*, Z. Vgl. Physiol. *40*, 9 (1957).
[6] *J. A. Klun, T. A. Brindley*, J. Econ. Entomol. *63*, 779 (1970); *W. L. Roelofs, A. Hill, R. Cardé*, J. Chem. Ecol. *1*, 83 (1975).
[7] *A. Butenandt, R. Beckmann, D. Stamm, E. Hecker*, Z. Naturforsch. *B 14*, 283 (1959).
[8] *G. Kasang, K. E. Kaissling, O. Vostrowsky, H. J. Bestmann*, Angew. Chem. *90*, 74 (1978); Angew. Chem. Int. Ed. Engl. *17*, 60 (1978).
[9] *O. L. Chapman, K. C. Mattes, R. S. Sheridan, J. A. Klun*, J. Am. Chem. Soc. *100*, 4878 (1978).

Intercalation Complexes of Metallocenes in Iron Oxide Chloride[**]

By *Hartwig Schäfer-Stahl* and *Raimund Abele*[*]

Iron oxide chloride (FeOCl) can accommodate guest atoms or molecules in its interlayer regions which are held together only by van der Waals forces. Amines[1], aromatic heterocycles[2], and alkali metals[3] may reduce some of the Fe^{3+} centers on inclusion. These inclusion compounds are of interest because of their semiconductor and superconductor properties and their catalytic behavior.

We prepared inclusion complexes from FeOCl and metallocenes in order to gain information about possible redox interactions.

As the host component we used violet-red FeOCl crystals (sieve fraction between 0.025 and 0.1 mm) which were obtained from Fe_2O_3 and $FeCl_3$ by annealing at 350—300 °C. Intercalation of the metallocenes can be accomplished between 20 and 110 °C in glyme under N_2, or directly from the gas phase in the case of $(C_5H_5)_2Fe$ and $(C_5H_5)_2Co$. The reaction was stopped on disappearance of the original FeOCl reflections in the Debye diagram. At higher temperatures other phases are formed; FeOCl reacts with the metallocenes of the alkaline earth metals and with $(C_5H_5)_2Mn$ and $(C_5H_5)_2V$ below room temperature with partial formation of $(C_5H_5)_2Fe$ and solvent-containing intercalation compounds[4].

The host crystal accommodates one guest molecule per five to seven formula units of FeOCl, *i.e.* (given two FeOCl units per unit cell) one guest molecule for about three unit cells. The expansion of the *b* axis (791.7 pm in FeOCl[5]) was about 518 pm in all cases. That is somewhat smaller than twice the van der Waals radius of the metallocenes for which 680 pm has been reported along the fivefold axis, and 560 pm perpendicular thereto. It could be demonstrated in the case of intercalation of $[C_5(CH_3)_5]_2Fe$ in FeOCl[7] that the planes of the intercalated rings are parallel to the *b* axis and project a little into the planes of the host lattice[8] with all the intermediate layers being occupied. Intercalation of the metallocenes in FeOCl is illustrated schematically in Figure 1. A similar situation has already been assumed in the intercalation compounds of metallocenes in dichalcogenides[6].

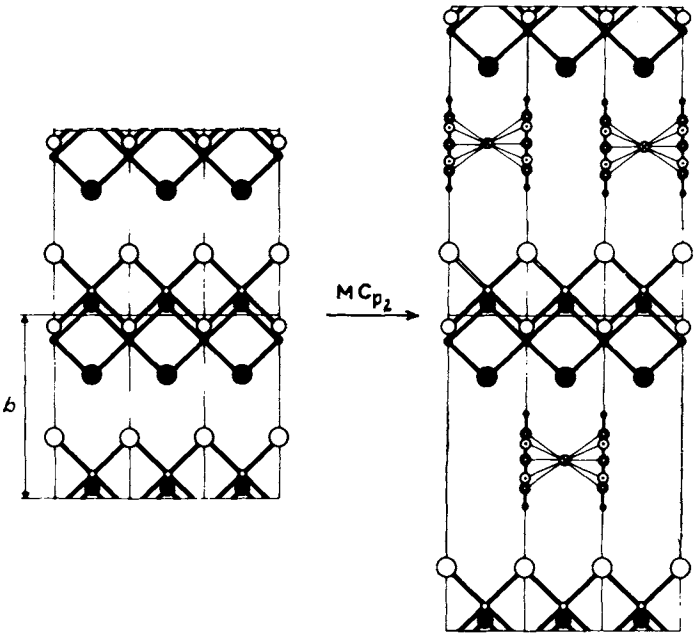


Fig. 1. Inclusion of metallocenes in FeOCl, schematic. • Fe^{3+}, $z=1/2$; • O^{2-}, $z=1/2$; ● Cl$^-$, $z=1/2$; ○ Fe^{3+}, $z=0$; ○ O^{2-}, $z=0$; ○ Cl$^-$, $z=0$; ⊗ M^{2+}, ○ C, • H.

The Mössbauer spectra of the intercalation complexes show a doublet. The quadrupole splitting is somewhat smaller than for FeOCl (Table 1). It must be concluded from the almost unchanged chemical shift that the high-spin Fe^{3+} state of the host lattice is retained on inclusion, *i.e.* that no reduction to Fe^{2+} occurs.

Table 1. Production and characterization of FeOCl intercalation complexes.

	Reaction conditions t [d]/T [°C]/solvent	b [pm]	Mössbauer parameters δFe	ΔE^Q [mm/s]
$NiCp_2 \cdot 6.6\,FeOCl$	8/ 20/Glyme	1310	0.49	0.69
$CoCp_2 \cdot 5.5\,FeOCl$	8/ 20/Glyme	1310	0.50	0.67
$FeCp_2 \cdot 6.3\,FeOCl$	8/ 20/Glyme	1310	0.48$_5$	0.64
$FeCp_2 \cdot 7.5\,FeOCl$	5/110/(Vacuum)	1310	0.49	0.66
$FeCp_2 \cdot 6.4\,FeOCl$	5/ 80/Glyme	1310	0.49	0.68
$CrCp_2 \cdot 7.1\,FeOCl$	8/ 20/Glyme	1310	0.49	0.69
FeOCl	30/350—300/(Vacuum)	792	0.41	0.92

Interestingly, the typical Mössbauer absorptions (quadrupole splitting $\Delta E^Q = 2.37$ mm/s) of ferrocene have completely disappeared in $FeCp \cdot 6\,FeOCl$. The transformation of ferrocene into the ferrocene cation is established by the appearance of the Mössbauer absorption band of the guest molecule, which is masked in the room temperature spectrum, as a singlet of chemical shift $\delta = 0.49$ mm/s at 4 K (alongside the 6-line system of the completely magnetically ordered iron

[*] Dr. H. Schäfer-Stahl, Dipl.-Chem. R. Abele
Fakultät für Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We are grateful to Dipl.-Chem. *A. Möller* for preliminary conductivity measurements.

centers of the host lattice). This corresponds to the singlet of $FeCp_2^+Cl^-$[9].

The observation that ferrocene is oxidized to the $FeCp^+$ ion on intercalation while the host lattice remains unchanged and shows only high-spin Fe^{3+} centers compellingly demonstrates that the intercalation compound must contain "free" electrons; we therefore propose the formulation $[Fe(C_5H_5)_2]^+ \cdot [6\,FeOCl] \cdot e$. The conductivity of the crystals is accordingly about 10^4 times greater than that of FeOCl. A compressed powder sample shows a conductivity of 10^{-3} $\Omega^{-1}\,cm^{-1}$ at room temperature, which lies in a region corresponding to typical semiconducting materials (*e.g.* doped germanium)[10].

Received: February 15, 1979;
supplemented: September 7, 1979 [Z 478 IE]
German version: Angew. Chem. 92, 493 (1980)

CAS Registry numbers:
$NiCp_2 \cdot FeOCl$, 73770-93-1; $CoCp_2 \cdot FeOCl$, 69952-12-1; $FeCp_2 \cdot FeOCl$, 69952-13-2; $CrCp_2 \cdot FeOCl$, 73770-94-2; FeOCl, 13870-10-5

[1] *P. Hagenmuller, J. Rouxel, J. Portier*, C. R. Acad. Sci. *254*, 2000 (1962); *P. Hagenmuller, J. Portier et al.*, Z. Anorg. Allg. Chem. *355*, 209 (1967).

[2] *F. Kanamaru, M. Shimada, M. Koizumi*, J. Solid State Chem. *7*, 297 (1973); Inorg. Chem. *15*, 2195 (1976).

[3] *P. Palvadeau, L. Coic, J. Rouxel, J. Portier*, Mater. Res. Bull. *13*, 221 (1978); *A. Weiss, E. Sick*, Z. Naturforsch. *B 33*, 1087 (1978).

[4] *H. Schäfer-Stahl, R. Abele*, Z. Anorg. Allg. Chem. *1980*, in press; Mater. Res. Bull., in press.

[5] *M. D. Lind*, Acta Crystallogr. *B 26*, 1058 (1970).

[6] *M. B. Dines*, Science *188*, 1210 (1975). 560 pm appears rather small for twice the van der Waals radius of the ring. A value of 664 pm results from the C—C and the C—H distance and from the van der Waals radius of the hydrogen atoms (143, 109, and 101 pm, respectively).

[7] *H. Stahl*, Inorg. Nucl. Chem. Lett. *16*, 271 (1980).

[8] In accord with this concept, the intensity of the IR bands decreases on inclusion of the metallocenes; and the longest wavelength band is concomitantly shifted to shorter wavelengths (*ca.* 20 cm^{-1} relative to the metallocene cations, *ca.* 30—70 relative to the metallocenes); *H. P. Fritz, R. Schneider*, Chem. Ber. *93*, 1171 (1960).

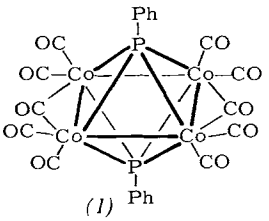
[9] *E. A. Koerner von Gustorf, F. W. Grevels, I. Fischler:* The Organic Chemistry of Iron. Vol. 1. Academic Press, New York 1978, p. 197; *H. Schäfer-Stahl*, Mater. Res. Bull., in press.

[10] *Note added in proof: T. R. Halbert, J. Scanlon*, Mater. Res. Bull. *14*, 415 (1979); *T. R. Halbert, D. C. Johnston, L. E. McCandlish, A. T. Thompson, J. C. Scanlon, J. C. Dumesic*, Physika *99B*, 128 (1980), have meanwhile reported the inclusion of $CoCp_2$, $Fe[C_5(CH_3)_4C_2H_5]_2$, and $FeCp_2$ in FeOCl from toluene at 80—100 °C. However, the resulting intercalation compounds do not exhibit an enhanced conductivity. Other physical data also indicate that these phases differ from those which we have obtained at room temperature.

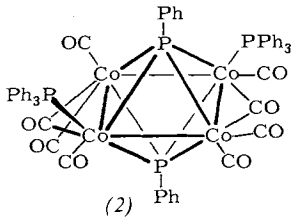
Catalysis of Hydroformylation by $Co_4(CO)_{8-x}(\mu_2\text{-}CO)_2(PPh_3)_x(\mu_4\text{-}PPh)_2$, $x = 0$ or 2: Clusters as Catalysts[**]

By *Charles U. Pittman, Jr., Gary M. Wilemon, W. Dean Wilson*, and *Robert C. Ryan*[*]

Soluble transition metal cluster compounds have recently attracted a great deal of interest as, *inter alia*, homogeneous catalysts, and as models for catalysis at metal surfaces[1-3]. A key problem is the tendency of clusters to fragment under the reaction conditions into homonuclear moieties[2-4]. So far there has been no definitive evidence demonstrating conclusively that a cluster actually serves as the active catalyst. To synthesize non-fragmenting clusters we have advocated the use of elements of the first transition series that are bound both by metal-metal bonds and by stable, nonfluxional bridging ligands[1,2,5]. We report here on hydroformylation of 1- and 2-pentene in the presence of cobalt clusters *(1)* and *(2)*, where the effect of added phosphanes on selectivity and rate of this reaction appears to rule out fragmentation of the clusters to catalytically active homonuclear fragments.

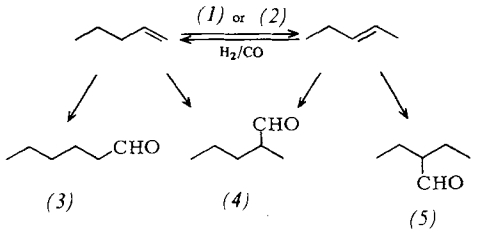


(1)



(2)

Cluster *(1)* was prepared by a known route[6] and converted by refluxing in toluene/PPh_3 into *(2)*, which could be isolated by chromatography on neutral Al_2O_3 and elution with deoxygenated hexane and hexane/toluene. The structures of *(1)* and *(2)* were established by elemental analysis, IR spectroscopy, and single crystal X-ray structural determinations[7]. Hydroformylations of 1- and 2-pentene to aldehydes were catalyzed in high yields and under mild conditions (120–150 C, 17—100 bar, CO/H_2 1:1); aldehydes were the major products. Some representative results are given in Table 1.



After completion of hydroformylation the cluster *(1)* could be recovered in high yield (95%). High pressure liquid chromatography (HPLC) was used to show that the concentration of *(1)* did not decrease within the limits of detection (*ca.* 0.5%) during reactions at 145 °C and 68.9 bar. No other metal-containing complexes could be detected by HPLC or TLC. The selectivity, *i.e.* the ratio of normal (*(3)*) to branched aldehydes (*(4)* + *(5)*), in the reaction of 1-pentene increased from 1.5 (31.3 bar) to 3.8 (80.0 bar) at 130 °C and from 2.5 (30.3 bar) to 4.7 (75 bar) at 110 °C, similarly as observed for $Co_2(CO)_6(PR_3)_2$-catalyzed hydroformylations where the active species is $HCo(CO)_3(PR_3)$[8]. Addition of PPh_3 to *(1)* decreases the rate (entries 5—7, Table 1). The selectivity increases from 1.4 to 2.9 (150 °C, 41.4 bar) upon the addition of two moles of PPh_3 per mol of *(1)* and to 3.6 on addition of four moles of PPh_3 per mol of *(1)*. The isomerization *(1)* ⇄ *(2)* competes with hydroformylation, both in the presence and in the absence of PPh_3.

Several key points were noted. First, very little alcohol is formed (≤5%) on hydroformylation of 1-pentene with *(1)* and PPh_3 at 150 °C and 34.5—48.3 bar, even with long reaction times. In contrast, in the $Co_2(CO)_8$-catalyzed hydroformylation the addition of PPh_3 (or $P(n\text{Bu})_3$) leads to high yields of alcohols[9]. $Co_2(CO)_8$ fragments under these conditions to $HCo(CO)_3PPh_3$[4b]. Accordingly, in the presence of PPh_3, *(1)* cannot fragment to $HCo(CO)_3PPh_3$. Secondly, only *(1)* was isolated or detected (TLC, HPLC) in hydroformyla-

[*] Prof. Dr. C. U. Pittman, Jr., G. M. Wilemon, W. D. Wilson, Dr. R. C. Ryan
Department of Chemistry, University of Alabama
Alabama 35486 (USA)

[**] Metal Cluster Catalysis, Part 4. Support for this work by the National Science Foundation (Grant CHE-77-06810) is gratefully acknowledged.—Part 3: [1].

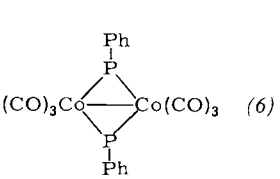
Table 1. Influence of added phosphanes on selectivity in the hydroformylation of 1- and 2-pentene with H_2/CO (1:1) in the presence of the catalysts *(1)* or *(2)*.

No.	Catalyst [a]	Substrate	Phosphane [a]	T [°C]	p [b] [bar]	Yield [%] [c] Aldehydes	Alcohols	t [h]	Selectivity [d]
1	*(1)*	1-pentene	None	130	33.8—28.9	65.0	0	63.5	1.5
2	*(1)*	1-pentene	None	130	47.6—43.4	62.5	0	88.0	2.6
3	*(1)*	1-pentene	None	130	62.0—55.4	94.8	3.4	23.0	2.7
4	*(1)*	1-pentene	None	130	82.6—78.5	49.9	0	30.0	3.9
5	*(1)*	1-pentene	None	150	41.4	67.1	0	12.4	1.4
6	*(1)*	1-pentene	PPh_3(2)	150	41.4	59.8	4.1	30.0	2.9
7	*(1)*	1-pentene	PPh_3(4)	150	41.4	48.4	3.2	52.0	3.6
8	*(1)*	1-pentene	PPh_2-(-CH_2-)$_2$-PPh_2	150	41.4	26.2	0	44.5	3.8
9	*(1)*	1-pentene	PPh_2-(-CH_2-)$_3$-PPh_2	150	41.4	47.7	0	45.0	2.5
10	*(1)*	1-pentene	PPh_2-(-CH_2-)$_4$-PPh_2	150	41.4	46.1	28.4	47.0	3.8
11	*(2)*	1-pentene	None	150	41.4	45.9	1.5	34.0	3.1
12	*(2)*	1-pentene	PPh_3(2)	150	41.4	51.7	5.4	72.3	3.8
13	*(1)*	2-pentene	None	130	35.5—29.6	87.4	0	72.0	1.2
14	*(1)*	2-pentene	None	130	64.8—58.6	88.7	1.0	70.5	1.3
15	*(1)*	2-pentene	None	150	77.1—68.2	95.2	0	22.5	0.6
16	*(1)*	2-pentene	Ph_2P-(-CH_2-)$_4$-PPh_2	150	41.4	44.4	39.5	75.0	1.5

[a] Phosphane refers to the phosphane added to the catalyst solution. The number in brackets indicates the number of moles of phosphane per mol of *(1)* or *(2)*. All chelating phosphanes $Ph_2P(CH_2)_xPPh_2$ were used in the ratio 1 mol per mol of *(1)* [*i. e.* P: *(1)* = 2:1]. [b] Pressure range refers to initial and final pressures (± 5%) at the reaction temperature. Those entries with one pressure were done under constant pressure during the entire reaction. [c] Yields are based on pentene consumed. Major products: hexanal *(3)*, 2-methylpentanal *(4)* and 2-ethylbutanal *(5)*. The amounts of pentane formed were ≤2% in all cases. [d] Selectivity = *(3)*/(*(4)* + *(5)*).

tions conducted with a fourfold excess of PPh_3. This behavior contrasts with that of $Co_2(CO)_8$-catalyzed reactions where only $[Co(CO)_3PPh_3]_2$ could be isolated when PPh_3 was the added ligand. Thus, cluster *(1)* could not have fragmented to $HCo(CO)_4$ or $HCo(CO)_3PPh_3$ during the hydroformylation. Thirdly, the selectivity increased from 2.9 to 3.8 and the rate decreased (entries 6 and 8, Table 1) when PPh_3 was replaced by $Ph_2PCH_2CH_2PPh_2$ as the ligand. This response of selectivity and rate is just the opposite of that observed for $Co_2(CO)_8$ when PPh_3 was replaced by $Ph_2PCH_2CH_2PPh_2$: there was a decrease in selectivity (from 1.9 to 1.3) and an increase in rate[9]. Taken together, these results show that *(1)* does not fragment to mononuclear species.

Despite the effect of PPh_3 on selectivity and rate, when *(2)* was used as the catalyst, only *(1)* could be recovered at the end of sample reactions. Use of HPLC demonstrated that under hydroformylation conditions (145 °C, 68.9 bar) *(2)* was rapidly converted into $Co_4(CO)_7(\mu_2\text{-}CO)_2(PPh_3)(\mu_4\text{-}PC_6H_5)_2$ and then into *(1)*.



(6)

Since both *(1)* and *(2)* contain two stable PPh bridges, they cannot easily dissociate to mononuclear species. If such dissociation did occur, it is difficult to imagine how such fragments would be able to reassemble into *(1)* at 100—150 °C and 30—100 bar CO/H_2. Our results do not rule out possible fragmentation to *(6)* during the reaction, although the reconversion of *(6)* to *(1)* would require loss of two CO ligands.

Received: October 8, 1979 [Z 479 IE]
German version: Angew. Chem. 92, 494 (1980)

CAS Registry numbers:
(1), 58092-22-1; *(2)*, 73804-98-5; 1-Pentene, 109-67-1; 2-Pentene, 109-68-2; PPh_3, 603-35-0; $Ph_2P(CH_2)_2PPh_2$, 1663-45-2; $Ph_2P(CH_2)_3PPh_2$, 6737-42-4; $Ph_2P(CH_2)_4PPh_2$, 7688-25-7

[1] *C. U. Pittman, Jr., R. C. Ryan*, Chemtech *1978*, 170; *A. L. Robinson*, Science *194*, 1150 (1976); *E. L. Muetterties, ibid. 196*, 839 (1977).
[2] *E. L. Muetterties*, Bull. Soc. Chim. Belg. *84*, 959 (1975); *85*, 451 (1975); *C. U. Pittman, Jr., R. C. Ryan*, Chemtech *1978*, 170; *A. L. Robinson*, Science *194*, 1150 (1976); *E. L. Muetterties, ibid. 196*, 839 (1977).
[3] *E. L. Muetterties, T. N. Rhodin, E. Band, C. F. Brucker, W. R. Pretzer*, Chem. Rev. *79*, 91 (1979).
[4] a) *T. J. Meyer*, Prog. Inorg. Chem. *19*, 1 (1975); b) *M. Orchin, W. Rupilius*, Catal. Rev. *6*, 85 (1972); c) *E. Cesarotti, A. Fusi, R. Ugo, G. M. Zanderighi*, J. Mol. Catal. *4*, 205 (1978).
[5] *R. C. Ryan, C. U. Pittman, Jr., J. P. O'Connor*, J. Am. Chem. Soc. *99*, 1986 (1977).
[6] *R. C. Ryan, L. F. Dahl*, J. Am. Chem. Soc. *97*, 6904 (1975).
[7] *R. C. Ryan, J. P. O'Connor, C. U. Pittman, Jr.*, unpublished.
[8] *E. R. Tucci*, Ind. Eng. Chem. Prod. Res. Develop. *7*, 32, 125, 227 (1968); *9*, 516 (1970).
[9] *L. H. Slaugh, R. D. Mullineaux*, J. Organomet. Chem. *13*, 469 (1968).

Extreme ^{13}C-NMR Data as Information on Organometal Radicals[**]

By *Frank H. Köhler, Karl-Heinz Doll*, and *Wolfram Prössdorf*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

The problem of numerous radicals failing to give any ESR spectra has been resolved step by step in recent years, particularly regarding organometal radicals: at first by paramagnetic ^{1}H- and later by ^{13}C-NMR spectroscopy (cf. earlier communications in this series). Unfortunately, however, the applicability of ^{13}C-NMR spectroscopy was hitherto greatly restricted. Signals broader than *ca.* 500 Hz are routinely regarded as unobservable; the not very satisfactory results obtained by *Kreilick et al.*[1] with a spectrometer of special construction confirmed this view.

We have now obtained ^{13}C-NMR spectra of the partially substituted nickelocenes *(1)*—*(7)*[2], whose individual signals have halfwidths >5000 Hz (signal groups > 20000 Hz) and cover a range of >2200 ppm. A typical example is shown in Figure 1. Nickelocenes, for which we had predicted very broad signals[3], are a special test case for the extension to other types of compounds, since here very narrow and very

[*] Prof. Dr. F. H. Köhler, Dipl.-Chem. K.-H. Doll, Dr. W. Prössdorf
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] NMR spectroscopy of paramagnetic complexes, Part 21.—Part 20: *F. H. Köhler*, Z. Naturforsch. *B 35*, 187 (1980).

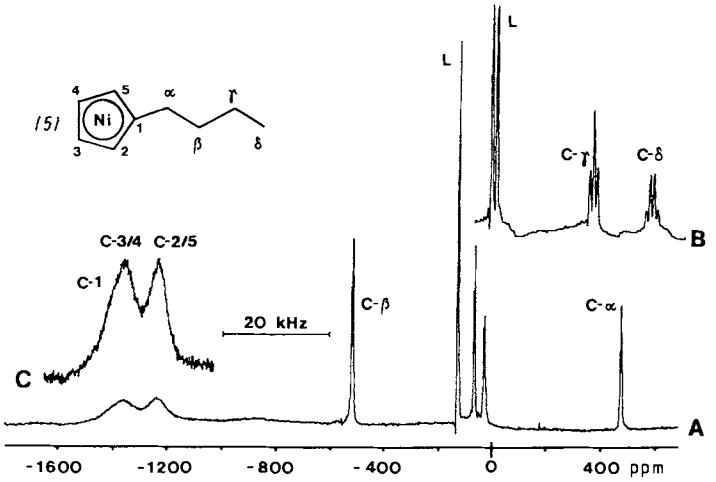


Fig. 1. ^{13}C-NMR spectrum of $(n\mathrm{BuC_5H_4})_2$Ni *(5)* in C_6H_6 at 77 °C. A) Overview; B) C-1 to C-5 amplified; L solvent, C_α and C_β expanded.

broad signals occur close to each other at the same time. As Figures 1B and 1C show, the spectrum of $(n\mathrm{BuC_5H_4})_2$Ni provides information on C-H coupling[4] and the symmetry of the five-membered ring. The poorly developed shoulder for C-1 is clearly recognizable in the spectrum of $(t\mathrm{BuC_5H_4})_2$Ni *(6)* (Fig. 2). This spectrum also provides the long sought[5]

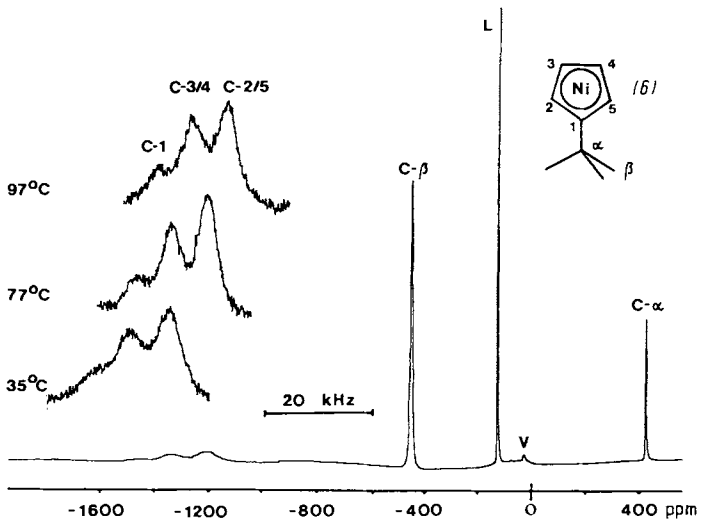


Fig. 2. ^{13}C-NMR spectra of $(t\mathrm{BuC_5H_4})_2$Ni *(6)* in C_6D_6 at 35, 77 and 97 °C; C-1 to C-5 amplified; V = impurity.

evidence for strong temperature dependence of the shifts and halfwidths.

The ^{13}C-NMR data of the nickelocenes investigated are collected in Table 1.

According to these data the nickelocenes *(1)—(6)* are radicals, which, with two unpaired electrons, shift in particular the signals of the five-membered ring C-atoms to an extreme, characteristic region. The number and position of the signals afford proof of structure just as easily as in the case of diamagnetic molecules.

Surprisingly, the C-1 signal in the compounds $(\mathrm{RC_5H_4})_2$Ni *[(3)—(6)]* is shifted further than the rest of the five-membered ring signals. In analogy to cobaltocenes[5b] the opposite was to be expected. It can be concluded, therefore, that the unpaired electrons in both metallocenes are in e_{1g} orbitals[7a], but slight perturbation of the degeneration (by substitution with R) leads to e_{1g}^+ and e_{1g}^-[7b], each of which give opposite signal splittings. In substituted cobaltocenes apparently the

Table 1. δ(^{13}C) values [a] of the nickelocenes *(1)—(6)* at 298 K [b]; syntheses of *(1)* and *(3)—(6)*: [5b], of *(2)*: [9].

	Cpd. [c]	C-1	C-2/5 [d]	C-3/4 [d]	other C
(1)	$(C_5H_5)_2$Ni		−1446 ± 2		
(2)	$(C_5D_5)_2$Ni		−1438 ± 2		
(3)	$(MeC_5H_4)_2$Ni	−1536	−1510	−1356	α 635.9
(4)	$(EtC_5H_4)_2$Ni	−1518	−1504	−1367	α 600.3; β −506.0
(5)	$(n\mathrm{BuC_5H_4})_2$Ni	−1532	−1509	−1368	α 599.3; β −571.5; γ − 51.1; δ − 18.6
(6)	$(t\mathrm{BuC_5H_4})_2$Ni	−1547	−1470	−1332	α 522.8 β −487.4

[a] Measured rel. to solvent *[(1)—(4)*: tetrahydrofuran; *(5)* and *(6)*: benzene], calculated rel. to analogous ferrocene [6]; accuracy [ppm] (if not otherwise quoted): C-1 to C-5: ± 10; other C: ± 1; downfield shift negative. [b] After recalculation from the measuring temperatures according to the Curie law. [c] Concentration [mol-%]: *(1)* = 15.5; *(2)* = 15.9; *(3)*, *(4)*, *(6)* = 15—25; *(5)* = 47.4. [d] Proposed assignment (cf. Text).

one, in substituted nickelocenes the other orbital determines the transfer of unpaired electrons to the ligand. Hence, the assignment of C-3/4 and C-2/5 (cf. Table 1) should also be opposite to that in cobaltocenes[8].

We have checked the accuracy with which such ^{13}C-NMR spectra are obtainable with perdeuterated nickelocene. Table 1 shows the very small difference of 8 ppm between the signals of *(1)* and *(2)*, which to our knowledge is, nevertheless, the largest ^{13}C-NMR isotope shift observed so far. This value falls neatly in line with our findings on other metallocenes[9].

Received: November 30, 1979 [Z 480 IE]
German version: Angew. Chem. *92*, 487 (1980)

CAS Registry numbers:
(1), 1271-28-9; *(2)*, 51510-35-1; *(3)*, 1293-95-4; *(4)*, 31886-51-8; *(5)*, 60064-87-1; *(6)*, 32964-16-2

[1] *G. F. Hatch, J. W. Neely, R. W. Kreilick*, J. Magn. Res. *16*, 408 (1974).
[2] Spectrometer: Bruker CXP 200; typical parameters: frequency 50.3 MHz, spectral width 125 and 166 kHz, pulse width 8 and 6 μs, 32 K accumulations, data collection time 44 min, data points 8 K (after zero point filling).
[3] *F. H. Köhler*, Z. Naturforsch. *B 29*, 708 (1974).
[4] The signals of C_α and C_β are also observable as triplets after using appropriate filter functions.
[5] a) We could not reproduce the preliminary results quoted in [5b]; b) *F. H. Köhler*, J. Organomet. Chem. *110*, 235 (1976).
[6] *F. H. Köhler, G. Matsubayashi*, J. Organomet. Chem. *96*, 391 (1975); *F. H. Köhler*, Z. Naturforsch. *B 31*, 1151 (1976).
[7] a) *M. Nussbaum, J. Voitländer*, Z. Naturforsch. *A 20*, 1417 (1965). b) Simplified. On going from $(C_5H_5)_2M$ to $(RC_5H_4)_2M$ with staggered conformation, D_{5d} changes to C_{2h}.
[8] *F. H. Köhler*, J. Organomet. Chem. *160*, 299 (1978).
[9] *F. H. Köhler, W. Prossdorf*, J. Am. Chem. Soc. *100*, 5970 (1978).

N-Isocyanoiminotriphenylphosphorane: Synthesis, Coordination Chemistry, and Reactions at the Metal[**]

By *Bernd Weinberger* and *Wolf Peter Fehlhammer*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

Isodiazomethane ($CNNH_2$) cannot be obtained as a pure substance owing to its ready decomposition[1]; it can however

[*] Prof. Dr. W. P. Fehlhammer, Dipl.-Chem. B. Weinberger
Institut für Anorganische Chemie der Universität Erlangen-Nürnberg
Egerlandstrasse 1, D-8520 Erlangen (Germany)

[**] Metal complexes of functional isocyanides. Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: [2].

be stabilized by coordination to a metal. Unfortunately, $CNN[Si(CH_3)_3]_2$, the precursor for the synthesis of $Cr(CO)_5CNNH_2$[2] is not easily accessible[3].

In search of a suitable "form of storage" of isodiazomethane we have now been able to prepare *N*-isocyanoiminotriphenylphosphane *(1)*[4] according to

$$HCO\quad NHNH_2 + 2PPh_3 + 2CCl_4 + 2NEt_3 \rightarrow \rightarrow CNNPPh_3 + 2HCCl_3 + 2[NEt_3H]Cl + OPPh_3$$

(1)

The surprising stability (dec. pt. 159—160 °C) of this functional *N*-isocyanide is apparently due to the masking of the primary amine function.

Apart from synthetic route and IR spectrum [(KBr): 2067 w (ν(CN)), 1117 s, 1009 sh (ν(P=N)) cm^{-1}] it is particularly its strong tendency to form complexes, which proves *(1)* to be an isocyanide. Thus, the stable[5] complexes *(2a—c)* and *(3)* are formed smoothly from tetrahydrofuran or bromo derivatives and *(1)*, respectively. No more problems arise in the syntheses of *(4)* and *(5)* by, respectively, addition of *(1)* to

$M(CO)_5CNNPPh_3$ *(2a—c)*, M = Cr, Mo, W

$Mn(\eta\text{-}C_5H_5)(CO)_2CNNPPh_3$ *(3)*

$PdI_2[CNNPPh_3]_2$ *(4)*

$[PtCl(CNNPPh_3)(PPh_3)_2][BF_4]$ *(5)*

PdI_2 and cleavage of the bridge in $[PtCl(PPh_3)_2]_2[BF_4]_2$. Complex formation is accompanied by an increase Δν(CN) in the ν(CN) frequency, which in the case of *N*-isocyanides reaches values up to 130 cm^{-1} (Pt^{II} complexes)[6]. In view of the high Δν(CN) values found here, and the low-lying CO bands of the pentacarbonylmetal moiety [*(2a)*: KBr: 2055 s [A_1], 1924 vs [E] cm^{-1}] *(1)* is primarily a donor ligand, *i.e.* bonding in metal complexes of *(1)* is perhaps best described by the resonance formula

$$L_n\overset{\ominus}{M} \leftarrow C\equiv\overset{\oplus}{N}\text{—}\overset{\ominus}{N}\text{—}\overset{\oplus}{P}Ph_3$$

As expected, the iminophosphorane bond in *(2)* can be cleaved hydrolytically under conditions leaving the rest of the molecule untouched. The isodiazomethane complexes *(6)*[2] formed in >70% yield according to

$$(2) + H_2O \xrightarrow{H^{\oplus}} M(CO)_5C\equiv N\text{—}NH_2 + OPPh_3$$

(6)

are stable enough to be sublimed after chromatographic separation from phosphane oxide.

(2) reacts with aldehydes and ketones in a Wittig-type reaction to give complexes *(7)* with *N*-isocyanoiminoalkane ligands

$$(2) + RR'C{=}O \xrightarrow{H^{+}} M(CO)_5C\quad N\quad N\quad CRR' + OPPh_3$$

(7)

e.g. R = R′ = CH_3; R = C_6H_5, R′ = H

In this way, a class of compounds becomes readily accessible in metal complexes, of which only one representative—$CNN{=}C(CH_3)C_6H_4\text{-}p\text{-}OCH_3$—has so far been characterized in free form[7].

There is definitely more synthetic potential in pentacarbonylmetal(6A) complexes of *(1)* as shown by the acid-catalyzed isomerization to the complex cyanamide *(8)*, which is complete in 2—3 d at room temperature[8]. This reaction proceeds particularly smoothly and quantitatively in the presence of palladium(II) compounds in a CO atmosphere.

$$(2) \xrightarrow{H^{\oplus}} M(CO)_5N\equiv C\text{—}N\text{—}PPh_3 \quad (8)$$

Procedures

All solvents and reagents must be anhydrous and, where necessary, saturated with N_2.

(1): A suspension of PPh_3 (157.4 g, 0.6 mol) in CH_2Cl_2 (600 ml) is treated with 50.6 g (0.5 mol) of NEt_3 and 15.3 g (0.25 mol) of formylhydrazine and heated to 50—60 °C. CCl_4 (77.0 g, 0.5 mol) is added dropwise to the mixture, which is kept at 50—60 °C for 4—5 h. After removal of the volatile components at room temperature, the residue is dried in a high vacuum, pulverized, stirred in 200 ml ethanol/water (1:1.5), filtered, and recrystallized from hot ethanol; yield 31.7 g (42%) *(1)* as orange-brown crystals.

(2c): A solution of $W(CO)_6$ (1.76 g, 5 mmol) in tetrahydrofuran (100 ml) is irradiated until ≈110 ml of CO have evolved. The solution is then cooled to −30 °C, mixed with 1.39 g (4.6 mmol) of *(1)*, stirred for 2 h at −30 °C, and for 1 h at 0 °C. After removal of the solvent (0 °C, high vacuum) and sublimation of $W(CO)_6$, the residue is extracted with 6 × 50 ml boiling petroleum ether (40—60 °C), the extract filtered rapidly through filter-cellulose, concentrated to *ca.* 1/3 of its volume and transferred to a refrigerator. Pale yellow *(2c)* crystallizes out; yield 2.91 g (93%).

(7), M = W, R = R′ = CH_3: Dry HCl gas is passed into a solution of *(2c)* (0.63 g, 1 mmol) in acetone (30 ml) for *ca.* 1/2 min. The solution is stirred for 2 h, the solvent removed, and the mixture chromatographed on silica gel with CH_2Cl_2/*n*-hexane (4:1). After evaporation of the solvent 0.20 g of a pale yellow solid (50%, m.p. 86.5 °C) are left behind.

Received: January 2, 1980 [Z 484 IE]
German version: Angew. Chem. 92, 478 (1980)

[1] *E. Müller, P. Kästner, R. Beutler, W. Rundel, H. Suhr, B. Zeeh*, Justus Liebigs Ann. Chem. *713*, 87 (1968).
[2] *W. P. Fehlhammer, P. Buračas, K. Bartel*, Angew. Chem. *89*, 752 (1977); Angew. Chem. Int. Ed. Engl. *16*, 707 (1977).
[3] *N. Wiberg, G. Hübler*, Z. Naturforsch. *B 31*, 1317 (1976).
[4] Similar results have been obtained with Br_2PPh_3/NEt_3 [*L. Horner, H. Oediger*, Justus Liebigs Ann. Chem. *627*, 142 (1959); *H. J. Bestmann, J. Lienert, L. Mott, ibid. 718*, 24 (1968)] in the place of the Appel three-component reagent [*R. Appel*, Angew. Chem. *87*, 863 (1975); Angew. Chem. Int. Ed. Engl. *14*, 801 (1975)].
[5] In contrast, $Ph_3PN\text{—}NCO$ and $Ph_3PN\text{—}NCS$ which, according to the "6-electron chalcogen atom/16-electron metal fragment" analogy should be comparable with metal complexes of *(1)*, were formulated only as labile intermediates: *R. Appel, G. Siegemund*, Z. Anorg. Allg. Chem. *363*, 183 (1968).
[6] *W. P. Fehlhammer*, Habilitationsschrift, Universität München 1976.
[7] *I. Hagedorn, U. Eholzer*, Angew. Chem. *74*, 499 (1962); Angew. Chem. Int. Ed. Engl. *1*, 75 (1962).
[8] $Cr(CO)_5NCNPPh_3$ had been synthesized previously (by photolysis of $Cr(CO)_6$ in the presence of $NCNPPh_3$) and studied IR spectroscopically: *H. Bock, H. tom Dieck*, Z. Anorg. Allg. Chem. *345*, 9 (1966).

B_8S_{16}—An "Inorganic Porphine"[**]

By *Bernt Krebs* and *Hans-Ulrich Hürter*[*]

The preparation and characterization of boron sulfides is difficult. The only compound to have been unequivocally identified in the solid state is B_2S_3, which has a polymeric structure made up of B_3S_3 six-membered rings and B_2S_2 four-membered rings[1]. The existence of $B_{12}S$, B_4S, BS, and B_2S_5[2] as defined phases has not yet been confirmed. The

[*] Prof. Dr. B. Krebs, Dipl.-Chem. H.-U. Hürter
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

[**] This work was supported by the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie.

only evidence for a species of composition BS_2 has so far come from mass spectrometry and thermal analysis[2, 3].

During our studies on binary and ternary boron sulfides[1, 4a, b] we have now obtained a new boron disulfide of molecular formula B_8S_{16} by two different routes. Rapid heating of a B_2S_3/S mixture (molar ratio 1:1.5) to *ca.* 300 °C at *ca.* 10^{-4} bar in a sealed quartz glass tube[4c], which has been graphitized or protected by a boron nitride coating, in a two-zone furnace with a sharp temperature profile (300/100 °C) leads to deposition of a crystalline product within a narrow region in the colder zone of the reaction tube. The colorless needles are up to 2 mm long, extremely sensitive to hydrolysis, and decompose above 115 °C in a sealed vessel under normal pressure (N_2).

The compound [elemental analysis B:S = 1:2.01(2)] forms monoclinic crystals (space group $P2_1/c$), $a = 12.158(3)$, $b = 4.089(1)$, $c = 21.961(4)$ Å, $\beta = 107.65(3)°$, $Z = 16$ BS_2, $V = 1040.4$ Å^3, $\rho_{calc} = 1.913$, $\rho_{exp} = 1.90(2)$ g cm^{-3}. As shown by the complete X-ray structure analysis (1349 diffractometer data, $R = 5.5\%$), solid boron disulfide is made up of discrete exactly planar B_8S_{16} molecules whose porphine type skeleton contains four 1,2,4,3,5-trithiadiborolane rings linked by sulfur bridges. Figure 1 shows the molecular structure with distances and angles averaged over chemically equivalent bonding parameters. Within the limits of experimental accuracy the molecule has D_{4h} symmetry (exact symmetry in the crystal is C_i). The average B—S bond length (1.811 Å)

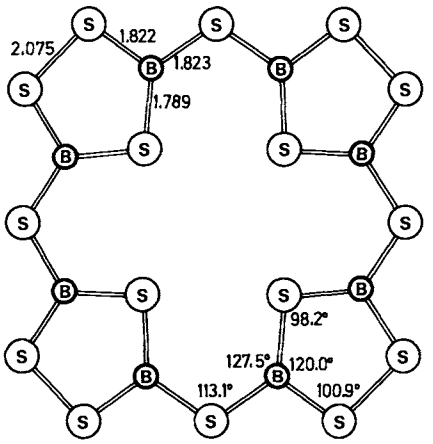
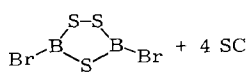


Fig. 1. B_8S_{16} molecule with bond lengths [Å] and bond angles ($\sigma = 0.003$ Å and 0.1°, respectively).

corresponds approximately to that in B_2S_3 (1.808 Å[1]) and once again, in agreement with the planarity of the molecule, is indicative of strong (p-p)π interactions. The significant difference between the two types of B—S bond lengths in the five-membered rings (Fig. 1) provides the first confirmation of the differing π bond orders estimated by CNDO calculations on trithiadiborolanes[5]. The similarity of the structural characteristics to those of dimethyl- and dichloro-1,2,4,3,5-trithiadiborolane in the gas phase[6] demonstrates the remarkable, substituent-independent constancy of the bonding in the stable five-membered ring.

A second synthetic route leading to B_8S_{16} was found in the thiolysis of the halogenated trithiadiborolanes described by *Schmidt* and *Siebert*[7]. Thus reaction of 3,5-dibromo-1,2,4,3,5-trithiadiborolane with trithiocarbonic acid as an H_2S generator[8] in dilute CS_2 solution according to



affords the porphine-like B_8S_{16} in *ca.* 6% yield along with polymeric $(B_2S_4)_x$ chains made up of S-linked B_2S_3 five-membered rings[9]. Cyclization can be promoted in the reaction mixture by addition of d^8 or d^9-transition metal compounds; the geometry of the B_8S_{16} molecule permits formation of interesting transition metal complexes having square-planar coordination of the tetradentate ligand (transannular S···S distance in B_8S_{16}: 4.667 Å).

In addition to other fragmentation products, the mass spectrum shows $B_2S_3^+$ as fragment of maximum intensity. The Raman spectrum contains bands at 942, 935, 883, 861, 835, 590, 530, 518, 462, 439 (vs), 344, 328 cm^{-1} in the region of stretching vibrations.

Received: January 8, 1980 [Z 485 IE]
German version: Angew. Chem. *92*, 479 (1980)

CAS Registry numbers:
B_8S_{16}, 73825-17-9; 3,5-dibromo-1,2,4,3,5-trithiadiborolane, 13863-77-9; $SC(SH)_2$, 594-08-1

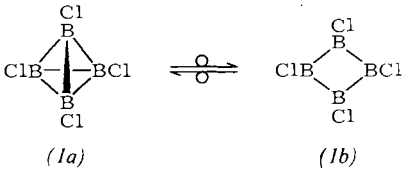
[1] *H. Diercks, B. Krebs*, Angew. Chem. *89*, 327 (1977); Angew. Chem. Int. Ed. Engl. *16*, 313 (1977).
[2] Cf. Gmelin Handbuch der Anorganischen Chemie, Ergänzungswerk zur 8. Aufl., Bd. 19, Borverbindungen Teil 3, pp. 6ff. Springer-Verlag, Berlin 1975; and further references cited therein.
[3] *F. T. Greene, P. W. Gilles*, J. Am. Chem. Soc. *86*, 3964 (1964); *H. Chen, P. W. Gilles*, ibid. *92*, 2309 (1970).
[4] a) *B. Krebs, H. Diercks*, Acta Crystallogr. *A 31*, S66 (1975); b) Inorg. Chem., in press; c) *B. Krebs, H.-U. Hürter*, Z. Naturforsch. *B*, in press.
[5] *O. Gropen, P. Vassbotn*, Acta Chem. Scand. *27*, 3079 (1973).
[6] *H. M. Seip, R. Seip, W. Siebert*, Acta Chem. Scand. *27*, 15 (1973); *A. Almenningen, H. M. Seip, P. Vassbotn, ibid. 27*, 21 (1973).
[7] *M. Schmidt, W. Siebert*, Angew. Chem. *76*, 687 (1964); Angew. Chem. Int. Ed. Engl. *3*, 637 (1964); Chem. Ber. *102*, 2752 (1969); and further references cited therein.
[8] *B. Krebs, G. Gattow*, Z. Anorg. Allg. Chem. *338*, 225 (1965).
[9] Under milder conditions, this condensation reaction of $(XB)_2S_3$ with $SC(SH)_2$ can be used to prepare new boron-carbon-sulfur compounds.

Hexakis(dimethylamino)cyclohexaborane, a Boron(I) Compound without Electron Deficiency

By *Heinrich Nöth* and *Hans Pommerening*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The molecular structures of boron(I) compounds in the solid state are characterized by B_n-polyhedral frameworks: B_4Cl_4 a tetrahedron *(1a)*[1a], B_8Cl_8 a square antiprism[1b], $(BCl)_{10}(CH)_2$ and $B_{12}H_{12}^{2-}$ an icosahedron[1c, d]. Surprisingly, however, in solution B_4Cl_4 shows a ^{11}B-NMR signal at $\delta = 85$ relative to $BF_3 \cdot OEt_2$[2a], which would contradict a *closo* structure, yet support presence of threefold coordinated boron (the same applies for B_4Br_4[2b]). According to *Williams*[3] B_4Cl_4 could therefore adopt the four-membered ring structure *(1b)* in solution. If this assumption is supported by further findings, then a polyhedral ring rearrangement



(1a) *(1b)*

would be demonstrated for the first time in the realm of boron chemistry[4]. Apparently, neither the energy difference between the two structural isomers is particularly large, nor the

[*] Prof. Dr. H. Nöth, Dr. H. Pommerening
Institut für Anorganische Chemie der Universität
Meiserstr. 1, D-8000 München 2 (Germany)

activation energy to bring about the rearrangement. Weak BCl π-bonds could contribute to the stabilization of *cyclo*-B_4Cl_4 *(1b)*. Thus dimethylamino groups, which are capable of stronger π-interactions with boron, should promote the monocyclic isomer. *Urry et al.*[5] assumed that the product of the dimethylaminolysis of B_4Cl_4 has a ring structure, since bands typical for the B_4 tetrahedron are not present in the IR spectrum; however, unequivocal characterization of the presumed $B_4[N(CH_3)_2]_4$ is still lacking.

Dehalogenation of (dialkylamino)boron chlorides with Na/K alloy leads to products with B—B bonds[6a], of which the first four members of the series $B_n[N(CH_3)_2]_{n+2}$ ($n=2$—5) have been completely characterized; there is evidence for the formation of higher members[6b].

We have now found that orange-red prisms, m.p. 163 °C (dec.), slowly crystallize from the distillation residues of the dehalogenation of $[(CH_3)_2N]_2BCl$. In [D_8]toluene solution they show a single ^{11}B-NMR signal at $\delta=65$. Likewise only one ^{1}H-NMR and one ^{13}C-NMR signal ($\delta=2.87$ and 46.65, respectively) could be observed. The mass spectrum shows a characteristic isotopic pattern for six B atoms at $m/e=330$. These findings are consistent with the composition $B_6[N(CH_3)_2]_6$ with boron of coordination number 3, since the resonance of the $(CH_3)_2NB(B)_2$ groups of $B_3[N(CH_3)_2]_5$ and $B_4[N(CH_3)_2]_6$ lie in the same $\delta(^{11}B)$ region (50—60)[6b]. The cyclic structure of the new compound was confirmed by X-ray structure analysis.

cyclo-$B_6[N(CH_3)_2]_6$ crystallizes monoclinically (space group C2[7]), $a=951.9(9)$, $b=1747.9(11)$, $c=713.8(4)$ pm, $\beta=108.77(6)°$, $Z=2$, $\rho_{calc}=0.974$ g cm^{-3}. Figure 1 shows the ORTEP plot of a molecule which has the symmetry of point group C_2 in the solid state but according to the NMR spectra, must however have a higher symmetry (D_{3d}?) in solution.

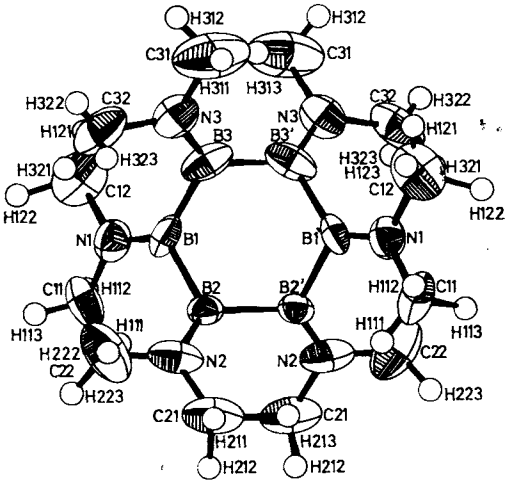


Fig. 1. Molecular structure of hexakis(dimethylamino)cyclohexaborane in the crystal. Selected bond distances [pm]: B1B2 170.4(13), B1B3 177.8(9), B3B3' 167.6(10), B1N1 139.7(5), B2N2 139.0(7), B3N3 140.7(7); bond angles [°]: B2B1B3 112.2(6), B1B2B2' 109.2(5), B1B3B3' 111.1 (5), B2B1N1 121.8(7), B3B1N1 124.9(7), B1B2N2 124.0(5), B2'B2N2 125.9(5), B1B3N3 123.1(5), B3'B3N3 124.5(5). The angle between the planes through B1B2B3 and B2B2'B3B3' is 57.6°; the C_2NB planes are twisted at an angle of *ca.* 65° to the NBB_2 planes.

All B and N atoms are planar coordinated. The twisting of the C_2NB planes w.r.t. the NBB_2 planes (Fig. 1) permits strong, though not optimum BN(pp)π bonding. The average BN distance of 140 pm is correspondingly longer than the shortest known BN distances (136 pm) in monoaminoboranes. The mean value of the unequal B—B bond distances in the solid state corresponds to that found in other six-membered ring systems containing B—B bonds (170 pm)[8].

The B_6 ring has a chair confirmation. Hence, as a consequence of the relatively strong BN(pp)π bonding, $B_6[N(CH_3)_3]_6$ also does not show any structural characteristics of an electron-deficient compound in the solid state. Structurally, the cyclohexaborane derivative resembles the radialenes[9a], particularly the isoelectronic $C_6(CHCH_3)_6$, whose C_6 ring is likewise not planar but shows a chair conformation[9b]. A more detailed comparison of the two isosteric systems will afford valuable information about the molecular states of the new boron compound. This opens an entry to further derivatives, since R_2N groups can easily be substituted.

Procedure

8.2 g of the distillation residue, obtained on preparation of $B_2[N(CH_3)_2]_4$ by reaction of 87.6 g of $ClB[N(CH_3)_2]_2$ with 25.6 g of Na/K alloy (1:3) in 350 ml hexane, was redistilled to remove $B_3[N(CH_3)_2]_5$ and $B_4[N(CH_3)_2]_6$[6b]. From the brown viscous oily residue *ca.* 30 mg of dark orange crystals separated out over four months; after decanting and washing with cold pentane, the crystals melt at 163—165 °C.

Received: March 12, 1980 [Z 486 IE]
German version: Angew. Chem. 92, 481 (1980)

CAS Registry numbers:
$B_6[N(CH_3)_2]_6$, 73825-16-8; $B_2[N(CH_3)_2]_4$, 1630-79-1; $ClB[N(CH_3)_2]_2$, 6562-41-0

[1] a) *M. Atoji, W. N. Lipscomb*, J. Chem. Phys. *21*, 172 (1953); Acta Crystallogr. *6*, 547 (1953); b) J. Chem. Phys. *31*, 601 (1959); c) *L. I. Zakharkin, G. G. Zhigareva*, Izv. Akad. Nauk SSSR, Ser. Khim. *1965*, 932; d) *J. Wunderlich, W. N. Lipscomb*, J. Am. Chem. Soc. *82*, 4427 (1960).

[2] a) *T. Davan, J. A. Morrison*, Inorg. Chem. *18*, 3194 (1979); b) *W. Haubold*, private communication (October 1979).

[3] *R. E. Williams*, IMEBORON IV, Snowbird, July 1979.

[4] See also, calculations of the relative stability of $B_2C_4H_6$ as diboracyclohexadiene and as *nido*-tetracarbahexaborane: *R. N. Camp, D. S. Marynick, G. D. Graham, W. N. Lipscomb*, J. Am. Chem. Soc. *100*, 6781 (1978), and experiments by *P. Binger*, Tetrahedron Lett. *24*, 2675 (1966). – *Note added in proof:* According to *D. A. Kleier, J. Bicerano*, and *W. N. Lipscomb*, Inorg. Chem. *19*, 216 (1980), square B_4H_4 and B_4F_4 may be stable intermediates of the degenerate rearrangement of *tetrahedro*-B_4H_4 and -B_4F_4, respectively.

[5] *G. Urry, A. G. Garrett, H. I. Schlesinger*, Inorg. Chem. *2*, 396 (1963).

[6] a) *R. J. Brotherton, A. L. McCloskey, L. L. Petterson, H. Steinberg*, J. Am. Chem. Soc. *82*, 6242 (1960);

[7] According to the systematic extinctions (*hhl* with $h+k=2n$) the space groups C2/m, Cm and C2 were to be taken into consideration. Although statistics suggested the centrosymmetric space group C2/m, the structural model (with 807 structural factors $I>3.29\sigma(I)$) refined only in the space group C2. With anisotropic temperature factors for the non-hydrogen atoms and isotropic ones (B=8) for the H atoms, the BLOCK refinement converged at $R_1=R_2=0.07$. The complete list of all structural parameters is available on request from the authors.

[8] *H. Nöth, H. Fussstetter, H. Pommerening, T. Taeger*, Chem. Ber. *113*, 342 (1980).

[9] a) *F. P. van Remoortere, F. P. Boer*, Angew. Chem. *81*, 567 (1969); Angew. Chem. Int. Ed. Engl. *8*, 597 (1969); b) *H. Hopff, A. K. Wick*, Helv. Chim. Acta *44*, 19 (1961); *E. Weltin, F. Gerson, J. N. Murrell, E. Heilbronner, ibid. 44*, 1400 (1961).

Boron Trifluoride: Crystal Structure of a Metastable Phase[**]

By *Dietrich Mootz* and *Michael Steffen*[*]

The trigonal-planar molecular structure of boron trifluoride and the B—F bond length of 1.31 Å were determined directly by spectroscopic and electron diffraction measurements in the gas phase[1]. We report here on the determination of the crystal structure of this simple compound.

[*] Prof. Dr. D. Mootz, Dipl.-Chem. M. Steffen
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstr. 1, D-4000 Düsseldorf (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

The growth of a single crystal in a sealed glass capillary on a diffractomer was achieved by slow cooling in a stream of cold gas to $-131\,^{\circ}C$ (m.p. $-127.1\,^{\circ}C$). All X-ray diffraction measurements were also carried out at this temperature. They were consistent with the monoclinic space group $P2_1/c$, giving the lattice constants $a = 4.779$, $b = 14.00$, $c = 7.430$ Å, $\beta = 107.60^{\circ}$ and eight molecules of BF_3 in the unit cell[2].

The molecules are planar; the B—F bond lengths (uncorrected for thermal motion) and the FBF angles vary between 1.26 and 1.31 Å (mean value 1.287 Å) and between 118 and 122°, respectively. Taking into consideration B...F contacts between 2.68 and 2.71 Å, the boron atoms have trigonal-bipyramidal coordination (Fig. 1).

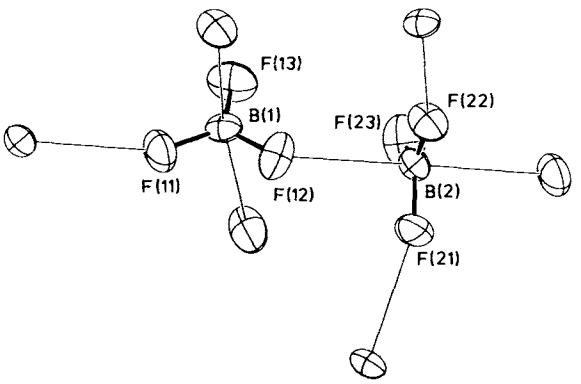


Fig. 1. The two independent BF_3 molecules with intermolecular B...F contacts (ORTEP diagram).

Each molecule is linked *via* such contacts with a total of four molecules of the other independent kind into a three-dimensional array. Linked molecules are always almost vertical to each other, since the two independent molecules are oriented almost vertical and parallel to the b axis. In each independent molecule one fluorine atom does not participate in this linking.

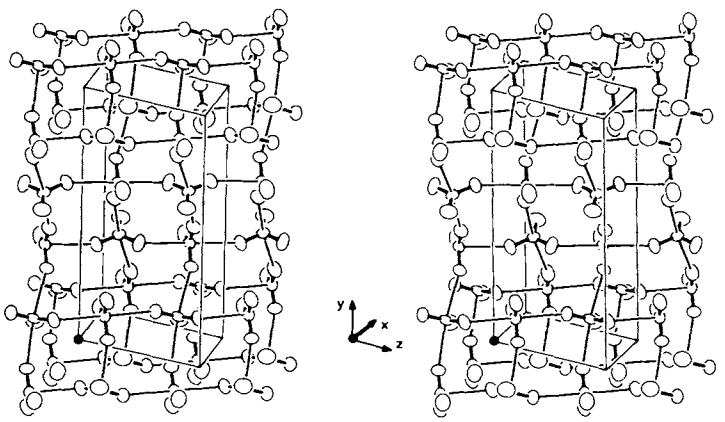


Fig. 2. Stereoscopic ORTEP diagram of the crystal structure of BF_3.

Thus, the crystal structure fundamentally differs from that of the other trihalides of boron with parallel orientation of only two molecules in a hexagonal unit cell[3]. This, and in particular marked interactions of eight molecules per unit cell in boron trifluoride, could already be concluded from IR and Raman crystal spectra[4,5]. The same cell content also results from single crystal X-ray photographs at $-173\,^{\circ}C$[5]; however, with similar latter constants the crystal system is described as triclinic. With X-ray powder measurements (Guinier-Simon technique) we could observe an enantiotropic phase change at $-147\,^{\circ}C$. The crystal structure given here is that of a yet another, metastable phase.

Received: October 1, 1979 [Z 487 IE]
revised: March 26, 1980
German version: Angew. Chem. 92, 481 (1980)

CAS Registry number:
Boron trifluoride, 7637-07-2

[1] Gmelin Handbuch der Anorganischen Chemie, Ergänzungswerk zur 8. Aufl., Bd. 53, Borverbindungen Teil 19, p. 49—62. Springer-Verlag, Berlin 1978 (Germany).

[2] Four circle diffractometer Syntex $P2_1$ with modified cooling device LT-1. Because of rapid decomposition of the crystals, measurements were carried out on three different single crystals. $Mo_{K\alpha}$, ω scan, $2\theta_{max} = 50°$, 842 reflections, of which 650 observed ($|F| > 3\sigma_F$), program system MULTAN 78 and EXTL, $R_1 = 0.096$.

[3] *M. A. Ring, J. D. H. Donnay, W. S. Koski*, Inorg. Chem. *1*, 109 (1962).

[4] *D. Dows*, J. Chem. Phys. *31*, 1637 (1959).

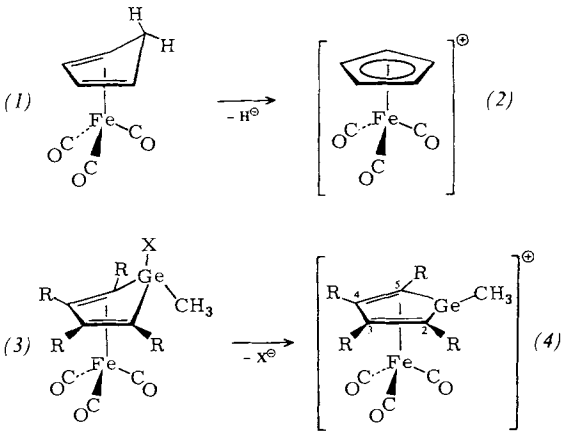
[5] *O. S. Binbreck, J. K. Brandon, A. Anderson*, Can. J. Spectrosc. *20*, 52 (1975).

The $(Ph_4C_4GeMe)Fe(CO)_3$ Cation: Synthesis, Structure, and Bonding[**]

By *Peter Jutzi, Alfons Karl,* and *Peter Hofmann*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

Tricarbonyl(η^4-cyclopentadiene)iron *(1)* can be transformed into tricarbonyl(η^5-cyclopentadienyl)iron cation *(2)* by elimination of hydride[1]. We have now also succeeded in eliminating the anionic ligand X from the germanium-containing complexes *(3a)* and *(3b)*[2]: quantitative removal of the hydride ion from *(3a)* can be accomplished by reaction with Ph_3CBF_4 in CH_2Cl_2, and that of the chloride ion from *(3b)* by treatment with $AgBF_4$ or $AgSbF_6$ in liquid SO_2. The resulting yellow salts *(4a)* and *(4b)* are amorphous to X-rays, very sensitive to hydrolysis, and thermolabile. On heating, preferably in a vacuum, they afford the fluorine compound



[*] Prof. Dr. P. Jutzi, Dr. A. Karl
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

Present address:
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)

Doz. Dr. P. Hofmann
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. *A. K.* is indebted to the Studienstiftung des Deutschen Volkes for a study grant. We wish to thank Dr. *J. Pebler*, Fachbereich Chemie der Universität Marburg, for recording the Mössbauer spectra.

(3c) together with BF_3 or SbF_5. Conductivity measurements in CH_3NO_2 confirm that *(4a)* and *(4b)* are 1:1 electrolytes.

(3a—c), R = C_6H_5, X = H, Cl, F; *(3d)*, R = H, X = F
(4a, b), R = C_6H_5, anion = $BF_4^{\ominus}$ or $SbF_6^{\ominus}$; *(4c)*, R = H

Interestingly, the cation in the salts *(4a)* and *(4b)* is not to be regarded as an η^5-germacyclopentadienyl complex—by analogy with *(2)*—but as an η^4-diene complex in which the positive charge is localized mainly at the germanium atom. The proposed structure follows from a comparison of the spectroscopic data of *(4a, b)* and *(3a—c)*. Table 1 contains the principal data for *(3c)* and *(4b)*.

Table 1. Selected physical data of *(3c)* and *(4b)*.

(3c): ^{1}H-NMR (CS_2, CH_2Cl_2 int.): $\delta = 1.18$ (d, CH_3, $J = 5.1$ Hz); $^{13}C\{^1H\}$-NMR (CD_2Cl_2): $\delta = -1.2$ (d, CH_3, $J = 11.8$ Hz), 75.0 (d, C-2, 5, $J = 14.7$ Hz), 110.8 (C-3, 4), 211.1 (d, CO, $J = 52$ Hz); IR (cyclohexane: νCO = 2044, 1985 cm^{-1}; ^{57}Fe-Mössbauer spectrum: $\delta = +0.325$ mm/s rel. to $Na_2[Fe(CN)_5NO]\cdot H_2O$, $\Delta E^Q = 1.484$ mm/s
(4b): ^{1}H-NMR (CD_3NO_2): $\delta = 2.01$ (CH_3); $^{13}C\{^1H\}$-NMR (CD_3NO_2): $\delta = 0.58$ (CH_3), 82.8 (C-2, 5), 112.3 (C-3, 4), 209.2 (CO); IR (CH_3NO_2): νCO = 2049, 1989 cm^{-1}; ^{57}Fe-Mössbauer spectrum: $\delta = +0.355$ mm/s, $\Delta E^Q = 1.528$ mm/s; ^{121}Sb-Mössbauer spectrum: $\delta = +10.92$ mm/s rel. to SbIn, $\Delta E^Q < 3$ mm/s

While *(1)* and *(2)* differ significantly in their ^{13}C-NMR, ^{57}Fe Mössbauer, and νCO IR data, this is not the case for *(3)* and *(4)*. As demonstrated by the ^{13}C-NMR data of the ring carbon atoms, the CO frequencies in the IR spectra, and the ^{57}Fe Mössbauer data, the electronic conditions are very similar in the tricarbonyl(diene)iron units of the complexes *(3)* and *(4)*. The downfield shift of the ^{1}H- and ^{13}C-NMR signals of the methyl groups on going from *(3)* to *(4)* likewise constitutes indirect evidence for the positive charge on the germanium atom; the relatively slight effect suggests shielding by the $Fe(CO)_3$ unit of coordination or solvent molecules to three-coordinate germanium.

The similarity in bonding and in the $Fe(CO)_3$ coordination in the cation of the salts *(4a, b)* and in the diene complexes *(3a—c)* is confirmed by MO model calculations[3] on *(3d)*, *(4c)*, and *(2)*. A perturbation treatment of the interactions between the $Fe(CO)_3$ fragment and its valence orbitals[4] with the relevant orbitals of the pertinent organic ligand leads to a clear comparative description. The typical picture of a butadiene- or cyclopentadiene-$Fe(CO)_3$ complex[5] results for *(3d)* with strong bending of the ring center not bonded to iron, as known for analogous molecules[6]. The calculations on the cation *(4c)* show that incorporation of the electropositive Ge atom into the cyclic ligand leads to a kind of bonding far more similar to that in tricarbonyl(diene)iron complexes and thus in *(3a—d)* than to that in *(2)*. The changes occurring in the π system of the cyclopentadienyl ligand on replacement of a CH by a $GeCH_3$ group are shown in Figure 1.

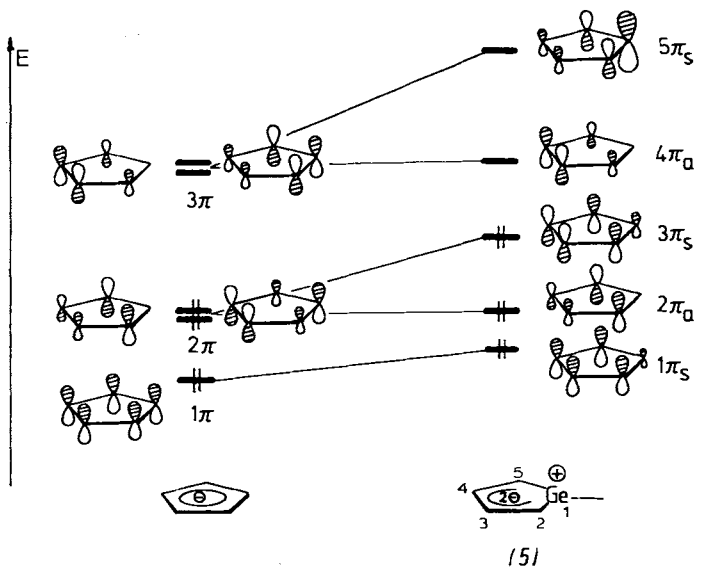


Fig. 1. Bonding in cyclopentadienide and 1-methylgermacyclopentadienide ion [resonance formula *(5)*].

The destabilization of the orbitals $1\pi_s$, $3\pi_s$, and $5\pi_s$ compared to those in the C_5H_5 parent conserves the butadiene character of the cyclic ligand, even for cations of type *(4)*. The small orbital coefficients at Ge in the $1\pi_s$ and $3\pi_s$ MOs lead to more pronounced localization of the positive charge on the electropositive ring atom, which is predicted by the rules of perturbation theory to play a significant role in the wave function only in the highest π orbital $5\pi_s$. The model calculations require that the $Fe(CO)_3$ unit be shifted from the center of the ring[7] towards the C^3—C^4 bond and that the $GeCH_3$ group be bent upwards by about 10°[7]. In terms of resonance theory, the butadienoid character of the $C_4H_4GeCH_3^{\ominus}$ ligand and the positive charge on the germanium could be expressed as participation of the resonance formula *(5)* in the ground state.

Received: December 7, 1979 [Z 481 IE]
German version: Angew. Chem. 92, 496 (1980)

CAS Registry numbers:
(3a), 73836-74-5; *(3b)*, 73836-80-3; *(3c)*, 73770-98-6; *(3d)*, 73789-38-5; *(4a)*, 73771-00-3; *(4b)*, 73771-01-4; *(4c)*, 73771-02-5

[1] *T. H. Whitesides, J. Shelly*, J. Organomet. Chem. *92*, 215 (1975).
[2] *P. Jutzi, A. Karl*, J. Organomet. Chem. *128*, 57 (1977).
[3] Extended Hückel MO calculations: *R. Hoffmann*, J. Chem. Phys. *39*, 1397 (1963).
[4] *M. Elian, R. Hoffmann*, Inorg. Chem. *14*, 1058 (1975); *T. A. Albright, P. Hofmann, R. Hoffmann*, J. Am. Chem. Soc. *99*, 7546 (1977); *P. Hofmann*, Z. Naturforsch. *B 33*, 251 (1978).
[5] Cf. *e.g. T. A. Albright, R. Hoffmann, P. Hofmann*, Chem. Ber. *111*, 1591 (1978).
[6] *R. Hoffmann, P. Hofmann*, J. Am. Chem. Soc. *98*, 598 (1976).
[7] Ring center here refers to the midpoint between Ge and the C^3—C^4 bond. For details of the optimized molecular geometry of *(4c)*, see *P. Jutzi, A. Karl, P. Hofmann*, to be published.

An Experimental and Theoretical Study of the Degenerate Carbon Skeleton Isomerization of the Cyclopentyl Cation in the Gas Phase[**]

By *Wilfred Franke, Helmut Schwarz, Helga Thies, Jayaraman Chandrasekhar, Paul von Ragué Schleyer, Warren J. Hehre, Martin Saunders*, and *Gary Walker*[*]

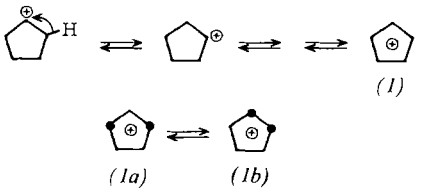
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

While the degenerate isomerization of the cyclopentyl cation *(1)* by sequential hydride shifts is well established[1],

[*] Prof. Dr. H. Schwarz, Dipl.-Chem. W. Franke, H. Thies
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Prof. Dr. P. v. R. Schleyer, Dr. J. Chandrasekhar
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)
Prof. Dr. W. J. Hehre
Department of Chemistry, University of California
Irvine, Calif. 92717 (USA)
Prof. Dr. M. Saunders, G. Walker
Department of Chemistry, Yale University
New Haven, Conn. 06520 (USA)

[**] This work was supported by the Fonds der Chemischen Industrie and by the Gesellschaft von Freunden der Technischen Universität Berlin.—Based on a lecture (*H. S.*) delivered at the 1979 Chemiedozententagung, Darmstadt (Germany).

rearrangements involving reorganization of the C-skeleton, *(1a)* ⇄ *(1b)*, have not yet been demonstrated.



(1)

(1a) *(1b)*

We have now studied this possibility experimentally in the gas phase. Dissociative ionization (electron impact MS at 70 eV and at 12 eV) of doubly ^{13}C labeled isotopomeric precursors, the bromocyclopentanes *(2a)* and *(2b)* and the acyclic 5-bromo-1-pentenes *(3a)* and *(3b)*, led to $C_5H_9^+$ ions. The unimolecular elimination of ethylene from these $[M-Br]^+$ ions (whose lifetime was $\approx 10^{-5}$ s), was followed by the MIKES method[2] (Fig. 1).

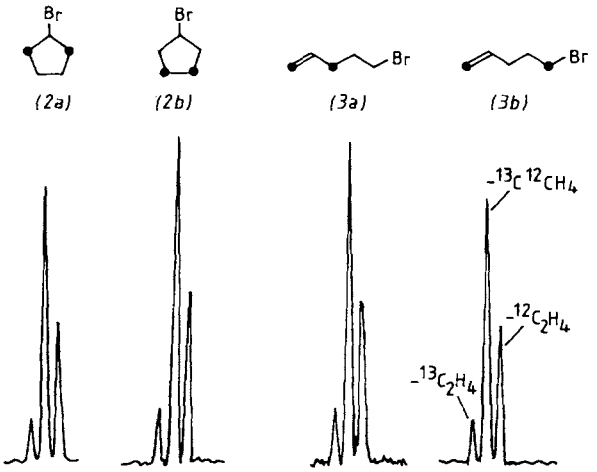
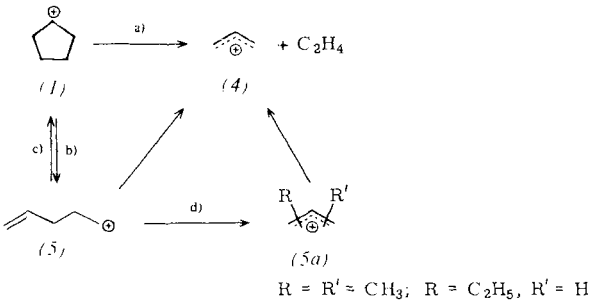


Fig. 1. Unimolecular ethylene elimination from the $[M-Br]^+$ ions of *(2a)*, *(2b)*, *(3a)*, and *(3b)*. (●) Indicates a ^{13}C-labeled center.

Table 1. $^{13}C/^{12}C$-Isotope distribution [%] on ethylene elimination from the $[M-Br]^+$ ions of *(2a)*, *(2b)*, *(3a)*, and *(3b)*. The data were obtained from the areas of the peaks shown in Figure 1.

Ethylene	Precursor				Calculated
	(2a)	*(2b)*	*(3a)*	*(3b)*	for C-equilibration
$^{13}C_2H_4$	10.4	9.9	10.4	9.8	10
$^{13}C^{12}CH_4$	59.0	59.7	61.6	58.8	60
$^{12}C_2H_4$	30.6	30.4	28.0	31.4	30

The data in Table 1 are convincing: $C_5H_9^+$ ions from both cyclic and acyclic precursors undergo statistical carbon scrambling before C_2H_4 is eliminated. These results are not consistent with a number of mechanistic models which have been discussed in the literature[1b,3], *e.g.*, a) cycloreversion,



(1)→*(4)*, b) two stage decomposition of *(1)* *via* *(5)*, c) head/tail cyclization, *(1)* ⇄ *(5)*, followed by ethylene elimination, or d) hydride shift along the C_5 chain, *(5)*→*(5a)* before heterolysis to *(4)*.

We now propose an alternative mechanism which is consistent with all available evidence. This is shown in Figure 2, which summarizes reaction profiles obtained from MINDO/3 calculations; all minima and transition states are geometry-optimized. Figure 2 indicates that carbon scrambling in the cyclopentyl carbon *(1)* can, in principle, proceed either *via* the bisected cyclobutylcarbinyl cation *(6)* or *via* the non-classical, pyramidal cation *(7)*[4]. The transition states, TS_1 and TS_2, for both these rearrangements lie well below TS_3, which represents our proposed transition state for ethylene elimination from *(7)*. In contrast, ethylene elimination from *(6)* or from acyclic $C_5H_9^+$ ions are less likely energetically. Of all the paths we have investigated by calculation, the most favorable involves pyramidal *(7)*, which thus serves both as the carbon scrambling intermediate and as the species from which ethylene elimination can take place. Electronic reorganization in *(7)* leads to transition state *(8)* which can be regarded as a partially opened cyclopropyl cation "solvated" by interaction with C_2H_4[5].

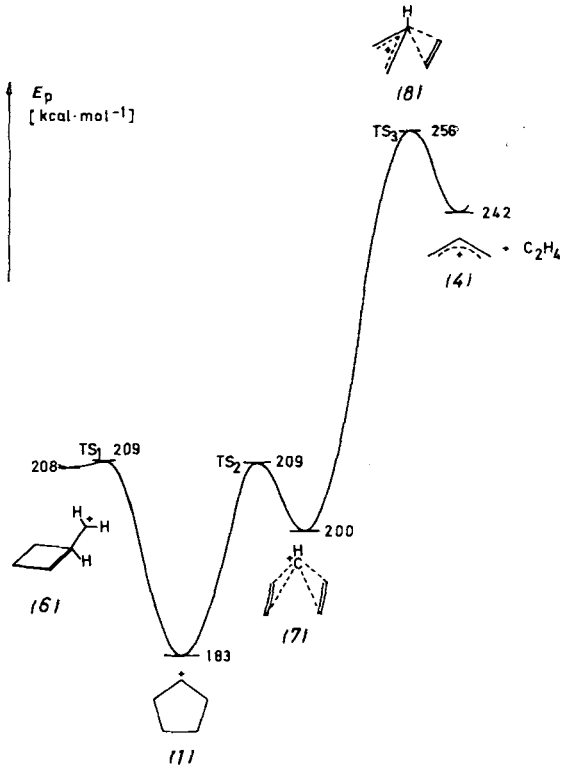


Fig. 2. MINDO/3 reaction profiles for the C-equilibration in the cyclopentyl cation *(1)* and for the reaction $C_5H_9^+ \rightarrow C_5H_7^+ + C_2H_4$.

It seems unlikely that acyclic pentyl cations *(5)* are involved in any of the reaction processes (ionization, Br^--loss, C-equilibration, or ethylene elimination)[3]; such primary carbocations are not expected to be minima on the potential energy surface. Instead, rearrangements concerted with ion formation should take place. Hydride shifts would lead to acyclic allyl cations which would split off ethylene only with difficulty energetically. The experimental observation that the $[M-Br]^+$ ion from *(3)* also undergoes complete carbon scrambling is consistent with the assumption that *(1)* [or *(6)*] rather than *(5)*, is the first intermediate, formed by π-electron participation during the ionization process[6]. *(1)* or *(6)*

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0606-486 $ 02.50/0

would then react further according to the scheme in Figure 2.

Does the equilibration, *(1a)*⇌*(1b)*, also take place in condensed phases? This question cannot be answered as yet. In SbF_5—SO_2ClF solution, the ^{13}C-NMR chemical shift of *(1b)* is 10 Hz upfield and of *(1a)* 4 Hz downfield from the normal cyclopentyl cation ^{13}C-NMR chemical shift. This means that the interconversion *(1a)*⇌*(1b)* could easily be detected experimentally. However, experiments at −20 °C or at lower temperatures indicated no such scrambling; the barrier must thus be greater than about 16 kcal mol^{-1}, in general agreement with the theoretical results. If complications with ion decomposition can be overcome, experiments at higher temperatures may provide additional information.

(7) is one of the simplest representatives of an increasingly populated class of pyramidal carbocations formally comprised of a CH^+ "cap" interacting with various four electron systems[4]. At the *ab initio* theoretical level, *(7)* is also found to be an energy minimum, but lying higher than the classical

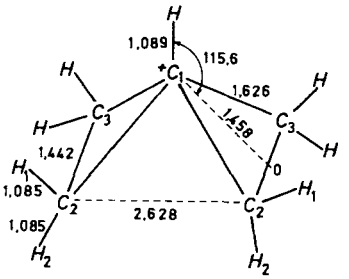


Fig. 3. *Ab initio* geometry of *(7)* calculated with the STO-3G basis set: C_{2v} symmetry; ∢ $H_1C_2O = 119.9$, ∢ $H_2C_2O = 119.7$, ∢ $H_1C_2OC_1 = 260.9$, ∢ $H_2C_2OC_1 = 105.4°$ (o is the midpoint of C_2C_3).

cyclopentyl cation *(1)* by 45.4 kcal mol^{-1} (STO-3G basis set optimized) or 30.8 kcal mol^{-1} (4-31G//STO-3G). The calculated STO-3G geometry is indicated in Figure 3.

Received: April 1, 1980 [Z 488 IE]
German version: Angew. Chem. *92*, 488 (1980)

CAS Registry numbers:
(1), 25076-72-6; *(2)*, 137-43-9; *(3)*, 1119-51-3; *(5)*, 35512-98-2

[1] a) *G. A. Olah, J. Lukas*, J. Am. Chem. Soc. *90*, 933 (1968); *G. A. Olah, A. M. White, ibid. 91*, 3954 (1969); b) *M. S. Shaw, R. Westwood, D. H. Williams*, J. Chem. Soc. *B 1970*, 1773; c) for a review of degenerate carbocation rearrangements, see *R. E. Leone, J. C. Barborak, P. v. R. Schleyer* in *G. A. Olah, P. v. R. Schleyer*: Carbonium Ions, Vol. 4, Wiley, New York 1973, Ch. 33, p. 1837.

[2] For the method see: *J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger, T. Y. Ridley*, Anal. Chem. *45*, 1023 A (1973); *U. P. Schlunegger*, Angew. Chem. *87*, 731 (1975); Angew. Chem. Int. Ed. Engl. *14*, 679 (1975); *K. Levsen, H. Schwarz, ibid. 88*, 589 (1976) and *(15)*, 509 (1976).

[3] *K. B. Tomer, J. Turk, R. H. Shapiro*, Org. Mass Spectrom. *6*, 235 (1972); *B. J. Stapleton, R. D. Bowen, D. H. Williams*, Tetrahedron *34*, 259 (1978).

[4] For further examples of pyramidal carbocations of this type see: *H. Hogeveen, P. W. Kwant*, Acc. Chem. Res. *8*, 413 (1975); *C. W. Jefford, J. Mareda, J. C. Perlberger, U. Burger*, J. Am. Chem. Soc. *101*, 1370 (1979); *G. A. Olah, G. K. S. Prakash, G. Liang, P. W. Westerman, K. Kunde, J. Chandrasekhar, P. v. R. Schleyer, ibid.*, in press; *C. W. Jefford, V. de los Heros*, Tetrahedron Lett. *21*, 913 (1980).

[5] The process *(7)*→*(8)*→*(4)* + C_2H_4 is closely related to the elimination of H_2 from $C_3H_7^+$. A transition state for the latter involving a similar partially opened cyclopropyl cation "solvated" by H_2, has been postulated on the basis of MINDO/3 calculations: *H. Schwarz, W. Franke, J. Chandrasekhar, P. v. R. Schleyer*, Tetrahedron *35*, 1969 (1979).

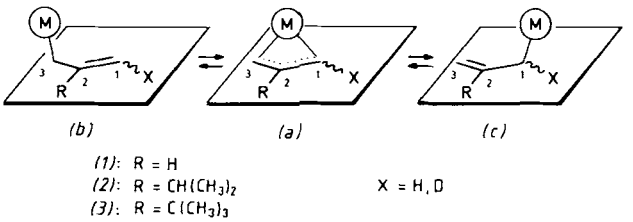
[6] Following *Baldwin*'s rules, the process, *(3)*‡ → *(6)* + Br$^{\cdot}$, should be favored over the alternative, *(3)*‡ → *(1)* + Br: *J. E. Baldwin*, J. Chem. Soc. Chem. Commun. *1976*, 734.

Allylic Compounds of Magnesium, Lithium, and Potassium: σ- or π-Structures?[**]

By *Manfred Schlosser* and *Manfred Stähle*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Hitherto, organic compounds of alkali and alkaline-earth metals have only rarely been obtained in crystalline form, and even then required mostly complexation with an unusual ligand such as tetramethylethylenediamine[1]. Owing to a lack of X-ray structure data, the question of the bonding between metal and the carbon skeleton in, say, allyllithium remains open. Even if they could reliably provide the desired accuracy of 1—3 kcal/mol, quantum chemical calculations[2a] will continue to be unrealistic as long as they assume "naked" rather than peripherally solvated metals[2b]. Nor has NMR spectroscopy provided unequivocal information about the bonding involved. Magnetic equivalence of the two terminal sites of allyllithium[3] is equally compatible with a ground state having mirror symmetry (π-structure *(1a)*, X = H, η^3-allyl ligand) as with fast, reversible transition between two identical and asymmetric metallomers (σ-structures *(1b)* and *(1c)*, X = H, η^1-allyl ligand). Nevertheless, the degree of uncertainty can be reduced: for instance, if the ^1H- and ^{13}C-NMR spectra of 2-isopropylallylpotassium *((2)*, X = H)[4] fails to show diastereotopism of the methyl groups even at −155 °C then the activation barrier for the oscillation of the metal cannot exceed 4 kcal/mol, provided that such a motion takes place at all.



We hoped to gain clearer insight by use of the isotopic perturbation technique developed by *Saunders et al.*[5] to distinguish between "classical" and "non-classical" carbocations. Owing to the lower zero point energy of the CD, as compared to the CH bond[6], the heavy hydrogen isotope should show a significantly greater preference than the light one for an olefinic carbon atom if it has a choice between such an atom and a saturated one. Thus, on introduction of deuterium into one of the allylic termini the proportion of metallomer *(b)* should increase at the expense of *(c)* if they are present in equilibrium (dynamic isotope effect). Independently of the exchange rate, separate signals should appear for the two terminal carbon nuclei, to the right and the left of the original signal. In the case of a symmetrical structure *(a)*, on the other hand, the deuterium would merely lead to a slight, isotope-specific upfield shift (static isotope effect).

We have recorded the ^{13}C-NMR spectra of some deuterium-free and mono-deuterated allyl-metal compounds *((1)—(3)*, X = H and D, Table 1 and Figures 1 and 2), obtained by metalation of propene, [3-^{2}H]propene[7a], 2,3-dimethyl-1-butene, 2-([^{2}H]methyl)-3-methyl-1-butene[7a], 2,3,3-trimethyl-1-butene, and 2-([^{2}H]methyl)-3,3-dimethyl-1-butene[7a] with

[*] Prof. Dr. M. Schlosser, Chem. techn. M. Stähle
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Projects 2.467.0.75, 2.693.0.76 and 2.128.0.78).

Table 1. Deuterium-free or mono-deuterated allyl-, 2-isopropylallyl, and 2-*tert*-butylallylmagnesium, -lithium, and -potassium (*(1)*, *(2)*, and *(3)*) in tetrahydrofuran solution at 25 °C: chemical shifts [a] (rel. to TMS) of the ^{13}C atoms in the allyl moiety.

M	X	*(1)*			*(2)*			*(3)*		
		$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$	$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$	$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$
MgBr	H	57.5	149.5	57.5 [b]		—			—	
	D [d]	56.6	149.5	58.0 [b, c]		—			—	
Li	H	51.1	147.0	51.1		—		48.3	169.5	48.3
	D [d]	51.1	147.0	51.2		—		48.2	169.5	48.2
K	H	52.9	144.1	52.9	50.2	164.3	50.2	50.5	166.4	50.5
	D [d]	52.9	144.1	52.7	50.2	164.3	50.0 [e]	50.3	166.4	50.1 [e]

[a] The absolute chemical shifts may vary by up to 0.5 ppm from sample to sample since they are temperature- and, in particular, concentration-dependent. The chemical shift difference between two neighboring signals is reproducible with a reliability of at least 0.05 ppm. [b] Owing to the possible effect of solvent on the Schlenk equilibrium (cf. *Stucky et al.*, J. Am. Chem. Soc. *92*, 1150 (1970)) the spectra of the diethyl ether solutions of the organomagnesium compounds were also measured; the chemical shifts were almost identical [$\delta(C^3)=58.7$ and 57.7, $\delta(C^2)=148.2$ and 148.3, $\delta(C^1)=58.7$ and 59.1 for the deuterium-free and the monodeuterated compound]. [c] At −35 °C (in diethyl ether) the individual signals are farther apart [$\delta(C^3)=57.5$, $\delta(C^2)=147.9$, $\delta(C^1)=59.2$] and overlap only slightly. [d] Leads to splitting of the $\delta(C^1)$ signal to a 1:1:1 triplet ($J=21$—23 Hz). [e] Accurate determination was impossible since the triplet of the deuterated carbon atom is not cleanly split.

trimethylsilylmethylpotassium[7b] and, where appropriate, by subsequent treatment with lithium bromide or magnesium dibromide. Allylmagnesium bromide *(1)*-MgBr is accordingly seen to have a *monohapto* structure ("σ-compound") in tetrahydrofuran and diethyl ether. The signal of the deuterated and hence split (1:1:1 triplet) carbon atom C^1 and that of its next-but-one neighbor C^3 are distinctly separated. The difference of *ca.* 1.9 ppm [$\delta(C^1)-\delta(C^3)$; +0.4 ppm for the static isotope effect] reveals an equilibrium distribution of *(1b)*-MgBr : *(1c)*-MgBr (at 24 °C) between 51:49 and 52:48[8]. In the lithium compounds *(1)*-Li and *(3)*-Li, however, deuteration gives rise to only a slight downfield shift (0.1 ppm).

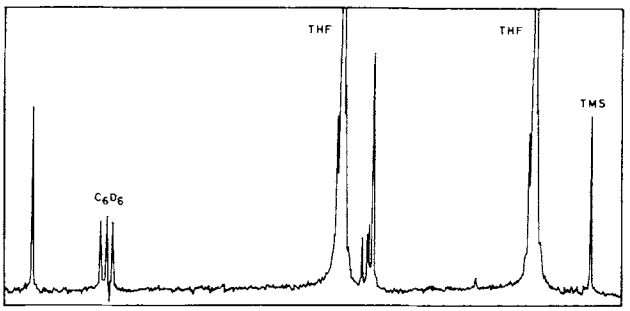


Fig. 1. ^{13}C-NMR spectrum of terminally monodeuterated allylmagnesium bromide in THF at 24 °C. The differences relative to the spectra of allyllithium and -potassium are not very large, they only become noticeable on stretching the spectra (Fig. 2).

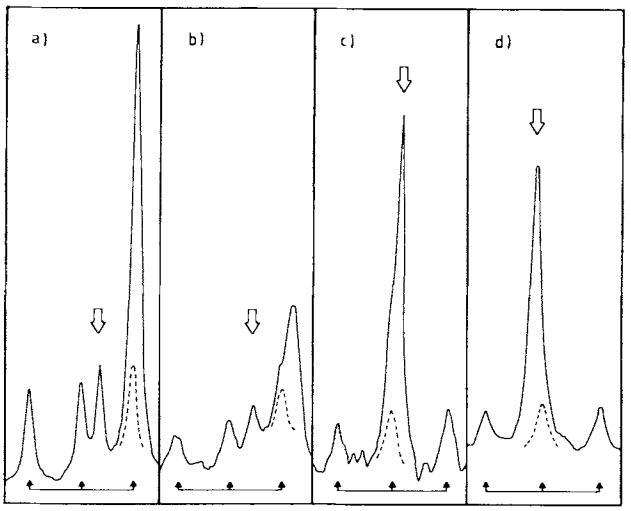


Fig. 2. ^{13}C-NMR spectra of a) [1-^{2}H]magnesium bromide contaminated with a small amount of allylmagnesium bromide (broad arrow!) at +24 °C; b) at −35 °C; c) and d) [1-^{2}H]allyllithium and potassium in THF at +24 °C. The position of the 1:1:1 triplet assigned to the deuterated carbon atom is shown in all cases by a three-pronged rake, and masked parts of signals are indicated by broken lines.

Table 2. ^{13}C-NMR data of allyl, crotyl, and prenyl-magnesium bromide, lithium, and -potassium (*(1)*, *(4)*, and *(5)*) in tetrahydrofuran solution at 25 or −40 °C [a]: chemical shifts (rel. to TMS) [b—d].

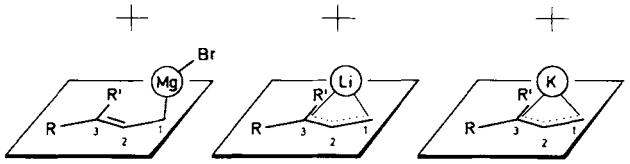
M	*(1)*			*(4)*					*(5)*		
	$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$	$\delta(CH_3)$	$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$	$\delta(CH_3)$	$\delta(C^3)$	$\delta(C^2)$	$\delta(C^1)$
H [e]	115	*135*	19	*11* *16*	124 125	*124* *125*	11 16	*17* *26*	132	*119*	17
MgBr	57 [f]	*150*	57 [f]	*15*	102	*141*	17	[g]	107	*135*	16
Li [h]	51 [f]	*147*	51 [f]	*14* *19*	76 79	*143* *145*	30 32	*18* *28*	87	*140*	26 [i]
K	53	*144*	53	*15* *18*	63 64	*139* *142*	45 43	*17* *27*	69 [i]	*136*	39

[a] The samples of *exo*-2-butenylpotassium and of prenyllithium and -potassium must be kept below −40 °C since they are otherwise unstable. [b] Crotyl = 2-butenyl; prenyl = 3-methyl-2-butenyl. [c] Where two series of numbers are given for a crotyl derivative *(4)*, the upper values apply to the *endo(cis)* isomer and the lower ones for the *exo(trans)* isomer; the upper value in the $\delta(CH_3)$ column of prenyl derivatives *(5)* refers to the *endo(cis)* and the lower one to the *exo(trans)* methyl group. [d] The $\delta(C^3)$ and the $\delta(C^1)$ values are informative; the other signals (in italics) are given only for the sake of completeness. [e] The chemical shifts of the hydrocarbons propene, 2-butene, and 3-methyl-2-butene are given for comparison; the single methyl group is always referred to as C^1. [f] Mixed signals arising by fast and reversible transition between two mirror-image structures; for "frozen" structures we would expect approximately 92 and 22 for the $\delta(C^3)$ and $\delta(C^1)$ values of allylmagnesium bromide and 57 and 45 for those of allyllithium. [g] Not recognizable at 25 °C since probably excessively broadened by coalescence; on cooling (to −30 °C) two separate signals appear at 18 and 26 ppm (the latter is masked by THF) and a mixed signal appears at 22 ppm on warming. [h] Data for crotyllithium: *J. P. C. M. van Dongen, H. W. D. van Dijkman, M. J. A. de Bie*, Rec. Trav. Chim. Pays-Bas *93*, 29 (1974). [i] Masked by signals of the usual solvent THF ($\delta=68$ and 26), visible in dimethyl ether ($\delta=59$).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0606-488 $ 02.50/0*

Hence we conclude that allyllithium possesses a non-symmetrical π-structure with similar, but not identical C^1Li and C^3Li bond lengths. Asymmetrically distorted π-complexes of transition metals are already known[9]. In contrast, allylpotassium *(1)*-K, 2-isopropylallylpotassium *(2)*-K, and 2-*tert*-butylallylpotassium *(3)*-K apparently form (closely or perfectly) symmetrical "π-complexes" in tetrahydrofuran and in diethyl ether[10] as a result of an essentially regular *trihapto* interaction between metal and allyl moiety. The signal of the deuterated carbon atom is shifted upfield by 0.2 ppm relative to the other terminal site.

We then examined whether the conclusions drawn for the allyl series also apply to the homologous crotyl- and prenylmetal compounds. This is confirmed by the chemical shifts (Table 2). The spectra of the magnesium compounds resemble those of the corresponding hydrocarbons (*(4)* and *(5)*, M = MgBr and H). Thus, as already assumed by *Roberts et al.*[11] on the basis of the ^{1}H-NMR spectra, σ-structures with the metal attached to the primary carbon atom have to be attributed to all allylic Grignard compounds. The relative upfield shift of the $\delta(C^3)$ signal indeed suggests a certain accumulation of electron density at the substituted end of the allylic moiety. Moreover, a polarizing interaction between metal and double bond (a kind of partial valence) may also be considered. The downfield shift of the $\delta(C^2)$ signal would be compatible with such an effect. Conversely, on the basis of the NMR data, crotyl and prenyl-potassium [*(4)*-K and *(5)*-K] belong to the essentially symmetrical π-structures. The large atomic radius of the metal favors the η^3-bonding state in two respects: potassium readily spans the allylic ligand from one end to the other and the gain in energy on addition of a further solvent molecule (cf. [2b]) would be smaller than in the case of lithium or magnesium[12]. The lithium compounds *(4)*-Li and *(5)*-Li are regarded as unequally distorted π-complexes, with the bond to the secondary or tertiary carbon atom appearing to become longer and weaker with increasing degree of substitution. While allyllithium itself presumably exhibits only slight asymmetry, prenyllithium probably occupies a position intermediate between the η^1 and η^3 bond types.



(1): R = R' = H
(4): R = H, R' = CH_3 (*endo*); R = CH_3, R' = H (*exo*)
(5): R = R' = CH_3

More detailed structural knowledge should provide a better understanding of the regioselectivity of allylmetal reactions and thus permit their directed modification. However, it should not be overlooked that large energy differences are not to be expected between σ- and π-allyl compounds of alkali and alkaline earth metals. *Structural changes immediately prior to reaction* can consequently not be ruled out *a priori*.

Received: March 14, 1980 [Z 489 IE]
German version: Angew. Chem. 92, 497 (1980)

CAS Registry numbers:
(1) · MgBr, 1730-25-2; *(1)* · Li, 3052-45-7; *(1)* · K, 7329-38-6; *(2)* · K, 73891-64-2; *(3)* · Li, 73891-65-3; *(3)* · K, 73891-66-4; *(4)* · MgBr, 6088-87-5; *(4)* · Li, 16327-44-9; *(4)* · K, 73891-67-5; *(5)* · MgBr, 63847-45-0; *(5)* · Li, 50585-10-9; *(5)* · K, 73891-68-6

[1] *G. Stucky*, Adv. Chem. Ser. *130*, 56 (1974); *M. Schlosser:* Struktur und Reaktivität polarer Organometalle. Springer-Verlag, Berlin 1973; *G. D. Stucky, W. Rhine*, J. Am. Chem. Soc. 97, 737 (1975) and further references cited therein.

[2] a) *H. L. Clarke*, J. Organomet. Chem. *80*, 155 (1974); *A. Bongini, G. Cainelli, P. Palmieri, A. Umani-Ronchi, ibid. 110*, 1 (1976); *T. Clark, E. J. Jemmis, P. v. R. Schleyer, J. S. Binkley, J. A. Pople, ibid. 150*, 1 (1978).—b) In general, a σ-allylmetal compound requires one more solvent molecule (or ligand) than a π-allylmetal compound in order to complete its coordination shell. Occasionally, mere addition of a more polar solvent should suffice to transform an η^3- into an η^1-species.

[3] *P. West, J. I. Purmont, S. V. McKinley*, J. Am. Chem. Soc. *90*, 797 (1968); *L. D. McKeever* in *M. Szwarc:* Ions and Ion Pairs in Organic Reactions, Vol. *1*, p. 263. Wiley-Interscience, New York 1972.

[4] *M. Stähle, J. F. M. Oth, M. Schlosser*, unpublished (1976); see also *M. Schlosser, G. Rauchschwalbe*, J. Am. Chem. Soc. *100*, 3258 (1978).

[5] *M. Saunders, L. Telkowski, M. R. Kates*, J. Am. Chem. Soc. 99, 8070 (1977); *M. Saunders, M. R. Kates, ibid.* 99, 8071 (1977); *M. Saunders, M. R. Kates, K. B. Wiberg, W. Pratt, ibid.* 99, 8072 (1977); cf. also *M. Saunders, P. Vogel, E. L. Hagen, J. Rosenfeld*, Acc. Chem. Res. *6*, 53 (1973).

[6] *L. Melander:* Isotope Effects on Reaction Rates. Ronald Press, New York 1960; *M. J. S. Dewar:* Hyperconjugation. Ronald Press, New York 1962.

[7] a) Prepared by metalation of the hydrocarbon with butyllithium in the presence of potassium *tert*-butoxide and quenching with heavy water.—b) *J. Hartmann, M. Schlosser*, Helv. Chim. Acta *59*, 453 (1976).

[8] We set the difference between the individual signals $\delta(C^1)$ and $\delta(C^3)$, which would be observed for "frozen" metallomerism, at 70 ppm (see Table 2, footnote [f]).

[9] *T. J. Greenhough, P. Legzdins, D. T. Martin, J. Trotter*, Inorg. Chem. *18*, 3268 (1979); *J. W. Faller, D. F. Chodosh, D. Katahira*, J. Organomet. Chem. *187*, 227 (1980).

[10] The spectra of 2-*tert*-butylallyllithium and -potassium recorded in diethyl ether (DEE) or tetrahydrofuran (THF) are almost identical. The insufficient solubility of allylpotassium in pure DEE precludes such a comparison for this compound. In a 1:1 mixture of DEE/THF close pairs of peaks are found at the same positions where single lines occur in pure THF (δ = 144 and 53). This doubling could be due to aggregate formation (coexistence of dimers and monomers or boat-like and chair-like dimers?).

[11] *J. E. Nordlander, J. D. Roberts*, J. Am. Chem. Soc. *81*, 1769 (1959); *J. E. Nordlander, W. G. Young, J. D. Roberts, ibid. 83*, 494 (1961); *G. W. Whitesides, J. E. Nordlander, J. D. Roberts, ibid. 84*, 2010 (1962).

[12] Concerning the hydration energies of metal ions in the gas phase, cf., *e.g., S. K. Searles, P. Kebarle*, Can. J. Chem. *47*, 2619 (1969).

The First "Small Ring" in Fluorometalates: $Ba_6F_4(F_4AlF_{2/2})_4$ = "$Ba_3Al_2F_{12}$"

By *Rainer Domesle* and *Rudolf Hoppe*[*]

In contrast to many "cation-rich" oxometalates, not one of the hundreds of known fluorometalates possesses a polynuclear anion (such as $Na_{10}[Co_4O_9]$[1a]) or cyclic anion (such as $K_4[Ag_4O_4]$[1b]).

The number of hexafluorometalates such as $Na[Rh^VF_6]$[2a], $K_2[Ni^{IV}F_6]$[2b], or $Cs_2K[Ag^{III}F_6]$[2c] is especially large. A naturally occurring example of such fluorides of aluminum is $Na_3[AlF_6]$, cryolite. In place of the octahedral structural unit AlF_6, octahedra are linked to form an *infinite chain* in the fluorine-poorer compounds such as $Tl_2[AlF_5] = Tl_2[AlF_{4/1}F_{2/2}]$[3a], to form a *two-dimensional sheet* in $K[AlF_4] = K[AlF_{2/1}F_{4/2}]$[3b], and to form a *three-dimensional skeleton* in others such as $Cs[AgF_3] = Cs[AgF_{6/2}]$[3c]; $Cs[AlF_4] = Cs_3[(F_2AlF_{2/2}F_{2/2})_3]$ represents a remarkable special case having a "one-dimensional three-stranded chain" of three mutually *cis*-linked octahedra[3d].

What is the structure of $Ba_3Al_2F_{12}$? Is it a simple analogue of cryolite conforming to $Ba_3[AlF_6]_2$? Does the "counterpolarizing" action of Ba^{2+} lead to structural peculiarities, as for instance in $Ba_2ZnF_6 = Ba_2F_2[ZnF_{2/1}F_{4/2}]$[4]?

We have obtained the low-temperature form α-$Ba_3Al_2F_{12}$ for the first time from the flux (650 °C) as lustrous, colorless,

[*] Prof. Dr. R. Hoppe, Dr. R. Domesle
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

transparent, multi-faceted single crystals. Contrary to earlier claims[5], powder data show α-$Ba_3Al_2F_{12}$ to form orthorhombic crystals in Pnnm-D_{2h}^{12} with $a = 10.18_7$, $b = 9.86_9$, $c = 9.50_2$ Å, $Z = 4$, $\rho_{calc} = 4.82$ and $\rho_{exp} = 4.79$ g cm^{-3}.

As shown by structural elucidation [four-circle diffractometer PW 1100, $Mo_{K\alpha}$, 1958 I_0 (*hkl*); $R = 7.2_9$, and $R_w = 5.6_7\%$]—cf. motifs of mutual assignment in Table 1—there are no "isolated" [AlF_6] octahedra present. Surprisingly, this is the first case of a fluorometalate containing a tetrameric structural unit according to $Ba_6F_4[(F_{4/1}AlF_{2/2})]_4$, a "ring" such as has only been encountered previously in a few neutral molecules $(MF_5)_4$ with M = Mo, Ru, *etc.*[6]. In those cases ring formation was discussed as an effect of the d orbitals[7]. We consider it remarkable that they can play no role in the present case.

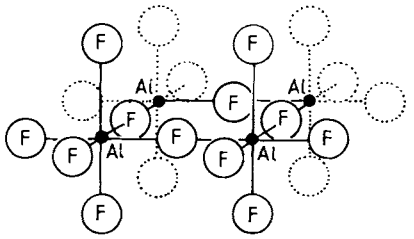


Fig. 1. The $[(F_4AlF_{2/2})_4]^{8-}$ "ring".

Four Al atoms situated in a plane form an almost square (edge length 3.50_1 and 3.54_2 Å) rectangle. Two of the four bridging F atoms lie in the same plane but are slightly displaced towards the center of the ring; the other two are not only displaced outwards but also in a manner slightly suggestive of a "chair" conformation. Four further terminal F atoms complete the octahedra around each Al. The coordination number of Ba is 10—11; however, naive counting proves difficult for Ba(2) and Ba(3) (cf. Table 1). The "rings" are in a space-saving arrangement (Fig. 2).

The Madelung part of the lattice energy (MAPLE[8]) for $Ba_3Al_2F_{12}$ (5141 kcal/mol) is in good agreement ($\Delta = 0.7\%$) with the sum of the MAPLE values of the binary fluorides (5179 kcal/mol). It remains to be investigated whether, and if so to what extent, paramagnetic ions of transition metals can be incorporated into the ring in place of Al^{3+}.

Received: January 11, 1980 [Z 491 IE]
German version: Angew. Chem. *92*, 499 (1980)

CAS Registry number:
$Ba_3Al_2F_{12}$, 25165-46-2

Table 1. Motifs of mutual assignment [a] (and distances in pm), as well as naively counted coordination numbers (C.N.) and effective coordination numbers (E.C.N.) [b] calculated *via* mean effective ionic radii (MEFIT) for $Ba_6F_4[(F_4AlF_{2/2})_4]$. [Starting values $r(Ba^{2+}) = 1.61$, $r(Al^{3+}) = 0.53$, $r(F^-) = 1.30$ Å.]

	F(1)	F(2)	F(3)	F(4)	F(5)	F(6)	F(7)	F(8)	C.N.	E.C.N.
Ba(1)	—	—	2/2 (280)	2/2 (279)	2/1 (278)	2/1 (270)	—	2/1 (280)	10	10.0
Ba(2)	(2/2) (338)	(1/1) (327)	1/1 (259)	1/1 (267)	2/1 (278)	2/1 (273)	2/1 (290)	2/1 (296)	10 (+3)	10.4
Ba(3)	—	1/1 (307)	1/1 (266)	1/1 (284)	2/1 (277)	2/1 (298)	2/1 2/1 (287, 289)	(2/1) (344)	11 (+2)	11.0
Al	1/2 (182)	1/2 (186)	—	—	1/1 (178)	1/1 (182)	1/1 (175)	1/1 (177)	6	5.9
C.N.	2 (+2)	3 (+1)	4	4	4	4	4	3 (+1)		
E.C.N.	3.2	3.9	3.8	3.9	4.0	3.8	3.9	3.3		

[a] For example, if 2/1 is given as motif for Ba(1)/F(6), that means that Ba(1) has two F(6) as neighbors while F(6) has only one Ba(1). [b] *R. Hoppe*, Z. Kristallogr. *150*, 23 (1979).

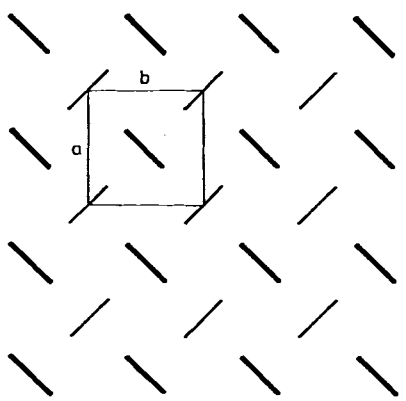


Fig. 2. Orientation of $[Al_4F_{20}]^{8-}$ rings in α-$Ba_3Al_2F_{12}$, viewed along [001] (schematic; bold lines refer to $z = 1/2$, thin lines to $z = 0$).

[1] a) *W. Burow, R. Hoppe*, Angew. Chem. *91*, 71 (1979); Angew. Chem. Int. Ed. Engl. *18*, 61 (1979); b) *H. Sabrowsky, R. Hoppe*, Z. Anorg. Allg. Chem. *358*, 241 (1968).
[2] a) *V. Wilhelm, R. Hoppe*, J. Inorg. Nucl. Chem., Suppl. *1976*, 113; b) *W. Klemm, E. Huss*, Z. Anorg. Allg. Chem. *258*, 221 (1949); c) *R. Hoppe, R. Homann*, Naturwissenschaften *53*, 501 (1966).
[3] a) *C. Brosset*, Thesis, University of Stockholm 1942; b) Z. Anorg. Allg. Chem. *239*, 301 (1938); c) *R.-H. Odenthal, R. Hoppe*, Monatsh. Chem. *102*, 1340 (1971); d) *R. Lösch, Ch. Hebecker*, Z. Naturforsch. *B 34*, 131 (1979).
[4] *H. G. von Schnering*, Z. Anorg. Allg. Chem. *353*, 13 (1967).
[5] *J. Ravez*, Bull. Soc. Chim. Fr. *1969* (5), 1583.
[6] *A. J. Edwards, R. D. Peacock, R. W. H. Small*, J. Chem. Soc. *1962*, 4486; *J. A. Holloway, R. D. Peacock, R. W. H. Small, ibid. 1964*, 644.
[7] *B. K. Morrell, A. Zalkin, A. Tressaud, N. Bartlett*, Inorg. Chem. *12*, 2640 (1973).
[8] *R. Hoppe*, Angew. Chem. *78*, 52 (1966); Angew. Chem. Int. Ed. Engl. *5*, 95 (1966); Adv. Fluorine Chem. *6*, 387 (1970).

Zintl Phases with Complex Anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$[**]

By *Brigitte Eisenmann* and *Herbert Schäfer*[*]

The halides and chalcogenides of the alkali and alkaline earth metals exhibit essentially heteropolar bonding character, with increasing admixture of metallic bonding compo-

[*] Prof. Dr. H. Schäfer, Dr. B. Eisenmann
Abteilung II für Anorganische Chemie im
Eduard-Zintl-Institut der Technischen Hochschule
Hochschulstrasse 4, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We wish to thank Dr. *H. Paulus*, Abt. Strukturforschung der TH Darmstadt, and Dr. *W. Massa*, Fachbereich Chemie der Universität Marburg, for the single crystal measurements.

nents on going to the corresponding compounds of elements of Groups V and IV[1]. Heteropolar interactions are also characteristic of the alkali and alkaline earth metal salts of acids with complex anions (*e.g.* sulfates, phosphates, *etc.*), and yet there is a lack of systematic studies on compounds with complex anions with analogous metallic bonding components. We have now synthesized the compounds $Sr_3Si_2As_4$ *(1)* and $Sr_3Ge_2As_4$ *(2)* which have a metallic luster but appear red by transmitted light when viewed as thin layers; complete X-ray structure analysis on single crystals[2] showed them to contain networks of infinite chains which are to be interpreted in this way (Figs. 1 and 2).

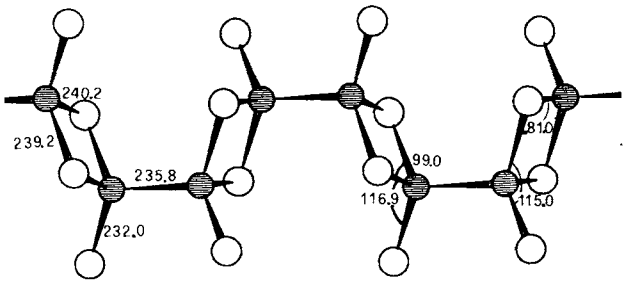


Fig. 1. $[Si_2As_4^{6-}]_n$ anion in $Sr_3Si_2As_4$ *(1)*: ⊜ Si, ○ ≙ As.

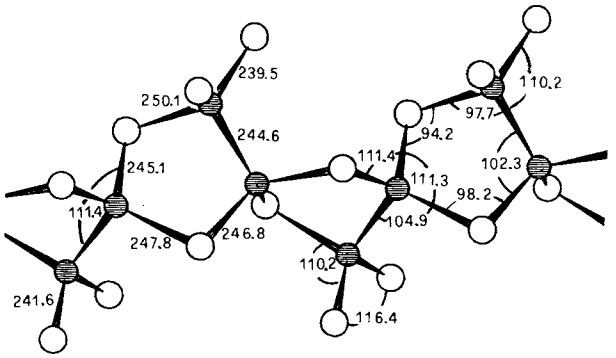


Fig. 2. $[Ge_2As_4^{6-}]_n$ anion in $Sr_3Ge_2As_4$ *(2)*: ⊜ Ge, ○ ≙ As.

In the two novel compounds *(1)* and *(2)* the Si and Ge atoms are surrounded tetrahedrally by three As atoms and one neighbor of the same kind. Thus As_3Si—$SiAs_3$ and As_3Ge—$GeAs_3$ units arise, which, in the case of the silicon compound, are linked by shared edges (cf. Fig. 1) to form one-dimensionally infinite chains. In contrast, the As_3Ge—$GeAs_3$ units in the germanium compound are joined together in such a way that all three As atoms of a $GeAs_3$ group form bridges while only one As atom of the other $GeAs_3$ group contributes to the network; two As atoms are still terminal (Fig. 2). In both cases, chain anions result which are shown by their composition and the coordination of their components (Zintl-Klemm concept[1]) to require description as $(Si_2As_4^{6-})_n$ and $(Ge_2As_4^{6-})_n$. The six negative charges are compensated by three Sr^{2+} ions.

Our results clearly show that transition from salts with complex anions to ternary intermetallic compounds leads to transitions in bonding similar to those demonstrated previously for numerous binary compounds[1].

Experimental

Stoichiometric amounts of the elements are heated to 1150 °C under argon in a corundum crucible in an evacuated quartz bomb kept at that temperature for 1 h, and then cooled at a rate of *ca.* 100 °C per hour. Crystalline platelets can be broken out of the homogeneous reguli.

Received: November 8: 1979 [Z 490 IE]
German version: Angew. Chem. *92*, 480 (1980)

[1] *H. Schäfer, B. Eisenmann, W. Müller*, Angew. Chem. *85*, 742 (1973); Angew. Chem. Int. Ed. Engl. *12*, 694 (1973).

[2] *(1):* monoclinic, space group C2/c, $Z=4$, $a=920.5(4)$, $b=1683.2(5)$, $c=737.6(4)$ pm, $\beta=122.46(3)°$; four circle diffractometer Stoe Stadi 4, 836 symmetry-independent reflections, $R=0.056$.
(2): monoclinic, space group $P2_1/c$, $Z=4$, $a=763.1(5)$, $b=1851.2(7)$, $c=743.9(5)$ pm, $\beta=111.88(8)°$; CAD 4 four-circle diffractometers, 867 symmetry-independent reflections, $R=0.101$. – Solution by direct phase-determination methods [SHEL-X-76 program, *G. M. Sheldrick* (1976), unpublished]

Catalytic Graphite-Intercalation with Alkali Metals in Solution[**]

By *Hans-Friedrich Klein, Joachim Gross,* and *Jürgen O. Besenhard*[*]

Liquid or evaporated alkali metals A form stoichiometric lamellar intercalation compounds AC_x with graphite or graphite-like samples of carbon. These compounds differ in the number n of carbon planes between two layer vacancies occupied by A (compounds of the n-th stage) and in the occupation of the interlayer vacancies.

When A = K, Rb, Cs, then $x = 8$, 24, 36, 48, 60 for compounds AC_x of the 1st to 5th stage[1a], whereas other compositions were found for A = Li, Na, *e.g.* LiC_6 and LiC_{12} for the 1st and 2nd stage[1b].

The formation of AC_x can also be accomplished in metallic reducing solutions, *e.g.* of A in liquid ammonia[2a], by alkali metal salts of organic radical anions such as naphthalenesodium in ethers[2b], and by electrochemical reduction of graphite in aprotic solutions of $A^{\oplus}$ salts[2c].

However, these procedures require strongly polar solvents which solvate $A^{\oplus}$ and lead to ternary compounds $A(solv)_yC_x$ which are generally extremely labile.

Solvate-free alkali metal intercalation compounds have so far only been accessible from the elements at elevated temperature, with intercalation usually being performed in high vacuum from the vapor phase[3].

We have now found a catalytic method of generating non-solvated compounds KC_8, RbC_8, and CsC_8 from graphite[4] in an apolar medium, at room temperature, and in short reaction times [reaction (1)].

$$\text{A + flake graphite} \xrightarrow[\text{pentane, 25°C}]{\text{[catalyst]}} AC_8 \qquad (1)$$
$$A = K, Rb, Cs$$

The catalysts used are monoolefintris(trialkylphosphane)cobalt(0) complexes which are reversibly reduced in an apolar medium. A reduced form of the catalyst A[Co(olefin)$(PR_3)_3]_2$[5] transports the alkali metal through the hydrocarbon solution to the graphite where the cobalt(0) complex is regenerated (Fig. 1). R is preferably methyl.

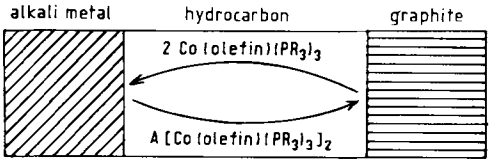


Fig. 1. Catalytic intercalation of graphite (A = K, Rb, Cs).

[*] Prof. Dr. H.-F. Klein, Dipl.-Chem. J. Gross, Doz. Dr. J. O. Besenhard
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

In polar solvents ternary compounds $A(solv)_yC_x$ are expectedly formed according to eq. (1); this also provides the first one-step entry to such compounds solvated with arenes[6a]. Thus, reaction of HOPG (highly oriented pyrolytic graphite) with excess potassium (10% $Co(C_2H_4)(PMe_3)_3$ in benzene, 8 d, 25 °C) gave the C_6H_6-solvated compounds of the 1st and 2nd stage, for which the compositions $K(C_6H_6)_yC_{24}$ and $K(C_6H_6)_yC_{48}$ and basal spacings of 930 and 1260 pm, respectively, are given[6b]. For the 2nd stage, however, we found a basal spacing of only 1245 pm[7]. Although the composition and X-ray diffraction data of the nonsolvated and the solvated alkali metal-graphite compounds correspond to those reported in the literature, some of the properties of the catalytically generated species are modified:

On rigorous exclusion of air, KC_8 forms lustrous golden flakes. They swell on contact with benzene, turning black. "High-temperature" KC_8 has been described as inert towards this arene[6a]. During the synthesis of KC_{24} we observed that a small portion of the graphite flakes adopts a golden sheen immediately after dissolution of the potassium, while the major part appears unchanged.

Only after prolonged reaction times (10% $Co(C_2H_4)(PMe_3)_3$ in pentane, 5 d, 25 °C) are all the flakes uniformly dark blue and have the same basal spacing. Equation (2) describes the overall reaction. The cobalt complex also catalyzes equilibration between phases of different degrees of intercalation.

$$K + \boxed{C_x} \xrightarrow[\text{pentane, 1 d, 25 °C}]{\text{[catalyst]}} \boxed{KC_8} \xrightarrow[\text{pentane, 4 d, 25 °C}]{\text{[catalyst]}} \boxed{KC_{24}} \qquad (2)$$

The reaction mechanism was confirmed by X-ray powder diagrams for nonsolvated K, Rb, and Cs compounds: After short reaction times only the compounds of the 1st stage (AC_8) were generally observed along with unchanged graphite. On prolonged reaction times compounds of higher stages could be prepared with appropriate quantities of potassium.

Thus, intercalation according to reaction (1) is kinetically controlled. Nucleation of the AC_x phases appears to be the rate determining step. In contrast, electrochemical intercalation is thermodynamically controlled, *i.e.* the reaction proceeds starting from graphite *via* higher stages to the 1st stage as the final product[2c].

The unusual reactivity of catalytically generated KC_8 is probably attributable to disorder effects. In general, solid state reactions performed at room temperature lead to less ordered, and hence frequently more "active" products than high temperature reactions.

Catalytic intercalation in solution permits the first transformation of highly oriented carbon fibers into good electrical conductors by conversion into KC_8[8].

Preliminary experiments have shown that solution intercalation of alkali metals can also be accomplished with metal chalcogenides having layer structures (MoS_2, WS_2). Catalytic reductions with Li are also feasible. Thus gray antimony (1.7 g, 1% $Co(C_5H_8)(PMe_3)_3$ in tetrahydrofuran (10 ml), 48 h, 25 °C) quantitatively yields the cubic low-temperature phase β-Li_3Sb. The potential of these highly reducing solutions is estimated at 2.5—3 V.

Received: December 11, 1979 [Z 482 IE]
German version: Angew. Chem. 92, 476 (1980)

CAS Registry numbers:
KC_8, 12081-88-8; RbC_8, 12193-29-2; CsC_8, 12079-66-2; $Co(C_2H_4)(PMe_3)_3$, 73770-97-5

[1] a) *W. Rüdorff*, Adv. Inorg. Chem. Radiochem. *1*, 224 (1959); *G. R. Hennig*, Progr. Inorg. Chem. *1*, 125 (1959); *W. Rüdorff, E. Schulze*, Z. Anorg. Allg. Chem. *277*, 156 (1954); *A. Schleede, N. Wellmann*, Z. Phys. Chem. *B 18*, 1 (1932); *M. A. M. Boersma*, Catal. Rev. *10*, 243 (1974); b) *D. Billaud, A. Hérold*, Carbon *17*, 183 (1979), and references cited therein.
[2] a) *W. Rüdorff, E. Schulze, O. Rubisch*, Z. Anorg. Allg. Chem. *282*, 232 (1955); b) *I. B. Rashkov, I. M. Panayotov, V. C. Shishkova*, Carbon *17*, 103 (1979); c) *J. O. Besenhard, ibid. 14*, 111 (1976).
[3] *A. Hérold*, Bull. Soc. Chim. Fr. *22*, 999 (1955).
[4] Manufacturer: Kropfmühl, Passau (Germany), RFL 99.5.
[5] Structure of the catalytically active species: *H.-F. Klein, J. Gross, J. M. Basset, U. Schubert*, Z. Naturforsch. *B 35*, 614 (1980).
[6] a) *G. Merle, I. Rashkov, C. Mai, J. Golé*, Mater. Sci. Eng. *31*, 39 (1977); b) *L. Bonnetain, P. Touzain, A. Hamwi, ibid. 31*, 45 (1977).
[7] For samples prepared in presence of air we obtained basal spacings of 1260—1270 pm.
[8] *J. O. Besenhard, H.-F. Klein, J. Gross, H. Möhwald, J. J. Nickl*, Synth. Metals, in press.

Nonstoichiometric Alkali Metal Titanium Sulfides with Channel Structure

By *Robert Schöllhorn, Wolfgang Schramm,* and *Dieter Fenske*[*]

The reduction of binary transition metal chalcogenides M_yX_z in alkali metal halide melts represents a suitable technique for the preparation of ternary chalcogenides $A_xM_yX_z$ (A = alkali metal, M = transition metal, X = S, Se, Te)[1]. In a study on the Ti/S system we observed the formation of the ternary sulfide $K_{0.3}Ti_3S_4$, which crystallizes in a structure type not described so far for the alkali metal titanium sulfides. Reduction of TiS_2 in a KCl melt at 1300 K with potassium metal (TiS_2:K = 1:1.7) leads to formation of a solid phase consisting of gray, needle-shaped crystals with a metallic luster; analytical data correspond to a ratio K/Ti/S = 0.3/3/4. Direct reduction of TiS_2 with K in titanium vessels at 1300 K yields the same compound, which, however, is contaminated by additional phases. Guinier powder diagrams and Weissenberg single crystal photographs showed $K_{0.3}Ti_3S_4$ to be hexagonal ($a = 950.5$, $c = 341.4$ pm, $Z = 2$). The structure was determined from automatic diffractometer data (MoK_α, 590 symmetry independent reflections, space group $P6_3/m(C_{6h}^2)$. There are two different sulfur positions in the unit cell; Ti and S(2) atoms occupy the position 6 h, whereas the S(1) atoms occupy the positions 2(c) (for positional parameters see Table 1). With Ti and S parameters only the structure model gave an agreement factor of $R = 0.081$. In a subsequent difference Fourier synthesis maxima could be detected on the positions 2a (0, 0, 1/4) and 2b (0, 0, 0). With the assumption of a statistical distribution of K^+ on these positions R showed a minimum at 0.30(5) K/Ti_3S_4; the agreement factor was $R = 0.065$.

Table 1. Positional parameters of Ti and S atoms in $K_{0.3}Ti_3S_4$.

	x	y	z
Ti	0.4867(2)	0.3546(2)	1/4
S(1)	1/3	2/3	1/4
S(2)	0.6928(3)	0.6437(3)	1/4

The structure can be described in terms of distorted TiS_6 octahedra joining common faces and edges to form a three-dimensional framework which is characterized by wide channels parallel to the hexagonal c axis which are incompletely occupied by potassium atoms (Fig. 1). The Ti atoms are displaced from the center of the TiS_6 octahedra so that

[*] Prof. Dr. R. Schöllhorn, Dipl.-Chem. W. Schramm, Priv.-Doz. Dr. D. Fenske
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

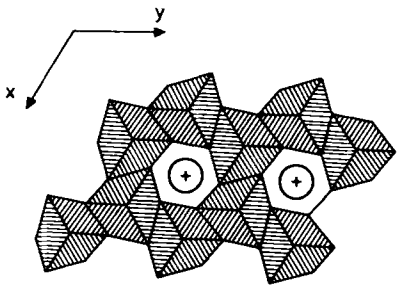


Fig. 1. Scheme of $K_{0.3}Ti_3S_4$ structure (cross section perpendicular to channel axis; circles indicate positions of $K^{\oplus}$ ions).

metal-metal zig-zag chains are formed; the Ti—Ti distance of 315.2(3) pm is close to that in titanium metal. The S(1) atoms are surrounded by six Ti atoms at the corners of a trigonal prism, while the S(2) atoms form the "channel wall" and have strongly asymmetric environment. Similarly to $Tl_xTi_6Se_8$[2], $A_xNb_3S_4$ and $A_xNb_3Se_4$[3] the ternary sulfide $K_{0.3}Ti_3S_4$ can thus be considered as a partially filled up structural version of the Nb_3Se_4 type[4].

Chalcogenides with channel type structure (*e.g.* Nb_3S_4, Mo_6S_8) have recently been shown by us to undergo reversible topotactic redox reactions at ambient temperature by electron/ion transfer[3, 5]. Like layered structures[6] they are of interest regarding their application as reversible electrodes in high density batteries. We found that the ternary titanium sulfide phase described here contains highly mobile $K^{\oplus}$ ions and is able to react in a similar way according to:

$$Ti_3S_4 + x\,e^{\ominus} + x\,A^{\oplus} \rightleftarrows A_x^{\oplus}[Ti_3S_4]^{x\ominus} \qquad (1)$$

Anodic oxidation of polycrystalline $K_{0.3}Ti_3S_4$ electrodes in $K^{\oplus}/H_2O$ electrolyte yields Ti_3S_4, while on cathodic reduction $K_{1/3}Ti_3S_4$ is obtained at the upper phase limit. The reduction of Ti_3S_4 in organic $Li^{\oplus}$/propylene carbonate electrolyte results in the reversible formation of $Li_{0.8}Ti_3S_4$; the steps appearing in the potential/charge transfer curve (Fig. 2) indicate the existence of intermediate phases. As a consequence of the rigid host lattice matrix changes in the lattice parameters with x are very small.

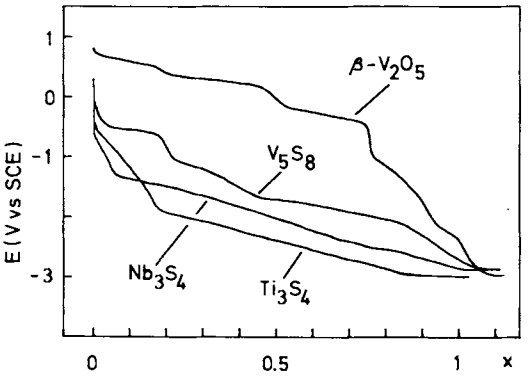


Fig. 2. Potential/charge transfer curves for topotactic cathodic reduction of Ti_3S_4, Nb_3S_4, V_5S_8 and β-V_2O_5 in 1 M $Li^{\oplus}$/propylene carbonate at 298 K; charge transfer $x = e^{\ominus}$/unit formula.

The ternary phases TlV_5S_8 and β-$Cu_{0.5}V_2O_5$, both of which are characterized by channel type structures[7], revealed a topotactic redox behavior basically similar to that of $K_xTi_3S_4$. The lattice channels in these compounds are occupied by Tl and Cu atoms, respectively, which according to our results are mobile at ambient temperature. Oxidation of TlV_5S_8 results in the formation of V_5S_8 (residual Tl content corresponding to $Tl_{0.07}V_5S_8$) with the monoclinic lattice parameters $a = 1139.9$ pm, $b = 664.5$ pm, $c = 1129.3$ pm, $\beta = 91.49°$. On cathodic reduction in aqueous or organic electrolytes V_5S_8 may take up reversibly mono- and bivalent cations with an ionic radius up to *ca.* 140 pm; for $Li^{\oplus}$/propylene carbonate a maximum degree of reduction corresponding to $Li_1V_5S_8$ was observed (Fig. 2).

On anodic oxidation of β-$Cu_{0.5}V_2O_5$ a binary metastable phase β-V_2O_5 is obtained after a transfer of $1.0\,e^{\ominus}$/$Cu_{0.5}V_2O_5$; the upper phase limit on cathodic reduction of V_2O_5 in $Cu^{2\oplus}/H_2O$ electrolyte is equivalent to $Cu_{0.65}V_2O_5$. For $Li_xV_2O_5$ phases, which can be prepared, *e.g.*, from $Li^{\oplus}$/propylene carbonate, the maximum guest ion content corresponds to $Li_{1.1}V_2O_5$ (Fig. 2). In contrast to $A_xM_3X_4$ phases the vanadium sulfide and oxide phases show clear changes in lattice parameters with the guest cation content. This reflects a higher flexibility of the host lattice matrix due to lower symmetry and less dense lattice framework.

Received: December 20, 1979 [Z 483 IE]
German version: Angew. Chem. *92*, 477 (1980)

CAS Registry numbers:
$K_{0.3}Ti_3S_4$, 39306-71-3; Ti_3S_4, 12067-25-3; Nb_3S_4, 12266-24-9; V_5S_8, 12067-28-6; β-V_2O_5, 1314-62-1

[1] *R. Schöllhorn, M. Kümpers, D. Plorin*, J. Less-Common Metals *58*, 55 (1978); *R. Schöllhorn, A. Lerf*, J. Less-Common Metals *42*, 89 (1975).
[2] *K. Klepp, H. Boller*, Abstracts of the 6th Int. Conf. on Solid Compounds of the Transition Elements 66 (1979).
[3] *R. Schöllhorn, W. Schramm*, Z. Naturforsch. *34b*, 697 (1979).
[4] *R. Huisman, F. Kadijk, A. J. Wagner, F. Jellinek*, Acta Cryst. *B 24*, 1614 (1968); *K. Selte, A. Kjekshus*, Acta Cryst. *17*, 1568 (1964).
[5] *R. Schöllhorn, M. Kümpers, A. Lerf, E. Umlauf, W. Schmidt*, Mat. Res. Bull. *14*, 1039 (1979); *R. Schöllhorn, M. Kümpers, J. O. Besenhard*, Mat. Res. Bull. *12*, 781 (1977).
[6] *M. S. Whittingham*, Progr. Solid State Chem. *12*, 41 (1978); *J. O. Besenhard, R. Schöllhorn*, J. Power Sources *1*, 267 (1977).
[7] *L. Fournès, M. Vlasse, M. Saux*, Mat. Res. Bull. *12*, 1 (1977); *J. Galy, D. Lavaud, A. Casalot, P. Hagenmuller*, J. Solid State Chem. *2*, 531 (1970).

Polymer-Polymer Miscibility. By *O. Olabishi, L. M. Robeson,* and *M. T. Shaw.* Academic Press, New York 1979. xii, 370 pp., bound, $ 42.50.

In the last decade, polymer mixtures have been studied with increasing interest. In the literature one finds two lines of research; on the one hand there exist numerous papers supplying more or less detailed experimental information, and on the other, theoreticians have tried to develop molecular models for such systems.

This book gives an excellent survey of both approaches. Starting from first principles the authors give an extensive review of recent developments of classic statistical thermodynamic considerations about the subject. The physical meaning of the parameters introduced in the various molecular models is discussed thoroughly.

With respect to the experimental data in the literature the authors first critically review the methods for determining the state of the mixture. Miscible (co-)polymer blends reported so far are conveniently listed together with some comments about the result. For immiscible polymer pairs the reader is referred to other publications.

As is well known, most polymer pairs are partially miscible. A lot of research is being carried out nowadays in the enhancement of polymer miscibility. The authors discuss several methods that can be used for this purpose.

The aim of most work in polymer mixtures is to obtain a significant diversification of physical properties. In this book a broad field of physical properties of miscible polymer and copolymer mixtures is treated in relation to theoretical models and experimental findings. Some industrial applications, including two phase systems, are given to illustrate the commercial importance of 'versatile' polymer blends.

Summarizing one may conclude that this book offers the academic polymer specialist an up-to-date guide for necessary future investigations, while industrial researchers will find practical possibilities of miscible polymer systems. In addition it will serve as an excellent source-book.

L. A. Kleintjens [NB 510 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Analytical Atomic Absorption Spectroscopy. Selected Methods. By *J. C. Van Loon.* Academic Press, New York 1980. x, 337 pp., bound, $ 35.00.—ISBN 0-12-714050-6

Advances in Chemical Physics, Vol. XLII. Potential Energy Surfaces. Edited by *K. P. Lawley.* John Wiley & Sons, Chichester 1980. 610 pp., bound, £ 27.00.—ISBN 0-471-27633-2

Experimental Methods in Polymer Chemistry. Physical Principles and Applications. By *J. F. Rabek.* John Wiley & Sons, Chichester 1980. xxv, 861 pp., bound, £ 48.00.—ISBN 0-471-27604-9

NMR Spectroscopy. By *H. Günther.* John Wiley & Sons, Chichester 1980. xiv, 436 pp., sewn, £ 7.95.—ISBN 0-471-27579-4

Equilibrium Thermodynamics for Engineers and Scientists. By *R. W. Haywood.* John Wiley & Sons, Chichester 1980. xxv, 430 pp., sewn, £ 7.95.—ISBN 0-471-27630-8

An Infrared Spectroscopy Atlas for the Coatings Industry. Edited by The Infrared Spectroscopy Committee of the Chicago Society for Coatings Technology. Federation of Societies for Coatings Technology, Philadelphia 1980. xi, 896 pp., bound, $ 75.00.—ISBN 0-934010-00-5

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form - by photoprint, microfilm, or any other means - nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar,* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 7
July 1980
Pages 495–574

The Principle of Minimum Chemical Distance (PMCD)[***]

By Clemens Jochum, Johann Gasteiger, and Ivar Ugi[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The principle of minimum chemical distance (PMCD) allows one to formulate the isoprene rule, the conversion of tetrahydrodicyclopentadiene into adamantane, five syntheses of colchicine, and the syntheses of C_{16}-hexaquinacene, morphine and strychnine as optimization problems which can be solved by computers in less than a second. The principle of minimum chemical distance is based on an algebraic theory of constitutional chemistry. The PMCD, a corollary to the well known principle of minimum structure change, is a quantitative heuristic rule which serves as the foundation of the computer-assisted combinatorial solution of a great variety of chemical problems, particularly in substructure analysis, the study of reaction mechanisms, and the design of syntheses.

1. Introduction

Since the introduction of the concept of chemical constitution around the middle of the last century, chemists have relied on the assumption that chemical reactions proceed generally with minimum structural change in the participating molecules. This heuristic rule has been used with great success in the solution of many problems in organic chemistry, and it has gradually acquired the status of a principle, namely the *principle of minimum structure change* (*Hückel*[1a], *Wheland*[1b]). *Hine*[2] has recently discussed the relation between the principle of minimum structure change and various other heuristic rules and principles which have been postulated for chemical reactions. The first of such principles to be formulated was the Rice-Teller principle[3], which led to the principle of least nuclear motion, and the principle of least change in electronic configuration. The Schuler principle[4] and the Woodward-Hoffmann rules[5] should also be mentioned in this context. Neither the principle of minimum structure change nor any one of the latter principles has been stated in a quantitative form in which it may directly serve as the basis for combinatorial algorithms and computer programs by which some expected minimum can be found.

The topic of this article is the *principle of minimum chemical distance* (PMCD) and its applications. It is a heuristic principle which is a corollary to the principle of minimum structure change. In contrast to the latter, it is directly usable in the computer assisted solution of a great variety of chemical problems.

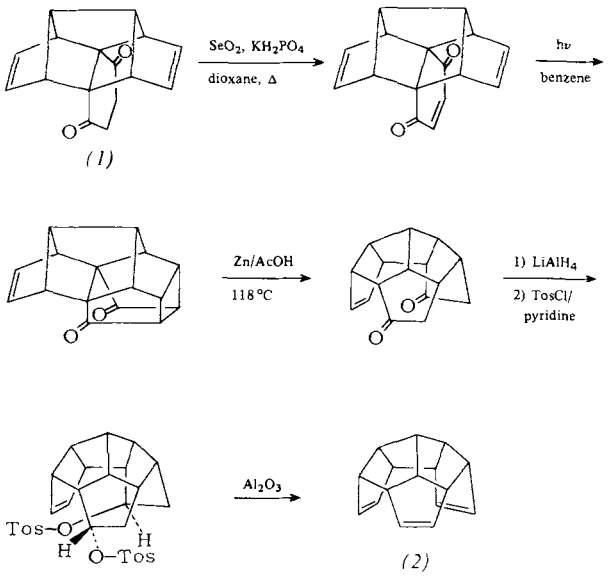
[*] Prof. Dr. I. Ugi, Dr. C. Jochum [**], and Dr. J. Gasteiger
Institut für Organische Chemie der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Present address: Department of Chemistry, University of Washington, Seattle, Washington (USA).

[***] Abbreviations: PMCD = principle of minimum chemical distance; *EM* = ensemble of molecules; *FIEM* = family of isomeric *EM*.

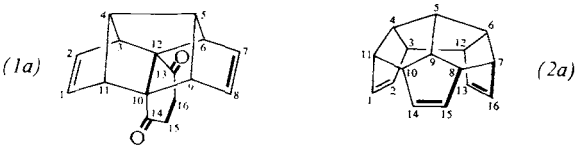
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0707-0495 $ 02.50/0*

The following example may serve as an introductory illustration for potential applications of the PMCD. A recently published synthesis[6] of C_{16}-hexaquinacene *(2)* involves the conversion of *(1)* as follows:



(1) *(2)*

The structural changes which lead from *(1)* to *(2)* appear to be rather deep-seated and complex. However, an efficient scheme for the overall conversion of *(1)* into *(2)* was found in extremely little computation time (0.03 s, Cyber 175) by a computer program which is based on the principle of minimum chemical distance. It involves the breaking of the bold-faced bonds in *(1a)* and the linking of the bold-faced bonds in *(2a)*. It corresponds to an atom onto atom mapping as shown by the indexing of *(1a)* and *(2a)*. It is interesting to note that the bonds which were actually broken and made in the published synthesis of *(2)* from *(1)* coincide precisely with the bonds indicated in *(1a)* and *(2a)*.



(1a) *(2a)*

2. The Principle of Minimum Chemical Distance (PMCD)

In 1973 a mathematical model of the logical structure of families of isomeric ensembles of molecules *(FIEM)*, an algebraic theory of constitutional chemistry, was published[7]. According to this theory the isomeric ensembles of molecules *(EM)* which can be formed from a collection of n atoms are representable as points in $\mathbb{R}^{n^2}$, an n^2-dimensional euclidean space. According to this theory the number of valence electrons that are redistributed during a real or conceivable chemical reaction corresponds to a distance between the points representing the isomeric *EM*s which participate in the reaction from the educts to the products. The term *chemical distance* has been introduced for the number of valence electrons which must be shifted in order to interconvert isomeric *EM*[*] under a given atom onto atom mapping. The chemical distance between two isomeric *EM*s is a quantitative measure for the chemical relatedness of molecular systems. This permits the formulation of the principle of minimum structure change in quantitative terms as the *principle of minimum chemical distance* (PMCD):

Most chemical reactions proceed along a pathway of minimum chemical distance, i. e. with a redistribution of a minimum number of valence electrons.

The translation of the principle of minimum structure change into PMCD is quite obvious. Since a reaction pathway of minimum chemical distance corresponds to a reaction in which a minimum number of valence electrons is being redistributed, it is also a reaction pathway with minimum breaking and making of bonds, as well as minimum involvement of free valence electrons. Thus it proceeds with minimum structure change.

The term "minimum chemical distance" is used in this article instead of "minimum number of redistributed valence electrons", in order to remind the reader of the fact that the chemistry of a family of isomeric ensembles of molecules *(FIEM)* is of a metric nature. We also wish to call attention to the fact that we really exploit the metric properties of the representation spaces of *FIEM* in our computer programs for finding an atom onto atom mapping for isomeric *EM*s with minimum chemical distance[8,9].

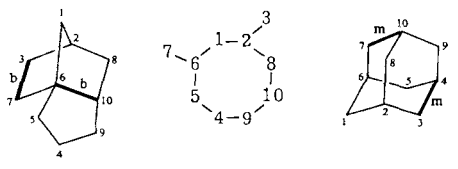
3. Scope of the Principle

The scope of the PMCD is the interconversion of ensembles of molecules regardless of whether or not this interconversion is actually possible or only conceivable. We have investigated three major types of applications of the PMCD: substructure matching, the elucidation of reaction mechanisms, and the evaluation of syntheses.

3.1. Substructures

Any atom by atom matching of two isomeric ensembles of molecules has a characteristic chemical distance. In a matching with minimum chemical distance we have maximum coincidence of substructures. Therefore the PMCD may be used to correlate substructures: The chemical similarity of two isomeric ensembles of molecules in terms of common substructures is obtained by an atom onto atom mapping under the aspect of minimum chemical distance.

The PMCD leads to a well-defined procedure for finding substructures which are common to a pair of ensembles of molecules. The corresponding search procedure detects the ensemble structures, which can be generated by breaking a minimum number of bonds in one, or both ensembles (largest set of largest substructures).

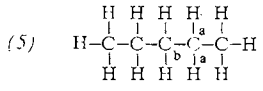


(3) *(4)*

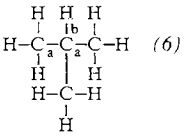
[*] A factor of two which stems from the algebra of BE- and R-matrices and was part of the original definition [7] has been omitted for simplicity.

Intuitively, a six-membered ring might be seen as the largest substructure common to molecules *(3)* and *(4)*. According to the PMCD the conversion of *(3)* into *(4)* can be achieved by breaking ("b") and making ("m") the bonds indicated. This corresponds to an atom onto atom mapping as shown by the indexing of structures *(3)* and *(4)*. As can be seen from this result, *(3)* and *(4)* have a disubstituted eight-membered ring as largest common substructure.

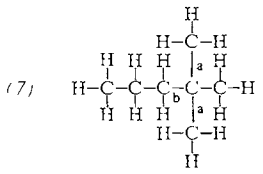
Note that our approach which looks for the *largest set of largest substructures* might give results which are different from those obtained with other substructure search procedures which perceive only the *largest common substructures*.



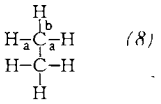
(5)



(6)

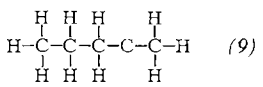


(7)

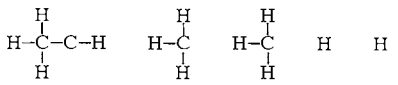


(8)

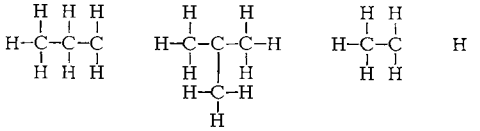
Obviously, the largest substructure which is common to the two ensembles {*(5)*, *(6)*} and {*(7)*, *(8)*} is *(9)*; the complementary substructures of *(9)* are shown underneath. The interconversion of {*(5)*, *(6)*} and {*(7)*, *(8)*} with preservation of these substructures requires the breaking of the bonds labeled by "a"; the chemical distance for this conversion is eight. In the ensemble of substructures 25 bonds are retained.



(9)



Our procedure yields the following four substructures: The correlation is obtained by breaking the bonds with label "b". The chemical distance between *(5)* and *(6)*, and *(7)* and *(8)* is four; 27 bonds are retained. This example illustrates that in



the correlation of substructures the search for the largest one may be chemically less meaningful than the search for the largest set of largest substructures which leads to a maximum overall coincidence.

3.2. Chemical Reactions

The correlation of the atoms in the educts and products of a reaction often depends on the reaction mechanism. Conversely, conclusions about the mechanism can be drawn if one knows for each atom in the products the corresponding atom in the educts. This is the working basis for any elucidation of reaction mechanisms by isotopic labeling. In essence our present computer program labels all atoms involved and finds a correlation of labelings which corresponds to a minimum chemical distance.

In the elucidation of reaction mechanisms the minimum chemical distance is a measure of the minimum mechanistic complexity of the reactions: the minimum chemical distance is twice the minimum number of arrows which are needed for describing the reaction by an "electron shifting pattern". For a given overall reaction there may be several mechanistic pathways which correspond to the same minimum chemical distance.

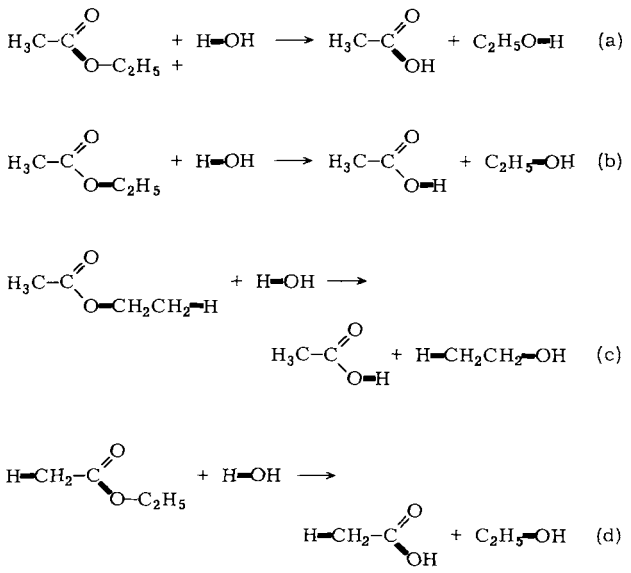
Chemical reactions are generally sequences of elementary steps. They are here treated as a single overall process. The chemical distance they cover is given by the overall displacement of electrons. The number of valence electrons which may have participated in the individual mechanistic steps of the reaction may be larger than is seen in the chemical change which determines the chemical distance.

With increasing complexity of reactions, *i.e.* with an increase in the number of elementary steps, the chance is enhanced that the reaction proceeds with an overall displacement of more valence electrons than the minimum number required. However, even then the number of valence electrons shifted deviates only slightly from the minimum chemical distance. This is always the case when a reaction mechanism involves the intermediate formation of a bond which is broken again in a later step and vice versa, or when an intermediate redox process occurs, which is later followed by a reverse process. Catalytic reactions proceeding through intermediates are typical representatives of such reactions whose actual pathways are "longer" than the minimum chemical distance. The reason for the preference of certain longer pathways is that they avoid some high energy barriers which sometimes obstruct the shortest pathway. Even in such cases investigation of the minimum chemical distance leads to valuable insights, for "mechanistic detours" tend to be as short as possible. The correlation of educts and products from the aspect of minimum chemical distance indicates the least changes which must be accomplished in the overall process.

The hydrolysis of ethyl acetate may serve as a simple illustration. For this reaction the four schemes (a)—(d) are conceivable.

The minimum chemical distance of four corresponds to two of the known mechanistic types of ester hydrolysis, *i.e.* O-acyl (a) and O-alkyl cleavage (b). Reaction path (c) involves the intermediacy of ethylene and (d) that of ketene. In both cases the chemical distance is six. Reactions corresponding to path (c) and (d) are conceivable but do not occur in simple cases.

Thus, determination of the minimum chemical distance and the corresponding bond shifting processes affords a good starting point for studying the mechanism of the reaction. It should be noted that the sum of the chemical distances of the individual mechanistic steps of path (a) is larger than the overall chemical distance: The hydrolysis of ethyl acetate proceeds *via* a tetracoordinated intermediate which is formed by attack of the nucleophile on the carbonyl-carbon. The



carbonyl double bond is later restored by elimination of the leaving group. In this way the direct O-acyl cleavage is generally avoided. Further, on acid catalysis an O—H bond is formed which is broken again later.

3.3. Multistep Syntheses

The PMCD is not only applicable to chemical reactions but also to sequences of reactions. Hence, PMCD provides guidance in the design of multistep syntheses.

Under given conditions the mechanistic pathways for chemical reactions are determined by the educts and products, whereas in synthesis the pathways for the conversion of given starting materials into the desired synthetic target are chosen by the chemist. In the design of syntheses, the principle of minimum structure change, which we apply in the form of the PMCD, cannot only be used in the selection of synthetic pathways with a given beginning and end, but it is also potentially useful in the choice of starting materials for a given synthetic target. It helps, *inter alia,* to avoid wasteful use of starting materials.

With very few exceptions, the great multistep syntheses of natural products would appear to have been designed according to the principle of minimum structure change. Syntheses which follow this principle have some natural appeal (cf. Section 5.3).

In a multistep synthesis the conversion of given starting materials into the synthetic target is achieved with minimum structural change, if the synthesis proceeds with an overall displacement of a minimum number of valence electrons. Thus it is desirable to find pathways of minimum structure change, because in these pathways only those bonds participate whose opening and closing is absolutely necessary. The choice of such pathways generally leads to a minimum number of synthetic steps.

Often a synthesis not only requires the operations and materials which are directly needed, but also the protection and deprotection of functional groups which might otherwise undergo undesirable reactions. Obviously the group protection techniques increase the number of synthetic operations to be performed and the amount of material being used. This is reflected by an increase in the chemical distance. However, we wish to emphasize that minimum chemical distance is just one criterion for the evaluation of syntheses. A synthesis along a pathway of minimum chemical distance may not necessarily be feasible, or best in yield. Sometimes a pathway with a moderate detour may be more effective in practice.

4. Solution of the Minimization Problem

In this section we briefly discuss the logic of the approach (cf. [8], for details see [10]). Every chemical reaction can be regarded as an isomerization of an ensemble of molecules *(EM)*. The conversion of an $EM(\mathbf{B})$ at the beginning of a reaction or sequence of reactions into an $EM(\mathbf{E})$, which contains the synthetic target, may be represented by a transformation $\mathbf{B} \rightarrow \mathbf{E}$ of the corresponding BE-matrices $\mathbf{B} = (b_{ij})$ and $\mathbf{E} = (e_{ij})$ by the addition of an R-matrix $\mathbf{R} = (r_{ij})$[*] according to

$$\mathbf{B} + \mathbf{R} = \mathbf{E} \tag{e}$$

The BE-matrices **B** and **E** of the ensembles $EM(\mathbf{B})$ and $EM(\mathbf{E})$ which contain the same collection of n atoms are symmetric $n \times n$ matrices, whose rows and columns are assigned to the atoms in the isomeric *EM*; the i-th row and the i-th column both represent the core of the i-th atom A_i. The entries b_{ij}, and e_{ij} $(i \neq j)$ respectively, are the formal orders of the covalent bonds between the atoms A_i and A_j and the entries b_{ii}, e_{ii} are the numbers of the valence electrons of the atoms A_i.

The n rows/columns of an $n \times n$ BE-matrix may be assigned to the n atoms of an *EM* in n! different ways. Thus a given $EM(\mathbf{B})$ is representable by up to n! distinct BE-matrices, which are interconvertible by row/column permutation. Therefore any two BE-matrices **B** and **B'** represent the same $EM(\mathbf{B})$, if **B** is transformed into **B'** according to:

$$\mathbf{B}' = \mathbf{P} \cdot \mathbf{B} \cdot \mathbf{P}^t \tag{f}$$

Here $\mathbf{P} = (p_{ij})$ is an $n \times n$ permutation matrix, and $\mathbf{P}^t$ its transposed matrix. Since each permutation can also be expressed by a mapping which reorders the numbers 1,..., n, equation (f) can also be written as:

$$b'_{ij} = b_{\pi(i)\,\pi(j)} =: \pi(\mathbf{B}) \qquad i,j = 1,\ldots,n \tag{f'}$$

$$\text{with} \quad \pi: \{1,\ldots,n\} \rightarrow \{1,\ldots,n\}$$

The n^2 entries in a BE matrix can be regarded as coordinates in a n^2-dimensional euclidean space ($\mathbb{R}^{n^2}$). The matrices **B** and **E** correspond to a pair of points in $\mathbb{R}^{n^2}$. The function

$$D(\mathbf{E},\mathbf{B}) = \frac{1}{2}\sum_{i,j}|e_{ij} - b_{ij}| = \frac{1}{2}\sum_{i,j}|r_{ij}| \tag{g}$$

[*] The abbreviation BE-matrix was chosen to point out that it describes *b*onds and *e*lectrons in molecules as well as the *b*eginning and *e*nd of a reaction.

corresponds to the "city block distance" between the points in $\mathbb{R}^{n^2}$ which represent **E** and **B**. We call $D(\mathbf{E},\mathbf{B})$ the *chemical distance* between $EM(\mathbf{E})$ and $EM(\mathbf{B})$, since it has a direct chemical meaning: It is the number of valence electrons which are displaced in the reaction $EM(\mathbf{B}) \rightarrow EM(\mathbf{E})$. In contrast, the euclidean distance

$$d(\mathbf{E},\mathbf{B}) = \sqrt{\sum_{ij}(e_{ij}-b_{ij})^2} \qquad (h)$$

has no direct chemical meaning. However, as a metric of $\mathbb{R}^{n^2}$ the euclidean distance is topologically equivalent to the chemical distance, because

$$\frac{1}{2}d(\mathbf{E},\mathbf{B}) \leq D(\mathbf{E},\mathbf{B}) \leq \frac{1}{2}n^2 \cdot d(\mathbf{E},\mathbf{B}) \qquad (i)$$

The BE-matrices **B** and **E** correspond to an arbitrarily fixed indexing of the atoms in $EM(\mathbf{B})$ and in $EM(\mathbf{E})$. If the indexing of the atoms in $EM(\mathbf{E})$ is maintained while the indexing of the atoms in $EM(\mathbf{B})$ is permuted according to eq. (f), the chemical distance

$$D(\mathbf{E},\mathbf{PBP}^t) = \frac{1}{2}\sum_{ij}|e_{ij}-b_{p(i),p(j)}| = F(\mathbf{P}) \qquad (j)$$

is a function of the permutation **P** acting on the row/column indices of **B**. The minimum $F(\mathbf{P}) = \text{min!}$ is a measure of the inherent chemical dissimilarity of the isomeric *EM*. Since the function $F(\mathbf{P})$ can only be minimized by trial and error, some other way must be found to correlate the atoms in pairs of isomeric *EM* according to their minimum chemical distance.

In operations research quadratic assignment algorithms[11, 12] are used which can be modified to find the maximum of the scalar product

$$G(\mathbf{P}) = \sum_{i,j} e_{ij} \cdot b_{p(i),p(j)} = \text{max!} \qquad (k)$$

It can be shown that the maximization of $G(\mathbf{P})$ is equivalent to the minimization of the euclidean distance $d(\mathbf{B},\mathbf{E})$ between **B** and **E**. It can further be shown that the solutions for the maximum of eq. (k) include all solutions for the minimum of eq. (j). Thus the minimization problem of eq. (j) for the chemical distance can be solved by maximizing eq. (k). These quadratic assignment algorithms[12-14] to maximize eq. (k) are based on the construction and searching of a decision tree. Each node of the decision tree consists of a number of already fixed assignments. Nodes and branches starting from a certain node indicate additional fixed assignments. Since there are n! different assignments possible the whole decision tree has n! different branches which differ in at least one node. The algorithm now detects the necessary and sufficient criteria for pruning branches and leading to an optimum solution.

At each node a lower bound is determined for solutions which all have certain fixed assignments determining this node. In addition, an optimum solution for this node, *i.e.* an optimum solution with respect to these certain fixed assignments is determined. If this solution is better than a previously found solution, it is stored and considered as an upper bound to all possible solutions. If a lower bound of a certain node is higher than the upper bound (of all solutions), the nodes starting from this node do not have to be treated since they cannot contain an optimum solution and all branches starting from this node can be pruned. These algorithms are often called branch-and-bound algorithms since they determine bounds to and among branches of a decision tree.

5. Applications of the Principle

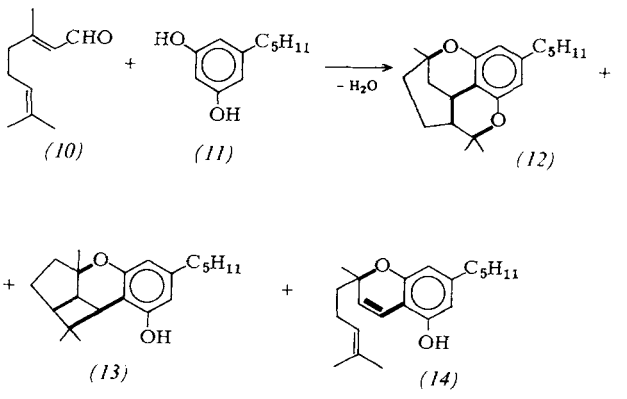
The preceding parts of this article demonstrate that the PMCD is universal in nature and can be applied to the solution of many substantially different types of problems. In this section, its usefulness, scope, and limitations will be illustrated.

5.1. Correlation of Substructures

The correlation of substructures by the PMCD does not only differ from other methods of substructure correlations by leading to the largest set of largest substructures but also by providing a direct atom onto atom mapping.

The terpenes are a class of natural products with an unusually high degree of structural variety. Here, the isoprene rule is a powerful principle of order. The validity of the isoprene rule and deviations from it can be checked by a substructure analysis of the terpenes according to the PMCD. Had our program existed before the discovery of the isoprene rule, this rule would have been found as follows: The occurrence of C_5-subunits can be recognized from the empirical formulas of the terpenes. Starting with combinations of all conceivable C_5-subunits the PMCD would have led to isoprene as the universally occurring substructure. For the individual terpenes as well as the whole set of the known terpenes isoprene would have been found as "precursor". Furthermore, this approach matches the isoprene units with the terpene atom by atom. Thus this atom to atom matching shows how the isoprene subunits have been incorporated into the terpene structure. The recognition of isoprene subunits in the structures of natural products by PMCD is not confined to compounds where the skeleton consists only of isoprene units but it may also be extended to molecules with other skeletal subunits.

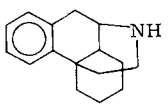
The condensation of citral *(10)* with olivetol *(11)* yields three products: the tetracycle *(12)*, cannabicyclol *(13)*, and cannabichromene *(14)*, which differ significantly in molecular structure[15].



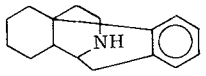
(10) *(11)* *(12)* *(13)* *(14)*

The analysis of the educts and products of this reaction by the PMCD program shows in detail the incorporation of the starting materials into the products and the placement of the isoprene subunits. The bonds in bold face are made during the reactions. The chemical distance from olivetol *(11)* and citral *(10)* to both the skeletons of *(12)* and *(13)* is eight, to the skeleton of *(14)* it is six.

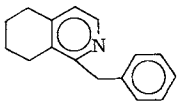
A further example of the application of the PMCD is the correlation of 1-benzyl-5,6,7,8-tetrahydroisoquinoline *(15)* and morphinan *(16)*. The structure of morphinan can be drawn in different ways—*e.g.* as *(16a)* or *(16b)*—with implicit emphasis of various kinds of substructures, each suggesting some synthetic approach.



(16a)



(16b)



(15)

It is customary to represent the structure of morphinan by formulas of type *(16a)* which emphasizes the relation to its degradation product phenanthrene. It must have been the recognition of the structural relation between 1-benzyl-5,6,7,8-tetrahydroisoquinoline *(15)* and morphinan in its form *(16b)* that led *Grewe et al.* to the design of their morphinan synthesis[16]. This important correlation of substructures was also found by the PMCD program. The chemical distance between the skeletons of *(15)* and *(16)* is only two, demonstating the close relationship between them.

5.2. Elucidation of Reaction Mechanisms

The preparation of adamantane required laborious multistep syntheses until *Schleyer*'s discovery of the conversion of the readily available tetrahydrodicyclopentadiene *(17)* into adamantane *(18)*. This conversion proceeds directly from tetrahydrodicyclopentadiene to adamantane through a sequence of carbonium ions without any directly observable intermediates, although a multistep sequence of rearrangements must undoubtedly be involved. The mechanism of this rearrangement presents an intriguing and not yet completely solved problem.

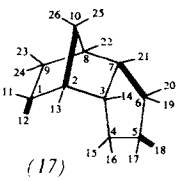
Whitlock[17] proposed a network of conceivable pathways, which consists of 1—2 shifts only. One of the pathways was selected by *Schleyer*[18] as the likeliest one by molecular mechanics calculations.

PMCD provides new insights into this process. Beginning with an arbitrary indexing of tetrahydrodicyclopentadiene *(17)*, we find an indexing of adamantane *(18)* which corresponds to a minimum chemical distance of eight. In comparison, the sum of the chemical distances of the individual

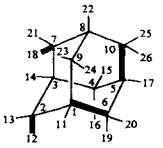
Table 1: Minimum chemical distance between the carbonium ions of tetrahydrodicyclopentadiene *(17)* and adamantane *(18)* [numbered according to *(17a)* and *(18a)*, respectively].

Reaction No.	Carbonium ions in *(17a)*	Carbonium ions in *(18a)*	Disconnected H-Atoms in *(17a)*	Disconnected H-Atoms in *(18a)*	Chemical Distance	Broken Bonds in *(17a)*	Made Bonds in *(18a)*
1	1	1	11	12	6	2–10 6–7 5–18	2–3 4–9 7–20
2	2	1	13	12	8	1–12 2–10 5–18 6–7	1–11 2–3 4–9 7–20
3	3	1	14	12	8	3–4 5–18 8–10 9–24	1–11 5–17 4–9 8–10
4	4	1	15	12	6	1–9 3–7 6–20	3–4 6–7 9–24
5	5	1	17	12	6	1–12 2–10 6–7	2–3 4–9 7–20
6	10	1	26	12	8	1–9 3–7 4–16 6–20	3–4 5–17 7–10 8–23
7	1	10	12	26	8	1–11 2–10 5–18 6–7	2–3 5–17 7–20 8–10
8	2	10	13	26	8	3–4 5–18 8–10 9–24	1–11 4–9 5–6 8–23
9	3	10	14	26	8	1–12 2–10 5–18 6–7	1–2 5–6 8–23 9–24
10	4	10	16	26	8	1–9 3–7 4–15 6–20	1–6 5–17 8–23 9–10
11	5	10	18	26	8	3–4 5–17 8–10 9–24	3–15 5–17 6–7 8–10
12	10	10	26	26	10	1–11 1–12 2–10 5–18 6–7	2–3 3–15 5–18 7–20 8–10

steps of the pathways suggested by *Schleyer*[18] is twenty. If the reaction proceeded from hydrocarbon to hydrocarbon the bonds indicated in bold face in *(17)* would be broken, and those in *(18)* would be made. The numbering of the atoms in *(18)* indicates their origin in *(17)*.

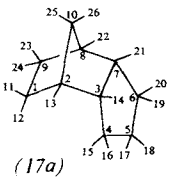


(17)

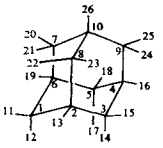


(18)

We are investigating whether the overall change in bonds corresponding to the PMCD can be broken down into mechanistically reasonable steps. In order to obtain a gross classification of the pathways we compared the minimum chemical distance of the 12 pathways which lead from one of the six isomeric carbonium ions of *(17)* to one of the two carbonium ions of adamantane *(18)* (cf. Table 1).



(17a)



(18a)

In all examples the atoms in *(17)* are indexed as in *(17a)*, and the atoms in *(18)* as in *(18a)*, in order to have a reference for the bonds broken and made. Interconversion of the hydrocarbons requires the involvement of two more bonds than the interconversion of the carbonium ions.

Thus a minimum chemical distance of six can be expected for the carbonium ions. This minimum is only found for the pairs in rows 1, 4 and 5. It is noteworthy, that all pathways with a minimum chemical distance of six lead from a secondary carbonium ion of *(17)* to a secondary carbonium ion of *(18)*. In each one of these cases the secondary carbonium ion center in *(18)* corresponds to an initially tertiary carbon atom in *(17)*.

5.3. The Study of Chemical Syntheses

Synthetic strategies involve the ability "to look ahead" from the target molecule to the starting materials along the reverse pathways[19,20]. In general this looking ahead covers only parts of synthetic pathways, and only a few most ingenious syntheses seemed to have been designed with a complete "look ahead" from the target to the starting materials.

With the PMCD we have a tool in our hands which allows us to find the largest set of largest substructures in a pair of isomeric *EM*s. In synthetic planning these two ensembles comprise, on the one hand, the target and its coproducts, and on the other, a set of starting materials taken from a list of all available compounds. The selection of an appropriate collec-

Atomic indices in *(17a)* assigned to atoms in *(18a)*																							
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
2	1	6	5	4	3	7	10	8	9	[12]	13	11	19	17	18	16	20	15	14	21	26	22	23	24	25
2	1	6	5	4	3	7	10	8	9	13	11	[12]	19	17	18	16	20	15	14	21	26	22	23	24	25
3	2	1	9	10	7	6	5	4	8	14	15	13	[12]	24	25	26	17	20	21	19	18	16	11	22	23
3	2	1	6	5	4	9	10	7	8	14	15	13	11	[12]	19	17	18	16	24	25	26	20	21	22	23
2	1	6	5	4	3	7	10	8	9	13	20	11	19	17	18	[12]	16	15	14	21	26	22	23	24	25
3	2	8	10	9	4	5	6	7	1	14	15	13	22	26	17	24	25	16	23	18	19	20	21	11	[12]
10	7	6	1	2	8	5	4	9	3	17	[26]	21	19	11	12	13	20	22	23	18	16	24	25	14	15
7	10	8	5	4	3	2	1	6	9	20	21	[26]	22	17	18	16	23	14	15	13	12	19	11	24	25
2	8	10	7	6	1	9	4	3	5	13	24	22	[26]	20	21	19	23	11	12	25	16	14	15	17	18
1	2	8	10	7	6	5	4	9	3	11	12	13	22	23	[26]	20	21	19	17	18	16	24	25	14	15
1	2	3	7	10	9	4	5	6	8	11	12	13	14	20	21	17	[26]	24	25	16	18	19	15	22	23
10	7	6	1	2	8	5	4	9	3	15	18	21	19	11	12	13	20	22	23	17	16	24	25	14	[26]

tion of starting materials from the list involves the comparison of various combinations of starting materials. Any eligible combination of molecules in the list must contain substructures whose union covers the target. The remaining substructures in the starting materials must yield a combination of feasible coproducts. With this concept, synthetic design consists of two parts: first, the selection of a suitable collection of starting materials and coproducts, and secondly a search for optimum synthetic pathways from the starting materials to the target (and its coproducts).

In order to explore the performance and merits of the PMCD program for this latter part of synthetic design with a complete "look ahead", we applied the program to the target and its coproducts together with the known starting materials of various published syntheses. We now consider the pathways which begin with the same ensemble of starting materials *EM*(**B**) and end with the same target ensemble *EM*(**E**) containing the target compound and its products. Generally there are many conceivable pathways for the synthesis of a target ensemble *EM*(**E**) from a given ensemble of starting materials *EM*(**B**). Besides the compounds involved, the bonds which are broken and made as well as the sequence of these changes are characteristic for individual synthetic pathways.

In a multistep synthesis each step has its characteristic chemical distance, and the sum of these distances is a typical feature of a given multistep synthesis. An electron shifting pattern with a characteristic chemical distance may be associated with the overall changes in valence electron distribution which take place in the synthesis. In such a pattern intermediate changes which cancel out in the net results are neglected, *e.g.* bonds which are made and broken in protecting group techniques. Obviously the sum of the chemical distances of the individual steps of a synthesis may be larger than the overall chemical distance, and this in turn may be larger than the minimum chemical distance between *EM*(**B**) and *EM*(**E**).

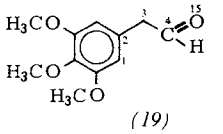
We conjecture that in the design of syntheses the best synthetic routes from a given *EM*(**B**) to *EM*(**E**) will be found among those for which the characteristic overall chemical distance is equal, or close, to the minimum chemical distance. This is illustrated by the following examples in which some published syntheses or their essential parts are analyzed by minimization of chemical distance. We deliberately chose sequences of synthetic reactions corresponding to complex chemical changes which are not immediately obvious.

Because of its interesting pharmacological properties and its unusual structure, colchicine *(21)* has attracted much attention from synthetic chemists. Of the numerous syntheses we chose five; they all involve rather complex chemical changes. Within each of these syntheses a sequence of steps was selected which reflects the essential concept of the whole synthesis. For none of the investigated sequences of reactions can one tell off-hand the pattern according to which the precursors are incorporated into the target molecule.

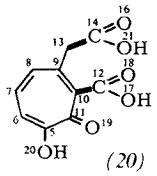
In the syntheses of natural products the construction of the molecular framework is the main task. Therefore and because changes in the placement of hydrogen atoms take place easily and can be treated separately, only bonds between nonhydrogen atoms were taken into account to determine the minimum chemical distance.

In the following synthetic schemes the bonds broken and made are shown in boldface.

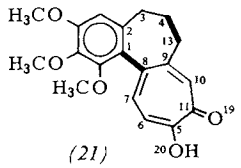
The synthesis by *Scott et al.*[21] is probably the one in which the mapping pattern of incorporation of the two starting materials in desacetamidocolchicine *(21)* is easiest to guess.



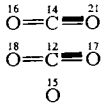
(19)



(20)

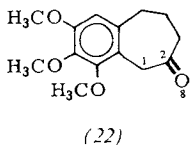


(21)

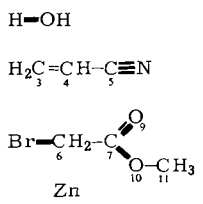


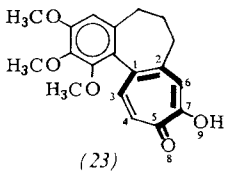
With the PMCD program we obtain the minimum chemical distance and a substructure matching for the conversion of *(19)* and *(20)* into *(21)* + O + 2 CO_2, which corresponds to the overall breaking and making of bonds in the actual synthesis. The brevity and elegance of the synthesis is reflected in the rather low value of the minimum chemical distance of eight.

The conversion of *(22)*, acrylonitrile and methyl bromacetate into *(23)* is the centerpiece of the synthesis of *van Tamelen et al.*[22]. For this we find a minimum chemical distance of 18 and an overall scheme of bond breaking and making which agrees with the published synthesis. The higher value for the minimum chemical distance in this synthesis relative to the synthesis of *Scott et al.* is a consequence of the small size of the substructures which are combined, as well as of the bond shifting in a multiple bond system.

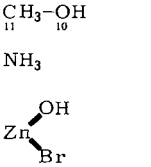


(22)



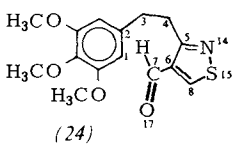


(23)

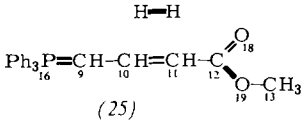


In the colchicine synthesis of *Woodward et al.*[23] the overall changes in the construction of the molecular framework [*(24)* + *(25)* → *(26)*] are also achieved with the minimum chemical distance (= 14)[*].

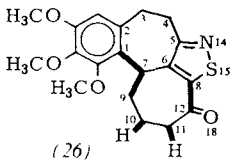
[*] In this synthesis the participation of some hydrogen atoms must be taken into consideration.



(24)



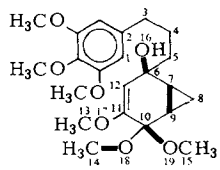
(25)



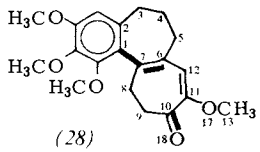
(26)



The main feature of the colchicine synthesis of *Evans et al.*[24] [*(27)*→*(28)*] is a deep-seated rearrangement of the bond system. Thus it may be surprising that the PMCD program found precisely the scheme of bond breaking and making which underlies this conversion. The minimum chemical distance for the conversion *(27)*→*(28)* is eight.



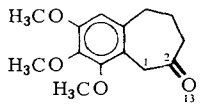
(27)



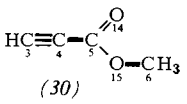
(28)



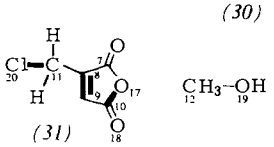
The colchicine synthesis of *Eschenmoser et al.*[25] demonstrates that in synthesis planning the PMCD is not a rule without exceptions. The essential overall changes in this synthesis correspond to the breaking and making of bonds according to the scheme below [*(29)* + *(30)* + *(31)* + *(32)*] and has a chemical distance of 20.



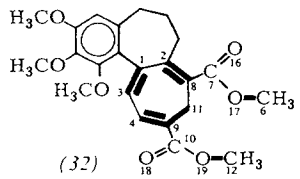
(29)



(30)



(31)

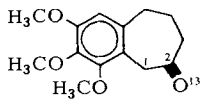


(32)

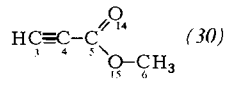


For the same conversion our program finds a minimum chemical distance of 14 for the following bond breaking and making scheme.

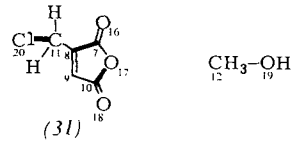
In the formulation of the PMCD we carefully avoided the categoric requirement that the results of each and any sequence of reactions must be achieved through a pathway of minimum chemical distance. A reaction or a sequence of reactions must not necessarily proceed with the displacement of a minimum number of valence electrons. It may well be possible that for a given chemical conversion a pathway with a higher chemical distance than the minimum is more favorable than one with the minimum chemical distance.



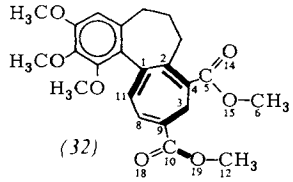
(29)



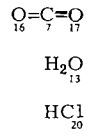
(30)



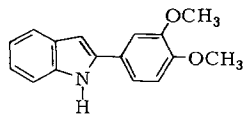
(31)



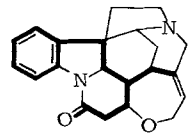
(32)



Strychnine! For its molecular size it is the most complex structure known. These words characterize well the total synthesis of strychnine by *Woodward et al.*[26] as one of the milestones in organic synthesis. One of the ingenious features in this synthesis is the use of veratrol derivative *(33)* as a starting material and its incorporation into the target *(34)* (bold face).



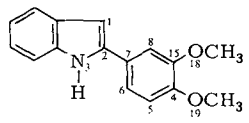
(33)



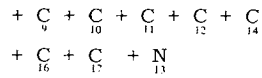
(34)

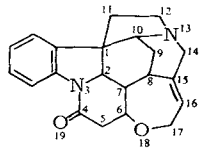
We considered the complex synthetic problem of strychnine as a suitable test case for studying the scope and limitations of the PMCD program.

First we wanted to see how the program would use the veratrol derivative *(33)* as a starting material for strychnine. For



(33)





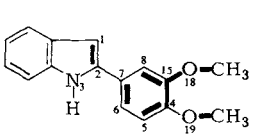
(34)

+ 2 CH_3

this, *(33)* was augmented by seven carbon atoms and a nitrogen atom to yield an *EM* which has the same set of non-hydrogen atoms as strychnine. Two optimal matchings were obtained. One of them corresponds to the incorporation of *(33)* into strychnine by *Woodward et al.*

The other matching is only different by coincidence of carbon atom C-15 in *(33)* and C-9 (instead of C-15) in strychnine. This result could hardly have been achieved by any one of the customary substructure search programs. In the customary approach to substructure search either the entire structure of *(33)* or a heuristically defined substructure (*e.g.* indolyl or dimethoxyphenyl) would be compared with strychnine. The heuristic definition of substructures must be chosen, because the set of all substructures is prohibitively large [there are up to 19! substructures in *(33)*]. In our approach we search for the largest set of largest substructures by selectively breaking bonds during the matching process with the chemical distance as a guideline. Thus, it is not surprising that with the PMCD program a benzene ring is matched with a chain of six carbon atoms.

In *Woodward*'s synthesis, in addition to *(33)*, two C_2-units (acetylene and ethyl glyoxylate), a C_1-unit, and a C_2N-unit (from formaldehyde and cyanide) were used for the construction of the strychnine skeleton. As a second part of our study we therefore investigated the matching of *(33)* and these buildings blocks onto strychnine. Several matchings corresponding to the minimum chemical distance were found, including also the pattern of *Woodward*'s synthesis. In formula *(34a)* the bonds which are made during the synthesis are indicated by bold face lines.



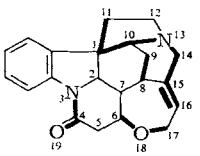
(33)

$+ \overset{11}{C}-\overset{12}{C}-\overset{13}{N}$

$+ \overset{9}{C}-\overset{10}{C}$

$+ \overset{16}{C}\equiv\overset{17}{C}$

$+ \overset{14}{C}$



(34a)

$+ 2\ CH_3$

This result is particularly noteworthy because of the very large number of synthetic steps which are needed to reach strychnine. This example illustrates the "look-ahead" capabilities of this program. It also shows that the PMCD program can be used to minimize those parts of starting materials which are not built into the target but enter the unwanted coproducts.

The atom by atom matchings and "electron shifting" patterns of multistep syntheses are obtained by minimization of the chemical distance with complete neglect of the stereochemical aspect. It should, however, be noted that any efficient synthetic pathway which also accounts for the stereochemistry should belong to the set of pathways with minimum chemical distance. The examples which we have analyzed confirm this.

6. Conclusion

The PMCD is a principle which is widely applicable in chemistry. Because many general rules which reflect chemical experience, *e.g.* the rule of "minimum structure change", are closely related or equivalent to the PMCD most chemists who learn about it, feel that, intuitively, they have already known the principle. Thus it should be pointed out again that the chemical distance is a quantitative measure of the "efficiency" of chemical reactions which has evolved from an algebraic theory of constitutional chemistry.

The reason for the long delay in its formulation lies in the fact that, despite the conceptual simplicity of the PMCD, its application is practically impossible without an algorithm which permits one to overcome the combinatorial barriers. By the minimum chemical distance program which is described here, it has become possible to apply the PMCD and explore its scope and limitations. Many applications are foreseeable for the PMCD program as a tool in its own right. The real importance of the PMCD program lies, however, in its future uses as a subunit of modular computer programs. Predictably, the computer-assisted design of syntheses, and the elucidation of reaction mechanisms will make increasing use of the PMCD program.

In the future, the development of computer programs for the solution of chemical problems will be characterized by efforts to consider all conceivable solutions. On the other hand, to avoid a "combinatorial explosion", heuristic rules and principles free of arbitrariness have to be developed to select optimum solutions. The large number of alternatives has compelled one, up to now, to disregard many conceivable solutions more or less arbitrarily by rejecting entire categories of solutions or by limiting oneself on empirical information, only. The search for non-arbitrary selection rules and measures of chemical relatedness and their algorithmic treatment will be of decisive importance for progress in that field.

The PMCD is a quantitative heuristic rule and a step in that direction.

We gratefully acknowledge the financial support of the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We appreciate valuable suggestions and helpful advice by Professors R. E. Burkard, J. Dugundji, J. C. Martin, A. Streitwieser Jr., M. R. Willcott III, and J. S. Showell.

Received: January 25, 1979 [A 323 IE]
supplemented: April 14, 1980
German version: Angew. Chem. *92*, 503 (1980)

[1] a) *W. Hückel:* Theoretische Grundlagen der Organischen Chemie. Akademische Verlagsgesellschaft, Leipzig 1934; b) *G. W. Wheland:* Advanced Organic Chemistry. Wiley, New York 1960.
[2] *J. Hine*, Adv. Phys. Org. Chem. *15*, 1 (1977).
[3] *F. O. Rice, E. Teller*, J. Chem. Phys. *6*, 489 (1938).
[4] *K. E. Schuler*, J. Chem. Phys. *21*, 624 (1953).
[5] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[6] *L. A. Paquette, R. A. Snow, J. L. Muthard, T. Cynowski*, J. Am. Chem. Soc. *100*, 1600 (1978).
[7] *J. Dugundji, I. Ugi*, Top. Curr. Chem. *39*, 19 (1973).
[8] *I. Ugi, J. Bauer, J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert*, Angew. Chem. *91*, 99 (1979); Angew. Chem. Int. Ed. Engl. *18*, 111 (1979).
[9] *I. Ugi, J. Bauer, J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert, J. Dugundji:* Informal Commun. Math. Chem. *6*, 159 (1979).

[10] C. Jochum, J. Gasteiger, I. Ugi, J. Dugundji, J. Chem. Soc. Perkin II, submitted.
[11] R. E. Burkard: Methoden der ganzzahligen Optimierung. Springer, Wien 1972.
[12] R. E. Burkard, K. H. Stratmann, Naval Res. Logistics Quart. 25, 129 (1978).
[13] R. E. Burkard, Z. Operat. Res. 19, 183 (1975).
[14] K. H. Stratmann, Diplomarbeit, Universität Köln 1976.
[15] V. V. Kane, R. K. Razdan, J. Am. Chem. Soc. 90, 6551 (1968).
[16] R. Grewe, A. Mondon, Chem. Ber. 81, 279 (1948).
[17] H. W. Whitlock, Jr., M. W. Siefken, J. Am. Chem. Soc. 90, 4929 (1968).
[18] E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, P. von R. Schleyer, J. Am. Chem. Soc. 95, 5769 (1973).
[19] A. Todd: Perspectives in Organic Syntheses. Wiley-Interscience, New York 1956.
[20] S. Turner: The Design of Organic Syntheses. Elsevier, New York 1976.
[21] A. I. Scott, F. McCapra, R. L. Buchanan, A. C. Day, D. W. Young, Tetrahedron 21, 3605 (1965).
[22] E. E. van Tamelen, T. A. Spencer, D. S. Allen, R. L. Orvis, Tetrahedron 14, 8 (1961).
[23] R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, R. B. Kelly, J. Chem. Soc. 1957, 1131.
[24] D. A. Evans, D. J. Hart, P. M. Koelsch, J. Am. Chem. Soc. 100, 4593 (1978).
[25] J. Schreiber, W. Leimgruber, M. Pesaro, P. Schudel, T. Threlfall, A. Eschenmoser, Helv. Chim. Acta 44, 540 (1961).
[26] R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daniker, K. Schenker, J. Am. Chem. Soc. 76, 4749 (1954); Tetrahedron 19, 247 (1963).

High-Resolution Transmission Electron Microscopy Re-examined as a Tool in Solid State Chemistry

By Reginald Gruehn and Wilhelm Mertin[*]

Transmission electron microscopy (TEM) can be used with crystalline solids to obtain direct images of small structural groups comprising a few coordination polyhedra with resolution nearly down to atomic scale ("lattice imaging"). More exact knowledge of the conditions required for direct imaging, as well as improvements in the instruments themselves, have now made it possible to examine very small defect regions (microdomains), faults in the stacking sequence of structural groups or atom layers (planar or Wadsley defects), and isolated defects in narrowly delimited areas that may actually be below the dimensions of the unit cell. The structural principle of the very smallest ordered regions can even be determined when X-ray structure analysis proves unable to do this. "Block structures" are particularly suitable as models for the testing and further development of the high-resolution method; the detection of three-dimensional, two-dimensional, and one-dimensional defects has been studied on such structures.

1. Introduction

A great deal of information is currently available on the structure of solids, and particularly in the case of the crystalline solids the number of known crystal structures is almost beyond computation. The positional parameters of individual atoms, ions, or structural groups (complex ions, molecules, "clusters") in crystalline substances can be determined, most commonly by diffraction methods, and primarily by X-ray structure analysis supplemented by neutron and electron diffraction. However, these diffraction techniques are at their most effective[1] only when a sufficiently large number of adjacent structural elements (unit cells) are ordered, *i.e.* when some structural principle imposes a periodic recurrence over a large region of the solid material (Section 3.7). When this condition is largely satisfied, as is the case with many crystalline materials, then it can be considered that single crystal X-ray diffraction is the most powerful method of structural investigation available to date.

X-Ray structure analysis requires a crystalline region with a uniform structure, *e.g.* with a size of about 1000 Å in all directions; it follows that the picture of the crystal structure obtained is one that has been "averaged" over a large number of unit cells.

Detailed information about structural irregularities in narrowly delimited regions cannot be obtained by such methods, or only at the cost of a great amount of labor, since it is difficult for the X-ray beam to "see" disordered departures from the periodicity. Defects the size of a unit cell, or even ones extending over no more than a few atoms, could be detected until recently only by indirect physical measurements. In particularly favorable cases (as in the metals W, Pt, and Au) point defects could be made directly visible by field ion microscopy (*E. W. Müller* 1956)[2-4].

[*] Prof. Dr. R. Gruehn, Dr. W. Mertin
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0707-0505 $ 02.50/0*

The direct imaging of structural defects[*] found wider application after *Wadsley*, together with *Allpress* and *Sanders* in 1967, had succeeded[6] in examining thin, suitably oriented crystal fragments by transmission electron microscopy. Since that time, direct imaging has enriched the repertoire of techniques available to solid state chemists, mineralogists, and crystallographers.

In the meantime, the examination of solids at a resolution of about 3—4 Å has been achieved in several laboratories[7–13]. In special cases, in which the objective was to develop the technique rather than to obtain the information itself (*e.g.* with Au[14], Si[15], or Ge[16]), even higher resolutions (1—2 Å) have been reached; this is quite possible in principle, but generally requires special specimen-preparation techniques.

2. Trends of Development in the Last 15 Years

2.1. Previous Developments

Whereas ordinary electron microscopy in the transmission mode (transmission electron microscopy, TEM[**]) goes back to *E. Ruska* (1932)[17], since about 1965 it has been complemented and to some extent displaced by scanning electron microscopy (SEM)[18]. The scanning methods, in combination with an analytical evaluation of the emitted X-rays, are not limited to the investigation of surface structures; scanning-transmission methods (STEM) can achieve still more, even yielding information about the bulk of the object under examination. In one new field of application, the investigation of the atomic structure in crystalline solids by high-resolution direct lattice imaging, transmission electron microscopy is however preferred to any other method, even to the STEM combination.

A first decisive step along this path had already been taken by *Menter* (Cambridge), who around 1956 studied the copper and platinum phthalocyanines using a Siemens-Elmiscope 1. The large structural elements of these solid compounds produce conditions favorable to the imaging of the lattice plane separations of 10.3 and 12.0 Å. With foresight, *Menter* wrote about this: "It is suggested that this method may be extended to the study of crystals of even smaller lattice dimensions than the phthalocyanines, making possible the direct study of imperfections in a wide range of materials in relation to properties known to be affected by them such as strength, plastic flow and fracture"[19]. In this case it was also significant that the crystals investigated were stable to the electron beam. In general, organic molecular compounds cannot withstand the beam irradiation at the highest magnifications; however, new impetus resulted from work on high-melting inorganic crystals.

2.2. Block Structures as a Springboard

A whole decade passed after *Menter*'s original success before investigations on Nb_2O_5 and Nb_2O_5-rich ternary oxides led to a major methodological step forward. This development was favored by the two-dimensionally extended unit cells with large structural elements ("blocks") of Nb–O octahedra (Fig. 1), which constitute an unusually variable structural principle (Fig. 2) in systems such as NbO_2–Nb_2O_5 and TiO_2–Nb_2O_5, and also in the Nb_2O_5-rich portions of the systems Nb_2O_5–WO_3 and Nb_2O_5–NbO_2F[20–22].

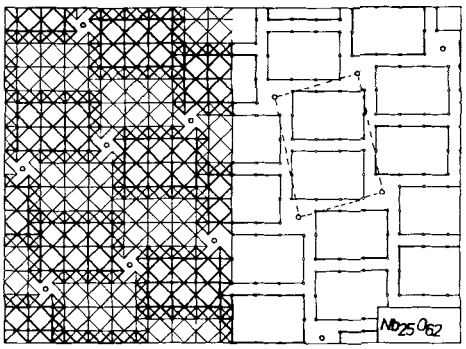


Fig. 1. Ideal structure of $Nb_{25}O_{62}$ as an example of a block structure [20]. The niobium is surrounded octahedrally by oxygens. The niobium atoms in tetrahedral positions between the blocks are indicated by circles. The left-hand side of the figure shows the idealized octahedra, which can be regarded as square-base bipyramids. The direction of view is from an apex down onto the basal plane, so that in projection the apexes appear to be at the points of intersection of the base diagonals. Within the blocks the octahedra are interconnected *via* the apexes in all directions; where the blocks abut against one another, the octahedra are linked with each other along edges. The outlines of the blocks are shown more clearly on the right; for the interconnection of the [3 × 4] blocks, see Figs. 2a and 2b. The different "heights" of the blocks in the direction of the short b-axis (perpendicular to the plane of the figure) are indicated by lines of different thickness; the unit cell is shown by broken lines.

For our knowledge of these concepts we are indebted to X-ray structure investigations, especially those carried out by *Wadsley et al.*[20,23]. More closely related structures can be grouped into "families" or "series", whose members differ in the extent of the blocks (mostly in the longitudinal direction, see Fig. 1), depending on the number n of octahedral layers involved. Together with the size of the blocks, there is also a stepwise change in the chemical composition of the phases (anion/cation ratio), with two-phase regions between them. As shown by the example of some phases in the Nb_2O_5–WO_3 system (Table 1), this concept seems to allow neither for "in-

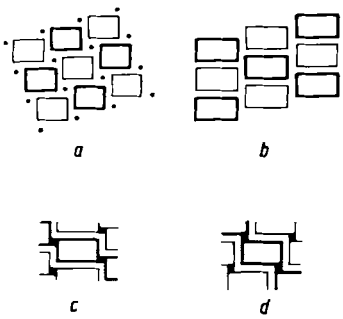


Fig. 2. Modes of interconnection of block structures [21]. a) The blocks are surrounded on all sides by (4/4) tetrahedral sites, *e.g.* $W_{4/4}Nb_{12}O_{33}$; b) the blocks are interconnected exclusively *via* the edges (both short edges), *e.g.* $MgNb_{14}O_{35}F_2$; c) detail of the connection *via* the short edges (see b); d) interconnection as in b and c, but *via* the longer edges (not known up to now in structurally uniform crystals).

[*] The term "Wadsley intergrowth defects" was coined by *Andersson* [5] in memory of *A. D. Wadsley* (1918—1969) (Section 4.3).

[**] The term electron microscopy was first used by *E. Brüche* [16a].

Table 1. Structural principle of some structurally related ternary oxides of the Nb_2O_5–WO_3 system. In the $M_{4n+1}O_{11n}$ series the block sizes of neighboring structures differ by one octahedral layer (n is an integer). The blocks are interconnected on all sides *via* tetrahedral sites ($W_{4/4}$) (see Fig. 2a). The block sizes correspond to the number of coordination polyhedra.

n	$Nb_2O_5:WO_3$	Structural principle [20]	Block size	$O/\sum M$ (M = Nb, W)
3	6:1	$W_{4/4}Nb_{12}O_{33}$	[4 × 3]	2.538
4	7:3	$W_{4/4}Nb_{14}W_2O_{44}$	[4 × 4]	2.589
5	8:5	$W_{4/4}Nb_{16}W_4O_{55}$	[4 × 5]	2.619

termediate phases" nor for phase widths. It was therefore at first surprising to find a further ternary oxide of composition $Nb_2O_5:WO_3 = 13:4$ *between* the 6:1 and the 7:3 phases of this system[24]. In other systems one can even find as many as four additional intermediate phases between the members of the $M_{3n+1}X_{8n-2}$ series ($7 \leq n \leq 11$ with M = Nb and X = O, F)

2.3. On the Road to Atomic-Scale Resolution

Like *Menter*[19], *Wadsley*'s working group first used a one-dimensional[29] imaging technique, *i.e.* the lattice planes of only *one* crystallographic direction were portrayed by selecting the corresponding diffraction spots. Lattice plane separations of *e.g.* 21, 14, and even 10.5 Å could be distinguished, but with the EM 200 electron microscope and side-entry goniometer used, a resolution better than 8—10 Å could not be achieved; in large measure this was due to the use of a goniometer (Section 3.6), which however, one cannot do without. Soon afterward *Allpress*[20] reported a two-dimensional technique, which yields information simultaneously about lattice planes in various crystallographic directions. In this case the diffractogram is not composed of the diffraction spots of only *one* direction, *e.g.* the h00 or 00l spots (direction of incidence along the b-axis) as in the one-dimensional case, but of h0l spots, which also increases the number of

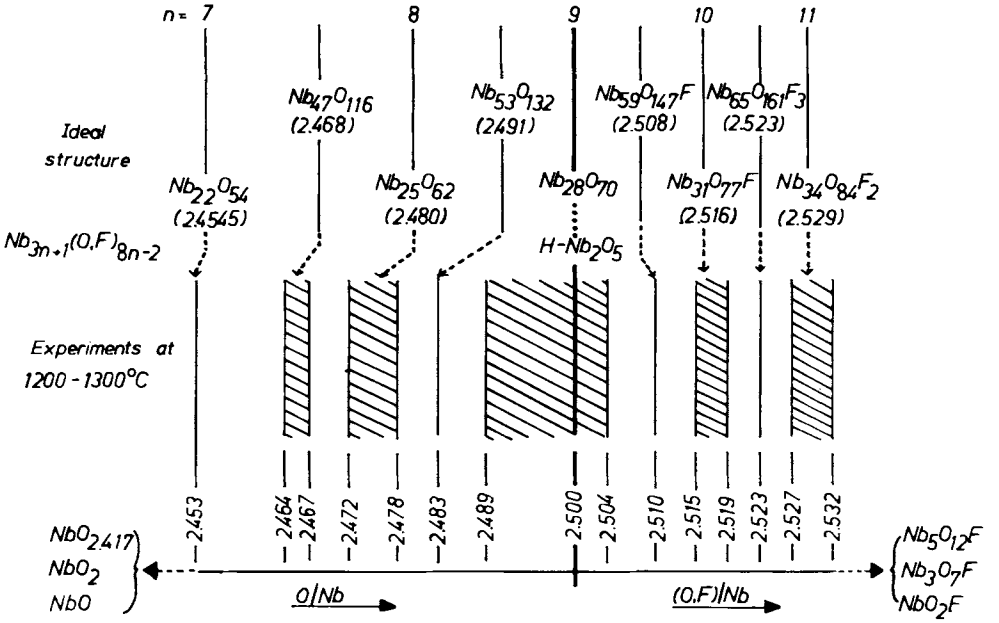


Fig. 3. The NbO_2–Nb_2O_5 and Nb_2O_5–NbO_2F systems at high temperatures [22]. In the representation of the Nb_2O_5-rich partial systems, not to scale, $Nb_{12}O_{29}$ has been omitted as a member of the $Nb_{3n}O_{8n-3}$ ($n = 4$) series. Note the very small but definite differences between the experimentally determined compositions and the ideal structures.

(Fig. 3)[25-27]. As shown by an X-ray structure analysis rendered highly elaborate because of the large unit cells[28], the 13:4 intermediate phase contains the structural elements of the two adjacent phases in a periodic arrangement thus consisting of alternating rows ("layers", see Section 4.3) of blocks with sizes of [4 × 3] and [4 × 4].

This first discovery, that blocks of different sizes can be combined coherently ("intergrowth"[23]) into a new structure ("hybrid phase"[21]), may—like the existence of additional intermediate phases, the then structurally inexplicable phase widths, the observed deviations of the narrow phases from the composition of their ideal structure (Fig. 3), and the joint discussion of the details of these questions at Münster[5]—have inspired *Wadsley* and *Allpress* and *Sanders* in 1967[6] to begin applying transmission electron microscopy to this field. At the same time they gave impetus to the development of a new investigation method.

spots that contribute to forming the picture (Section 3.5). Gradually, greater experience led to increasing confidence that this did not involve any "artefacts" but that the true characteristics of the crystal structure in question were being portrayed. It was recognized that one could come close to a direct lattice imaging (1:1 representation) of the crystal structure projected onto a plane, and this has been confirmed both theoretically[1] and by computer simulation[30,31].

Improved resolution soon led to further advances in the lattice imaging of crystal structures; several teams were especially successful as the result of using electron microscopes with top-entry goniometer stages[8,9,32]. As early as 1971, *Iijima*[32], a member of *Cowley*'s team, led the field in resolution capability (*ca.* 3 Å). The advances made in as little as five years are illustrated in Figure 4 on the example of WO_3, whose structure, analogous to that of ReO_3 (apex-connected W-O octahedra), is shown in Figure 4c in projection along a

diagonal of an octahedron. Edge connections between the coordination octahedra can appear if there is a slight oxygen deficiency (reduction), corresponding to some composition that may be denoted by WO_{3-x}; the edge-connected octahedra are arranged in planes of a determined crystallographic direction (shear planes, see Fig. 4c). When the oxygen deficit

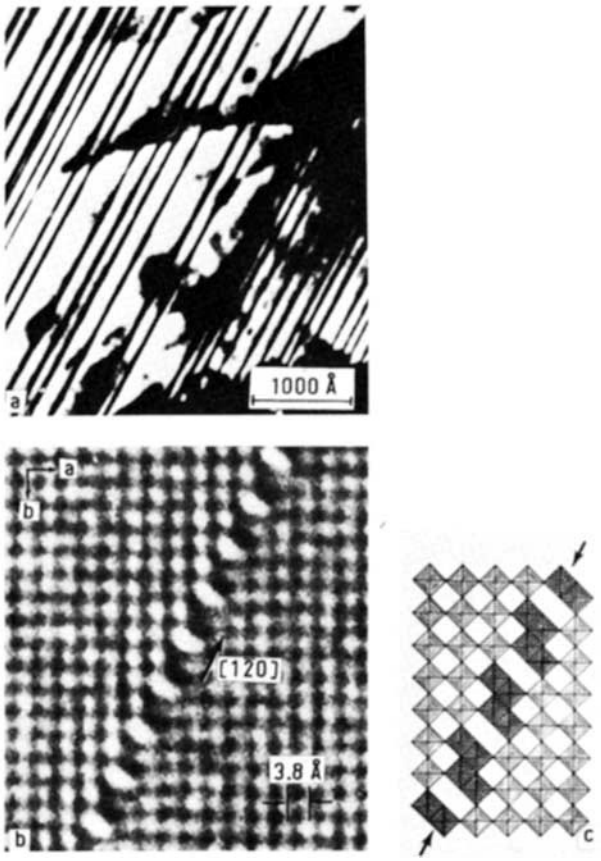


Fig. 4. Transmission electron micrographs of partially reduced tungsten trioxide (WO_{3-x}) with so-called planar defects. a) "One-dimensional" photograph [33] with nonperiodic shear planes in the [1$\bar{2}$0] direction; b) high-resolution "two-dimensional" image [34]; the centers of the W–O octahedra are recognizable, as are characteristic features of the octahedral interconnection (cf. c) along a [1$\bar{2}$0] shear plane; c) idealized model of the structure of WO_3 with apex-interconnected W–O octahedra. A [1$\bar{2}$0] shear plane is indicated, with characteristic edge interconnection of the octahedra.

x is small, the shear planes may fail to form a periodic sequence (cf. Section 4.3); when the sequence is periodic, they constitute an important structural element of many crystal structures, *e.g.* the block structures (Fig. 1). As shown by Figure 4a, nonperiodic shear planes can even be shown up by one-dimensional imaging[33], but in this case their structure cannot be made out. High-resolution two-dimensional images (Fig. 4b) reveal the individual coordination polyhedra (*i.e.* their most strongly scattering W centers) with their respective connections[34].

3. Foundations of Transmission Electron Microscopy

3.1. Structural Principles of the Microscope

The design of the microscope column is in principle similar in all transmission electron microscopes (Fig. 5). At the top there is an electron gun, and beneath this the anode, the condenser system (two lenses), and the objective lens with the specimen chamber. Underneath the objective lens there

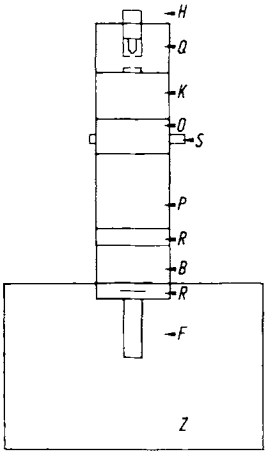


Fig. 5. Schematic sketch of a transmission electron microscope with a side-entry goniometer. H = high voltage input, Q = electron gun (see Fig. 6), K = condenser system, O = objective lens with specimen chamber (see Fig. 7), S = specimen airlock of the goniometer, P = projector system, R = recording camera (35 mm film), B = observation chamber with fluorescent screen, R = sheet film or plate camera, F = television camera, Z = electronics, pumps, *etc.*

is a projector system comprising three or four lenses, which project the image formed by the objective lens onto a fluorescent screen situated at the bottom of the column for direct observation. Modern electron microscopes have special magnetic lenses[35]. In most instruments the images can be recorded on 35 mm, sheet film, or photographic plates, and it is also possible to mount a television camera or a 70 mm cine camera as an attachment. The space comprising the electron gun, the interior of the microscope column, the specimen chamber, and the observation chamber with its fluorescent screen and plate camera must be under high vacuum. In most instruments the high-voltage generator, the control electronics, and the vacuum pumps are housed in a desk console below the column itself.

3.2. Electron Generation

In order to produce electrons as coherent as possible and to achieve a sufficient light intensity for observation and photography, several types of electron gun have been developed. In TEM the electrons are usually produced by incandescent emission from a hairpin cathode (tungsten wire about 0.1 mm thick) surrounded by a metal cap (Wehnelt cylinder) to control the electron emission; this cap is maintained at a slightly negative potential (*ca.* -100 V) (Fig. 6). The tip of the hot filament, bent into the shape of a hairpin, is situated opposite the aperture in the Wehnelt cylinder.

Apart from the simple hairpin cathode, variously shaped point cathodes have been proposed, which up to now have been used mostly for scanning electron microscopy. For example, some pointed cathodes have hairpins with the smallest possible radius of curvature, while in others the bent portion is drawn to a point[35]. Greater brightness can be attained by using LaB_6 cathodes[36], but these are more difficult to make than hairpin cathodes. Likewise, for some years

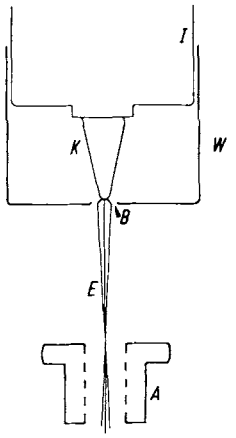


Fig. 6. Sketch of an electron gun. I = Insulator with high-voltage input, K = hairpin cathode, W = Wehnelt cylinder, B = Wehnelt aperture, E = electron beam, A = anode.

field emission electron sources have been available for routine use. These produce more coherent electron beams and give a high beam directionality, but their emission surface area is very small[37]; they are thus particularly suitable for scanning transmission electron microscopy (STEM) or for surface imaging (SEM). All these electron sources of special design may become particularly significant in high resolution transmission electron microscopy.

3.3. The Operating Principle of the Microscope

The electrons emitted from the tip of the hairpin cathode are accelerated toward the anode. Accelerating voltages of up to about 100 kV can be applied in most of the usual commercial electron microscopes. The wavelength of the accelerated electrons can be calculated from de Broglie's equation[35] (Table 2). The wavelengths of the electron beam is considerably shorter than that of the X-ray beams commonly used for the investigation of crystal structures (*e.g.* $Cu_{K\alpha} = 1.5418$ Å).

Table 2. Wavelengths of accelerated electrons.

U [kV]	80	100	120	200	500	1000
λ [Å]	0.041_7	0.037_6	0.033_5	0.025_1	0.014_2	0.008_7

The accelerated electrons oriented close to the optical axis pass through the anode, which has an aperture in the beam direction, into the condenser system (Fig. 6). This system can be used to adjust the beam diameter and the convergence of the beam incident on the specimen.

The specimen is imaged by the objective lens (Fig. 7), which is thus the most important lens of the electron microscope; its properties essentially determine the performance of the instrument. The position of the lens function exerted by the coils of the objective lens lies between the pole-pieces of the lens coils, so that the space available for the specimen between the pole-pieces is determined by the coil and pole-piece geometry. On the one hand, the separation of the pole-pieces should be as large as possible to enable the necessary mechanical devices to fit in; for example, there must be room for the specimen holder, diaphragm screens, and a cold trap, while for the investigations described here it should also be possible to raise or tilt the specimen by means of a goniometer. On the other hand, the separation of the pole-pieces should be as small as possible to reduce lens aberrations (particularly spherical aberration).

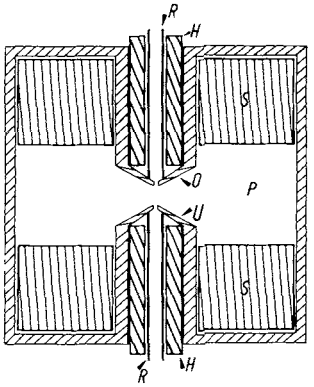


Fig. 7. Sketch of the objective lens. R = evacuated inner tube of the microscope column, H = auxiliary coils, S = main coils, O = upper pole-piece, U = lower pole-piece, P = specimen chamber.

After the objective lens the electrons pass into the projector system, which comprises the diffraction lens, one or more intermediate lenses, and one or more projector lenses. This enables one to vary the image magnification or to switch from the imaging to the diffraction mode (see Fig. 8), by varying the lens currents and so the focal lengths of the lenses, or by switching the lenses on and off. Since the electrons follow spiral paths when passing through the magnetic fields of the lenses[35], the image is rotated with respect to the specimen itself, the axis of rotation coinciding with the optical axis. The amount of rotation depends upon the setting of the lenses of the magnification system.

3.4. Crystallographic Adjustment of the Specimen

The orientation of crystalline specimens can be identified from the diffraction pattern of the crystal; this is done using the method of selected area diffraction[38,39] (Section 3.5). If the instrument is fitted with a goniometer, the orientation of the crystal can be changed until the desired diffraction pattern has been obtained. The electron beam is then perpendicular to the desired plane of the reciprocal lattice of the crystal (Sections 3.6 and 3.9). With a eucentric goniometer the image of the crystal can be kept within the diffraction diaphragm during the tilting or rotation.

3.5. Selected Area Diffraction

At low magnifications (*e.g.* × 20000) the specimen is moved about until an image of a seemingly suitable area of the crystal to be examined by diffraction is obtained. This image is brought within the aperture of the diffraction diaphragm visible on the fluorescent screen, this aperture having previously been centered in the middle of the field of view. The diffraction diaphragm is arranged in the microscope column in such a way that it lies in the image plane of the objective lens and can also be imaged sharply by the dif-

fraction lens (Fig. 8). With a sharply imaged diffraction diaphragm, the image of the crystal is focused in the plane of the diaphragm, *i.e.* both the diaphragm and the crystal are sharply imaged on the observation screen. The microscope is then switched into the diffraction mode. This type of diffraction is known as selected area diffraction[38,39].

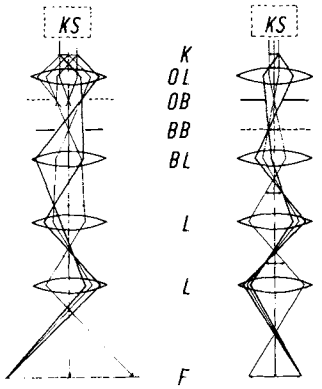


Fig. 8. Simplified ray diagram of the electron microscope. Left: Selected area diffraction, right: imaging mode. KS = condenser system, K = crystalline specimen, OL = objective lens, OB = objective aperture, BB = diffraction aperture, BL = diffraction lens, L = other lenses in the projector system, F = film plane.

Since the wavelength of the electrons is very short, the diffraction angles θ are small, up to about 3°. This can be seen directly from the Bragg equation:

$$n \cdot \lambda = 2d \sin\theta$$

(n = diffraction order, λ = wavelength, d = lattice plane separation, θ = angle between the lattice plane and the diffracted beams). The crystals must be very thin in the transmission direction (phase object, see Section 3.6)[1,7]. Under these conditions the number of structural units available to diffract the beam is small, and for this reason the diffraction maxima in this direction are not very sharp. The diffraction spots are in this direction elongated into so-called spikes. When the electron beam makes a right angle with a plane of the reciprocal lattice of a crystal, the situation is as shown in Figure 9. Although no spot lies with its mid-point exactly on the surface of the Ewald sphere, *i.e.* though the Bragg condition is not exactly satisfied for any of the points, very many of the rodlet-shaped spots intersect or touch the sphere. This is the starting point for later high resolution imaging (Section 3.6).

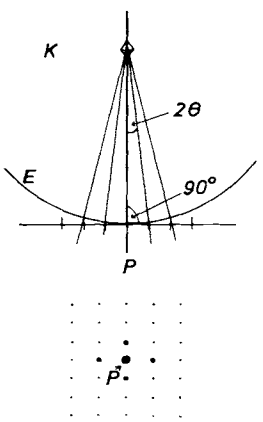


Fig. 9. Sectional view through the Ewald sphere and multibeam pattern. Top: production of a beam pattern [39]; crystal orientation required for high-resolution work. Bottom: schematic view of the corresponding diffraction pattern. K = crystal, E = Ewald sphere, P = primary beam, θ = glancing angle.

The diffraction pattern of an object is sharply imaged by the objective lens at its back focal plane[35]. In this plane there is also the perforated diaphragm known as the objective diaphragm (Fig. 8). In the diffraction mode, the diffraction lens is so adjusted that it forms a sharp image of what appears at the back focal plane of the objective lens. This image is projected onto the observation screen, or onto photographic film, by the intermediate and projector lenses further down. The diffraction pattern of a correctly oriented crystal, obtained here on account of the pointed (rod-shaped) intensity distribution of the spot intensity from a fixed crystal (Fig. 9), looks like a Buerger precession diagram made with X-rays. The spot intensities in themselves are of no direct use, but in regard to the spot separations and the angles between spot series the pattern can be evaluated like a precession pattern[39,40]:

$$a^* = \frac{A}{\lambda \cdot L}$$

(a^* is the separation between two spots in the reciprocal lattice, A the separation between two points on the film, and L the camera length, *i.e.* the apparent distance between the crystal and the film). With orthogonal crystal systems this yields the lattice plane separation r in the real lattice, $r = 1/a^*$[41]. With oblique-angled crystal systems the calculation is more complicated[40]. In contrast to the case of a precession camera, with an electron microscope it is easy to vary the camera length, and with it the scale of the image, within wide limits. The camera length can be calibrated for various settings of the instrument with the aid of a known substance.

3.6. High Resolution Lattice Imaging[1,7]

The orientation of the crystal with respect to the electron beam must be set accurately to within about 0.1—0.2°, since otherwise the image will show contrast variations and distortion. When the crystal has been oriented (Section 3.4), a correctly centered objective aperture in the back focal plane of the objective lens is used to pick out the number of diffraction spots required to contribute to the image.

Spots too far out from the primary beam, such as those admitted by too large an aperture, will be affected by additional phase alterations because of lens aberrations and will produce contrast errors and spurious detail in the image. All these factors affect the resolving power of the instrument. A decision must therefore be made concerning which spots may sensibly be allowed to contribute to the image, *i.e.* what size of objective aperture should be selected (*e.g.* about 50 μm for one of the block structures mentioned).

Spots that lie far out from the primary beam are produced by lattice planes whose mutual separation is very small. The smallest distance between two points on the object that can be resolved with an electron microscope can be evaluated from the following relationship[1]:

$$\Delta x \approx 0.6 \cdot C_s^{1/4} \cdot \lambda^{3/4}$$

(Δx = smallest resolvable separation, C_s = error constant of spherical aberration).

When, after the spots have been selected, the instrument is switched over to the image mode, the projector system will produce the "normal" image generated by the objective lens approximately in the plane of the diffraction aperture (Fig. 8). It is advisable to focus the image sharply, making the Fresnel fringes at a crystal edge or at a hole in the supporting film (Section 3.8) disappear completely, or making the supporting film (carbon film) appear with the least possible contrast. To allow the best possible correction of the astigmatism of the instrument, the primary magnification must be increased to at least 400000—500000. The contrast of high resolution images is especially sensitive to the influence of astigmatism, which therefore has to be corrected extremely thoroughly. To achieve this, we have found it very useful to inspect a part of the image using CCTV. The focus is then adjusted in the smallest possible steps. With a certain degree of underfocus (500—1000 Å), the correct image contrast is set to its clearest level[1, 7, 35]; this approximately compensates for phase changes of the electron waves occasioned by lens aberrations. It is recommended to take a picture for each focusing step, and pick out the best image later. The part of the crystal that is to be imaged at very high magnification must be very thin in the beam direction to constitute an effective phase object (*ca.* 100 Å; the edges of crystal flake fragments are suitable)[1, 7]. Under these conditions it is permissible to correlate contrast phenomena of the image directly with structural elements of the crystal.

The exposure time should not exceed 2—4 s, mainly because otherwise mechanical instabilities of the instrument will lead to blurring of the image. It can be difficult to obtain sufficiently intense illumination at very high magnifications, since in order not to allow too great a beam divergence ($<0.05°$)[1], an aperture size of about 100 μm should be chosen in the second condenser lens. The total observation time of a crystal can run to hours. Thus, it is important to maintain a good vacuum in the electron microscope, so as to decrease the deposition of organic impurities onto the sample (contrast reduction).

Our own TEM photographs reproduced in this article were taken using an EM 400 Philips electron microscope with an HMG high resolution side-entry goniometer; the accelerating voltage was 120 kV. For this instrument, in which the vacuum was very good (ion getter pump), a largely vibration-free mounting position was chosen.

3.7. Comparison between X-Ray and Electron-Microscopic Methods

The fundamental difference between these two methods of structure determination[1] is that since X-rays cannot be sufficiently affected to produce any lens-like effect, one cannot use "X-ray optical" methods to obtain an image from the diffraction pattern carrying phase information. Instead, the intensities of the diffraction phenomena must be measured for later computer generation of an image, and the phase information is lost during this process. The intensity is usually determined only at selected points that can be described by integral indices. X-Rays are less strongly scattered than electrons, and thus only relatively large crystals (mosaic crystals) are suitable for X-ray studies. As a result, the intensities obtained are averaged out and permit no conclusions about individual defect sites[1].

In contrast, in the electron microscope, after diffraction at the crystal, the beam can proceed without interruption, *i.e.* with all the pertinent phase relationships, so that an image of the crystal structure can be obtained. Which features are seen depends on the resolution and on the crystal structure itself (Section 3.10). The image is formed not only on the basis of the intensities of individual spots in the diffraction pattern, but rather of all the diffraction information from such electrons as pass through the selected objective aperture (structure determination by electron diffraction)[42, 43].

3.8. Specimen Preparation

The crystalline substances are placed on support grids (diameter 2 or 3 mm), usually copper grids covered with a perforated film of carbon (Fig. 10). The perforated film also serves to conduct away electrons. The preparation conditions for such perforated films (see *e.g.*[44]) are difficult to reproduce, and therefore we use our own method. The part of the crystal to be examined should be positioned over one of the holes in the film, so as to minimize loss of contrast due to an image background.

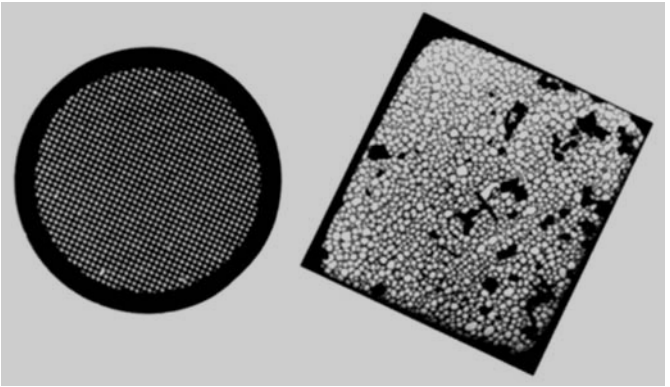


Fig. 10. Support grids. Left: copper grid (3 mm diameter); right: an individual mesh of this grid (about 0.04×0.04 mm^2) with perforated carbon film and crystals.

To obtain the thinnest possible crystal edges (Section 3.6), the specimen is first carefully crushed in a mortar, suspended in a liquid (chloroform, alcohol, water), and some of it is taken up onto a support grid. Even a dry crystalline powder can often be made to stick in sufficient quantity to the film.

During the comminution of the specimen care should be taken to avoid producing structural alterations such as may occur on milling in a mechanical mill[45]. In the investigations discussed here (Section 4) it was observed that the type of the defects present depended on the conditions of the chemical preparation (*e.g.* crystal growth from the vapor phase). By varying the preparation conditions, apart from severely disordered crystals it was also possible to obtain crystals free from a particular type of defect or ones that had only very low concentrations of structural defects. This provided confirmation that our way of comminuting the specimen, and also the irradiation in the microscope, did not generate any recognizable structural changes.

In special cases it is also possible to obtain regions of the preparations thin enough for direct imaging in other ways, *e.g.* by chemical etching or by polishing and ion-etching of the specimens[46].

The work on specimen preparation can be made negligible or at least reduced if the crystalline solid is in the form of a film, though it should be confirmed in each individual case whether the findings obtained with thin films can be extended to compact crystals[13].

3.9. Mounting the Specimen in the Microscope

The support grid is fitted into a specimen holder and inserted into the electron microscope. In instruments without a goniometer the positioning of the specimen is in principle mechanically more stable than with an arrangement in a goniometer. Consequently, up to now the highest resolutions had been attained in microscopes without goniometers[14 16]; however, such instruments have the decisive drawback that the inclination of the specimen with respect to the electron beam cannot be alterated. Thus, in this way one can only examine accurately pre-oriented crystal regions (*e.g.* [14 16]), or those crystal fragments that happen to be correctly oriented by pure chance[47,48].

Where a goniometer is needed, a choice has to be made between the top-entry and the side-entry types. The top-entry systems are mechanically quite stable, but up to now have not been available as eucentric goniometers. The support grid, fitted into a small specimen holder, is introduced from the top into the objective lens segment and is finally situated between the pole-pieces of the lens[13].

The side-entry goniometers currently available on the market are designed as uniaxial eucentric goniometers, *i.e.* the specimen holder is moved perpendicular to the longitudinal direction until the rotation axis of the goniometer passes through the specimen region that is to be observed. Thus, they are convenient to manipulate. The support grid is arranged at the leading end of a rod-shaped specimen holder; an electric motor is coupled to the other end in the case of the double-tilt or rotation and tilt holders. The holders are pushed into the microscope column through a generally pre-evacuated airlock; they are about 30 cm long, and are sealed and supported near the middle by an O-ring. Because of this type of bearing and their length, these holders are very sensitive to mechanical vibrations.

3.10. Specimen Requirements

The specimen-preparation techniques usual up to now (Section 3.8) for substances due to be examined in the electron microscope at very high resolutions have required that the material should not be sensitive to moisture, since crystal areas thin enough to be suitable for imaging could otherwise undergo rapid attack. The crystals should also be stable to electron irradiation within the microscope. There should be no unwanted phase transformations or other changes in the crystal structure; likewise, the crystals should not melt, vaporize, or decompose. For materials that are sensitive to air or moisture, *in situ* observation can offer advantages[13,49].

Thus, the high-resolution technique (lattice imaging) is particularly promising for structure investigation when the three-dimensional structure of the substance to be investigated can easily be projected onto a plane, so that the contrast will be as high as possible, *i.e.* the structural features will be clearly perceptible. It is advantageous if the beam can be directed along one of the short axes; a very small repeat period of *e.g.* about 4 Å (corresponding to one layer of polyhedra in the oxides we investigated) is particularly useful. Problems due to overlapping in projection of structural information from different parts of the unit cells are then minimal. Under these conditions, for example, structural defects can most easily be recognized when they extend through the entire depth of the crystal specimen in the direction of the beam.

4. A Broad Field of Application: Structural Defects

4.1. General Review

The direction of investigations carried out by the high-resolution technique has been decisively influenced[50 52] by questions relating to the structure of "nonstoichiometric" compounds[53]. Both this term and similar admittedly not very apt designations[50,52,53] indicate that the observed composition of the solid, *e.g.* the anion/cation ratio, cannot be described in terms of small whole numbers. In particular, variable compositions (phase widths) such as those in Nb_2O_5-rich systems (Fig. 3), that can be described neither in terms of a simple, periodically recurring unit cell nor by a statistical population of lattice planes, have given impetus to the electron-microscopic investigation of nonperiodic "deviations" from the matrix structure (structural defects) (Section 2.2).

The structural defects observed by electron microscopy show a very wide variation. In principle, the possibilities of the generation of different structural defects are especially numerous when the matrix structure is already highly variable, as *e.g.* in the case of "block structures"[20,21], "bronzes"[10,51,54,55], variants of the WO_3[34,51] and rutile[9,51] structures, and in many silicates[56,57]. Regions with different structures can then be connected to one another coherently, *i.e.* without undue deformation of their coordination polyhedra; this possibility extends even to a combination of the structural principle of "bronzes" with the WO_3 structure[10,51,55]. However, in the following sections, we shall only be able to deal with the situation relating to block structures. In block structures, bronzes, and WO_3 variants the variability and the coherence of the modes of interconnection depend upon the predominant presence of apex-to-apex and edge-to-edge connections of the coordination octahedra and in rutile variants also upon their additional connections by faces. Structural defects with noncoherent arrangement of their structural elements are also known[8].

Essentially, the observable structural defects (Section 3.10) are "extended" defects, among which three-dimensional, two-dimensional (planar), and one-dimensional defects may be distinguished[52]. The most important three-dimensional defects are the microdomains (Section 4.2); furthermore, nonperiodic clusters or defect clusters also play some part. In general, the microdomains are small regions within a crystalline matrix that possess their own (periodic) structure; if this conforms with the structure of one of the neighboring phases

in the system, then one can speak of a "microheterogeneity", especially when the homogeneous regions are large in comparison. Some authors also consider smaller *ordered* regions within an *unordered* matrix to be microdomains[58].

In general, the structural defects mentioned also differ in chemical composition (anion/cation ratio) from the surrounding part of the crystal; less frequently one observes defects that do not differ in composition, *e.g.* microdomains of a different modification, stacking faults, twin planes, and antiphase boundaries[50,51]. The anion/cation ratio in narrowly delimited defect zones of block structures can often be inferred from the structure observed in the electron microscope[48,59], especially when the structural elements of the disturbed region (*e.g.* the coordination polyhedra and their mode of interconnection) are well known from X-ray studies of the undisturbed matrix or of another related structure and it is assumed that a "fully populated" crystal structure is present. Isolated point defects, which cannot be detected by TEM, cannot be taken into account by this procedure. Notwithstanding their designation as "extended defects", the very small size of the microdomains and other defect zones, which in many cases cannot even be approached by selected area diffraction (Section 3.5), has up till now frustrated the direct determination of their composition by chemical analysis.

4.2. Microheterogeneities, Microdomains

In investigations of the phase relationships in a multicomponent system, the answer to whether a given specimen should still be regarded as homogeneous or already as heterogeneous is influenced not only by structural similarity but also, and in particular, by the particle sizes of the secondary phases to be detected. Thus, the Guinier method, which can be used for high-sensitivity X-ray investigations of polycrystalline or powdered specimens, is the *less* sensitive, the greater the similarity between the diffraction patterns. In other words, the closer is the structural relationship between the phases[22], the less accurate will be the localization of the phase boundary compositions in a multicomponent system. For example, in the TiO_2–Nb_2O_5 system, as little as 1% of the compound $(Ti,Nb)O_{2.33}$ can be detected in rutile, while the relative detection sensitivity for $(Ti,Nb)O_{2.483}$ side by side with $(Ti,Nb)O_{2.489}$ is only 17%, or an order of magnitude smaller, since the diffraction patterns of these two phases only differ in some very weak lines. X-Ray confirmation of phase purity is called into question when the particles or uniform regions of the secondary phase to be detected are too small for this method ("microheterogeneities"), as can be brought about *e.g.* by segregation. In the X-ray investigation of "single crystals" (mosaic crystals) it should be borne in mind that an apparently well ordered matrix structure may show a dispersion of coherently included regions ("microdomains") of one or more neighboring phases without any such structural defects being detectable by X-rays (Section 3.7).

Microheterogeneities can often be detected by electron microscopy in specimens that appear to be uniform to X-rays (Guinier method). Thus, in Guinier-pure $(Ti,Nb)O_{2.483}$, whose structural principle can be described in terms of the different composition $TiNb_{52}O_{132}$ (similar to $Nb_{53}O_{132}$; Fig. 3), *Allpress*[60] found microdomains of the lower neighboring phase $TiNb_{24}O_{62}$ and of the previously unknown compound $Ti_2Nb_{76}O_{194}$ ($TiNb_{38}O_{97}$). However, the electron-microscopically observed inhomogeneity of a substance such as $(Ti,Nb)O_{2.483}$ seems to us insufficient to classify the system as a two-phase one. For example, in this case if one were to ascribe to the pure phase a composition above $(Ti,Nb)O_{2.483}$, it would be difficult to see why the composition $(Ti,Nb)O_{2.485}$ is already heterogeneous to X-rays, as shown by the presence of the higher neighboring phase $(Ti,Nb)O_{2.489}$ with the H-Nb_2O_5 structure. The analogous situation in the NbO_2–Nb_2O_5 system (Fig. 3) lends support to the considerations concerning the demarcation of the phases present[22]. Since segregation during the cooling of the specimens can be excluded on account of the observed sluggishness of the reactions in these oxides, it seems here that equilibrium is not fully established within the solid material. This is also supported by observations in the Nb_2O_5–WO_3 system[61], where, in one and the same crystal fragment, regions of both the

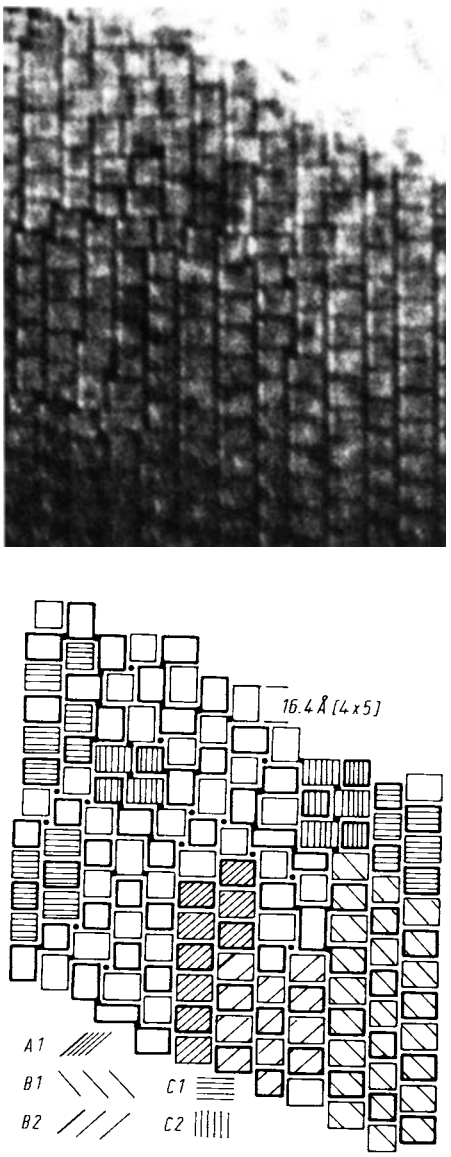


Fig. 11. a) Transmission electron micrograph and b) interpretation of a severely defective crystal region. Specimen composition $Nb_2O_5:WO_3 \approx 6:1$, deposition temperature 780 °C. Microdomains of five structure variations (Table 3) are indicated. Of the possible edge connections, only the unusual type of connection along the longer block edges is marked (as in Fig. 2d).

lower and the higher neighboring phases have been detected by electron microscopy.

It should be noted that microdomains of the compound $Ti_2Nb_{76}O_{194}$ can be formed before the final state has been reached. This compound was not observed in the stable

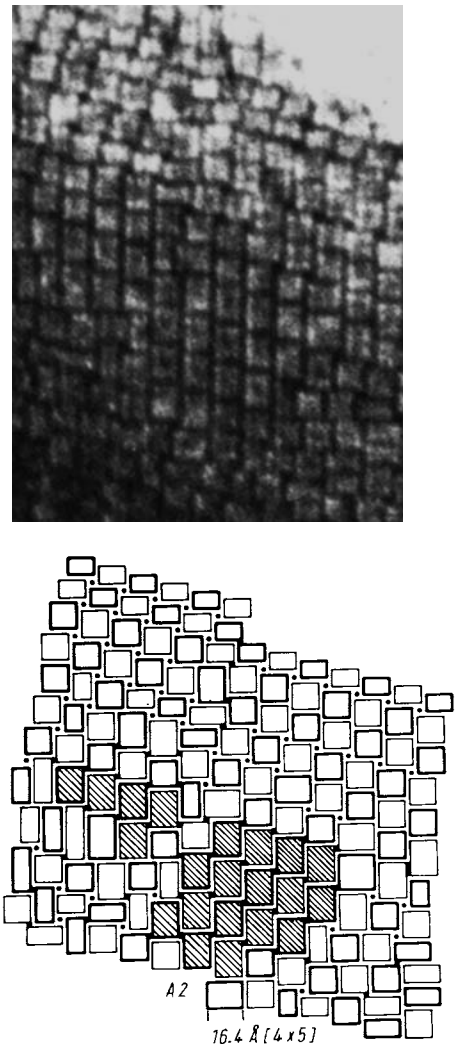


Fig. 12. a) Transmission electron micrograph and b) interpretation of a second crystal region of the same specimen as in Fig. 11. The unusual connection along the longer edges of the [4 × 5] blocks is marked.

TiO_2–Nb_2O_5 system, and is possibly metastable. There is a close structural relationship between the $TiNb_{52}O_{132}$ matrix and the microdomains of $Ti_2Nb_{76}O_{194}$. $TiNb_{52}O_{132}$ can be regarded as a 1:1 hybrid phase[21] of the structures $TiNb_{24}O_{62}$ and $Nb_{28}O_{70}$ (H–Nb_2O_5), and $Ti_2Nb_{76}O_{194}$ as a 2:1 hybrid phase with the same structural elements. Thus, the connection principle of the structural elements is the same in both structures.

Microdomains differing fundamentally from the matrix in the connection principle and in the size of the structural elements (blocks) have recently been discovered in the Nb_2O_5–WO_3 system, in crystals of the approximate composition $Nb_2O_5:WO_3 \approx 6:1$[62]. The 6:1-specimens crystallizing under conditions close to equilibrium possess a uniform structure of (3 × 4) blocks interconnected as shown in Figure 2a[20], but if

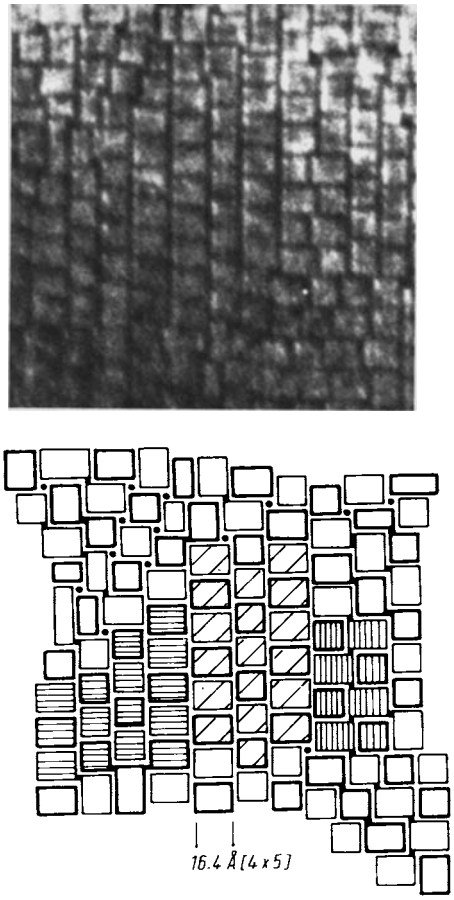


Fig. 13. a) Transmission electron micrograph and b) interpretation of a third crystal region of the specimen of Fig. 11. Microdomains of C1 and C2 (with zipper-like connections), and of B2, are clearly visible. In addition, as in Fig. 12, one can see individual blocks of dissimilar sizes (*e.g.* [3 × 6]) and with unusual types of interconnection (*e.g.* top right), see Section 4.4.

the crystals are deposited from the vapor phase by a chemical transport reaction[63] at a relatively low temperature of about 780 °C, their structure is severely disturbed. As shown in Figures 11—13, numerous microdomains of various structures can be detected even in a *single* crystal fragment[62].

Table 3. Structure of the microdomains in Figs. 11—13. The blocks are connected along the shorter (s) or longer (l) block edges (see Figs. 2c or d); monoclinic sequence of block rows = (m); orthorhombic = (o).

Region	Composition	O/$\sum$M (M = Nb, W)	Size and connection of the blocks
A1	$W_2Nb_{18}O_{51}$	2.55	[4 × 5] (s, m)
A2	$W_2Nb_{18}O_{51}$	2.55	[4 × 5] (l, m)
B1	$W_4Nb_{52}O_{142}$	2.536	[4 × 4] + 2 [4 × 5] (s, m)
B2	$W_4Nb_{52}O_{142}$	2.536	[4 × 4] + 2 [4 × 5] (s, o)
C1	$W_2Nb_{34}O_{91}$	2.528	[4 × 4] + [4 × 5] (s)
C2	$W_2Nb_{34}O_{91}$	2.528	[4 × 4] + [4 × 5] (l)

The edge interconnections are of particular interest; these hold the blocks together in a way never before observed in the Nb_2O_5–WO_3 system (Fig. 2b—d) and the blocks themselves have a size of [4 × 5] octahedra previously unknown for this type of connection. It is also unexpected to find the connections *via* the longer edges of the blocks (Fig. 2d) in re-

gions A2 and C2. Table 3 summarizes the unusual structures observed in the form of microdomains (for calculation of the compositions, see[48,59]). No macroscopically uniform specimens with any of the structures mentioned have yet been prepared. There is no doubt that nonequilibrium processes played a part at the relatively lower temperature at which these crystals were grown from the vapor phase.

4.3. Planar Defects, Wadsley Defects

As X-ray structure investigations have shown[64,65], particular structural elements, the shear planes, are characteristic[50] of regular series of closely adjacent and structurally related Hägg-Magnéli phases[22] (*e.g.* Fig. 3, Table 1 and the systems MoO_2–MoO_3, WO_2–WO_3, Ti_2O_3–TiO_2, V_2O_3–VO_2 *etc.*[64-67]. These can be described as planes in which the coordination octahedra are particularly closely connected to one another (along their edges or faces) (Fig. 4c); thus, the less dense "matrix" structure (*e.g.* of ReO_3 or rutile type) appears to be periodically divided into "layers" or "blocks". The separation of the connecting planes from one another can vary stepwise (structure-related series, *e.g.* Table 1), as also can their crystallographic direction. Both these features have been confirmed by electron microscopy[9,51,61].

If the composition of a crystal is very close to that of the matrix structure (*e.g.* WO_3 with ReO_3-like configuration in Fig. 4), the mutual separation of the "shear planes" is too great for an ordered distribution. Thus, sufficiently separated (see Fig. 4a)[33,34] shear planes should be regarded as nonperiodic structural defects, which become increasingly like the structural elements of ordered crystal structures (Hägg-Magnéli phases) as the separation decreases and they come closer together. This consideration is particularly applicable to systems or structurally related series that are limited at the upper end by a phase with the matrix structure (WO_3, TiO_2, VO_2); it fails, for example, in Nb_2O_5-rich systems where the connection planes (Fig. 1) of the block structures run perpendicular to one another. In this case a transition to what could be considered as a matrix structure, represented by the ReO_3 (or NbO_2F or WO_3) extraneous to the system, and an extensive "dilution" of the shear planes consequent upon this, cannot be achieved by chemical means (ReO_3), because "foreign" structures occur on approach to the limiting composition (NbO_2F, WO_3). In such materials it seems more meaningful to regard "blocks" or "rows of blocks" as the structural units. Both can occur nonperiodically as structural defects, since they can be included coherently in the structure matrix (for isolated blocks as structural defects, see Section 4.4).

Rows of blocks with irregular block sizes, known as Wadsley defects (Section 1), have been detected in many electron-microscopic investigations[5,60,61,68] as structural defects in block structures; Figure 14 shows a micrograph of a specimen of $W_3Nb_{14}O_{44}$ with two different block rows[62], one of $[4\times3]$ blocks, like those in the compound $WNb_{12}O_{33}$, and one of $[4\times6]$ blocks; up to now, no compound $W_7Nb_{18}O_{66}$ built up uniformly from this type of blocks has been re-

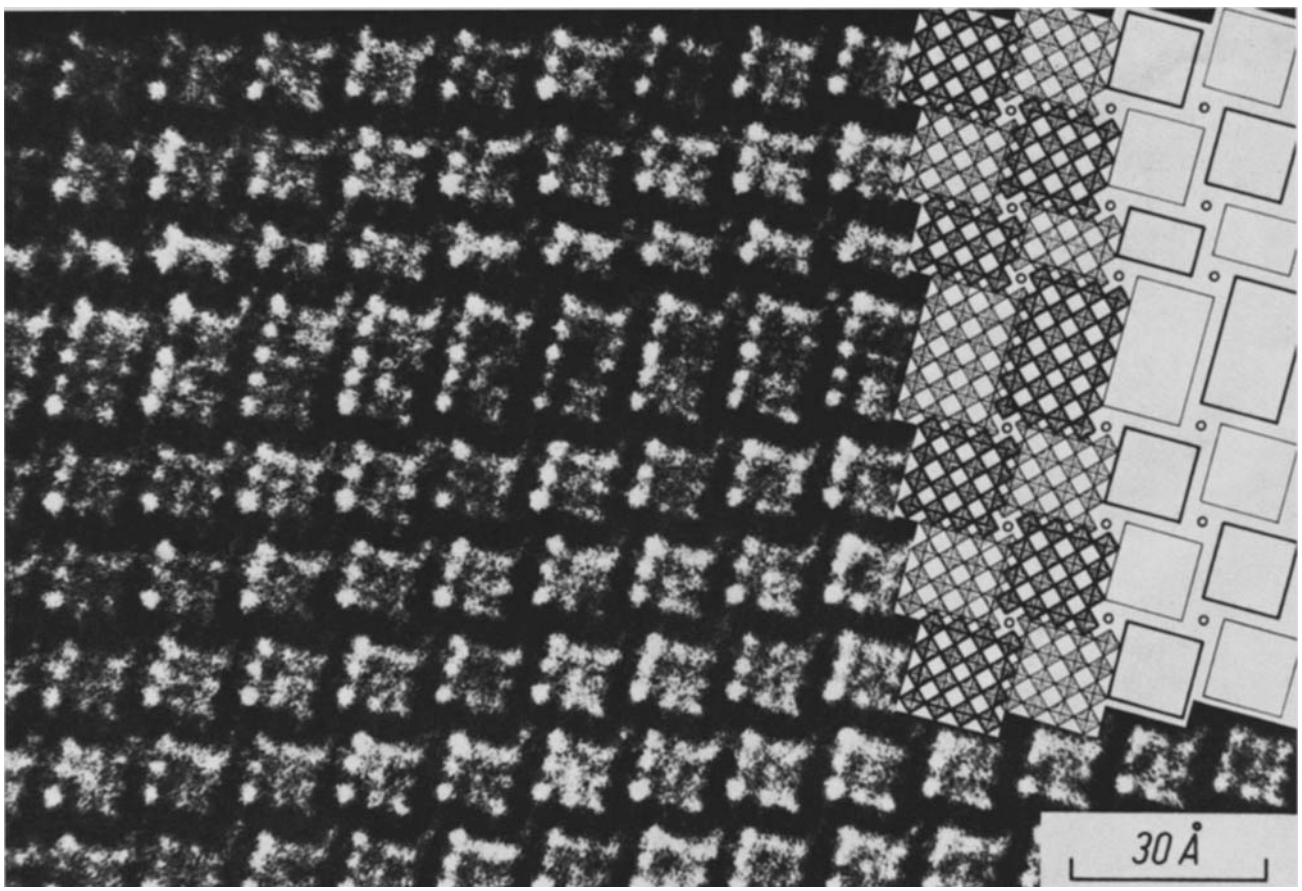


Fig. 14. Transmission electron micrograph of a specimen of $W_3Nb_{14}O_{44}$ with Wadsley defects. The manner of inerpretation is given (see Figs. 1 and 2a). The bright spots correspond to holes (perovskite holes) in the octahedra blocks, lying in the beam direction.

ported. The WO_3-deficit due to the [4 × 3] blocks (reduction of the $O/\sum M$ ratio) is overcompensated by the [4 × 6] blocks, so that the ratio $O/\sum M$ of the defect region amounts to 2.605, whereas for the matrix $W_3Nb_{14}O_{44}$ the $O/\sum M$ ratio is only 2.588[62]. If their compositions compensate partially or completely, the Wadsley defects can be healed by annealing[61]. Under these conditions the nonperiodically ordered shear planes (*e.g.* in WO_{3-x}) will attempt to achieve some degree of order, but they cannot disappear without a change in the overall composition of the specimen.

The block rows that can be seen in projection in an electron microscope image are three-dimensional "layers". Their layer thickness perpendicular to the viewing direction is determined by the size of the blocks; the total extent of a structural defect depends on the number of block rows that it comprises, *i.e.* for the two rows in Figure 14 together it amounts to about 30 Å. On account of their three-dimensional extension, these structural defects can scarcely be referred to as "planar defects", and we thus prefer the term Wadsley defects. As can be seen from the octahedron model (Fig. 4c), the individual shear planes, *e.g.* in a WO_3 matrix, also have an extension in space, and for this reason they cannot strictly be regarded as two-dimensional defects.

If several block rows with various types of blocks are *ordered* one after another, then it is difficult to decide whether such a region is a (large) Wadsley defect or a (small) microdomain (but with its own, new structure); we speak of a microdomain (Section 4.2) when two or more block rows are ordered in sequence[62]. The term "extended defect" is, however, appropriate in all the cases mentioned. It is not yet known for the materials in question how many periodically ordered layers are needed, before one can speak of a phase in the thermodynamic sense.

The occurrence of shear planes and Wadsley defects is not limited to structures made up predominantly of coordination octahedra. The large group of silicates offers an example of the usefulness of these concepts with structures comprising tetrahedral structural units[69].

4.4. From Macroscopic to Narrowly Delimited Defects

Crystals deposited from the vapor phase[48,62] by chemical transport[63] and examined by scanning electron microscopy[*] in many cases showed irregularities or "macroscopic" structural defects that take the form of channels or tubes running through the crystal in the growth direction[70,71]. An ex-

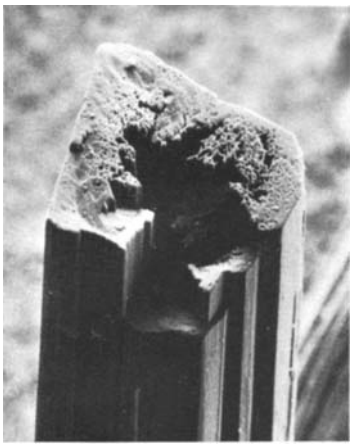


Fig. 15. Scanning electron micrograph of a $W_5Nb_{16}O_{55}$ crystal with tube-like cavities in the growth direction. Diameter of the needle-shaped crystal about 0.1 mm.

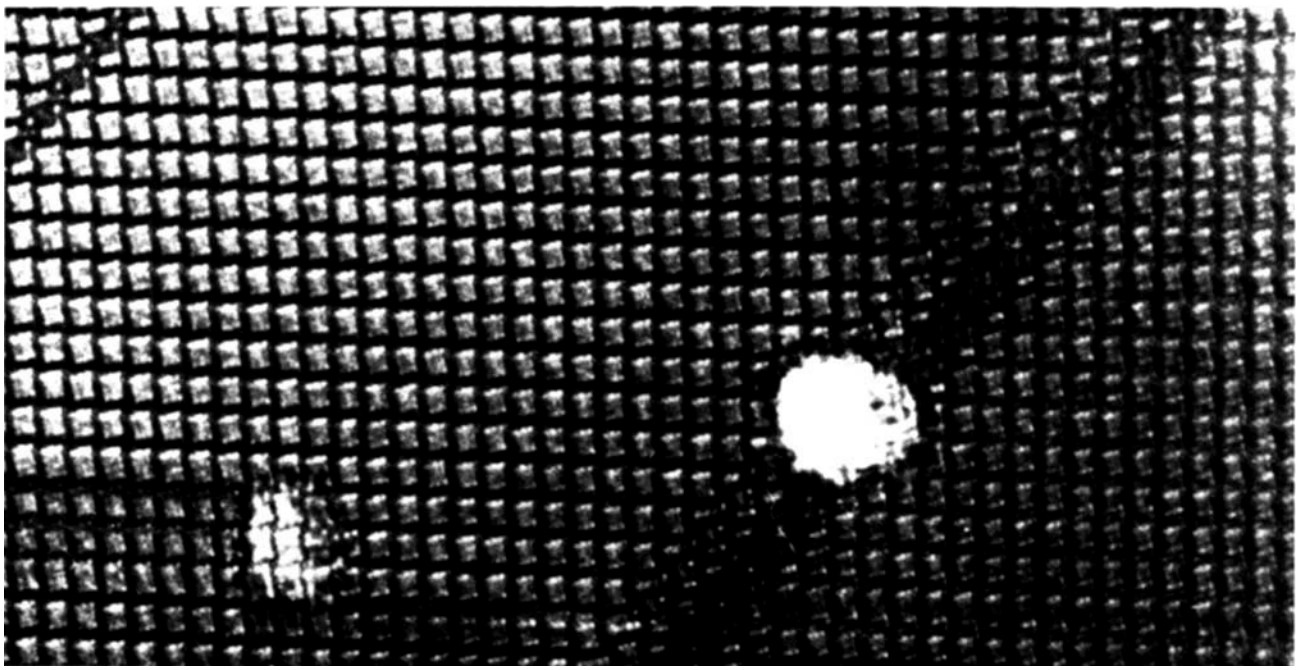


Fig. 16. Transmission electron micrograph of a fragment of the crystal in Fig. 15. The direction of the transmitted beam is along the short crystallographic axis (the growth direction). In a matrix of [4 × 5] blocks, in addition to other structural defects, two tubes can be seen in cross section (diameter about 50—60 Å), which do not pass completely through. The dark diagonal "bands" are defects in the b-direction (Section 6).

[*] The photographs were prepared at the Radiation Center of Giessen University.

ample of this can be seen in Figure 15, which shows a single crystal of the ternary oxide $Nb_2O_5:WO_3 = 8:5$[71]. Fragments of this preparation were examined by high-resolution transmission electron microscopy[72] in order to obtain comparative data on the "building-in" of structural defects during the longitudinal growth of such acicular or rod-shaped crystals. Apart from larger tube apertures, not reproduced here, one can observe defects of this type down to the order of magnitude of the unit cell (Fig. 16). The extremely small tube apertures recognizable in this case, whose size is *e.g.* below that of the Wadsley defects, could be regarded as "narrowly delimited" defects. The observations suggest that the processes involved in the formation and the "building-in" of the tube apertures and structural defects are evidently not different from each other in principle so far as the block structures in question are concerned. The situation may be different with crystals such as MoO_3 that grow in the form of flat plates, which in a few cases also have "holes" (about 1000 Å in diameter)[13].

Narrowly delimited defects of various types are found predominantly in specimens prepared under nonequilibrium conditions. Thus, deposition by chemical transport at relatively low temperatures gives particularly strongly defective crystals, *e.g.* in the Fe_2O_3–Nb_2O_5[47] or Nb_2O_5–WO_3[48,62] systems. As Figures 11—13 show, very few Wadsley defects (Section 4.3) occur at the deposition temperature of 780 °C selected in this case; apart from various microdomains (Section 4.2), there are some *individual* blocks that differ from their surroundings in size and mode of interconnection as well as in their anion/cation ratio[48,59], and that can be regarded as narrowly delimited structural defects like certain unusual types of interconnections.

Whether interconnections recognized from crystal structure determinations (Fig. 2a—c) are present or whether unusual types of interconnections are involved (*e.g.* Fig. 2d) is a question to be settled from the way the blocks are positioned with respect to one another and from the contrast phenomena observed. In this way sporadically occurring particular types of interconnection and "gaps" in the network of polyhedra can be inferred even when the limits of resolution of the electron microscope have been reached[48].

Figure 17 shows a severely defective region of a crystal of composition $Nb_2O_5:WO_3 \approx 7:3$ (deposition temperature 800 °C); an unusual connection around a bright spot can be seen within the circled area. Figure 18 shows the block arrangement in the form of a diagram, but no further attempt is made to interpret the interconnection in this region. If it is borne in mind that an arrangement comprising several terminal O-particles (octahedron apexes) is improbable[48], one arrives at an arrangement of the R1-type gap (tunnel) (for the nomenclature, see [48]) in Figure 19, which also illustrates a variety of other gaps; with the resolution attainable at present, it is not yet possible to decide between the two possibilities given for the S-type gaps[48]. Except for the R-type gaps, which constitute a structural element of the compound $NaNb_{13}O_{33}$[73], all the gaps known up to now have been found exclusively as structural defects. In this case the designation "narrowly delimited defect" may be the most appropriate one on account of their unusually small extension in the plane of observation.

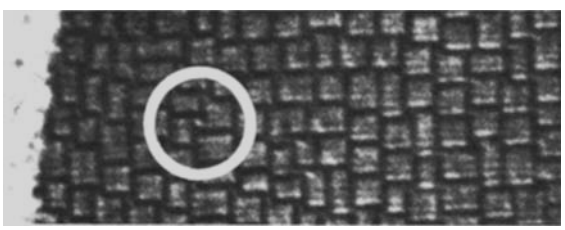


Fig. 17. Transmission electron micrograph of a specimen of $W_3Nb_{14}O_{44}$ with a narrowly delimited defect (circled). The bright spot indicates an interstice (see Figs. 18 and 19).

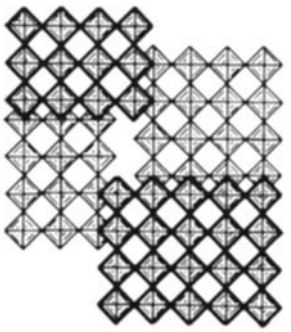


Fig. 18. Interpretation of the narrowly delimited defect of Fig. 17. The arrangement of the blocks can be inferred from the transmission electron micrograph and from crystallographic data. The situation at the center of the connection is left open (see text).

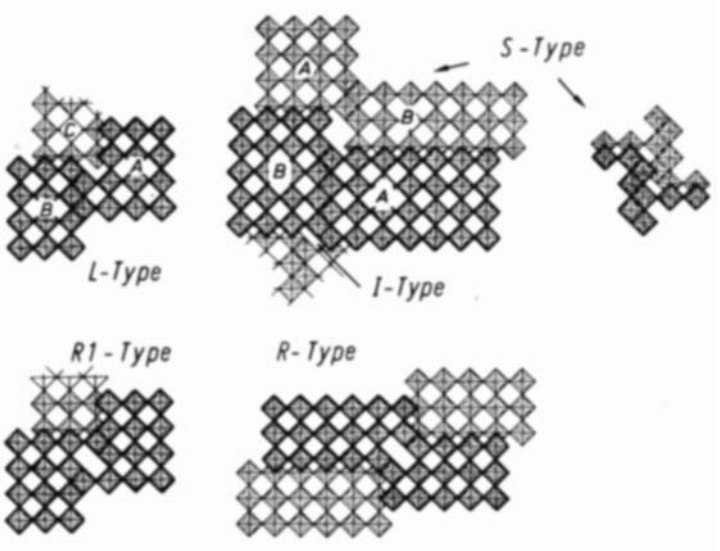


Fig. 19. Models of some narrowly delimited defects. The blocks include "gaps" because of unusual types of interconnection (see text). A, B, C denote blocks whose $O/\sum M$ values have to be evaluated in different ways.

5. Determination of the Crystal Structure

In favorable cases high-resolution transmission electron microscopy makes it possible to ascertain the crystal structure directly in exceptionally small specimens, though the determination of accurate positional parameters still remains the province of X-ray methods[42]. In addition to the information obtained by selected area diffraction, electron microscopy yields transmission micrographs showing a projection of the crystal structure in the selected favorable direction (see

Section 3.10). Fundamentally, the image can also be used to elucidate the structure, at least in regard to the principle of the latter, but to avoid faulty interpretations, it is indispensable to possess certain knowledge of the expected image contrast (Section 6). Furthermore, the reliability of the interpretation of an electron-microscopic picture is increased if one knows what images are produced by related well-known structures at high resolution; in general this is true of the works mentioned here. Investigations in the silicate field[57,74]—at first without any such comparison material—give an impression of the potential of this method. A clear example of an electron-microscopic structural picture is the micrograph of beryl (Fig. 20)[74], whose crystal structure has long been known from X-ray investigations.

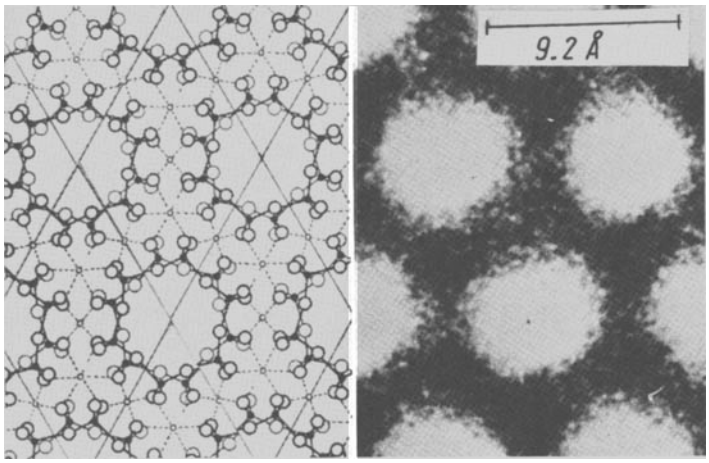


Fig. 20. Right: transmission electron micrograph of beryl [74]. The line of sight along the hexagonal c-axis makes the structural principle easy to recognize (rings of SiO_4 tetrahedra). Left: the ideal structure of beryl ($Al_2Be_3Si_6O_{18}$), drawn to the same scale.

As has been recognized for a long time (Section 2.2), the electron microscope is useful for the clarification of structures when it is difficult or impossible to apply other diffraction methods for the following reasons:

a) When the unit cells are particularly large, *e.g.* with superlattices or the hybrid phases mentioned in Section 2.2[21], in the case of stacking variants such as barium ferrites[75] or hexagonal polytypes of perovskite-related structures[76,77].
b) With structures that cannot be prepared as uniform crystals, *i.e.* that only exist in very small regions. This applies particularly to the structure determinations in microdomains, which sometimes cover only a few unit cells (see Section 4.2).

Furthermore, a transmission electron micrograph such as Figure 20 can very quickly yield an impression of the structural principle and thereby provide valuable indications for a detailed X-ray structural study.

In general, the factors a) and b) will both apply in the case of electron-microscopic investigations; this is true, for example, in the examination of Nb_2O_5-rich systems comprising block structures. The new structural variations recognizable in Figures 11—13, which up to now have only ever been detected in very small regions (microdomains, see Section 4.2), are for the most part hybrid phases (B1, B2, C1, C2 in Table 3); further structural variations in the Nb_2O_5–WO_2 system are known[62,78] or are at present being investigated[72]. An example from the TiO_2–Nb_2O_5 system[60] was mentioned in Section 4.2.

Metastable solids often cannot be obtained in the form of well crystallized specimens (or only with great difficulty), or are available only in exceptionally small amounts; this is also evident from the observations of microdomains mentioned earlier. Electron microscope studies can also achieve progress in this case (b); examples are a new metastable modification of $FeNbO_4$[79] or the oxidation products of $Nb_{12}O_{29}$ and other phases between $Nb_{12}O_{29}$ and Nb_2O_5[80,81].

6. Future Prospects

In this research review the applications of high-resolution transmission electron microscopy have been discussed taking as examples niobium oxides and niobium-oxide-containing systems; the method has also been used with other solids (*e.g.* [9,10,12,13,33,34,54–57,74–77]). Block structures have provided the impetus for this direction of work (Section 2.2), and they are also extremely suitable models for the study of structural defects and for the testing and further development of investigation methods, since they can be irradiated along their short crystallographic axis (Section 3.10).

In the interpretation of the results it was first assumed that, like the surrounding undistorted structure, the structural defects imaged continue with uninterrupted periodicity through the crystal *in the direction of the transmitted beam.* However, it has since been found that this is not an invariable rule—the observable "defects in the b-direction" (*e.g.* in Fig. 16), *i.e.* in the direction of irradiation[82] and *Ijima*'s point defects[83] cannot be discussed in detail here. Deviations in the occupation of the tetrahedral sites (likewise lying in the beam direction) (Figs. 1 and 2a), such as those first investigated more closely in $GeNb_{18}O_{47}$[84], are of special interest, since the differences between the compositions of the ideal and real structures shown in Figure 3 may possibly be elucidated with their help[21,51]. Particular attention should be paid in further work to the arrangement of defects in the beam direction.

In the investigations discussed here we have avoided mistaking for real observations any artefacts that may have been produced during the preparation process, during irradiation of the specimen (Section 3.8) or spuriously simulated by contrast effects. Further technical developments and systematic work, which will answer the following questions also for materials other than those investigated by us, seem to us to be urgently necessary:

1) Does the mechanical or other specimen pretreatment or comminution give rise to structural defects? (On the subject of mechanical-chemical reactions, see [45]).
2) How can one reduce the radiation load or how can one exclude the possibility of changes in the specimen's structure due to the electron beam? (On the production of point defects, see [13,83].)

Other points that still require discussion are how the influence of lens aberrations can be reduced and the correct in-

terpretation of contrast relationships. The lens aberration that can be influenced by the user is astigmatism. In the usual commercial instruments the basic astigmatism may be too great to allow high-resolution work, since the fine adjustment of the focus becomes meaningless under these circumstances.

Other desirable technical developments relate to the mechanical stability, *e.g.* the suppression of specimen "creep" during the time of the observation. The necessary stability of the high voltage ($\Delta E/E$) is improved when one changes, for example, from a 100 kV to a (technically much more complicated) 1000 kV microscope[11]; the radiation load of the specimen is not increased here in the same proportion. Organic molecular compounds are very sensitive to such irradiation[85]. Chlorinated copper phthalocyanine has proved to be a relatively stable model substance[86].

Niobium oxides and oxide fluorides, and also other particularly stable compounds with suitable structures known from X-ray structure analysis, have in the last ten years been used by physicists as model substances in order to perfect the theory of computer simulation of electron microscopic images. Computer methods are now in use that portray the crystal as being built up of layers (the multislice method[87]), and that make it possible to calculate the intensity relationships in a high-resolution microscope on the basis of the dynamical theory of electron diffraction (the dynamical n-beam multislice method)[30,31,88-90]. The effects of defocusing, spherical and chromatic aberration, the size of the objective aperture, *etc.* can all be taken into account. It is particularly important that model calculations can even be applied to structural defects, to the occupation of interstitial lattice points, and so on. Only by such model calculations can one interpret complicated contrast relationships in electron micrographs with a sufficient degree of reliability. Such parallel computer investigations are the more necessary, the more accurately are the real structures to be examined.

Our own investigations using the new method would not have been possible without enthusiastic co-workers; particular thanks must go to Dr. H. Brunner, Dipl.-Chem. G. Heurung, Dr. H. Hibst, and Dipl.-Chem. B. Meyer. We are indebted to Frau H. Geiss and to Herr M. Zahrt for technical assistance. Our work was generously supported by the Fonds der Chemischen Industrie and by the Deutsche Forschungsgemeinschaft.

Received: February 26, 1980 [A 325 IE]
German version: Angew. Chem. *92*, 531 (1980)

[1] *J. M. Cowley:* Diffraction Physics. North-Holland, Amsterdam 1975.
[2] *M. K. Sinha, E. W. Müller,* J. Appl. Phys. *35*, 1256 (1964).
[3] *M. J. Attardo, J. M. Galligan,* Phys. Rev. *161*, 558 (1967).
[4] *D. G. Ast, D. N. Seidman,* Appl. Phys. Lett. *13*, 348 (1968).
[5] *S. Andersson,* S. Solid State Chem. *1*, v—vi (1970).
[6] *J. G. Allpress, J. V. Sanders, A. D. Wadsley,* Phys. Status Solidi *25*, 541 (1968).
[7] *J. M. Cowley, S. Iijima,* Phys. Today *30*, 32 (1977).
[8] *J. S. Anderson, J. L. Hutchison, F. J. Lincoln,* Proc. R. Soc. *A 352*, 303 (1977).
[9] *L. A. Bursill,* J. Solid State Chem. *10*, 72 (1974).
[10] *A. Hussain, L. Kihlborg,* Acta Crystallogr. *A 32*, 551 (1976).
[11] *S. Horiuchi, K. Muramatsu, Y. Matsui,* Acta Crystallogr. *A 34*, 939 (1978).
[12] *L. Stenberg, S. Andersson,* J. Solid State Chem. *28*, 269 (1979).
[13] *J. R. Fryer:* The Chemical Applications of Transmission Electron Microscopy. Academic Press, London 1979.
[14] *H. Hashimoto, H. Endoh, A. Kumao,* Proc. 6th Eur. Congr. EM, Jerusalem, *1*, 137 (1976).
[15] *K. Izui, S. Furuno, H. Otsu,* JEOL (Jpn. Electron Opt. Lab.) News *15 E (2)*, 2 (1977).
[16] *A. Bourret, J. Desseaux,* JEOL (Jpn. Electron Opt. Lab.) News *14 E (4)*, 12 (1977).
[16a] *E. Brüche,* Naturwissenschaften *20*, 353 (1932).
[17] *M. Knoll, E. Ruska,* Ann. Phys. *12*, 607 (1932).
[18] *L. Reimer, G. Pfefferkorn:* Rasterelektronenmikroskopie. Springer, Berlin 1977.
[19] *J. W. Menter,* Proc. R. Soc. *A 236*, 119 (1956).
[20] *A. D. Wadsley, S. Andersson* in *J. D. Dunitz, J. A. Ibers:* Perspectives in Structural Chemistry. Vol. III, 1. Wiley, New York 1969.
[21] *R. Gruehn,* Nat. Bur. Stand. (U. S.) Spec. Publ. 364, Sol. State Chem., Proc. of 5th Mater. Res. Symp., July 1972.
[22] *R. Gruehn,* Habilitationsschrift, Universität Münster 1968.
[23] *A. D. Wadsley,* Acta Crystallogr. *14*, 664 (1961).
[24] *R. Gruehn,* Monatsh. Chem. *96*, 1789 (1965).
[25] *R. Gruehn, R. Norin,* Z. Anorg. Allg. Chem. *355*, 176 (1967).
[26] *R. Gruehn, R. Norin,* Z. Anorg. Allg. Chem. *367*, 209 (1969).
[27] *R. Gruehn,* Naturwissenschaften *54*, 645 (1967).
[28] *S. Andersson, W. G. Mumme, A. D. Wadsley,* Acta Crystallogr. *21*, 802 (1966).
[29] *J. G. Allpress,* Mater. Res. Bull. *4*, 707 (1969).
[30] *M. A. O'Keefe, J. V. Sanders,* Acta Crystallogr. *A 31*, 307 (1975).
[31] *A. J. Skarnulis, E. Summerville, L. Eyring,* J. Solid State Chem. *23*, 59 (1978).
[32] *S. Iijima,* J. Appl. Phys. *42*, 5891 (1971).
[33] *J. G. Allpress, R. J. D. Tilley, M. J. Sienko,* J. Solid State Chem. *3*, 440 (1971).
[34] *S. Iijima,* J. Solid State Chem. *14*, 52 (1975).
[35] *L. Reimer:* Elektronenmikroskopische Untersuchungs- und Präparationsmethoden. 2nd Edit. Springer, Berlin 1967.
[36] *H. Ahmed,* Proc. 5th Eur. Congr. EM, Manchester, 10 (1972).
[37] *Y. Harada, T. Goto, T. Someya,* 8th Int. Congr. EM, Canberra *1*, 110 (1974).
[38] *P. B. Hirsch, A. Howie, R. B. Nicholson, D. W. Pashley, M. J. Whelan:* Electron Microscopy of Thin Crystals. Butterworths, London 1971.
[39] *E. Hornbogen:* Durchstrahlungselektronenmikroskopie fester Stoffe. Verlag Chemie, Weinheim 1971.
[40] *K. W. Andrews, D. J. Dyson, S. R. Keown:* Interpretation of Electron Diffraction Patterns. Adam Hilger, London 1971.
[41] International Tables for X-Ray Crystallography. Vol. I. The Kynoch Press, Birmingham 1969.
[42] *J. M. Cowley,* Inst. Phys. Conf. Ser. *41*, 156 (1978).
[43] *P. Goodman,* Inst. Phys. Conf. Ser. *41*, 116 (1978).
[44] *W. Baumeister, J. Seredynski,* Micron *7*, 49 (1976).
[45] *H. Hibst, R. Gruehn,* Z. Anorg. Allg. Chem. *440*, 137 (1978).
[46] *H. Bach,* Beitr. Elektronenmikroskop. Direktabb. Oberfl. *12*, 277 (1979).
[47] *H. Brunner, R. Gruehn, W. Mertin,* Z. Naturforsch. *B 31*, 549 (1976).
[48] *G. Heurung, R. Gruehn, H. Brunner,* Z. Naturforsch. *B 34*, 553 (1979).
[49] *A. Maas,* 8th Int. Congr. EM, Canberra *1*, 524 (1974).
[50] *J. S. Anderson* in *M. W. Roberts, J. M. Thomas:* Surface and Defect Properties of Solids. Vol. 1. The Chemical Society, London 1972.
[51] *J. S. Anderson* in *M. W. Roberts, J. M. Thomas:* Surface and Defects Properties of Solids. Vol. 3. The Chemical Society, London 1974.
[52] *B. G. Hyde, L. A. Bursill* in *L. Eyring, M. O'Keeffe:* The Chemistry of Extended Defects in Non-metallic Solids. North Holland, Amsterdam 1970.
[53] *L. Mandelcorn:* Non-stoichiometric Compounds. Academic Press, London 1964.
[54] *T. Ekström, R. J. D. Tilley,* J. Solid State Chem. *24*, 209 (1978).
[55] *S. Iijima, J. G. Allpress,* Acta Crystallogr. *A 30*, 29 (1974).
[56] *H. R. Wenk:* Electron Microscopy in Mineralogy. Springer, Berlin 1976.
[57] *M. Czank, F. Liebau,* Fortschr. Mineral. *57*, Beih. 1, 23 (1979).
[58] *J. M. Cowley* in *L. Eyring, M. O'Keeffe:* The Chemistry of Extended Defects in Nonmetallic Solids. North Holland, Amsterdam 1970.
[59] *H. Hibst, R. Gruehn,* Z. Naturforsch. *B 33*, 884 (1978).
[60] *J. G. Allpress,* J. Solid State Chem. *1*, 66 (1969).
[61] *J. G. Allpress, R. S. Roth,* J. Solid State Chem. *3*, 209 (1971).
[62] *G. Heurung, R. Gruehn,* Z. Naturforsch. *B 34*, 1377 (1979).
[63] *H. Schäfer:* Chemische Transportreaktionen. Verlag Chemie, Weinheim 1962.
[64] *G. Hägg, A. Magnéli,* Rev. Pure Appl. Chem. *4*, 235 (1954).
[65] *S. Andersson, L. Jahnberg,* Ark. Kemi *21*, 413 (1963).
[66] *L. Kihlborg,* Adv. Chem. Ser. *39*, 37 (1963).
[67] *A. D. Wadsley,* Helv. Chim. Acta, Fasc. Extraord. Alfred Werner, 1967.
[68] *J. G. Allpress, J. V. Sanders, A. D. Wadsley,* Acta Crystallogr. *B 25*, 1156 (1969).
[69] *J. E. Chisholm* in *M. W. Roberts, J. M. Thomas:* Surface and Defect Properties of Solids. Vol. 4. The Chemical Society, London 1975.
[70] *H. Reuter, D. Söthe, J. Sturm,* unpublished.
[71] *G. Heurung,* Diplomarbeit, Universität Giessen 1976.
[72] *G. Heurung, R. Gruehn,* unpublished.

[73] *S. Andersson*, Acta Chem. Scand. *19*, 557 (1965).
[74] *P. R. Buseck, S. Iijima*, Am. Mineral. *59*, 1 (1974).
[75] *S. Amelinckx* in *J. A. Venables:* Developments in Electron Microscopy and Analysis. Academic Press, London 1976.
[76] *J. L. Hutchison, A. J. Jacobson*, J. Solid State Chem. *20*, 417 (1977).
[77] *R. J. D. Tilley*, J. Solid State Chem. *21*, 293 (1977).
[78] *J. G. Allpress, A. D. Wadsley*, J. Solid State Chem. *1*, 28 (1969).
[79] *H. Brunner, R. Gruehn*, Z. Naturforsch. *B 31*, 318 (1976).
[80] *H. Hibst, R. Gruehn*, Z. Anorg. Allg. Chem. *442*, 49 (1978).
[81] *B. Meyer, R. Gruehn*, unpublished.
[82] *J. G. Allpress*, J. Solid State Chem. *2*, 78 (1970).
[83] *S. Iijima*, Acta Crystallogr. *A 31*, 784 (1975).
[84] *A. J. Skarnulis, S. Iijima, J. M. Cowley*, Acta Crystallogr. *A 32*, 799 (1976).
[85] *W. Hoppe*, 8th Int. Congr. EM, Canberra, *1* (1974).
[86] *K. Kobayashi* in *J. A. Venables:* Developments in Electron Microscopy and Analysis. Academic Press, London 1976.
[87] *J. M. Cowley, A. F. Moodie*, Acta Crystallogr. *10*, 609 (1957).
[88] *J. G. Allpress, E. A. Hewath, A. F. Moodie, J. V. Sanders*, Acta Crystallogr. *A 28*, 528 (1972).
[89] *D. F. Lynch, M. A. O'Keefe*, Acta Crystallogr. *A 28*, 536 (1972).
[90] *P. M. Fields, J. M. Cowley*, Acta Crystallogr. *A 34*, 103 (1978).

Alkali Metal-Transition Metal π-Complexes[**]

By Klaus Jonas and Carl Krüger[*]

In this progress report a new principle is described for the synthesis of multimetal π-complexes with hitherto unknown structural features. The nickel(0)-olefin complexes 1,5,9-cyclododecatrienenickel(0) and bis(1,5-cyclooctadiene)nickel(0) react unexpectedly with main-group metals, in particular alkali metals, their hydrides, and organometallic compounds, to give nickel-ligand species with a surplus charge. These species endeavor to transfer the excess charge onto π-ligands such as olefins or dinitrogen. Multimetal complexes with electron rich transition metal π-ligand units can, in addition, be prepared from metallocenes, alkali metals, and unsaturated compounds. The syntheses, structures, and reactions of this new class of substances will be summarized.

1. Introduction

The main group metals—especially those of the first to third groups of the periodic table—their hydrides and organometallic compounds play an important role in the syntheses of organo-transition metal compounds. Their reactions with transition metal salts open the way for the preparation of low-valent transition metal complexes and permit the syntheses of well-defined hydrido- and organo-transition metal complexes as well as the construction of active catalytic systems such as the Ziegler catalysts[1].

Whereas electropositive main-group metals M_M[*], for example alkali metals, magnesium, or aluminum, reduce transition metal salts M_TX_n (eq. (a) to (c))[2-4], their organo-compounds M_MR_n or hydrides M_MH_n act primarily as sources of groups R or H atoms.

$$3\,CrCl_3 + 2\,Al \xrightarrow{6\,C_6H_6,\ 13\,AlCl_3} 3\,[(C_6H_6)_2Cr]AlCl_4(AlCl_3)_4 \qquad (a)$$

(1)

Examples of products from this double displacement reaction are organo-transition metal complexes with M_T—C σ-bonds such as *(4)*[5] and π-complexes like ferrocene *(5)*[6] and bis(π-allyl)nickel *(6)*[7]. From reduction of the transition metal come such compounds as the nickel(0) olefin complexes[8] $(CDT)Ni^0$ *(7)* or $(COD)_2Ni^0$ *(8)*.

In 1952 *Gilman et al.*[9] reported that poorly soluble methyl-copper, prepared as in eq. (e), dissolves in diethyl ether in the presence of methyl lithium (eq. (f)). Lithium dimethylcuprate *(9)* is formed showing that the tendency of main-group organo metallic compounds and hydrides to combine with their corresponding alkali metal derivatives to give metalates (atecomplexes) such as $Li[AlH_4]$ or $Li[B(C_6H_5)_4]$ [known from the early work of *Wanklyn*[10] and *Hein et al.*[11] together with the systematic investigations by *Wittig et al.*[12] and *Schlesinger et al.*[13]] is also found for a transition metal alkyl compound.

As in the synthesis of *(9)* and analogous cuprates[14,15], the first step in the numerous other syntheses of transition metal

[*] Priv.-Doz. Dr. K. Jonas, Priv.-Doz. Dr. C. Krüger [***]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim a. d. Ruhr (Germany)

[**] Extracts from the habilitation theses of *K. Jonas*, Universität Bochum 1979, *C. Krüger*, Gesamthochschule Wuppertal 1978. Preparative work by *K. Blum, T. E. G. Daenen, E. Deffense, D. Habermann, U. Häusig, K. Jonas, K. R. Pörschke*, and *L. Schieferstein*.

[***] X-ray analyses together with *D. J. Brauer, K. H. Claus, L. K. Liu, J. C. Sekutowski*, and *Y.-H. Tsay*.

[*] Abbreviations: M = metal, M_M = main-group metal, M_A = alkali metal, M_T = transition metal, acac = acetylacetonate, CDT = cyclododecatriene, COD = cyclooctadiene, COT = cyclooctatetraene, DME = dimethoxyethane, THF = tetrahydrofuran, TMEDA = *N,N,N',N'*-tetramethylethylenediamine. Interatomic distances in Å (10^{-10} m).

$$(CH_2)_2[P(C_6H_{11})_2]_2NiCl + Li \xrightarrow{Arene}$$

$$(CH_2)_2[P(C_6H_{11})_2]_2NiArene + LiCl \quad (b)$$

(2)

$$[C_6H_5(CH_3)_2P]_2MoCl_4 + 4\,Na \xrightarrow{2\,C_6H_5(CH_3)_2P,\ 2\,N_2}$$

$$[C_6H_5(CH_3)_2P]_4Mo(N_2)_2 + 4\,NaCl \quad (c)$$

(3)

$$M_TX_n + nM_MR(H) \rightarrow M_TR_n(H_n) + nM_MX$$

$$WCl_6 + 6\,Al(CH_3)_3 \rightarrow W(CH_3)_6 + 6\,(CH_3)_2AlCl$$

(4)

$$FeCl_2 + 2\,C_5H_5MgBr \rightarrow (\pi\text{-}C_5H_5)_2Fe + MgBr_2 + MgCl_2$$

(5)

$$NiBr_2 + 2\,C_3H_5MgBr \rightarrow (\pi\text{-}C_3H_5)_2Ni + 2\,MgBr_2$$

(6)

$$Ni(acac)_2 + 2\,AlR_3 \xrightarrow{CDT} (CDT)Ni^0 + 2\,R_2Al(acac) + 2[R^{\ominus}] \quad (d)$$

(7)

$$Ni(acac)_2 + 2\,AlR_3 \xrightarrow{2\,COD} (COD)_2Ni^0 + 2\,R_2Al(acac)_3 + 2[R^{\ominus}]$$

(8)

$$CuI + LiCH_3 \rightarrow CuCH_3 + LiI \quad (e)$$

$$CuCH_3 + LiCH_3 \rightarrow Li[Cu(CH_3)_2] \quad (f)$$

(9)

metalates is a double displacement reaction, in particular between transition metal halides and organo-alkali metal compounds. The addition of mM_AR to M_TR_n leading to the metalate can be considered as a separate step. This usually takes place on the intact M_TR_n species so that starting from M_TX_n a metalate of the form *(10)* results[15-17].

$$M_TX_n + (m+n)M_AR \rightarrow (M_A)_m[M_TR_{n+m}] + nM_AX$$

(10)

This is also true for the f-element metalate complexes that have been described so far[18]. Representative examples of *(10)* are the cuprates[14,19] such as *(9)*, which are gaining increasing importance in organic chemical syntheses, the transition metal alkynyl complexes $(M_A)_m[M_T(C{\equiv}C{-}R)_{m+n}]$ thoroughly investigated by *Nast*[20], the Hein chromium complexes[21] $Li_3[Cr(C_6H_5)_6]$ and $Na_2[Cr(C_6H_5)_5]$ as well as $Li_2[Ni(CH_3)_4]$[22] and $Li_2[W(CH_3)_8]$[5].

2. From the "Nickel Effect" to Isolable Organo-Alkali Metal-Nickel(0) π-Complexes

Transition metals are characteristic in their ability to interact with the π-systems of unsaturated hydrocarbons or their residues. The first example of a system of this type was an ethylene-platinum compound; it was first prepared by *Zeise*, who over 150 years ago obtained the salt $K[PtCl_3(C_2H_4)]H_2O$[23], which was named after him, from $PtCl_4$, KCl and ethanol. Transition metal metalates containing π-ligands and bearing only organic ligands at the M_T atom, such as $[Li(TMEDA)_2]^{\oplus}[CH_3{-}Ni(C_2H_4)_2]^{\ominus}$ *(16a)*, on the other hand, have only become known in recent years. We have reported these in brief[24,25].

The starting point of our investigations were studies on the mechanism of the "nickel effect"[26] discovered by *Ziegler* and *Holzkamp*. These studies were based on a comprehensive nickel chemistry developed, in particular, by *Wilke et al.*[27]. It was found that aluminum alkyl compounds not only react with salt-like nickel compounds by double displacement reactions as in eq. (d), but can also interact with nickel(0)[28,29]. The original observation by *Ziegler* and *Holzkamp* that the „Aufbau" reaction[30] of $Al(C_2H_5)_3$ with ethylene is transformed into dimerization of ethylene by addition of traces of nickel salts ("nickel effect")[26] depends on both of these factors, while the observation[28,29] that particular nickel(0)-olefin complexes such as *(7)* or *(8)* or tris(ethylene)nickel(0) *(11)*[31] are extremely effective catalysts for the alkyl exchange of higher molecular weight aluminum-alkyl compounds with olefins, for example eq. (g), depends on the latter.

$$Al(n\text{-}C_4H_9)_3 + 3\,C_2H_4 \xrightarrow[0\,^{\circ}C]{(C_2H_4)_3Ni^0\ (11)} Al(C_2H_5)_3 + 3\,C_4H_8 \quad (g)$$

The nickel(0)-catalyzed transalkylation [eq. (g)] very probably proceeds within a complex where the aluminum alkyl compound and the olefin are bound to nickel and a multicenter bond $R_2Al{-}R{-}Ni^0$ exists between R_3Al and nickel(0). Stereochemical observations and model considerations agree with this supposition[29].

This fundamental view of the "nickel effect" is supported by the fact that compounds could be obtained from reactions of nickel(0)-olefin complexes with more polar organometallic compounds than R_3Al, *i.e.* with organo-alkali metal compounds. These compounds, particularly those of lithium, form isolable multimetal compounds $(M_AR)_x(n\text{-donor ligand})_yNi^0(\pi\text{-ligand})_z$ with *n*-donor ligands, nickel(0), and olefins or other molecules with multiple bonds (π-ligands) in which up to three M_AR units per nickel atom can be bound. In several of these compounds multicenter bonding of the type $M_A{-}R{-}Ni^0$ has been demonstrated by X-ray structural analyses (see Section 4).

3. Salt-Like M_AR-, M_AH-, and M_APR_2-Nickel(0) π-Complexes

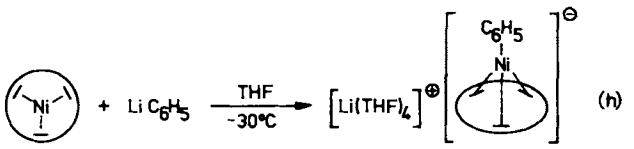
Both in the solid state[32,33] and in solution[34], organolithium compounds can, depending on the nature of R and on the solvation ability (n-donor strength)[35] of the solvent, be associated or exist as monomeric solvated ion pairs. Dissociation into freely moving ions plays but a minor role in solutions to which strong n-donors such as tetrahydrofuran (THF) or *N,N,N',N'*-tetramethylethylenediamine (TMEDA) have been added in order to stabilize the cations. Stabilization of the carbanion, on the other hand, is much better in promoting an ionic dissociation, which can be attained—as *Hein et al.*[11] were able to show, through conductivity measurements, for example on $Li_2[ZnR_4]$ and $Li[AlR_4]$—with main-group metal organometallic Lewis acids (here ZnR_2 and AlR_3, respectively).

3.1. Carbanion Complexes of Nickel(0)

We have found[24, 25, 36] that certain nickel(0)-olefin complexes or nickel(0) complex fragments with π-ligands can heterolytically cleave the Li—C bond in simple organolithium compounds provided that the lithium ion can be sufficiently stabilized with n-donors.

Thus the dark red coordinatively unsaturated $(CDT)Ni^0$ *(7)*, for example, reacts smoothly with phenyl lithium in THF to give the yellow 1:1 adduct *(12)*.

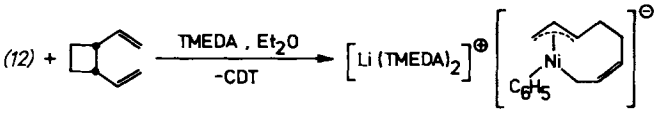
In *(12)* four THF molecules are bonded to the lithium cation, and the phenyl anion, acting as a two electron ligand, fills the fourth coordination site on nickel—as is known for phosphanes and phosphites[27]—to give the cyclododecatriene(phenyl)nickel(0) anion.



(h)

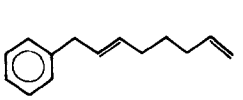
(7) *(12)*

(12) reacts with *cis*-divinylcyclobutane with the loss of the CDT-ligand and opening of the cyclobutane ring to give *(13)*[37]. In *(13)* the C_8H_{12} chain is bonded to nickel as a π-allyl group at one end and as a σ-allyl group at the other, as is observed for $(C_6H_{11})_3PNiC_8H_{12}$[38].

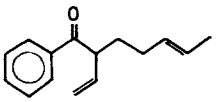


(13)

(13) reacts with carbon monoxide with transfer of a phenyl group or a benzoyl group, formed by CO insertion, to the C_8H_{12} chain on the nickel atom. The main products resulting from protonation are *(14)* and *(15)*[37].



(14)



(15)

The simplest nickel(0) π-ligand carbanion complexes *(16)* can be prepared from $(CDT)Ni^0$ *(7)* or $(COD)_2Ni^0$ *(8)*, organolithium compounds, TMEDA, and ethylene in diethyl ether (Et_2O)[24].

$$(CDT)Ni^0 + 1\,LiR + 2\,C_2H_4 + 2\,TMEDA \xrightarrow{Et_2O}$$

(7)

$$[Li(TMEDA)_2]^{\oplus}[R{-}Ni(C_2H_4)_2]^{\ominus} + CDT$$

(16)

(16a), R = CH_3; *(16b)*, R = C_2H_5; *(16c)*, R = *n*-C_4H_9; *(16d)*, R = C_6H_5

The ionic nature of *(16)* has been demonstrated by conductivity measurements and an X-ray structure analysis of *(16a)*. The complex salts *(16)* have about a 10^3 times higher specific conductivity than organolithium compounds (0.25 M in THF at −30 °C) and their conductivity corresponds to that of lithium perchlorate in THF solution.

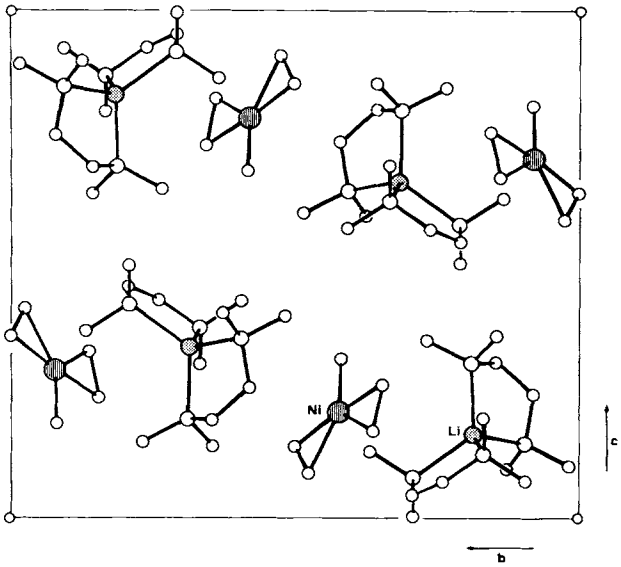


Fig. 1. Packing diagram of $[Li(TMEDA)_2]^{\oplus}[CH_3Ni(C_2H_4)_2]^{\ominus}$ *(16a)*, projected along −*a*.

The packing diagram of *(16a)* (Fig. 1) shows that the separated ions are arranged in a linear fashion. Each lithium cation, tetrahedrally coordinated by two TMEDA ligands, lies equidistant between two planar bis(ethylene)methylnickel anions. The relatively short C=C distances (1.36, 1.38 Å) of the complexed ethylene molecules indicate only a weak interaction with the metal; the Ni—C σ-bond at 1.91 Å is nevertheless exceptionally short[39].

Both ethylene molecules in *(16)* can be displaced by CO or cyclooctatetraene, while only one ethylene molecule is displaced with nitriles such as C_6H_5CN or CH_3CN at −30 °C. As a result, new complexes, *e.g. (17)*, can be isolated, in which an anionic phenyl group, an ethylene, and a benzonitrile are bonded to nickel.

$$(16d) + 1\,C_6H_5CN \xrightarrow[-TMEDA,\ -C_2H_4]{Et_2O}$$

$$Li(TMEDA)C_6H_5Ni(C_2H_4)(C_6H_5CN)$$

(17)

The carbanion ligands in *(16)* can be abstracted by several main-group organometallic Lewis acids, *e.g.* $Al(C_2H_5)_3$. Thus from *(16b)* and $Al(C_2H_5)_3$ in the presence of COD one obtains $(COD)_2Ni^0$ *(8)* and TMEDA-complexed lithium tetraethylaluminate *(18)* in high yields.

$$[Li(TMEDA)_2]^{\oplus}[C_2H_5{-}Ni(C_2H_4)_2]^{\ominus} + 1\,Al(C_2H_5)_3 + 2\,COD \rightarrow$$

(16b) (i)

$$(COD)_2Ni^0 + [Li(TMEDA)_2]^{\oplus}[Al(C_2H_5)_4]^{\ominus} + 2\,C_2H_4$$

(8) *(18)*

3.2. The Hydride Ion $H^{\ominus}$ as a Bridge between two Nickel Atoms

The reverse of reaction (i) using a hydridoaluminate, *i.e.* with $M_A[AlR_mH_{4-m}]$, results in hydride transfer onto the nickel atom, and can be used for the synthesis of novel alkali metal hydride-containing nickel olefin complexes[40]. Where-

as (CDT)Ni^0 *(7)* reacts with Na[Al(C_2H_5)$_3$H] or Li[AlH_4] to give the complex anions [(CDT)Ni—H—AlR_3]$^\ominus$ or [(CDT)Ni—H—AlH_3]$^\ominus$, in which the hydride ion bridges the nickel and aluminum atoms, the reaction with tris(ethylene)nickel(0) *(11)* results in complete hydride transfer to the nickel atom, and a complex salt is formed containing two nickel atoms in the anion, *e.g. (19).*

$$2(C_2H_4)_3Ni^0 + Li[Al(i\text{-}C_4H_9)_2H_2] \xrightarrow{2\,TMEDA}$$

(11)

$$[Li(TMEDA)_2]^\oplus[(C_2H_4)_2Ni—H—Ni(C_2H_4)_2]^\ominus + Al(C_2H_5)(i\text{-}C_4H_9)_2 + C_2H_4$$

(19)

The two nickel atoms in *(19)* are probably trigonally-planar coordinated [as in the carbanion-containing complex salts *(16)*] and the two parts of the anion are bound *via* a linear or bent two-electron three-center Ni—H—Ni bond (Fig. 2).

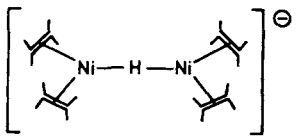


Fig. 2. Proposed structure for the bimetallic anion of [Li(TMEDA)$_2$]$^\oplus$[(C_2H_4)$_2$Ni—H—Ni(C_2H_4)$_2$]$^\ominus$ *(19)*.

3.3. The $R_2P^\ominus$ Anion as a Bridge between two Nickel Coordination Centers

Lithium diorganophosphides[41] have two available σ-donating electron pairs and can form complexes of type *(20)* or *(21)* with either one or two bis(ethylene)nickel(0) units, respectively[42,43].

$$\xrightarrow{LiPR_2}$$

$$+ (COD)_2Ni(0)\ (8),\ + 2\ C_2H_4,\ + 3\ THF \downarrow - 2\ COD$$

$$(THF)_3LiR_2PNi(C_2H_4)_2 \quad (20)$$

$$+ (COD)_2Ni(0)\ (8),\ + 2\ C_2H_4,\ + THF \downarrow - 2\ COD$$

$$[Li(THF)_4]^\oplus[(C_2H_4)_2Ni(PR_2)Ni(C_2H_4)_2]^\ominus \quad (21)$$

R = C_6H_{11}

The dinuclear complex *(21)* is a stronger electrolyte than *(20)*, since both electron pairs of the phosphorus atom in *(21)* are involved in bonding to the two (C_2H_4)$_2$Ni units, and none is available to interact with the lithium ion. Figure 3 shows the structure of *(21)* as determined by an X-ray analysis[44].

Each nickel atom is trigonally-planar coordinated and the coordination planes make an angle of 95° with each other; the Ni—P—Ni angle is 105.7°. The Ni—Ni distance of 3.57 Å indicates that a metal-metal interaction is unlikely. The different Ni—C(olefin) distances suggest there might be some steric interaction in the coordination planes of the nickel atoms. The bridging phosphorus atom is approximately tetrahedrally coordinated.

There are no preferred intermolecular contacts to be seen in the packing diagram of *(21)*, and the lithium to phosphorus and ethylene distances lie well into the region of an ionic interaction (Li—P = 7.88 Å, Li—C = 5.54—6.00 Å). Here there is an indication of an—albeit very weak—ion pair interaction between a main group metal and a π-bonded olefin.

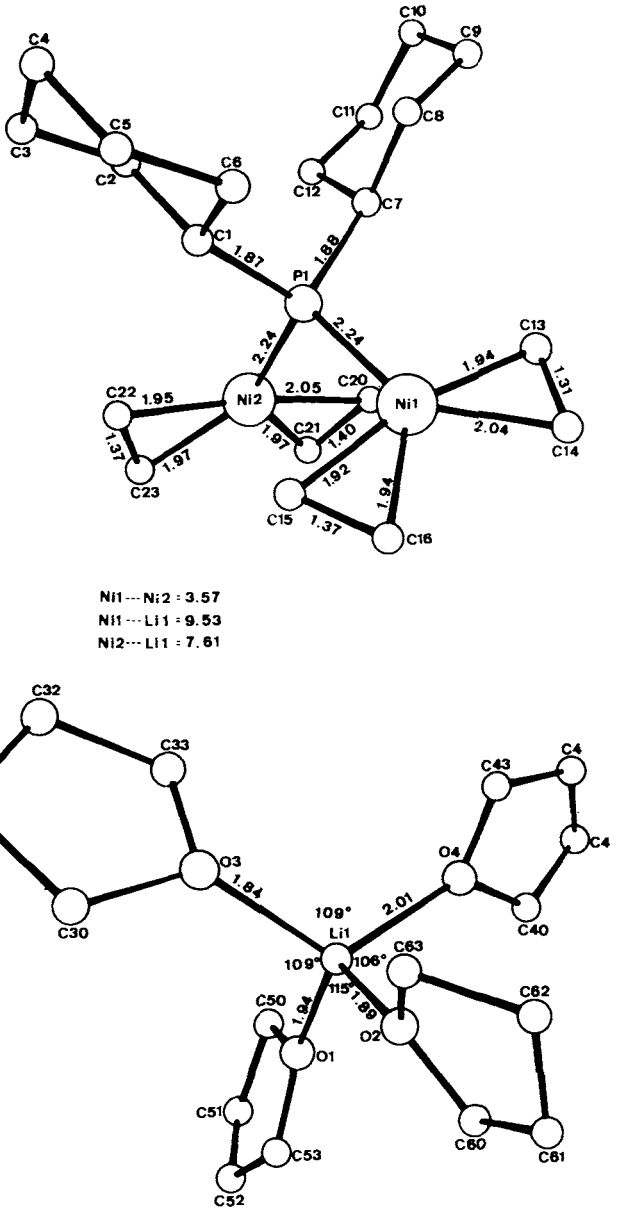


Fig. 3. Structure of [Li(THF)$_4$]$^\oplus$[(C_2H_4)$_2$Ni(PR_2)Ni(C_2H_4)$_2$]$^\ominus$, R = C_6H_{11} *(21)*.

Reaction of *(20)* with excess butadiene at room temperature gives exclusively polybutadiene. This suggests that *(20)*, like pure $LiPR_2$[43], initiates a fast anionic polymerization, which is unaffected by nickel. *(21)* reacts somewhat differently with butadiene. In addition to polybutadiene (*ca.* 50%) typical oligomerization products from nickel(0)-catalyzed reactions[27] such as C_8H_8 (COD, vinylcyclohexene, and divinylcyclobutane) and CDT are also formed. The product distribution obtained with *(21)* can be explained in terms of the interplay of known catalytic systems if one considers the following simplified dissociation equilibria:

$$\underset{I}{[Ni—PR_2—Ni]^\ominus} \rightleftarrows \underset{II}{[Ni]} + \underset{III}{[NiPR_2]^\ominus} \rightleftarrows 2\underset{II}{[Ni]} + \underset{IV}{[PR_2]^\ominus}$$

Acting as ligand-modified nickel(0) catalysts, I and possibly also III, effect the formation of C_8 products. II catalyzes the

cyclotrimerization (CDT formation), while IV and probably III are the polymerization catalysts.

The ionic complex *(22)*, formed by the reaction of *(21)* with butadiene at low temperature, is interesting in connection with the catalytic effect of I. It may well be an intermediate in the cyclodimerization of butadiene by *(21)*.

$$(21) + 4\,C_4H_6 \xrightarrow[-4\,C_2H_4]{} [Li(THF)_4]^{\oplus}[(C_6H_{11})_2P(NiC_8H_{12})_2]^{\ominus}$$

(22)

In *(22)* two butadiene molecules have linked on each nickel atom to give a C_8H_{12} chain, and according to the ^{13}C-NMR spectrum[46] the chains are bonded to the metal *via* π-allyl and σ-allyl attachments as in *(13)*[37] and $(C_6H_{11})_3PNiC_8H_{12}$[38] (see Fig. 4).

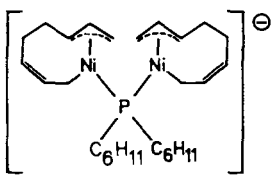
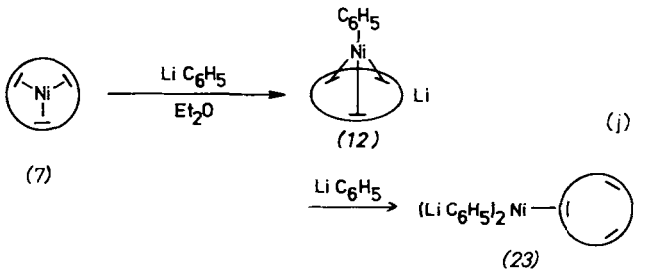


Fig. 4. Proposed structure for the anion of $[Li(THF)_4]^{\oplus}[(C_6H_{11})_2PNi(C_8H_{12})_2]^{\ominus}$ *(22)* (schematic).

4. Complex Formation between Unsaturated Molecules and the Bis(phenylalkali metal)nickel(0) Unit

4.1. Syntheses of Bis(phenylalkali metal)nickel(0) π-Complexes

If $(CDT)Ni^0$ *(7)* is reacted with phenyl lithium in the molar ratio of 1:2 in ether at 0 °C [eq. (j)] one obtains a yellow-red solution of $[(LiC_6H_5)_2(Et_2O)_y]Ni(CDT)$ *(23a)*. $[(LiC_6H_5)_2(THF)_4]Ni(CDT)$ *(23b)* or $[(LiC_6H_5)_2(TMEDA)_2]Ni(CDT)$ *(23c)* crystallizes[36] out of this solution at low temperatures after addition of THF or TMEDA. Similarly, $(COD)_2Ni^0$ *(8)* reacts with LiC_6H_5 (molar ratio 1:2) with the loss of a COD ligand to give *(24)*[*]. Crystals of *(24a)* or *(24b)* can be isolated after addition of THF or TMEDA, respectively[36].



(23) (j)

$$(COD)_2Ni^0 + 2\,LiC_6H_5 \xrightarrow[-COD]{THF} [(LiC_6H_5)_2(THF)_4]Ni(COD)$$

(8) *(24a)*

$$(8) + 2\,LiC_6H_5 \xrightarrow[-COD]{Et_2O,\ TMEDA} [(LiC_6H_5)_2(TMEDA)_2]Ni(COD)$$

(24b)

[*] *(24)* is likewise formed from *(8)* and $LiPb(C_6H_5)_3$ [47].

According to the ^{13}C-NMR[46] spectrum, the cyclododecatriene ligand in *(23)* is only coordinated to the nickel atom *via* one double bond; this is in contrast to what is seen in complexes *(7)* and *(12)*. The CDT ligand can be displaced by other molecules containing multiple bonds such as alkenes, alkynes, arenes, ketones, or nitriles. In this way, new bis(phenyllithium)nickel(0) π-complexes can be prepared, eq. (k); examples are given in Table 1.

$$(LiC_6H_5)_2Ni(CDT) + \pi\text{-Ligand} \xrightarrow{\text{n-Donor ligand}}$$

(23)

$$[(LiC_6H_5)_2(\text{n-Donor ligand})_x]Ni(\pi\text{-Ligand}) + CDT \qquad (k)$$

Table 1. Bis(phenyllithium)nickel(0) π-complexes obtained according to eq. (k).

π-Ligand	Complex	
Ethylene	$[(LiC_6H_5)_2Et_2O]NiC_2H_4$	*(25)*
Norbornene	$[(LiC_6H_5)_2Et_2O]NiC_7H_{10}$	*(26)*
3-Hexyne	$\{[(LiC_6H_5)_2(THF)_3]Ni\}_2C_2H_5C{-}CC_2H_5$	*(27)*
Naphthalene	$[(LiC_6H_5)_2(THF)_x]NiC_{10}H_8$	*(28)*
Phenanthrene	$[(LiC_6H_5)_2(THF)_4]NiC_{14}H_{10}$	*(29)*
Benzophenone	$[(LiC_6H_5)_2(THF)_3]Ni(C_6H_5)_2CO$	*(30)*
Acetonitrile	$[(LiC_6H_5)_2(THF)_3]NiCH_3CN$	*(31)*

The synthesis of pure bis(diethyl ether)ethylenebis(phenylsodium)nickel *(32)*[48] can be performed in ether by treating $(CDT)Ni^0$ *(7)* with a salt-free mixture of NaC_6H_5/LiC_6H_5 (Na:Li = 2—4:1) in the molar ratio $(NaC_6H_5 + LiC_6H_5):Ni^0 = 2:1$ in the presence of ethylene. The phenyllithium-containing nickel complex *(25)* remains in solution, and the complex *(32)* precipitates as an orange-red powder.

$$(CDT)Ni^0 + 2(m\,NaC_6H_5 + n\,LiC_6H_5) \xrightarrow[-CDT]{C_2H_4,\ Et_2O}$$

(7)

$$m[(NaC_6H_5)_2(Et_2O)_2]NiC_2H_4 + n \qquad (25)$$

(32)

$m:n = 2—4:1;\ m+n=1$

$[(NaC_6H_5)_2(THF)_{2.5}]NiC_2H_4$ *(32a)* $\qquad$ $[(NaC_6H_5)_2(DME)_2]NiC_2H_4$ *(32b)*

Exchange of the coordinated ether molecules in *(32)* by THF or dimethoxyethane (DME) gives the crystalline complexes *(32a)* or *(32b)*.

In the complexes *(23)*—*(32)*, containing two M_AR groups per nickel atom, there are no more than two n-donor atoms in the form of diethyl ether, tetrahydrofuran, dimethoxyethane, or *N,N,N',N'*-tetramethylethylenediamine bonded to each alkali metal atom. This is different from what is observed in the salt-like complexes $(M_AR)[Ni(C_2H_4)_2]$ and $(M_AH)[Ni(C_2H_4)_2]_2$ (Section 3). This observation together with their 10^2—10^3 times lower specific conductivity than $(M_AR)[Ni(C_2H_4)_2]$ (0.25 M in THF at −30 °C) indicate that ionic structures are unlikely for compounds *(23)*—*(32)*. Probably several of the free coordination sites on the lithium atoms, *i.e.* those not occupied by n-donors, are involved in multicenter or ion-pair interaction. The structures of *(32a)* and *(29)* are described in the next section.

4.2. Structures of Ethylenebis(phenylsodium)nickel(0) and Phenanthrenebis(phenyllithium)nickel(0)

We have characterized several of the bis(phenylalkalimetal)nickel(0) π-complexes by X-ray structure analyses. The results show surprising structural features which will be described for the compounds *(32a)*[49] and *(29)*.

(A) Ni---‖ (B) O, Na

The dimeric ethylenebis(phenylsodium)nickel compound *(32a)* (Fig. 5) contains two trigonal-planar $Ph_2Ni(C_2H_4)$ units A, in which Ni^0 is surrounded by two σ-bonded phenyl groups and one π-bonded ethylene molecule.

Four $Na(THF)_x$ units B ($x=1$, 2) are bound in different ways to these subunits. Two of these B groups ($x=1$) bridge the A groups and form a Ni_2Na_2 four-membered ring (Ni—Na = 2.883(1) Å). Comparable structural units are known in $Na_2Fe(CO)_4(dioxane)_{1.5}$[50] and disodium pentaphenylchromate[51]. In the first, for example, two $[Fe(CO)_4]^{2-}$ groups are linked by two sodium bridges to give a dimeric cluster (Fe—Na = 3.086 Å).

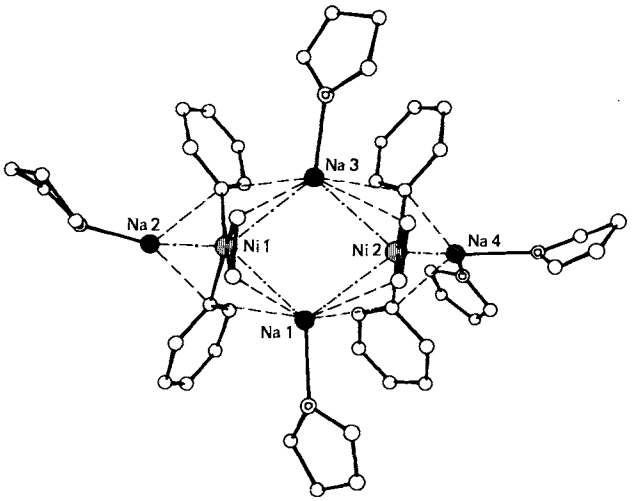


Fig. 5. The molecular structure of $\{[(NaC_6H_5)_2(THF)_{2.5}]NiC_2H_4\}_2$ *(32a)*.

Each of the two remaining B groups interacts with a different A group. The corresponding Ni—Na distances are longer and unequal. Their difference (Ni1—Na2 = 3.037 Å; Ni2—Na4 = 2.926 Å) can be explained as a consequence of the different occupations of the free coordination sites about the sodium atoms: whereas Na4 has two THF molecules bonded to it, Na2 has only one (as do Na1 and Na3). Consideration of the packing of the molecules in the unit cell provides an explanation. It is possible to ascribe a weak bond between Na2 of one molecule and a coordinated ethylene in a neighboring molecule. The molecules are therefore arranged in a one-dimensional polymeric fashion in the crystal lattice (see Fig. 6). The sodium atom Na2 sits on the opposite side of the ethylene molecule from nickel. Hence the electron density on ethylene might be high.

Semi-empirical MO calculations support this view. The arrangement of sodium atoms and phenyl groups in unit A suggest similar ion-pair interactions here (Fig. 5 and 6). In-

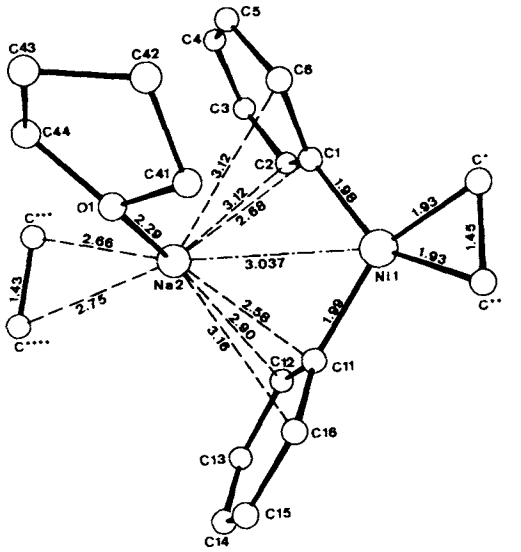


Fig. 6. Section from the polymeric molecular structure of *(32a)*.

teractions of this kind are known from structural analyses of both aryl- and alkyl-alkali metal compounds[33].

Bonding features found in *(32a)* can be seen again in the structure of *(29)* (Fig. 7).

Here a trigonally-planar coordinated nickel atom is surrounded by two σ-bonded phenyl groups (Ni—C15 = 1.950(4) Å, Ni—C21 = 1.963(4) Å) and a π-bonded phenanthrene molecule which, as expected[52], is bound *via* the 9,10-positions with its molecular plane lying almost perpendicular to the coordination plane of the nickel atom. The C9—C10 distance is lengthened from 1.341(7) Å, in free phenanthrene, to 1.445(6) Å; the Ni—C distances are

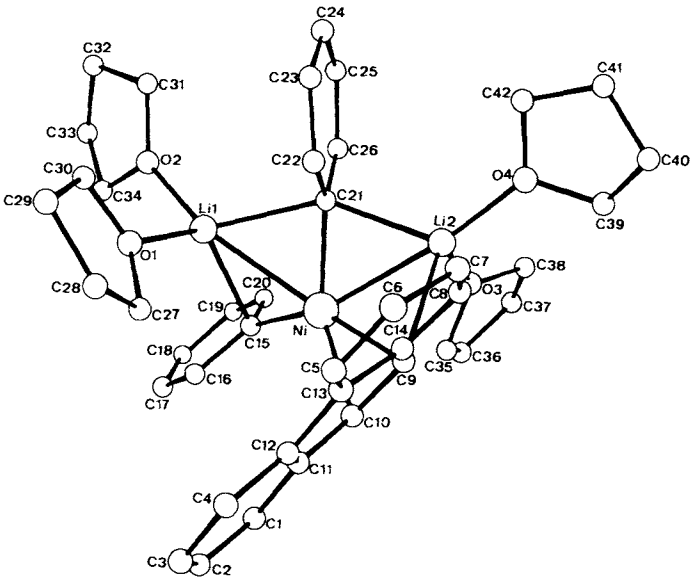
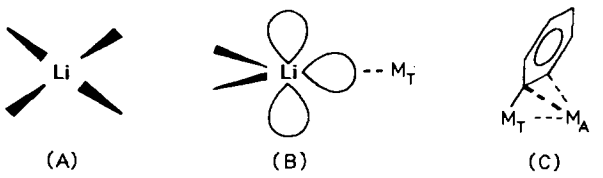


Fig. 7. Molecular structure of $[(LiC_6H_5)_2(THF)_4]NiC_{14}H_{10}$ *(29)*.

1.989(4) and 1.977(5) Å. The fact that Ni—C9 is longer than Ni—C10 can be explained in terms of the additional interaction of C9 with Li2. There is also an ion-pair interaction between one of the phenyl groups and both of the lithium atoms through C21. Such an interaction has also been observed in analogous cobalt compounds[53a] and in nickel dinitrogen complexes (see Section 6).

The second phenyl group on nickel and the phenanthrene molecule are, on the other hand, only adjacent to Li1. The

two out of four coordination sites on lithium in *(29)* and sodium in *(32a)* that are not occupied by tetrahydrofuran are preferentially directed towards the α-carbon atoms of the phenyl groups bonded to nickel. Although this geometry results in relatively short Li—Ni or Na—Ni distances, the question as to whether a direct alkali metal-nickel bond exists must remain open[79b]. The observed interaction of the alkali metal with delocalized π-systems could, in the case of a tetrahedral arrangement of ligands (sp^3) (A), be purely electrostatic in nature. If however, the alkali metal, especially lithium, is trigonally-planar coordinated (sp^2), one of the coordination sites being occupied by a transition metal (B), then there is an unoccupied p-orbital perpendicular to the coordination plane which is available to interact with delocalized π-systems.



Both interactions mentioned lead to a novel, unsymmetrical three-center arrangement (C), in which the charge flow takes place *via* bonds of different symmetry.

5. NMR-Data for Complexed Ethylene in Trigonal-Planar Nickel(0) Ethylene Complexes

The position of the ^{1}H- and ^{13}C-NMR signals (C=C—H) of olefins bonded to metals depends on, among other factors, the electron density at the double bond. Shifts of the signals to higher field on coordination of the olefin are usually observed when the π-back bonding contribution from the metal is greater than the σ-bonding contribution from the olefin

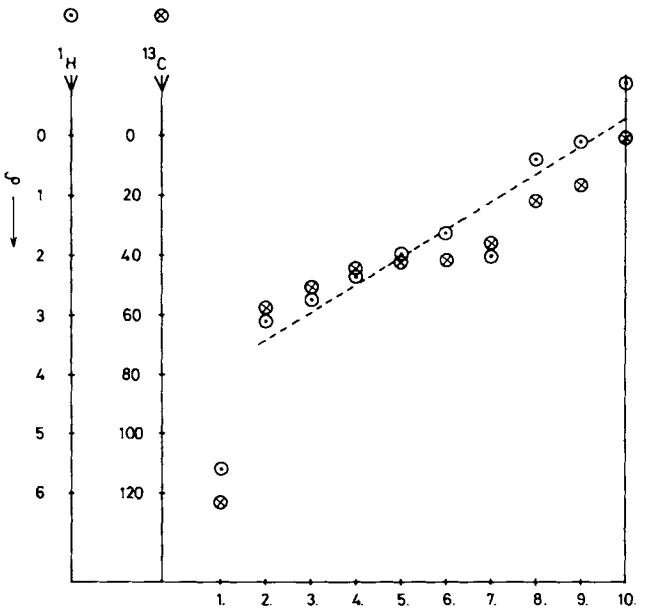


Fig. 8. ^{1}H- and ^{13}C-NMR data for free ethylene and ethylene bonded in trigonal-planar nickel(0)-ethylene complexes. 1, C_2H_4; 2, $(C_2H_4)_3Ni$ *(11)*; 3, $(C_6H_{11})_3PNi(C_2H_4)_2$ [45]; 4, $Li^{\oplus}[(C_6H_{11})_2P\{Ni(C_2H_4)_2\}_2]^{\ominus}$ *(21)*; 5, $Na^{\oplus}[(C_2H_4)_2Ni—H—Ni(C_2H_4)_2]^{\ominus}$ [cf. *(19)*]; 6, $Li^{\oplus}[C_2H_5—Ni(C_2H_4)_2]^{\ominus}$ *(16b)*; 7, $[(C_6H_{11})_3P]_2NiC_2H_4$; 8, $(NaC_6H_5)_2NiC_2H_4$ *(32)*; 9, $(LiC_6H_5)_2NiC_2H_4$ *(25)*; 10, $(LiC_2H_5)_2NiC_2H_4$ [65].

to the metal[54]. For several metal olefin cations only small upfield shifts or even downfield shifts are seen. Here a significant bonding contribution results from a charge flow from the olefin into an unoccupied metal orbital[55].

Figure 8 shows that for tris(ethylene)nickel(0) *(11)* (no. 2) the ^{1}H- and ^{13}C-NMR signals of the complexed ethylene molecules appear at a higher field than those in the free molecule (no. 1) ($\Delta\delta$-^{1}H ≈ 2.5, $\Delta\delta$-^{13}C ≈ 60). If one of the coordinated ethylenes is replaced by phosphane, phosphide, hydride, or $R^{\ominus}$ giving the complexes nos. 3—6, containing only 2 C_2H_4 per Ni, then an even stronger high-field shift is observed. The corresponding ^{1}H-NMR signals of the complexes nos. 8—10, those with only 1 C_2H_4 per Ni but now containing 2 M_AR per Ni, lie at only a slightly lower or even higher field (no. 10) than the signal of the internal standard tetramethylsilane! High-field shifts of the olefin signals on complexation with a zero-valent transition metal of this order are unusual. They indicate that the bis(organoalkali metal)nickel(0) unit is exceptionally electron rich and ideally suited for π-back bonding into the unoccupied orbitals of unsaturated molecules.

6. Dinitrogen Bonded Side-on to Nickel

The question whether dinitrogen can be bonded side-on to a metal atom M (Fig. 9c and d) has been the focus of interest ever since the instigation of intensive efforts to accomplish *in vitro* N_2 activation in a metal complex[56-58]. The recent findings by *Chatt et al.*[59] that dinitrogen end-on bonded (Fig. 9a) to molybdenum(0)-phosphane units, *e.g. (3)*, can be protonated by sulfuric acid and reduced to ammonia do not totally rule out a side-on fixation of dinitrogen during enzymatic N_2 activation. In fact, it might well be relevant[60] that some biological systems (nitrogenase) are able to reduce not only dinitrogen, $N_3^{\ominus}$, N_2O, CH_3NC, and RCN but also acetylene (C_2D_2 in H_2O and C_2H_2 in D_2O give *cis*-dideuteroethylene).

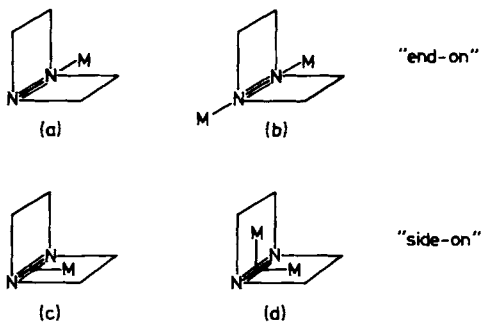


Fig. 9. Possible bonding modes of a N_2 molecule onto metal atoms.

Our nickel complexes *(33)*[62,63] and *(35)*[64] are the only[*] dinitrogen metal complexes with dinitrogen bonded side-on to a transition metal to have been structurally characterized by X-ray methods so far.

Stable dinitrogen transition metal complexes with end-on bonded N_2 molecules often contain transition metals in low oxidation states or activated by good donor ligands (*e.g.* $C_6H_5(CH_3)_2P$ in *(3)* or $(C_6H_{11})_3P$ in $[(C_6H_{11})_3P]_2Ni—N{\equiv}N—Ni[P(C_6H_{11})_3]_2$[66]). From this and

[*] In the X-ray analysis of $RhCl(N_2)[P(C_3H_7)_3]_2$ [61] a statistical disorder (Cl, N_2) about an inversion center was interpreted as a side-on bonded dinitrogen molecule.

spectroscopic data one is led to conclude that the stability of the M_T—N bond in most mononuclear dinitrogen transition metal complexes and the related destabilization of the N≡N triple bond mainly results from good d_π-p_π* back bonding[59,67]. This together with the NMR data for $[(LiC_2H_5)_2Et_2O]NiC_2H_4$[65] and $[(LiC_6H_5)_2Et_2O]NiC_2H_4$ *(25)* (see Fig. 8) led us to investigate the reactivity of organo-alkali metal-nickel(0) systems towards molecular nitrogen.

An ethereal solution of phenyllithium and (CDT)Ni^0 *(7)* in the molar ratio 3:1 absorbs molecular nitrogen (1 bar) at 0 °C. 1 N_2 is bound per 2 Ni. At the end of the reaction (after 1—2 h, corresponding to an absorption of *ca.* 280 Nml N_2 per 25 mmol of starting material *(7)*) some of the nickel N_2-complex *(33)* precipitates out as a yellow powder. Further *(33)* crystallizes out of solution within several weeks after addition of pentane (total yield *ca.* 50%). The ether content in *(33)* varies; generally there are 2—3 Et_2O per 6 LiC_6H_5.

$$4\,(CDT)Ni^0 + 12\,LiC_6H_5 + 2\,N_2 \xrightarrow[Et_2O]{0\,^\circ C} \underset{(33)}{\{[(LiC_6H_5)_3(Et_2O)_{1\ldots1.5}Ni]_2N_2\}_2} + 4\,CDT$$
(7)

In view of the formation of the adducts *(12)* and *(23)* from phenyllithium and (CDT)Ni^0 *(7)* and the structural data for *(33)*[63], the formation of *(33)* can be interpreted as follows:

$$\underset{(7)}{(CDT)Ni^0} + 1\,LiC_6H_5 \rightarrow \underset{(12)}{LiC_6H_5Ni(CDT)} \qquad (h)$$

$$(12) + 1\,LiC_6H_5 \rightarrow \underset{(23)}{(LiC_6H_5)_2Ni(CDT)} \qquad (j)$$

$$2\,(23) + 2\,LiC_6H_5 + 1\,N_2 \xrightarrow[-2CDT]{} [(LiC_6H_5)_3Ni]_2N_2 \qquad (33a)$$

$$2\,(33a) \xrightarrow{Et_2O} (33)$$

The 1:1 adduct *(12)*, formed from *(7)* and LiC_6H_5, reacts with further LiC_6H_5 to give *(23)*. The CDT ligand in this molecule is bonded to nickel by only one double bond and can be displaced by N_2 in the presence of LiC_6H_5. A formal $[(LiC_6H_5)_3Ni]_2N_2$ unit *(33a)* is formed when each N_2 molecule bonds to two nickel atoms; the crystalline final product *(33)* is a dimer.

Active solutions, which contain methyllithium or a mixture of NaC_6H_5/LiC_6H_5 in addition to (CDT)Ni^0 *(7)*, also take up 1 N_2 per 2 Ni at 0 °C[62,64]. With NaC_6H_5/LiC_6H_5 as the organo-alkali metallic component one obtains, among other products, the poorly soluble compound *(34)*. In this compound too there is 1 N_2 per 2 Ni, and approximately 3 M_AR per Ni. Eq. (l) is a typical reaction.

$$6\,(NaC_6H_5/LiC_6H_5) + 2\,(CDT)Ni^0 + 1\,N_2 \xrightarrow[Et_2O]{0\,^\circ C} \underset{(34)}{[(NaC_6H_5)_{2.44}(LiC_6H_5)_{0.67}(Et_2O)_{2.8}Ni]_2N_2} + 2\,CDT \qquad (l)$$

A further mixture of products crystallizes from the filtrate at 0 °C. This contains the nickel(0)-N_2 complex *(35)*, in which ethoxide groups resulting from ether cleavage are incorporated[64].

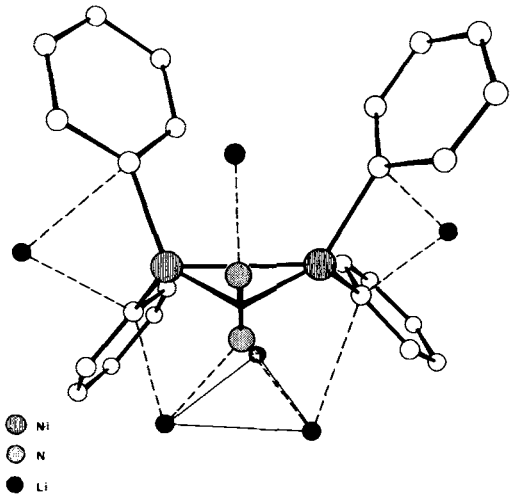


Fig. 10. Important structural features of a "half" of molecule *(33)*, *i.e.* a $[(LiC_6H_5)_3Ni]_2N_2$ unit *(33a)*. The two phenyl groups bonded to the Li_3-ring are not shown.

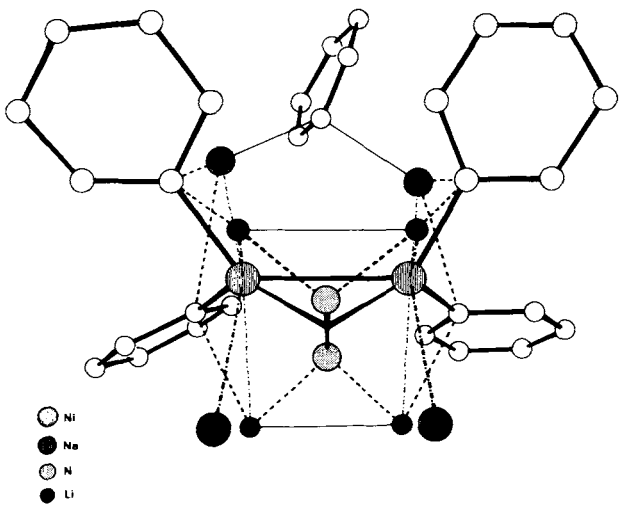


Fig. 11. Important structural features of a "half" of $\{C_6H_5(NaEt_2O)_2[(C_6H_5)_2Ni]_2N_2NaLi_6(OEt)_4Et_2O\}_2$, *(35)*.

$$\underset{(35)}{\{C_6H_5[NaEt_2O]_2[(C_6H_5)_2Ni]_2N_2NaLi_6(OEt)_4Et_2O\}_2}$$

Both N_2 complexes *(33)* and *(35)* show structural features similar to those already described for the related olefin complex *(32a)* (cf. Fig. 5 and 6). Their important structural subunits are reproduced in Figures 10 and 11. Two dinitrogen-bridged trigonal-planar diphenylnickel units form the central part of both molecules, and are so arranged as to allow a weak Ni—Ni bond. Comparable bridging arrangements are known for π-bonded alkynes[68] and azo compounds[69]. In the structures both bonds of σ-character and π-type, back bonding interactions between nickel and dinitrogen can be seen. Excess negative charge on dinitrogen is removed in the following two ways. Firstly, there is an end-on interaction between the lone pairs and the cationic lithium atoms. In *(33)* the chemical environment at each end of the N_2 molecule is different. At one end, the lone pair interacts with just one lithium ion, while at the other the lone pair is involved in a two-electron four-center bond with a Li_3 ring[70]. The sec-

ond apical position of the trigonal bipyramid defined using the Li_3 ring as the equatorial plane is occupied by a phenyl carbanion (not shown in Figure 10), so that overall a four-electron five-center bond arises. The bonding features are similar though somewhat simpler in *(35)*. In this case we observe similar two-electron three-center bonds to lithium at both ends of dinitrogen. Secondly, the system is stabilized by ion-pair interactions between lithium and dinitrogen on the opposite side of the dinitrogen molecule from nickel (cf. the analogous interactions in Fig. 6). The total effect of all interactions is to make the N≡N bond much weaker than in free N_2, and this manifests itself in the greatly enlarged N—N distances (1.34—1.36 Å) which lie within the range of those observed for single and double bonds.

The complexed dinitrogen in *(33)* can be displaced by carbon monoxide or ethylene. *(33)* reacts with ethylene in THF to give, in addition to the calculated amount of N_2, the nickel-ethylene complex *(25)*, free LiC_6H_5, and Et_2O. On hydrolysis of *(33)* in THF some of the dinitrogen (found 30—38%) is converted into ammonia, and the rest is liberated as N_2 gas. Hydrogen is not evolved.

$$3/2\ \{[(LiC_6H_5)_3(Et_2O)_{1.5}Ni]_2N_2\}_2 \xrightarrow[-78\ \text{to}\ 20\ ^\circ C]{\text{THF, } H_2O} 2NH_3 + 2N_2 + \cdots \quad \text{(m)}$$

(33)

The dinitrogen that is reduced according to eq. (m) can be found in the molecular structure of *(33)*; this is explained in Figure 12.

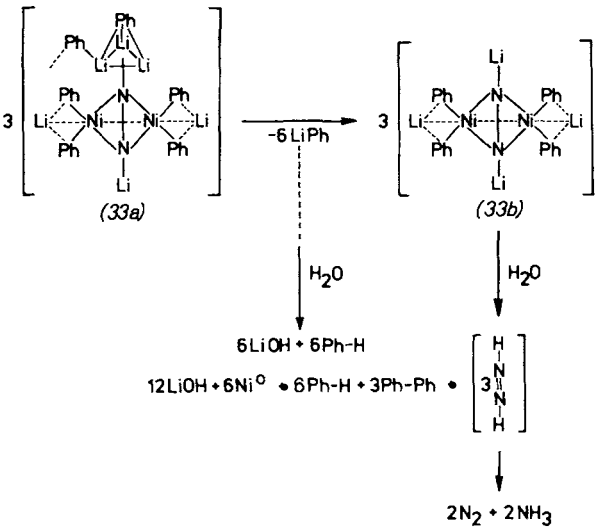


Fig. 12. Hydrolysis of $[(LiC_6H_5)_3Ni]_2N_2$ units *(33a)* and the conversion of side-on bonded dinitrogen into ammonia.

Of the four lithium atoms bonded to the nitrogen, the three in the Li_3 ring are additionally bonded to phenyl groups. *(33a)* is converted into *(33b)* after loss of two LiC_6H_5 molecules from the $Li_3(C_6H_5)_2$ group. In *(33b)* the two lithium atoms bonded to dinitrogen interact solely with nitrogen. A conceivable exchange of these Li atoms by $H^\oplus$ with concomitant transfer of two electrons from the side-on bonded $[Ni(C_6H_5)_2Li]$ units to nitrogen would lead to biphenyl and diimine. The latter could form N_2 and NH_3 in analogy with the N_2H_2 disproportionation[71] on low-valent titanium atoms.

The reaction scheme (Fig. 12) does not, of course, describe the exact mechanism for the hydrolysis of *(33a)* or *(33)*. It merely gives the total stoichiometry and shows that the yields of ammonia and biphenyl are equivalent. The reduction equivalents for the conversion of dinitrogen into ammonia are supplied by the carbanionic phenyl groups bonded to nickel. The nickel atoms, which are present after the hydrolysis as nickel(0), *i.e.* elemental nickel, just direct the electron flow from $C_6H_5^\ominus$ to N_2. Bearing this in mind, the hydrolysis reaction of *(33)* differs from that of the N_2 reductions which *Chatt et al.*[59] and *Bercaw et al.*[72] have described for Mo, W, or Zr with end-on bonded dinitrogen: Reduction and protonation of the N_2 ligand in this case results in oxidation of the transition metal.

7. Dilithium-Nickel-Olefin Complexes

7.1. Syntheses and Structures

In the reactions of nickel(0) olefin complexes with organoalkali metal compounds, alkali metal hydrides and alkali metal diorganophosphites, it was seen in Sections 3 to 6 that the charge on the alkali-metal atoms is transferred onto nickel atoms and π-ligands bonded to them *via* C, H or P atoms. The syntheses, structures, and NMR data[46,73] of compounds described in this section show that the charge on the alkali metal atom can also be transferred directly onto nickel(0) π-ligand systems.

The dilithium-nickel-olefin complexes *(36)* and *(37)* which result from the lithiation of $(CDT)Ni^0$ *(7)* or $(COD)_2Ni^0$ *(8)*[74] are examples of a new class of d-element compounds, in which alkali metals, acting as one-electron ligands, together with olefins are bonded to transition metal atoms.

$$(CDT)Ni^0 + 2Li + 2TMEDA \xrightarrow[0\ ^\circ C]{THF} [Li(TMEDA)]_2Ni(CDT)$$

(7) *(36)*

$$(COD)_2Ni^0 + 2Li \xrightarrow[-30\ \text{to}\ 0\ ^\circ C]{THF} [Li(THF)_2]_2Ni(COD)_2 \quad \text{(n)}$$

(8) *(37)*

The conversion of *(7)* into *(36)* with lithium can be attributed to the tendency of the coordinatively unsaturated 16e complex $(CDT)Ni^0$ *(7)* to attain the noble gas configuration; the two requisite electrons are supplied by the lithium atoms.

Nickel also has a noble-gas configuration in *(37)*. *(37)* is a fluxional molecule (Fig. 13). The low temperature ^{1}H-NMR spectrum of *(37)* shows four signals of equal intensity for the olefin protons; one, at $\delta = 5.4$, can be attributed to the protons of an uncomplexed double bond. At room temperature, however, only one signal for the olefin protons is seen which remains unaltered on the addition of COD (the signals of free COD are also unperturbed). The observed signal equivalencing depends, therefore, on an intramolecular exchange process involving the free double bond (identifiable in the IR spectrum, $\nu_{C=C} = 1655\ cm^{-1}$ (THF at 0 °C)). The fluxional process of the pentacoordinate complex cannot be satisfactorily described by a Berry pseudo-rotation or turnstile rotation[75,76] alone. The structure and the rearrangement mechanism, schematically represented in Figure 13, are in accord with the NMR and IR data.

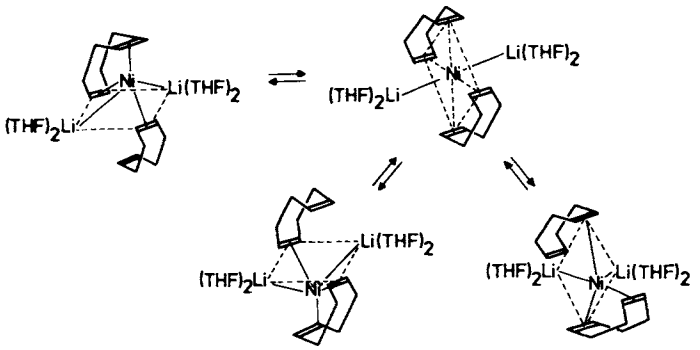


Fig. 13. The fluxional process in $[Li(THF)_2]_2Ni(COD)_2$ *(37)* (schematic).

The coordination geometry of the nickel atom is possibly tetragonal-pyramidal with the lithium atoms residing in *trans* positions. Breaking and remaking of the nickel-olefin bonds occur simultaneously with retention of the noble-gas configuration around nickel. Merely the slightest displacement at the nickel atom, *i.e.* a change in the Li—Ni—Li angle, is all that is required for this process.

The two cyclooctadiene ligands in *(37)* can be displaced by monoolefins or dienes, and new dilithium-nickel-olefin complexes are formed containing tetra- or pentacoordinate nickel atoms (see Table 2)[74, 77, 78].

$$[Li(THF)_2]_2Ni(COD)_2 + z\,\text{Olefin} \xrightarrow[-4\,THF]{2\,y\text{n-Donor ligand}} \underset{(37)}{} \qquad (o)$$

$$[Li(n\text{-Donor ligand})_y]_2Ni(\text{Olefin})_z + 2\,COD$$

Table 2. Dilithium-nickel-olefin complexes.

Olefin	Complex	
CDT	$[Li(TMEDA)]_2Ni(CDT)$	*(36)*
COD	$[Li(THF)_2]_2Ni(COD)_2$	*(37)*
N,N,N',N'-Tetramethyl-2-butene-1,4-diamine	$Li_2Ni[(CH_3)_2NCH_2CHCHCH_2N(CH_3)_2]_3$	*(38)*
N,N-Dimethyl-allylamine	$Li_2Ni[(CH_3)_2NCH_2CHCH_2]_4$	*(39)*
Ethylene	$[Li(TMEDA)]_2Ni(C_2H_4)_3$	*(40)*
Ethylene	$[Li_2(TMEDA)_{1.5}]Ni(C_2H_4)_2$	*(41)*
Norbornene	$[Li(TMEDA)]_2Ni(C_7H_{10})_2$	*(42)*
Norbornadiene	$[Li(TMEDA)]_2Ni(C_7H_8)_2$	*(43)*
Butadiene	$[Li(THF)]_2Ni(C_4H_6)_3$	*(44)*
Dimethyl butadiene	$[Li(TMEDA)]_2Ni(C_6H_{10})_2$	*(45)*
Styrene	$[Li(TMEDA)]_2Ni(C_6H_5CHCH_2)_2$	*(46)*
trans-Stilbene	$[Li(THF)_2]_2Ni(C_6H_5CHCHC_6H_5)_3$	*(47)*

Dilithium-nickel-olefin complexes are best classified as non-salt-like compounds. There are valid arguments for this: None of the compounds in Table 2 contains more than three n-donor atoms per lithium atom, most of them have only two; four n-donor atoms are required to stabilize a cationic, tetrahedrally coordinated lithium atom. Olefin ligands, particularly those with doubly alkyl-substituted double bonds (CDT, COD), are only relatively weak π-acceptors and are thus poorly suited to stabilize a doubly negatively charged nickel anion. Even carbon monoxide, a typical π-acceptor ligand, is unable to do this[*]. The complexes *(36)*, *(37)*, and *(38)* are soluble in benzene, toluene, and perceptibly so in pentane, and show only a slight conductivity in THF. The cryoscopic molecular weight determination of *(36)* in benzene gives the expected value. Finally, semi-empirical molecular orbital calculations[79b] on model compounds suggest that a completely salt-like structure for these compounds is unlikely.

We assume therefore that during the reductive addition of lithium to *(7)* and *(8)* to give *(36)* and *(37)*, respectively, an electron rich Li_2Ni skeleton is formed which remains intact during the olefin exchange reaction [eq. (o)], and in which the lithium atoms are connected to the nickel atom by covalent, strongly polarized metal-metal bonds ($Li^{\delta\oplus}$—$Ni^{\delta\ominus}$).

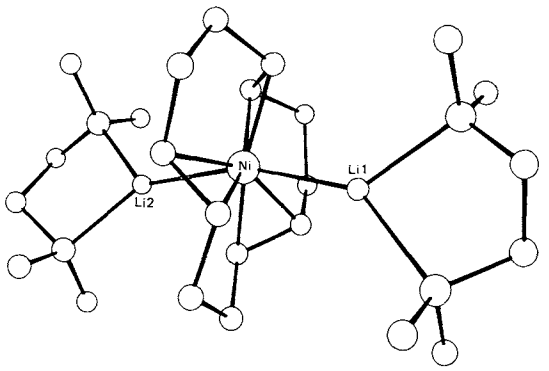


Fig. 14. Molecular structure of $[Li(TMEDA)]_2Ni(CDT)$ *(36)*.

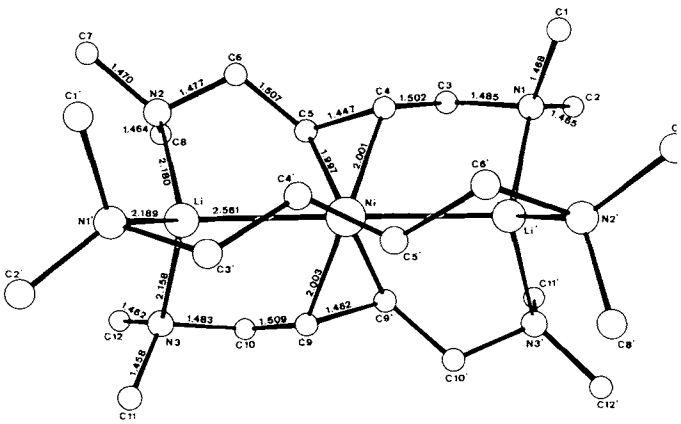


Fig. 15. Molecular structure of $Li_2Ni[(CH_3)_2NCH_2CHCHCH_2N(CH_3)_2]_3$ *(38)*.

Characteristic features of this class of compounds can be seen in the structures of *(36)* and *(38)* (Fig. 14 and 15)[79a]. Nickel has, in both cases, a trigonal-bipyramidal coordination geometry, the mid-points of the double bonds occupy equatorial positions and the lithium atoms sit at the vertices. A comparison of the two structures accentuates lithium's different coordination abilities; in *(38)* lithium adopts a tetrahedral sp^3-coordination geometry with a direct metal-metal bonding interaction with nickel (Ni—Li = 2.561 Å), while in *(36)* lithium is trigonally-planar coordinated (sp^2) (Ni—Li = 2.39 Å). As was described in Section 4.2, this latter arrangement allows interaction between the unoccupied p-orbital on lithium and the π-orbitals of the olefins bonded to nickel. In order to optimize this bonding the linear Li—Ni—Li skeleton seen in *(38)* distorts in *(36)* in such a way (∢ Li—Ni—Li = 162.2°) as to give the best overlap between the olefin and the lithium orbitals. The shorter Li—Ni distance in *(36)* may indicate a higher Ni—Li (p-d) π-back bonding than in *(38)*, and the greatly lengthened C—C bonds in *(38)*

[*] The tricarbonylnickelate dianion $[Ni(CO)_3]^{2\ominus}$ is as yet unknown.

(mean 1.452(9) Å) together with the related changes in angles are also characteristic of strong bonds between olefins and nickel.

The Ni—Li distances (2.381 Å) are extremely short in the square-planar, centrosymmetric 16e complex *(42)* (Fig. 16).

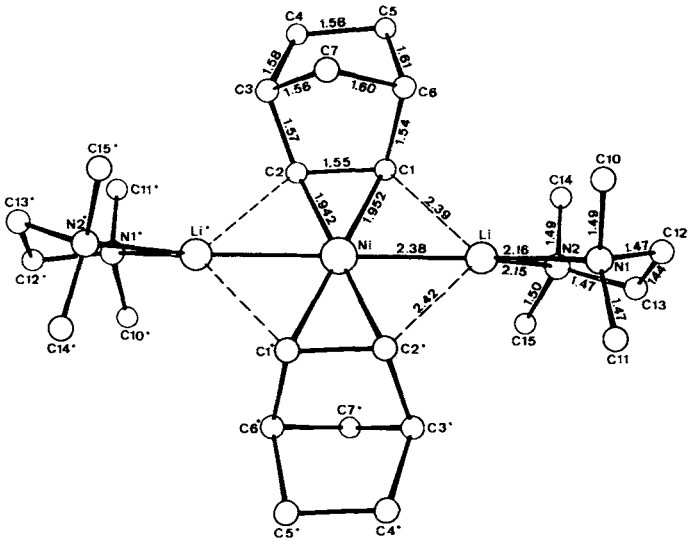


Fig. 16. Molecular structure of $[Li(TMEDA)]_2Ni(norbornene)_2$ *(42)*.

Here again the planes of the trigonally-planar coordinated lithium atoms are so oriented that optimal bonding to both olefinic carbon atoms of the norbornene ligands can be achieved. Short Li—C distances result, and there is a consid-

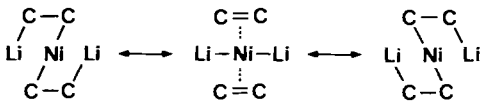


Fig. 17. Resonance structures for the central part of *(42)*.

erable lengthening of the olefinic double bonds (mean 1.551 Å). This molecular geometry may be formulated in terms of the mesomeric system shown in Figure 17.

7.2. Dilithium-Nickel-Olefin Complexes, a New Form of Soluble and Reactive Lithium

7.2.1. Nickel(0)-Olefin Complexes from Dilithium-Nickel-Olefin Complexes

An important criterion for the reactivity of dissolved alkali metals is their ability to reduce. In order to examine the dilithium-nickel-olefin complexes in this regard, we have reacted them with oxidants of different electron affinities.

The dilithium-nickel-olefin complexes *(36)* and *(37)* are converted into the nickel(0)-olefin complexes *(7)* and *(8)*[74], respectively, by relatively strong oxidants such as iodine or cyclooctatetraene (COT) and by observing the molar ratios given below.

$$[Li(TMEDA)]_2Ni(CDT) + 1\,COT \rightarrow \underset{(36)}{} \underset{(7)}{(CDT)Ni^0} + Li_2(COT) + 2\,TMEDA$$

$$[Li(THF)_2]_2Ni(COD)_2 + 1\,I_2 \rightarrow \underset{(37)}{} \underset{(8)}{(COD)_2Ni^0} + 2\,LiI + 4\,THF$$

When weaker oxidants such as aromatic hydrocarbons are used, it is possible to see that the reductive ability of the Li_2Ni unit depends in a characteristic way on the electron affinity of the complexed olefins. The reductive ability can thus be set by the choice of the olefin ligands[78,80] [see eq. (p) to (s)].

$$[Li(THF)_2]_2Ni(COD)_2 + 2\,Biphenyl \xrightarrow{THF} \underset{(37)}{} \underset{(8)}{(COD)_2Ni^0} + 2\,Li[Biphenyl] \quad (p)$$

$$[Li(THF)_2]_2Ni(COD)_2 + 2\,Naphthalene \xrightarrow{THF} \underset{(37)}{} \underset{(8)}{(COD)_2Ni^0} + 2\,Li[Naphthalene] \quad (q)$$

$$[Li(TMEDA)]_2Ni(C_2H_4)_3 + 2\,Naphthalene \xleftarrow{THF} \underset{(40)}{} \underset{(11)}{(C_2H_4)_3Ni^0} + 2\,Li[Naphthalene] \quad (r)$$

$$[Li(TMEDA)]_2Ni(C_2H_4)_3 + 2\,Anthracene \rightarrow \underset{(40)}{} \underset{(11)}{(C_2H_4)_3Ni^0} + 2\,Li[Anthracene] \quad (s)$$

Thus biphenyl is able to delithiate *(37)* in THF at low temperatures. According to the ^{1}H-NMR and ESR spectra the dark-green reaction solution contains *(8)* and biphenyllithium. *(8)* can also be isolated from the reaction solution of *(37)* and naphthalene. If olefins with greater electron affinities than COD are bonded to the Li_2Ni unit, such as ethylene molecules (*e.g.* in *(40)*), then the electron affinity of naphthalene is not sufficient to effect oxidation, and anthracene with its higher electron affinity must be used.

Several dilithium-nickel-olefin complexes are listed in Table 3 together with the arenes whose electron affinities are just sufficient for their oxidation.

Table 3. The oxidation of dilithium nickel olefin complexes by arenes.

$[Li(TMEDA)]_2Ni(CDT)$	*(36)*	Oxidized by biphenyl
$[Li(THF)_2]_2Ni(COD)_2$	*(37)*	
$[Li(TMEDA)]_2Ni(C_2H_4)_3$	*(40)*	Oxidized by anthracene,
$[Li_2(TMEDA)_{1.5}]Ni(C_2H_4)_2$	*(41)*	but not oxidized by biphe-
$[Li(TMEDA)]_2Ni(C_7H_{10})_2$	*(42)*	nyl or naphthalene
$[Li(TMEDA)]_2Ni(C_7H_8)_2$	*(43)*	
$[Li(THF)]_2Ni(C_4H_6)_3$	*(44)*	
$Li_2Ni[(CH_3)_2NCH_2CHCHCH_2N(CH_3)_2]_3$	*(38)*	Oxidized by perylene

The rule that the reductive ability of the Li_2Ni unit increases with decreasing electron affinity of the olefin ligands, fulfilled by complexes *(36)*—*(44)*, is not obeyed by *(38)*, although the electron affinity of the ligand *N,N,N',N'*-tetramethyl-2-butene-1,4-diamine is comparable with those of CDT and COD. This can be explained in terms of the chelating ef-

fect of the unsaturated diamine which, by coordinating to the nickel and both the lithium atoms, greatly stabilizes the Li_2Ni unit (cf. Figure 15).

7.2.2. The Nickel(0)-Induced Synthesis of Ethyllithium from Lithium, Hydrogen, and Ethylene

If dilithiumbis(cyclooctadiene)nickel *(37)* is reacted with molecular hydrogen (1 bar) in THF at $-60\,^{\circ}C$, the light yellow, almost insoluble, powdery *(48)* is formed after take-up of 1 H_2 and loss of 0.5 COD per Li_2Ni.

$$[Li(THF)_2]_2Ni(COD)_2 + 1\,H_2 \xrightarrow[-COD]{THF,\ -60\,^{\circ}C} \underset{(48)}{Li_2H_2(THF)_xNi(COD)_{1.5}} \quad (t)$$
(37)

The molecular structure of *(48)* is unknown at present as its insolubility precludes adequate spectroscopic characterization. From its chemical properties, it can be inferred that the lithium and hydrogen atoms in *(48)* behave as two particularly reactive lithium hydride molecules[25,77,81].

(48) dissolves in tetrahydrofuran in the presence of organometallic Lewis acids (*e.g.* $Al(C_2H_5)_3$) and COD. The complex-bonded Li and H atoms are released and are transferred as lithium hydride onto $Al(C_2H_5)_3$; the hydridoaluminate $Li[Al(C_2H_5)_3H]$ [isolated as *(49)*] and $(COD)_2Ni^0$ *(8)* are formed in high yields.

$$\underset{(48)}{Li_2H_2(THF)_xNi(COD)_{1.5}} + 2\,Al(C_2H_5)_3 + 0.5\,COD \xrightarrow[-30\,^{\circ}C]{THF} \underset{(8)}{(COD)_2Ni^0} + 2\,Li[Al(C_2H_5)_3H] \quad (u)$$

$$Li[Al(C_2H_5)_3H] \xrightarrow{TMEDA} \underset{(49)}{[Li(TMEDA)_2]^{\oplus}[Al(C_2H_5)_3H]^{\ominus}}$$

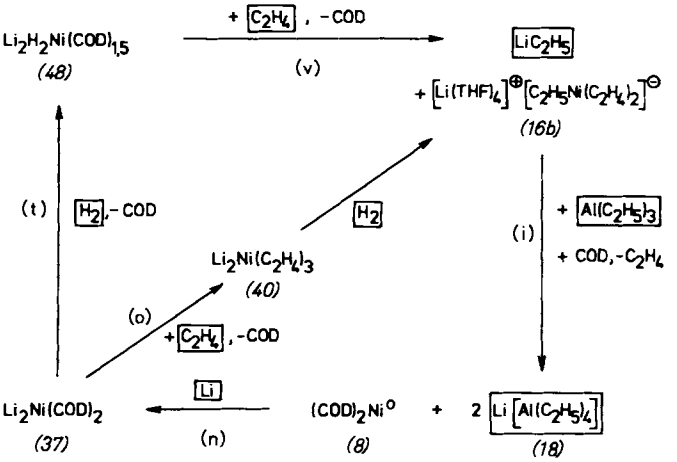
If one includes the lithiation of *(8)* to give *(37)* [eq. (n)], then equations (n), (t), and (u) describe a nickel(0)-induced stoichiometric synthesis of $Li[Al(C_2H_5)_3H]$ from lithium, hydrogen, and $Al(C_2H_5)_3$ which only requires very mild conditions.

$$2\,Li + 1\,H_2 + 2\,Al(C_2H_5)_3 \xrightarrow{Ni^0} 2\,Li[Al(C_2H_5)_3H]$$

A nickel(0)-catalyzed synthesis of the hydridoaluminate is not possible using *(8)*, lithium, and $Al(C_2H_5)_3$ because hydrogen does not bond to *(37)* in the presence of $Al(C_2H_5)_3$. Of course, the $(COD)_2Ni^0$ formed in equation (u) can be relithiated, *etc.* Thus it is possible to synthesize $Li[Al(C_2H_5)_3H]$ in a stepwise fashion (pseudo-catalytically).

Pure lithium hydride made from Li and H_2 does not add to C=C double bonds[82a]. The complexed "lithium hydride" in *(48)* is much more reactive. It is able to hydrolithiate C=C double bonds even at low temperatures, and the speed of addition depends on the structure of the olefin, as is the case for hydroalumination[82b].

The double bonds on the COD ligands in *(48)* are doubly substituted by alkyl groups. *(48)* is stable at room temperature; the addition of LiH to the complexed COD ligands is thus not observed. *(48)* dissolves slowly in THF with propylene below $-20\,^{\circ}C$. Probably propyllithium is formed; ethylene reacts with *(48)* to give ethyl lithium[25,77,81]. Following this reaction sequence the synthesis of alkyllithium compounds from lithium hydride and olefins, which *Ziegler* failed to accomplish in 1952[82a], can be achieved.



(48) reacts with ethylene at a satisfactory rate even at $-60\,^{\circ}C$ [eq. (v)]; the clear reaction solution contains *(16b)* and free ethyllithium. *(16b)* and $Li(C_2H_5)$ react with $Al(C_2H_5)_3$ and COD to give $Li[Al(C_2H_5)_4]$ *(18)* and $(COD)_2Ni^0$ *(8)*. The lithiation of *(8)* leads back to *(37)* [eq. (n)]. There is a second route from *(37)* to *(16b)* and LiC_2H_5 other than *via (48)* [eq. (t)], and that is by displacing the COD in *(37)* by ethylene [eq. (o)] to give *(40)* and then reacting this with hydrogen.

8. Olefin-Transition Metal and Alkali Metal-Olefin-Transition Metal Complexes from Metallocenes by Reductive C_5H_5-Abstraction

After it was found that nickel(0)-olefin complexes react with lithium to give dilithium-nickel-olefin complexes, we became interested in preparing alkali metal-olefin-transition metal complexes with other transition metals besides nickel. The number of other transition metal-olefin complexes for which alkali metalation might be possible is, however, limited, and their formation often requires a considerable experimental effort (co-condensation[83] of M_T atoms and olefins) so we sought a new way of preparing them.

Metallocenes $(\pi\text{-}C_5H_5)_2M_T$ are known for all 3d-elements except titanium. They can be synthesized from the corresponding halides and alkali metal- or alkaline-earth metal-cyclopentadienides in high yields [cf. *(5)* in Section 1]. Their reactions can be divided into two large groups. In one group the five-membered ring ligands remain attached to the transition metal. Among these are the thoroughly investigated substitution reactions of ferrocene *(5)*[84], such as Friedel-Crafts acylation, sulfonation, mercuration, or metalation[85] with organolithium compounds.

$$(\pi\text{-}C_5H_5)_2Fe \xrightarrow[-RH]{LiR} (\pi\text{-}C_5H_5)(\pi\text{-}C_5H_4Li)Fe \xrightarrow[-RH]{LiR} \pi\text{-}C_5H_4Li)_2Fe$$
(5)

Reactions belonging to the second group include those where the C_5H_5 ligands are displaced by other ligands, *e.g.* two-

electron ligands like CO, PR_3, PF_3, or RNC. Ring ligand displacement reactions[86] are less characteristic for metallocenes, since the breaking of the C_5H_5—M_T bond generally requires somewhat severe conditions. The 18-electron complex ferrocene *(5)* is particularly stable in this regard.

Since 1957 it has been known[87] that several metallocenes react with alkali metals to give alkali metal cyclopentadienides and transition metals, for example as in eq. (w).

$$(\pi\text{-}C_5H_5)_2Fe + 2Li \rightarrow 2LiC_5H_5 + Fe \qquad (w)$$
(5)

Remarkably, it has been overlooked that reactions of this type open a convenient route for the preparation of "naked" transition metals which should be well suited for the synthesis of low-valent transition metal organometallic complexes.

Our investigations on the $(\pi\text{-}C_5H_5)_2M_T$/alkali metal systems with M_T = Ni, Co, Fe[88-91] show that transition metal precipitation according to equation (w) is actually absent if the metallocenes are treated with alkali metals in the presence of molecules capable of functioning as π-ligands, *e.g.* olefins.

$$(\pi\text{-}C_5H_5)_2M_T \xrightarrow[-M_AC_5H_5]{M_A,\ Olefin} (M_A)_x(\pi\text{-}C_5H_5)M_T(Olefin)_z$$

$$\xrightarrow[-M_AC_5H_5]{M_A,\ Olefin} (Olefin)_zM_T \xrightarrow{M_A} (M_A)_xM_T(Olefin)_z$$

M_T = Ni, Co, Fe; M_A = Li, Na, K

After loss of the C_5H_5 ligands as $M_AC_5H_5$ from the transition metal, alkali metal-free or alkali metal-containing olefin-transition metal complexes are formed even at low temperatures (in yields of greater than 65% in THF, for example). These complexes contain one or two M_A atoms per M_T. In addition, by a particular choice of the molar ratio of reactants, of the reaction conditions, and of the transition metal, it is possible to remove one or both of the C_5H_5 ligands from the M_T atom; hence this method[92] can be used to prepare a variety of new transition metal-olefin complexes.

8.1. The Nickelocene/Lithium/Olefin System

$[Li(THF)_2]_2Ni(COD)_2$ *(37)* (see Section 7) can be prepared from nickelocene, cyclooctadiene, and lithium.

$$Cp_2Ni \xrightarrow[-2LiCp]{2Li,\ 2COD} \underset{(8)}{(COD)_2Ni^0} \xrightarrow[THF]{2Li} \underset{(37)}{[Li(THF)_2]_2Ni(COD)_2}$$

Cp = C_5H_5

Both C_5H_5 ligands can be removed from nickelocene using either the two lithium atoms complexed in *(37)* or lithium metal.

$$Cp_2Ni + \underset{(37)}{[Li(THF)_2]_2Ni(COD)_2} + 2COD \xrightarrow[-THF]{} \underset{(8)}{2(COD)_2Ni^0} + 2LiCp$$

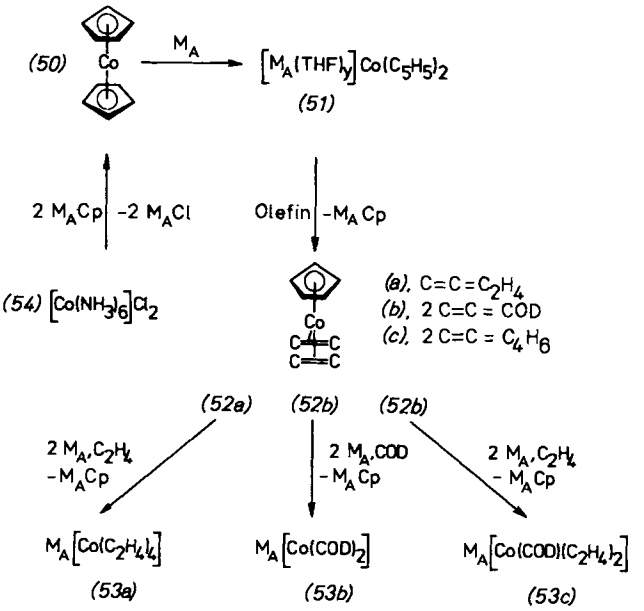
8.2. Cobalt-Olefin and Alkali Metal-Cobalt-Olefin Complexes from Cobaltocene

The removal of both C_5H_5 ligands from cobaltocene by alkali metals and the addition of an M_A atom to the Co atom proceeds *via* reduction of Co^{II} (d^7) in the 19e complex cobaltocene *(50)* to give Co^{-I} (d^{10}) in the $M_A[Co(C\equiv C)_4]$ complexes *(53)* (18e); three alkali metals are required for this process:

$$\underset{(53)}{Cp_2Co} + 4C\equiv C + 3M_A \xrightarrow[-60\text{ to }0\,^\circ C]{THF} M_A[Co(C\equiv C)_4] + \underset{(50)}{2M_ACp}$$

C ≡ C = Ethylene or 1/2COD; M_A = Li, Na, K

In the formation of the alkali metal-cobalt-olefin complexes *(53)* (yields 70–90%), alkali metal-containing and alkali metal-free intermediates are formed and these can be isolated[89,93].



In the absence of olefins, cobaltocene *(50)* reacts with an excess of lithium in THF at −30 °C to give *(51)* where the addition of just one Li atom has occurred. *(51)* crystallizes out of solution at −78 °C. It still contains both C_5H_5 ligands. Loss of the first C_5H_5-ring as $M_AC_5H_5$ only occurs when olefins are added, and even at temperatures as low as −30 to 0 °C complexes of the type *(52)* are formed. COD and butadiene give the exceptionally thermally stabile complexes *(52b)* and *(52c)* which have until now been prepared under more severe reaction conditions[94]:

$$Co_2(CO)_8 \xrightarrow[60\,^\circ C]{Cp-H} CpCo(CO)_2 \xrightarrow[130\,^\circ C]{COD} \underset{(52b)}{CpCo(COD)}$$

$$\underset{(50)}{Cp_2Co} \xrightarrow[130\,^\circ C]{C_4H_6} \underset{(52c)}{CpCoC_4H_6}$$

The more thermally labile $(\pi\text{-}C_5H_5)$Co(olefin) complexes like (η^5-cyclopentadienyl)bis(ethylene)cobalt *(52a)* cannot be prepared by conventional methods. We initially prepared

(52a) from *(51)* and ethylene[89], but we have also synthesized it directly from cobaltocene *(50)*[93].

$$[Li(THF)_n]CoCp_2 + 2C_2H_4 \xrightarrow{Et_2O} CpCo(C_2H_4)_2 + LiCp$$

(51) *(52a)*

$$Cp_2Co + 1K + 2C_2H_4 \xrightarrow[-20\text{ to }0\,^\circ C]{Et_2O} CpCo(C_2H_4)_2 + KCp$$

(50) *(52a)*

(52a) is stable at room temperature and can be prepared on a 50-g scale in yields of *ca.* 80%; the easy displacement of the ethylene ligands makes a variety of reactions possible[89,93,95].

If the complexes *(52)* are again treated with alkali metals (Li, Na, K) in the presence of olefins, the second C_5H_5 ligand is lost from cobalt, and the alkali metal-cobalt-olefin complexes *(53)* and corresponding alkali metal cyclopentadienides are formed in high yields. Reaction of the latter with $[Co(NH_3)_6]Cl_2$ regenerates cobaltocene *(50)*[96].

All in all, the C_5H_5 group fulfills the important role of a support ligand. It is transferred first to and then from cobalt, and without it even the synthesis of the C_5H_5-free cobalt complexes *(53)* would not have been possible. If one reduces cobalt(II) chloride with sodium in THF/pyridine/COD[97], for example, one obtains (η^4-1,5-cyclooctadiene)(η^3-cyclooctenyl)cobalt *(54)*, which can also be prepared electrolytically[98] from cobalt(II) acetylacetonate and COD or by reduction of cobalt(II) acetylacetonate and COD with R_2AlH[99] or from $M_A[Co(COD)_2]$ *(53b)* and methanol[92]. *(54)* does not react with alkali metals (Li, Na) to give *(53b)* but gives a dialkali metal cobalt complex *(55)*, *e.g.* the crystalline $[Li(TMEDA)]_2Co(C_8H_{13})(COD)$[92,100].

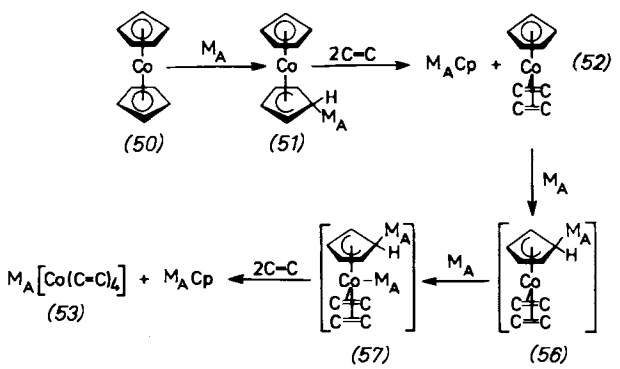
$$(\pi\text{-}C_5H_5)_2Co \xrightarrow[THF]{M_A,\ COD} M_A[Co(COD)_2]$$

(50) *(53b)*

$$M_A[Co(COD)_2] \xrightarrow{CH_3OH,\ -\ M_AOCH_3} CoCl_2 \xrightarrow[THF,\ Pyridine]{M_A,\ COD} (C_8H_{13})(COD)Co \xrightarrow{M_A} (M_A)_2Co(C_8H_{13})(COD)$$

(54) *(55)*

The different reaction course when using cobaltocene *(50)* as the cobalt(II) compound and the special advantage of the C_5H_5 ligand over and above typical anions like halides arise from the fact that metallocenes, are substantially more soluble in THF for example, and that both C_5H_5 ligands can be successively lost very easily from the transition metal even at



low temperatures. The latter seems to be the determining factor in the synthesis of the new cobalt olefin complexes *(52a)* and *(53a—c)*.

Several possibilities for the attack of a M_A atom on cobaltocene *(50)* might be envisaged. An electron could be transferred from a M_A atom onto *(50)*, resulting in the complex salt $[M_A]^\oplus[(C_5H_5)_2Co]^\ominus$. Polarographic investigations on $[(C_5H_5)_2Co]^\oplus[PF_6]^\ominus$, for example, have demonstrated[101,102] the existence of the cobaltocene anion, which is isoelectronic with nickelocene. If, on the other hand, the alkali metal—in particular lithium, which is the one most inclined to bond covalently—were to bond to *(50)*, it could add either to the ligands or to the metal. If the addition were to the ligands, as is the case for the isobutyronitrile radical ($^\ominus C(CH_3)_2CN$)[103], then *(50)* would be converted into *(51)* (see Scheme). In *(51)* the $M_AC_5H_5$ ring could be either diene-fashion bonded to cobalt, η^4, or allyl-fashion, η^3, as in the allyl group of $(\pi\text{-}C_5H_5)CoC_3H_5MgBr(THF)_2$[104]. Loss of the alkali metal cyclopentadienide and complexation of two olefinic double bonds give the 18e complex *(52)*. A second alkali metal could then form the 17e complex *(56)* with *(52)* or, alternatively, attach itself to the cobalt (radical center on the ligands), or even the formation of a $[C_5H_5Co(C{\cdots}C)_2]$ anion could be imagined[*]. In all cases, the addition of a second alkali metal would lead to *(57)*, which after loss of $M_AC_5H_5$ and addition of two olefinic double-bonds, would give the stabile 18e complex *(53)*.

The alkali metal-cobalt-olefin complexes $M_A[Co(C{\cdots}C)_4]$ *(53)*, in contrast to the dilithium-nickel-olefin complexes of Section 7, but like $M_A[Co(CO)_4]$[105], are inclined to dissociate into ions. Their specific conductivities in 0.25 M THF solution (−30 °C) are approximately $10^{-3}\ \Omega^{-1}\ cm^{-1}$. These are comparable with the values obtained for the salt-like nickel complexes $[Li(TMEDA)_2]^\oplus[R{-}Ni(C_2H_4)_2]^\ominus$ *(16)*. The observation that the cobalt complexes *(53)* can be prepared not only with lithium but also with sodium and potassium is also in agreement with the electrolytic character of these complexes. The number of n-donor atoms that are bound to an M_A atom in the crystalline complexes *(53)* can vary by large amounts; the number depends on the type of the M_A atom, the type of olefin ligands as well as the type of n-donor ligand itself. The temperature at which the particular cobalt complex in question crystallizes out of solution, and the pressure and temperature of drying the crystal will also affect this number. Thus $Li[Co(COD)_2]$ *(53b)* crystallizes with two THF or three DME molecules[88], of which certainly only two are bonded to the lithium ion. Hence a salt-like structure can be assumed for $[Li(DME)_2]^\oplus[Co(COD)_2]^\ominus \cdot DME$ *(53b)*, for crystalline $[Li(TMEDA)_2]^\oplus[Co(C_2H_4)_4]^\ominus$ *(53a)* and for $[Li(TMEDA)_2]^\oplus[Co(COD)(C_2H_4)_2]^\ominus$ *(53c)*.

If the C···C double bonds are able to move freely around the cobalt atom in *(53a)* the undisturbed $[Co(C{\cdots}C)_4]$ anion, which is not bonded by an ion pair bond to the M_A cation, will be tetrahedral. This is the most stable ligand arrangement for tetracoordinated d^{10} transition metal olefin complexes according to MO calculations[106] on the hypothetical $(C_2H_4)_4Ni^0$. Figure 18 shows a proposed structure for the tetrakis(ethylene)cobalt anion which is in accord with the ^{13}C-NMR spectrum[46] of *(53a)*.

[*] We were recently able to isolate the complexes $[Li(THF)_4]^\oplus[C_5H_5Co(COD)]^\ominus$ and $[K(THF)_2]^\oplus[C_5H_5Co(COD)]^\ominus$ at low temperatures [93].

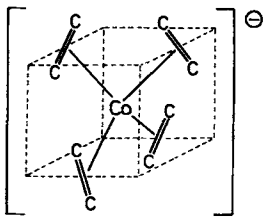


Fig. 18. Proposed structure for the $[Co(C_2H_4)_4]^{\ominus}$ anion *(53a)* (schematic).

In the presence of free ethylene the ^{13}C-NMR spectrum of $K[Co(C_2H_4)_4]$ *(53a)* shows two signals for the complexed ethylene molecules ($\delta = 55.5$ and 37.5) in $[D_8]$-THF at $-70\,^{\circ}C$. On warming the solution these signals broaden, and at room temperature only a broad signal at $\delta = 47$ appears. At all temperatures, the signal for free ethylene remains sharp and fixed. The broadening and coalescence of the ethylene signals can be traced back to a rotation of the ethylene ligands about the ethylene-cobalt bond.

The four ethylene ligands in *(53a)* or the two COD ligands in *(53b)* can be displaced by CO or butadiene even at low temperatures[88,89]. The diphosphane $(CH_2)_2[P(C_6H_{11})_2]_2$ reacts with *(53a)* at $0\,^{\circ}C$ with loss of only two ethylene ligands to give *(59)*[93]. These compounds ($M_A = Li$, K) react with molecular hydrogen to give novel alkali metal-phosphane-hydrido-cobalt complexes *(60)*, in which $2\,H_2$ are bonded per M_ACo.

$$M_A[Co(C{=}C)_4] + 2\,C_4H_6 \rightarrow M_A[Co(C_4H_6)_2] + 4\,C{=}C$$
(53a–c) *(58)*

$$M_A[Co(C_2H_4)_4] + (CH_2)_2(PR_2)_2 \xrightarrow[-2\,C_2H_4]{} M_A[(CH_2)_2(PR_2)_2Co(C_2H_4)_2]$$
(53a) *(59)*

$$(59) + 4\,H_2 \xrightarrow[-30\,^{\circ}C]{THF} M_A[(CH_2)_2(PR_2)_2CoH_4] + 2\,C_2H_6$$
(60)

$R = C_6H_{11}$

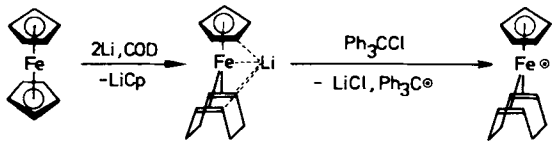
As in the anion of *(58)*, the butadiene ligands in $R_3Sn{-}Co(C_4H_6)_2$ ($R = CH_3$, C_6H_5) and $Zn[Co(C_4H_6)_2]_2$ bonded to the cobalt atom are not linked together. These three complexes are formed in high yields from *(58)* and R_3SnCl or $ZnCl_2$, and like *(58)* itself, are stable at room temperature[93].

$$2\,(58) + ZnCl_2 \xrightarrow[-2\,M_ACl]{} (C_4H_6)_2Co{-}Zn{-}Co(C_4H_6)_2$$

8.3. Iron-Olefin and Alkali Metal-Iron-Olefin Complexes from Ferrocene

As with cobaltocene *(50)*, one or both C_5H_5 ligands in ferrocene *(5)* can be displaced by olefins and alkali metals[43,90-92].

If ferrocene is treated with lithium and COD or ethylene in DME at -60 to $-40\,^{\circ}C$, only one C_5H_5 ligand is displaced and one obtains the complex $[Li(DME)](\pi\text{-}C_5H_5)Fe(COD)$ *(61a)* or the analogous ethylene complex. On addition of TMEDA, crystalline $[Li(TMEDA)](\pi\text{-}C_5H_5)Fe(COD)$ *(61b)* or $[Li(TMEDA)](\pi\text{-}C_5H_5Fe(C_2H_4)_2$ *(62)* is obtained.



(5) *(61)* *(63)*

(61) reacts with trityl chloride to give the monomeric, alkali metal-free $(\eta^5$-cyclopentadienyl$)(\eta^4$-1,5-cyclooctadiene)iron *(63)* which, in contrast to the dimeric $[(\pi\text{-}C_5H_5)Fe(CO)_2]_2$[107], contains one unpaired electron. The iron(I) complex *(63)* has a magnetic moment of 2.1 B.M. at room temperature, and the ESR spectrum shows an absorption signal ($g = 2.12 \pm 0.01$) with a peak width at half height of 39 gauss at $-100\,^{\circ}C$ and 106 gauss at $-30\,^{\circ}C$.

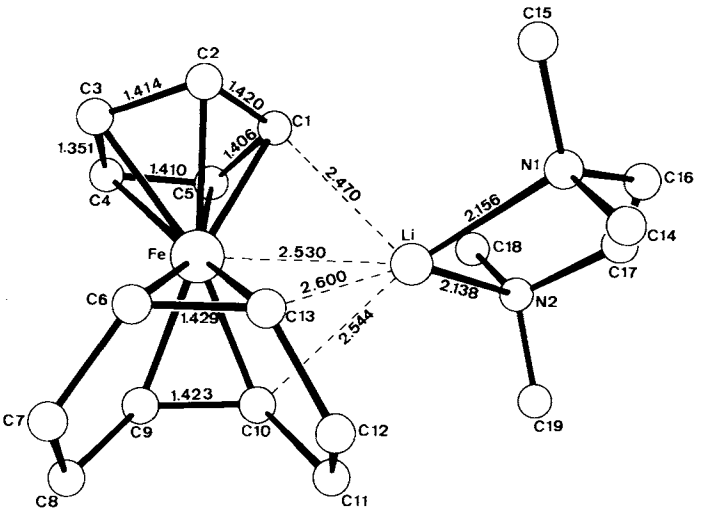


Fig. 19. Molecular structure of $[Li(TMEDA)](\pi\text{-}C_5H_5)Fe(COD)$ *(61b)*.

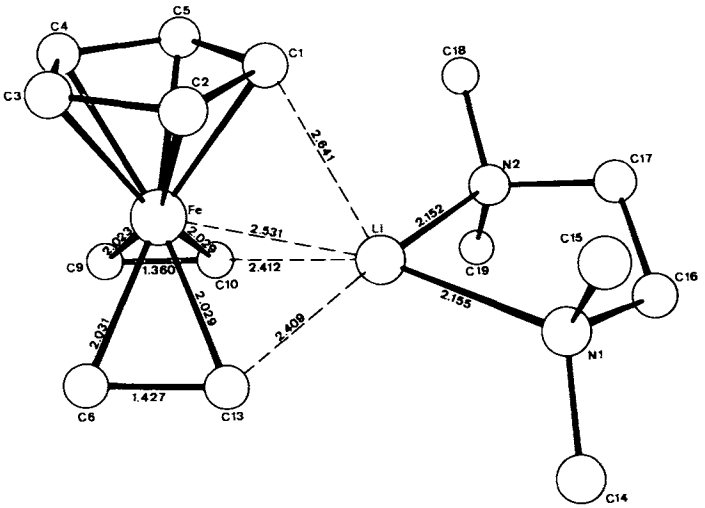


Fig. 20. Molecular structure of $[Li(TMEDA)](\pi\text{-}C_5H_5)Fe(C_2H_4)_2$ *(62)*.

As can be seen from Figures 19 and 20, the metal coordination geometries in the two compounds *(61b)* and *(62)* are very similar, and the organic ligands are arranged around the iron atom as they are around cobalt in the isoelectronic $(\pi\text{-}C_5H_5)Co(COD)$[53b]. The close proximity of the alkali metal,

however, causes changes in the C—C distances in the C_5H_5 ring which are consistent with the formulation of an increased double-bond character in the C—C bond most distant from lithium (C3—C4). In *(61b)* the distance from lithium to C1 of the cyclopentadienyl ring is shorter than to the carbon atoms on the neighboring olefins; in *(62)* the opposite is true. However, the Fe—Li distances are equal (2.531 Å) in both compounds so that a direct metal-metal interaction between the iron atom and the trigonally-planar coordinated lithium atom, in addition to the already mentioned ion-pair bond, might be a structure-determining factor.

The lithium-containing complexes *(61)* and *(62)*[43,90] and, in particular, the iron(I) compound $(\pi\text{-}C_5H_5)Fe(COD)$ *(63)*[108] are suitable starting materials for the synthesis of numerous new organo-iron compounds. Thus from *(61)* and $ZnCl_2$ one obtains the complex *(64)*, where the olefin ligands are bonded to iron, or the corresponding magnesium compound *(65) from (63)* and magnesium. Alkali metals react likewise with *(63)* to give *(61)*.

$$2\,Li[(\pi\text{-}C_5H_5)Fe(COD)] + ZnCl_2 \rightarrow Zn[(\pi\text{-}C_5H_5)Fe(COD)]_2 + 2\,LiCl$$
(61) *(64)*

$$2(\pi\text{-}C_5H_5)Fe(COD) + Mg \xrightarrow{THF} [Mg(THF)_6][(\pi\text{-}C_5H_5)Fe(COD)]_2$$
(63) *(65)*

$$(\pi\text{-}C_5H_5)Fe(COD) + M_A \rightarrow M_A[(\pi\text{-}C_5H_5)Fe(COD)]$$
(63) *(61)*

The new iron(II) complexes *(66)* or *(67)* are formed from *(61)*, HX ($(CH_3)_3COH$, CH_3OH, CH_3COOH) and ethylene or benzonitrile. The reaction probably proceeds *via* exchange of Li in *(61)* by H, addition of the Fe—H bond to a double bond on the cyclooctadiene ligand, and subsequent isomerization of the Fe—C_8H_{13} group to give the products. The ethylene or benzonitrile is displaced by carbon monoxide to give *(68)* which is stable at room temperature.

$$Li[(\pi\text{-}C_5H_5)Fe(COD)] + HX + C_2H_4 \xrightarrow[-LiX]{}$$
(61)

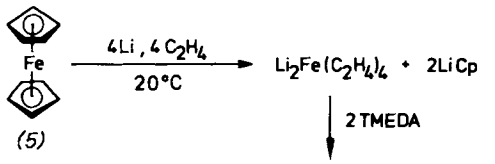
$$(\pi\text{-}C_5H_5)(\pi\text{-}C_8H_{13})FeC_2H_4$$
(66)

$$(61) + HX + C_6H_5CN \xrightarrow[-LiX]{} (\pi\text{-}C_5H_5)(\pi\text{-}C_8H_{13})Fe(C_6H_5CN)$$
(67)

$$(\pi\text{-}C_5H_5)(\pi\text{-}C_8H_{13})FeL + CO \xrightarrow[-L]{} (\pi\text{-}C_5H_5)(\pi\text{-}C_8H_{13})FeCO$$
(66) *(68)*

$L = C_2H_4$, C_6H_5CN

Ferrocene *(5)* reacts with lithium and ethylene in THF at room temperature with the loss of both C_5H_5 ligands from iron to give dilithium-tetrakis(ethylene)iron which can be isolated as crystalline $[Li(TMEDA)]_2Fe(C_2H_4)_4$ *(69)*[43,91,92].



(5)

$[Li(TMEDA)]_2Fe(C_2H_4)_4$ *(69)*

The structure[91] of the 18e complex *(69)* (Fig. 21) is reminiscent of that of the 16e Li_2Ni complex *(42)* (see Fig. 16). In this compound, a crystallographic twofold axis passes through the distorted octahedrally coordinated central iron atom and bisects the C1—C1* vector. There are short contacts between the trigonally-planar coordinated lithium atom and carbon atoms of the coordinated ethylenes (2.17—2.21 Å). Disregarding the iron-lithium bond (Fe—Li = 2.619 Å), the lithium atom appears to be tetrahedrally surrounded by ligands.

(69) takes up four equivalents of CO (1 bar) and four equivalents of C_2H_4 are lost. It reacts with COD at 40—70 °C to

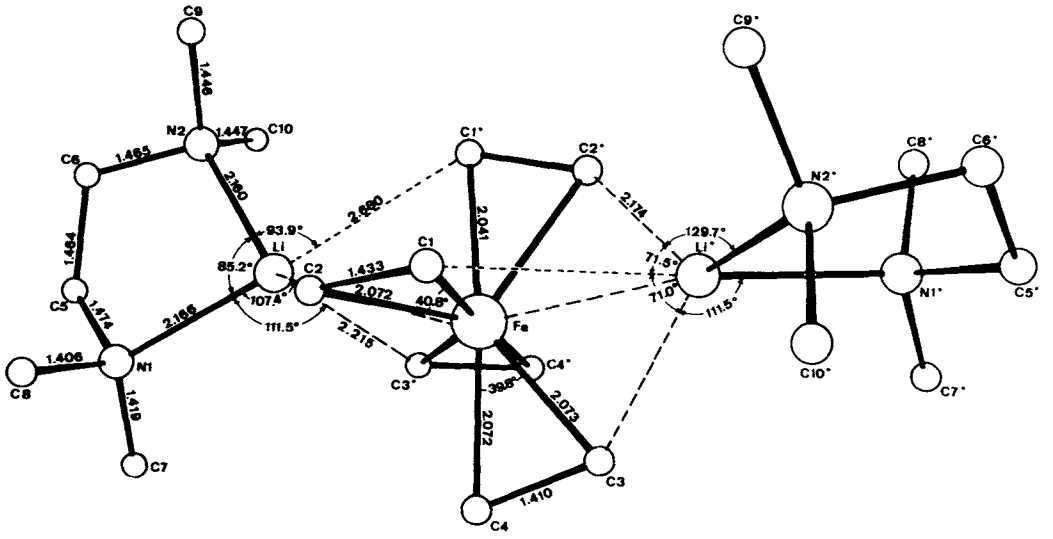
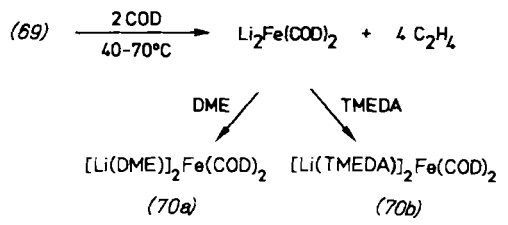


Fig. 21. The molecular structure of $[Li(TMEDA)]_2Fe(C_2H_4)_4$ *(69)*. Fe---Li = 2.619 Å.

give $Li_2Fe(COD)_2$ *(70)*—which can be isolated as crystalline *(70a)* or *(70b)*—whereupon the series of the isoelectronic cyclooctadiene complexes of the Group VIII 3d-elements, namely $(COD)_2Ni$ *(8)*, $M_A[Co(COD)_2]$ *(53b)*, and $Li_2Fe(COD)_2$ *(70)*, is complete.



9. Closing Remarks

The observations described here show that the combination of transition metal π-complexes and main-group metals, their hydrides, or organometallic compounds to give well-defined multimetal compounds is a new and attractive area of organometallic chemistry. The properties of these compounds not only reflect the structures and reactivities of the metal-containing starting components, but show new aspects as well. By pursuing the principles described here, we discovered new methods of synthesis, of which the reductive abstraction of C_5H_5 from metallocenes is particularly worthy of emphasis because of its efficiency and practicability. Examination of the breadth of application of this method for the synthesis of as yet unknown or difficultly prepared organometallic compounds seems to us to be especially worthwhile. Finally, detailed experimental investigations into the electron-density distributions together with model theoretical calculations should be attempted in order to gain a better insight into the bonding in the multimetal compounds described here.

We thank the members of both our groups who participated in obtaining the results presented here for their enthusiastic collaboration. Furthermore, we are indebted to numerous colleagues at the Max-Planck-Institut für Kohlenforschung for many discussions and analytical services. Our special thanks go to the director of the institute, Prof. Dr. Günther Wilke, for valuable discussions and the stimulating furtherance of our work.

Received: February 11, 1980 [A 324 IE]
German version: Angew. Chem. *92*, 513 (1980)
Translated by Dr. *R. Goddard*, Mülheim an der Ruhr, Germany

[1] *K. Ziegler, E. Holzkamp, H. Breil, H. Martin*, Angew. Chem. *67*, 426 (1955).
[2] *E. O. Fischer, W. Hafner*, Z. Naturforsch. *B 10*, 665 (1955); *E. O. Fischer*, Angew. Chem. *69*, 715 (1957); *E. O. Fischer, J. Seeholzer*, Z. Anorg. Allg. Chem. *312*, 244 (1961); *H. Werner*, Fortschr. Chem. Forsch. *28*, 157 (1972).
[3] *K. Jonas*, J. Organomet. Chem. *78*, 273 (1974).
[4] *T. A. George, C. D. Seibold*, Inorg. Chem. *12*, 2544 (1973).
[5] *A. L. Galyer, G. Wilkinson*, J. Chem. Soc. Dalton Trans. *1976*, 2235.
[6] *T. J. Kealy, P. L. Pauson*, Nature *168*, 1039 (1951); *E. O. Fischer, W. Pfab*, Z. Naturforsch. *B 7*, 377 (1952); *G. Wilkinson, M. Rosenblum, M. C. Whiting, R. B. Woodward*, J. Am. Chem. Soc. *74*, 2125 (1952).
[7] *G. Wilke, B. Bogdanović*, Angew. Chem. *73*, 756 (1961).
[8] *G. Wilke*, Angew. Chem. *72*, 581 (1960); *B. Bogdanović, M. Kröner, G. Wilke*, Justus Liebigs Ann. Chem. *699*, 1 (1966).
[9] *H. Gilman, R. G. Jones, L. A. Woods*, J. Org. Chem. *17*, 1630 (1952).
[10] *J. A. Wanklyn*, Justus Liebigs Ann. Chem. *108*, 67 (1858); *111*, 234 (1859); *140*, 211 (1866).
[11] *F. Hein, E. Petzchner, K. Wagler, F. A. Segitz*, Z. Anorg. Allg. Chem. *141*, 161 (1924); *F. Hein*, Z. Elektrochem. *28*, 469 (1922).
[12] *G. Wittig*, Angew. Chem. *62*, 231 (1950); *70*, 65 (1958); *G. Wittig*, Q. Rev. Chem. Soc. *20*, 191 (1966); *W. Tochtermann*, Angew. Chem. *78*, 355 (1966); Angew. Chem. Int. Ed. Engl. *5*, 351 (1966).
[13] *A. E. Finholt, A. C. Bond, H. I. Schlesinger*, J. Am. Chem. Soc. *69*, 1199 (1947).
[14] *J. F. Normant*, Synthesis *1972*, 63; *G. M. Whitesides, W. F. Fischer, Jr., J. S. Filippo, Jr., R. W. Bashe, H. O. House*, J. Am. Chem. Soc. *91*, 4871 (1969); *H. O. House*, Proc. Robert A. Welch Found. Conf. Chem. Res. *17*, 101 (1973).
[15] *P. J. Davidson, M. F. Lappert, R. Pearce*, Chem. Rev. *76*, 219 (1976).
[16] *R. R. Schrock, G. W. Parshall*, Chem. Rev. *76*, 243 (1976).
[17] *R. Taube, H. Drevs, D. Steinborn*, Z. Chem. *18*, 425 (1978).
[18] *H. Schumann*, Nachr. Chem. Tech. Lab. *27*, 393 (1979).
[19] *G. H. Posner*, Org. React. *19*, 1 (1972).
[20] *R. Nast*, Angew. Chem. *72*, 26 (1960).
[21] *F. Hein, R. Weiss*, Z. Anorg. Allg. Chem. *295*, 145 (1958); *F. Hein, K. Schmiedeknecht*, J. Organomet. Chem. *5*, 454 (1966).
[22] *R. Taube, G. Honymus*, Angew. Chem. *87*, 291 (1975); Angew. Chem. Int. Ed. Engl. *14*, 261 (1975).
[23] *W. C. Zeise*, Mag. Pharm. *35*, 105 (1830); Ann. Phys. Chem. *9*, 632 (1827); *21*, 497 (1831).
[24] *K. Jonas, K. R. Pörschke, C. Krüger, Y.-H. Tsay*, Angew. Chem. *88*, 682 (1976); Angew. Chem. Int. Ed. Engl. *15*, 622 (1976).
[25] *K. Jonas, K. R. Pörschke*, Angew. Chem. *91*, 521 (1979); Angew. Chem. Int. Ed. Engl. *18*, 488 (1979).
[26] *K. Ziegler*, Brennst.-Chem. *35*, 321 (1954); *K. Ziegler, E. Holzkamp, H. Breil, H. Martin*, Angew. Chem. *67*, 541 (1955).
[27] *P. W. Jolly, G. Wilke*: The Organic Chemistry of Nickel. Vol. I and II. Academic Press, New York 1974, 1975.
[28] *K. Fischer*, Dissertation, Universität Bochum 1973.
[29] *K. Fischer, K. Jonas, P. Misbach, R. Stabba, G. Wilke*, Angew. Chem. *85*, 1002 (1973); Angew. Chem. Int. Ed. Engl. *12*, 943 (1973).
[30] *K. Ziegler, H.-G. Gellert*, Justus Liebigs Ann. Chem. *567*, 195 (1950).
[31] *K. Fischer, K. Jonas, G. Wilke*, Angew. Chem. *85*, 620 (1973); Angew. Chem. Int. Ed. Engl. *12*, 565 (1973).
[32] *E. Weiss, E. A. C. Lucken*, J. Organomet. Chem. *2*, 197 (1964); *E. Weiss, G. Hencken, ibid. 21*, 265 (1970); *H. Dietrich*, Acta Crystallogr. *16*, 681 (1963).
[33] *R. Zerger, W. Rhine, G. D. Stucky*, J. Am. Chem. Soc. *96*, 6048 (1974); *G. D. Stucky*, Adv. Chem. Ser. *130*, 56 (1974); *J. P. Oliver*, Adv. Organomet. Chem. *15*, 235 (1977).
[34] *M. Schlosser*: Struktur und Reaktivität polarer Organometalle. Springer, Berlin 1973; *H. F. Ebel*, Tetrahedron *21*, 699 (1965); *24*, 459 (1968).
[35] *V. Gutmann*, Angew. Chem. *82*, 858 (1970); Angew. Chem. Int. Ed. Engl. *9*, 843 (1970).
[36] *U. Häusig, K. Jonas*, unpublished; *U. Häusig*, Ingenieurarbeit, Fachhochschule Aachen, Abt. Jülich, 1976.
[37] *R. Salz*, Dissertation, Universität Bochum 1976.
[38] *P. W. Jolly, I. Tkatchenko, G. Wilke*, Angew. Chem. *83*, 329 (1971); Angew. Chem. Int. Ed. Engl. *10*, 329 (1971).
[39] *P. Binger, M. J. Doyle, J. McMeeking, C. Krüger, Y.-H. Tsay*, J. Organomet. Chem. *135*, 405 (1977).
[40] *K. R. Pörschke, G. Wilke*, unpublished.
[41] *K. Issleib, A. Tzschach*, Chem. Ber. *92*, 1118 (1959).
[42] *K. Jonas, L. Schieferstein*, Angew. Chem. *88*, 682 (1976); Angew. Chem. Int. Ed. Engl. *15*, 622 (1976).
[43] *L. Schieferstein*, Dissertation, Universität Bochum 1978.
[44] *C. Krüger, J. C. Sekutowski, Y.-H. Tsay*, Z. Kristallogr. *149*, 109 (1979).
[45] *C. Krüger, Y.-H. Tsay*, J. Organomet. Chem. *34*, 387 (1972).
[46] *R. Mynott*, unpublished.
[47] *E. Uhlig, B. Hipler, P. Müller*, Z. Anorg. Allg. Chem. *442*, 11 (1978).
[48] *K. Jonas*, Angew. Chem. *88*, 51 (1976); Angew. Chem. Int. Ed. Engl. *15*, 47 (1976).
[49] *D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, Angew. Chem. *88*, 52 (1976); Angew. Chem. Int. Ed. Engl. *15*, 48 (1976).
[50] *H. B. Chin, R. Bau*, J. Am. Chem. Soc. *98*, 2434 (1976).
[51] *F. Hein, B. Heyn, K. Schmiedeknecht*, Monatsber. Dtsch. Akad. Wiss. Berlin *2*, 552 (1960); *E. Müller, J. Krause, K. Schmiedeknecht*, J. Organomet. Chem. *44*, 127 (1972).
[52] *D. J. Brauer, C. Krüger*, Inorg. Chem. *16*, 884 (1977).
[53] a) *H. Bönnemann, C. Krüger, Y.-H. Tsay*, Angew. Chem. *88*, 50 (1976); Angew. Chem. Int. Ed. Engl. *15*, 46 (1976); *H. Bönnemann, C. Krüger, Y.-H. Tsay*, unpublished; b) *C. Krüger, L.-K. Liu*, unpublished.
[54] *M. H. Chisholm, H. C. Clark, L. E. Manzer, J. B. Stothers*, J. Am. Chem. Soc. *94*, 5087 (1972); *M. H. Chisholm, S. Godlesk*, Prog. Inorg. Chem. *20*, 299 (1975).
[55] *R. G. Parker, J. D. Roberts*, J. Am. Chem. Soc. *92*, 743 (1970); *H. W. Quinn, J. S. McIntyre, D. J. Peterson*, Can. J. Chem. *43*, 2896 (1965); *J. C.*

Schug, R. J. Martin, J. Phys. Chem. *66*, 1554 (1962); *G. A. Olah, P. R. Clifford*, J. Am. Chem. Soc. *93*, 1261, 2320 (1971).
[56] *E. Ruch* in: 10 Jahre Fonds der Chemischen Industrie. Verband der Chemischen Industrie, Düsseldorf 1960, p. 163; *L. E. Orgel:* An Introduction to Transition Metal Chemistry. Methuen, London 1960, p. 137.
[57] *M. E. Vol'pin, V. B. Shur*, Dokl. Akad. Nauk SSSR *156*, 1102 (1964; Nature *209*, 1236 (1966).
[58] *A. D. Allen, C. V. Senoff*, Chem. Commun. *1965*, 621.
[59] *J. Chatt, J. R. Dilworth, R. L. Richards*, Chem. Rev. *78*, 589 (1978).
[60] *R. W. F. Hardy, R. D. Holsten, E. K. Jackson, R. C. Burns*, Plant. Physiol. *43*, 1185 (1968); *M. J. Dievorth*, Biochim. Biophys. Acta *127*, 285 (1966); *M. Kelly, ibid. 191*, 527 (1969).
[61] *C. Busetto, A. D'Alfonso, F. Maspero, G. Perego, A. Zazzetta*, J. Chem. Soc. Dalton Trans. *1977*, 1828.
[62] *K. Jonas*, Angew. Chem. *85*, 1050 (1973); Angew. Chem. Int. Ed. Engl. *12*, 997 (1973).
[63] *C. Krüger, Y.-H. Tsay*, Angew. Chem. *85*, 1051 (1973); Angew. Chem. Int. Ed. Engl. *12*, 998 (1973).
[64] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, J. Am. Chem. Soc. *98*, 74 (1976).
[65] *K. Jonas, R. Stabba*, unpublished; *R. Stabba*, Dissertation, Universität Bochum 1971.
[66] *P. W. Jolly, K. Jonas, C. Krüger, Y.-H. Tsay*, J. Organomet. Chem. *33*, 109 (1971).
[67] *D. Sellmann*, Angew. Chem. *86*, 692 (1974); Angew. Chem. Int. Ed. Engl. *13*, 639 (1974).
[68] *W. G. Sly*, J. Am. Chem. Soc. *81*, 18 (1959); *Y. Wang, P. Coppens*, Inorg. Chem. *15*, 1122 (1976); *F. A. Cotton, J. D. Jamerson, B. R. Stults*, J. Am. Chem. Soc. *98*, 1774 (1976).
[69] *A. Albini, H. Kisch*, Top. Curr. Chem. *65*, 105 (1976), and references cited therein.
[70] *J. G. Fripiat, K. T. Chow, M. Boudart, J. B. Diamond, K. H. Johnson*, J. Mol. Catal. *1*, 59 (1975/76).
[71] *Y. G. Borodko, I. N. Ivleva, L. M. Kachapina, S. I. Salienko, A. K. Shilova, A. E. Shilov*, J. Chem. Soc. Chem. Commun. *1972*, 1178; *E. W. van der Weij, J. H. Teuben*, J. Organomet. Chem. *120*, 223 (1976).
[72] *J. M. Manriquez, R. D. Sanner, R. E. Marsh, J. E. Bercaw*, J. Am. Chem. Soc. *98*, 3042 (1976).
[73] *R. Benn, K. Blum, K. Jonas, K. R. Pörschke*, unpublished.
[74] *K. Jonas*, Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975).
[75] *P. Gillespie, P. Hoffmann, H. Klusacek, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis, I. Ugi*, Angew. Chem. *83*, 691 (1971); Angew. Chem. Int. Ed. Engl. *10*, 687 (1971); *E. L. Muetterties, R. A. Schunn*, Q. Rev. Chem. Soc. *20*, 245 (1966).
[76] *M. R. Churchill, S. A. Bezman*, Inorg. Chem. *11*, 2243 (1972); *M. R. Churchill, K.-K. G. Lin*, J. Am. Chem. Soc. *96*, 76 (1974); *J. R. Shapley, J. A. Osborn*, Acc. Chem. Res. *6*, 305 (1973).
[77] *K. R. Pörschke*, Dissertation, Universität Bochum 1975.
[78] *K. Blum*, Dissertation, Universität Bochum 1978.
[79] a) *D. J. Brauer, C. Krüger, J. C. Sekutowski*, J. Organomet. Chem. *178*, 249 (1979); b) *R. Goddard, E. D. Jemmis, R. Hoffmann*, to be published.
[80] *R. Benn, K. Blum, K. Jonas*, unpublished.
[81] *T. E. G. Daenen, K. Jonas*, unpublished.
[82] a) *K. Ziegler*, Angew. Chem. *64*, 323 (1952); Brennst.-Chem. *33*, 193 (1952); b) *K. Ziegler, H.-G. Gellert, H. Martin, K. Nagel, I. Schneider*, Justus Liebigs Ann. Chem. *589*, 91 (1954).
[83] *P. L. Timms, T. W. Turney*, Adv. Organomet. Chem. *15*, 53 (1977); *P. S. Skell, M. J. McGlinchey*, Angew. Chem. *87*, 215 (1975); Angew. Chem. Int. Ed. Engl. *14*, 195 (1975); *P. L. Timms, ibid. 87*, 295 (1975) and *14*, 273 (1975); *E. A. Koerner von Gustorf, O. Jaenicke, O. Wolfbeis, C. R. Eady, ibid. 87*, 300 (1975) and *14*, 278 (1975); *J. R. Blackborow, D. Young:* Reactivity and Structure, Vol. 9. Springer, Berlin 1979.
[84] *D. W. Slocum, T. R. Engelmann, C. Ernst, C. A. Jennings, W. Jones, B. Koonsvitsky, J. Lewis, P. Shenkin*, J. Chem. Educ. *46*, 144 (1969); *D. E. Bublitz, K. L. Rinehart*, Org. React. *17*, 1 (1969).
[85] *A. N. Nesmeianov, E. G. Perevalova, Z. A. Beinoravichute*, Proc. Acad. Sci. USSR *112*, 439 (1957); *M. Walczak, K. Walczak, R. Mink, M. D. Rausch, G. Stucky*, J. Am. Chem. Soc. *100*, 6382 (1978).
[86] *H. Werner*, Fortschr. Chem. Forsch. *28*, 141 (1972).
[87] *D. S. Trifan, L. Nicholas*, J. Am. Chem. Soc. *79*, 2746 (1957); *G. W. Watt, L. J. Baye*, J. Inorg. Nucl. Chem. *26*, 2099 (1964); *J. M. Osgerby, P. L. Pauson*, J. Chem. Soc. *1961*, 4604; *A. N. Nesmeianov, E. V. Leonova, N. S. Kochetkova, L. Ya. Golovleva*, Dokl. Chem. *191*, 285 (1970); *H. P. Fritz, L. Schäfer*, Chem. Ber. *97*, 1829 (1964).
[88] *K. Jonas, R. Mynott, C. Krüger, J. C. Sekutowski, Y.-H. Tsay*, Angew. Chem. *88*, 808 (1976); Angew. Chem. Int. Ed. Engl. *15*, 767 (1976).
[89] *E. Deffense, K. Jonas*, unpublished.
[90] *K. Jonas, L. Schieferstein*, Angew. Chem. *91*, 590 (1979); Angew. Chem. Int. Ed. Engl. *18*, 549 (1979).
[91] *K. Jonas, L. Schieferstein, C. Krüger, Y.-H. Tsay*, Angew. Chem. *91*, 590 (1979); Angew. Chem. Int. Ed. Engl. *18*, 550 (1979).
[92] *K. Jonas*, DOS 2724111 (1979), Studiengesellschaft Kohle; Chem. Abstr. *90*, 121804 (1979).
[93] *D. Habermann, K. Jonas*, unpublished.
[94] *A. Nakamura, N. Hagihara*, Bull. Chem. Soc. Jpn. *33*, 425 (1960); *34*, 452 (1961); *R. L. Pruett, W. R. Myers*, US-Pat. 3 159 659; Chem. Abstr. *62*, 7800 (1965).
[95] *G. Koepe, K. Jonas*, unpublished.
[96] *J. F. Cordes*, Chem. Ber. *95*, 3084 (1962).
[97] *S. Otsuka, M. Rossi*, J. Chem. Soc. *A 1968*, 2630; *L. W. Gosser, M. A. Cushing*, Inorg. Synth. *17*, 112 (1977).
[98] *H. Lehmkuhl, W. Leuchte, E. Janssen*, J. Organomet. Chem. *30*, 407 (1971).
[99] *Ch. Grard*, Dissertation, Universität Bochum 1967; *G. Wilke*, Chem. Chem. Ind. (Japan) *20*, 1308 (1967).
[100] *H. Bönnemann, K. Jonas, C. Krüger*, J. Organomet. Chem., in press.
[101] *W. E. Geiger, Jr.*, Proc. VI. Int. Conf. Organomet. Chem. *1973*, 250; J. Am. Chem. Soc. *96*, 2632 (1974); *J. D. L. Holloway, W. E. Geiger, Jr., ibid. 101*, 2038 (1979).
[102] *N. El Murr, R. Dabard, E. Laviron*, J. Organomet. Chem. *47*, C 13 (1973); *N. El Murr, ibid. 112*, 189 (1976).
[103] *G. E. Herberich, J. Schwarzer*, Angew. Chem. *82*, 883 (1970); Angew. Chem. Int. Ed. Engl. *9*, 897 (1970).
[104] *K. Jonas, G. Koepe, C. Krüger*, unpublished.
[105] *W. F. Edgell, J. Lyford IV, A. Barbetta, C. I. Jose*, J. Am. Chem. Soc. *93*, 6403 (1971); *W. F. Edgell, J. Lyford IV, ibid. 93*, 6407 (1971); *W. F. Edgell, M. T. Yang, N. Koizumi, ibid. 87*, 2563 (1965).
[106] *N. Rösch, R. Hoffmann*, Inorg. Chem. *13*, 2656 (1974).
[107] *E. O. Fischer, R. Böttcher*, Z. Naturforsch. *B 10*, 600 (1955); *R. D. Fischer, A. Vogler, K. Noack*, J. Organomet. Chem. *7*, 135 (1967).
[108] *K. Jonas, L. Schieferstein*, unpublished.

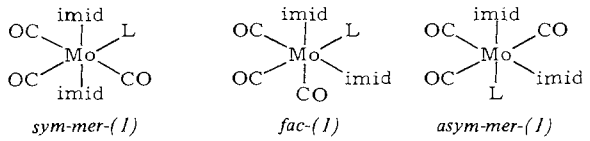
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

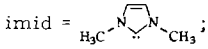
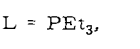
Electrochemical Oxidation of Dicarbene Complexes of the Type (Carbene)$_2$MoL(CO)$_3$: Interconversion Among Three Isomers *via* Electrochemical Redox Processes[**]

By *Reuben D. Rieke, Hiroyuki Kojima*, and *Karl Öfele*[*]

Carbenecarbonylmetal complexes constitute a relatively new class of organometallic compounds which are currently the subject of intensive investigation[1]. In 1970 *Öfele* and *Herberhold* reported the preparation of *cis*- and *trans*-dicarbenetetracarbonylmetal complexes[2]. We have been involved in a study of the redox properties of dicarbene metal carbonyl complexes and recently we reported on an unusual electrochemical isomerization without net current flow in the case of *trans*-dicarbenetetracarbonylmetal complexes[3].

We report here on further unusual isomerizations in neutral ligand-substituted dicarbenetricarbonylmolybdenum complexes of the type (imid)$_2$MoL(CO)$_3$ *(1)*: In these systems, we found that interconversion occurs among the three isomers *via* electrochemical redox processes.



imid =  ; *a*, L =  ; *b*, L = PEt_3, *c*, L = PPh_3, *d*, L = 

The compounds *(1a—c)* were synthesized by ligand exchange from (imid)$_2$Mo(py)(CO)$_3$ *(1d)*, which had been prepared photochemically from (imid)$_2$Mo(CO)$_4$ *(2)*, and were identified as the *sym-mer*-isomers by IR and NMR spectra. *sym-mer-(1)* was electrochemically oxidized in dichloromethane and propylene carbonate with tetrabutylammonium perchlorate (TBAP) as supporting electrolyte. Since the complexes *(1)*, except *(1a)*, are very air-sensitive, care was taken to exclude air from the cells. To prevent the possibility of the compounds isomerizing, preparation of the solutions and electrochemical measurements were performed at low temperature.

Cyclic voltammetry of *sym-mer-(1a)* yielded two oxidation waves at the peak potentials $E_p^a = -0.20$ and 0.09 V (*vs.* SCE) in dichloromethane (Fig. 1a). This voltammogram is very similar to that of *trans-(2)*[3]. The amplitude of the first wave is much smaller at room temperature and/or slow scan rates.

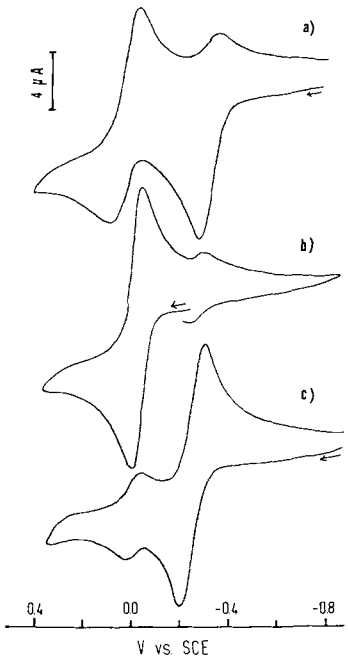


Fig. 1. Cyclic voltammogram of (imid)$_2$Mo(CN-*cyclo*-C_6H_{11})(CO)$_3$ *(1a)* in 0.25 M TBAP/dichloromethane solution at −20 °C; sweep rate 0.20 V/s. a) starting solution; *sym-mer-(1a)*; b) after electrooxidation of the first wave; conversion into *fac-(1a)*; c) after electrooxidation of the second wave, then electroreduction of the third wave; conversion into *asym-mer-(1a)*.

The electrolysis of the intense yellow solution was complete within a few minutes; the amount of current consumed was less than 10% of that required for a one-electron oxidation. The cyclic voltammogram of the resulting pale yellow solution showed that formation of the second wave was roughly reversible (Fig. 1b). This process turned out according to coulometry to correspond to a normal one-electron oxidation. However, on re-reduction a new wave appeared at a cathode potential $E_p^c = -0.27$ V. This suggests that the cation produced in the second wave converts to yet another new species. The neutral complex of this third species was obtained by successive bulk electrooxidation of the second wave and bulk electroreduction of the third wave, and it was characterized by its voltammogram (Fig. 1c).

These two new species corresponding to the waves at $E_p^a = 0.09$ V and $E_p^a = -0.20$ V were isolated after electrolysis by removing TBAP and were identified by NMR and IR

[*] Prof. Dr. R. D. Rieke, H. Kojima
Department of Chemistry, University of Nebraska-Lincoln
Lincoln, Nebraska 68588 (USA) and
William Rand Kenan, Jr., Laboratories of Chemistry, Department of Chemistry
University of North Carolina
Chapel Hill, North Carolina 27514 (USA)
Dr. K. Öfele
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the National Science Foundation.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0707-0538 $ 02.50/0*

spectra. The methyl protons of the imid ligand (N—CH_3) for the second species showed a single signal at $\delta = 3.42$ (60 MHz, TMS int., in C_6D_6), which was shifted upfield by 0.5 ppm compared to the signal of *sym-mer-(1a)* ($\delta = 3.86$); for comparison: $\delta = 3.98$ for *trans-*, 3.62 for *cis-(2)* (TMS int., [D_6]acetone). The consequent assignment of the second species as *fac-(1a)* is also supported by the similarity of the electrochemical behavior of *(1a)* and *trans-(2)*. In the case of the third species, the methyl protons appear as a doublet with a chemical shift ($\delta = 3.33$, 3.29; TMS int., in C_6D_6) similar to that of *fac-(1a)*. This species can be assigned the structure of the remaining *asym-mer*-isomer.

Additional support for these assignments was provided by the C≡N stretching frequency of the isocyanide ligand in *(1a)*[4]. Both *sym-mer-(1a)* and *fac-(1a)* showed a broad absorption band at about 2080 cm^{-1}, while *asym-mer-(1a)* showed this absorption at about 1980 cm^{-1}. Only the *asym-mer*-isomer has one of the imidazole ligands *trans* to the isocyanide; in the other isomers the isocyanide group has CO ligands *trans* to it. Since the carbene ligand is a poorer π-acceptor than CO, the assignment of the *asym-mer* structure to the third complex is consistent with the lower stretching frequency of the R—N≡C group.

$$2\,[\textit{asym-mer-(1b)}]^{\oplus} \longrightarrow [\textit{asym-mer-(1b)}]^{0} + [\textit{asym-mer-(1b)}]^{2\oplus}$$

$$[\textit{asym-mer-(1b)}]^{0} \longrightarrow [\textit{fac-(1b)}]^{0}$$

$$[\textit{fac-(1b)}]^{0} \longrightarrow \textit{cis-}(\text{imid})_2\text{Mo(CO)}_4 \quad \textit{cis-(2)}$$

$$[\textit{asym-mer-(1b)}]^{2\oplus} \longrightarrow \text{dec.}$$

showed very similar electrochemical behavior to that of the triethylphosphane complex *(1b)*. However, *fac-(1c)* is much less stable than *fac-(1b)* and forms the dicarbene complex *(2)* within a few hours. The pyridine complex *(1d)* decomposes very rapidly, especially in dichloromethane, with a change in color from purple-red to brown; however, it is fairly stable in propylene carbonate at low temperature. Electrochemical studies on this system showed a similar isomerization scheme as in the case of *(1a—c)*, but a much faster rate of formation of the dicarbene complex *(2)* was observed. Table 1 shows the half-wave oxidation potentials of each isomer and the estimated rates of isomerization of the complexes. The oxidation potentials vary considerably; in the case of *(1d)*, *e.g.*, by over 360 mV.

Table 1. Half-wave potentials and approximate isomerization rate of the complex $(imid)_2MoL(CO)_3$ *(1)* [a].

		$E_{1/2}$ [V *vs* SCE] [b]			k_1 [s^{-1}] at −20 °C			Formation of *cis-(2)*
	L	*sym-mer*	*fac*	*asym-mer*	[*sym-mer*]$^{\oplus}$ → [*fac*]$^{\oplus}$	[*fac*]$^{\oplus}$ → [*asym-mer*]$^{\oplus}$	[*asym-mer*]^{0} → [*fac*]^{0}	
(1d)	py [d]	−0.43	−0.08	−0.44	$t_{1/2} = 3$ s at 20 °C	$t_{1/2} = 10$ s	$t_{1/2} \approx 2$—3 min	immediately without py
(1b)	PEt_3	−0.33 [c]	−0.04	−0.34	2×10^{-2}	$> 3 \times 10^{2}$	4×10^{-2}	days
(1a)	CN-*c*-C_6H_{11}	−0.30	+0.05	−0.24	4×10^{-1}	$\sim 10^{-3}$	[e]	not detected
(1c)	PPh_3	−0.24 [c]	+0.01	−0.25	2×10^{-2}	$> 3 \times 10^{2}$	1×10^{-1}	hours

[a] Measurements as in [3] in 0.25 M TBAP/dichloromethane solution at −20 ± 2 °C except where otherwise stated. [b] The values were obtained by averaging the peak potentials of anodic and cathodic waves. [c] These values are approximate because of rapid isomerization. [d] In 10% pyridine solution. [e] Negligibly small.

The electrochemical behavior of the *sym-mer* complexes *(1b—d)* was similar to that of the *sym-mer-(1a)*, but in some cases it was more complex.

The triethylphosphane complex *fac-(1b)* did not give a corresponding wave on re-reduction, but gave the very stable cation [*asym-mer-(1b)*]$^{\oplus}$, even at scan rates of up to 100 V/s and at −20 °C. Its cyclic voltammogram showed another oxidation wave as well as the corresponding oxidation wave to this cation. This new wave turned out to correspond to *fac-(1b)*. It follows, therefore, that [*fac-(1b)*]$^{\oplus}$ is extremely rapidly converted into [*asym-mer-(1b)*]$^{\oplus}$, and that *asym-mer-(1b)* returns to the *fac*-isomer. As well as these isomerization reactions, there are other very slow chemical reactions, *fac-(1b)* slowly forms the dicarbene complex *cis-(2)* (within a few days) in solution. The complex was identified by the cyclic voltammogram and the spectral properties. Presumably, the ligand exchange reaction shown below takes place. The species *(3)* was not detected electrochemically.

$$4\,\underset{\textit{fac-(1b)}}{\textit{fac-}(\text{imid})_2\text{MoL(CO)}_3} \rightarrow 3\,\underset{\textit{cis-(2)}}{\textit{cis-}(\text{imid})_2\text{Mo(CO)}_4} + \underset{\textit{(3)}}{(\text{imid})_2\text{MoL}_4}$$

cis-(2) is also formed in a solution of [*asym-mer-(1b)*]$^{\oplus}$ after a few days at room temperature. This observation is best explained in terms of the following disproportionation of [*asym-mer-(1b)*]$^{\oplus}$. The triphenylphosphane complex *(1c)* showed very similar electrochemical behavior to that of the triethylphosphane complex *(1b)*. However, *fac-(1c)* is much less stable than *fac-(1b)* and forms the dicarbene complex *(2)* within a few hours. The pyridine complex *(1d)* decomposes very rapidly, especially in dichloromethane, with a change in color from purple-red to brown; however, it is fairly stable in propylene carbonate at low temperature. Electrochemical studies on this system showed a similar isomerization scheme as in the case of *(1a—c)*, but a much faster rate of formation of the dicarbene complex *(2)* was observed. Table 1 shows the half-wave oxidation potentials of each isomer and the estimated rates of isomerization of the complexes. The oxidation potentials vary considerably; in the case of *(1d)*, *e.g.*, by over 360 mV.

In some cases, the cations are more stable than that of the dicarbene complex *(2)*[3]. In the isomerization scheme (Fig. 2) the electrochemical redox processes are indicated by thick arrows, while spontaneous or non-spontaneous processes are indicated by thin arrows. There are several unusual features of the isomerization scheme: a) the direct conversion of *sym-mer-(1)* into *asym-mer-(1)* is inhibited, while either conversion of *sym-mer-(1)* into *fac-(1)* or [*fac-(1)*]$^{\oplus}$ into [*asym-mer-(1)*]$^{\oplus}$ can occur, and b) the *fac/asym-mer* conversion proceeds in opposite directions in the neutral and the cation states. These puzzling results suggest that there is a specific

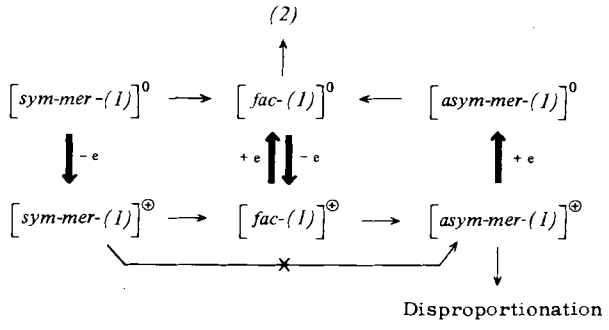


Fig. 2. Isomerization *via* electrochemical redox processes.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0539 $ 02.50/0

mechanism for the isomerization of these systems and that carbene ligands play an unusual and important role. We assume, firstly that dissociation of a CO group takes place at a selective position in an initial stage of the isomerization, and secondly that a substantial change of π-acceptability of the carbene ligand from the neutral to the cation states has to be invoked.

Received: August 6, 1979 [Z 456 IE]
revised: May 22, 1980
German version: Angew. Chem. 92, 550 (1980)

[1] *E. O. Fischer*, Rev. Pure Appl. Chem. *24*, 407 (1970); *30*, 353 (1972); *D. J. Cardin, B. Cetinkaya, M. F. Lappert*, Chem. Rev. *72*, 545 (1972); *F. A. Cotton, C. M. Lukehart*, Prog. Inorg. Chem. *16*, 487 (1972); *P. J. Krusic, U. Klabunde, C. P. Casey, T. F. Block*, J. Am. Chem. Soc. *98*, 2015 (1976); *P. G. Gassman, T. H. Johnson, ibid. 98*, 6055, 6057, 6058 (1976); *S. J. Lee, J. McGinnis, T. J. Katz, ibid. 98*, 7818 (1976).

[2] *K. Öfele, M. Herberhold*, Angew. Chem. *82*, 775 (1970); Angew. Chem. Int. Ed. Engl. *9*, 739 (1970); *C. G. Kreiter, L. Öfele, G. Wieser*, Chem. Ber. *109*, 1749 (1976).

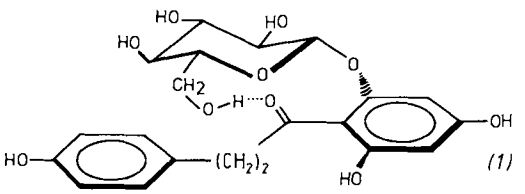
[3] *R. D. Rieke, H. Kojima, K. Öfele*, J. Am. Chem. Soc. *98*, 6735 (1976).

[4] Unfortunately, the CO stretching bands were not useful in the assignments of the structures because they were all too similar.

A Phlorizin Polymer as Affinity Gel for Sugar-Binding Proteins[***]

By *Jiann-Trzuo Lin* and *Rolf Kinne*[*]

Phlorizin *(1)*, a β-glycoside found in apple tree roots, was isolated in 1835[1] and synthesized in 1942[2]. Compound *(1)* is known as potent inhibitor of renal and intestinal sugar transport, and is therefore particularly suited for investigations on the properties of the sugar transport system[3]. Owing to the numerous phenolic hydroxyl groups it was possible to cross-link the aglucone moiety while leaving the sugar residue unchanged. As shown below, this polymer san serve as affinity gel for sugar-binding proteins. In contrast to the commonly used affinity gels based on agarose as matrix, both the matrix and the ligand are provided by the same molecule in the phlorizin polymer.



(1)

Phlorizin undergoes cross-linkage with formaldehyde and urea in the presence of acetic acid to give a white polymer. From the glucose content of the polymer[4] a phlorizin content of 3.05% can be estimated, and from the nitrogen content (32.53%) a molar ratio of 1:4:16 is found for phlorizin: urea:formaldehyde. Following the concepts developed for other resins[5], the polymer can be envisaged as composed of phlorizin molecules interconnected by $-CH_2-O-$ and $CH_2-NH-CO-NH-$ chains. The distance between the phlorizin molecules is governed by the amount of formaldehyde and the amount of urea used for synthesis. It has to be large enough to allow free rotation of the sugar moiety and for unrestricted access of the sugar-binding proteins.

In order to test the ability of the polymer to act as affinity gel for sugar-binding proteins the binding capacity for Concanavalin A (ConA) and lentil lectin was first determined. At 22 °C approximately 2×10^{-7} mol ConA and 8×10^{-8} mol lentil lectin were bound per gram of dry polymer. Then purified ConA was applied on a column of phlorizin polymer. In contrast to bovine serum albumin, ConA was adsorbed by the column and could be eluted by D-glucose (Fig. 1a). The polymer was also used to purify ConA from a crude extract of Jack beans. As shown in Figure 1b, most of the proteins present in the extract passed through the column. A small amout of protein was recovered by elution with D-glucose. The composition of this fraction is virtually identical to the composition of commercially available purified ConA (see Fig. 2).

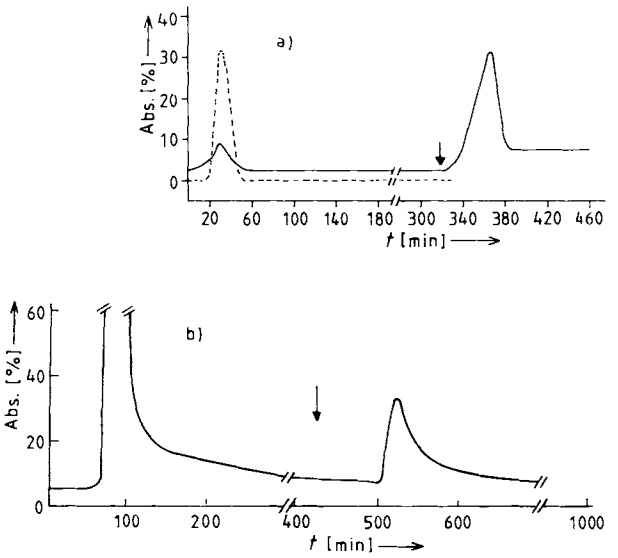


Fig. 1. Affinity chromatography on phlorizin polymer. a) 500 µl of a ConA solution (1.7 mg/ml) (– ·) or 200 µl of bovine serum albumin (4.7 mg/ml) in water were applied onto an affinity column (30 × 0.9 cm). The column was eluted with deionized water, rate 9 ml/h, fraction volume 3 ml. The protein content of the eluate was monitored at 279 nm. Concanavalin A could only be eluted with 0.2 mol/l of D-glucose (arrow). b) 400 µl of crude Jack bean extract in 0.1 M ammonium acetate, pH 7.0, were applied to a column. The proteins adsorbed to the column were eluted with D-glucose (0.5 mol/l), see arrow.

Preliminary experiments with extracts from hog kidney brush border membranes show that the protein fraction adsorbed on the column and eluted by D-glucose exhibits an at least five-fold higher transport activity than the membrane itself. The transport activity was determined after incorporation of the proteins into liposomes. Thus the phlorizin polymer seems to be suitable for the purification of a variety of proteins that show an affinity for D-glucose linked to the matrix by a β-glycosidic bond.

Procedure

Preparation of the polymer: A mixture of phlorizin (2 g), urea (30 g), 37% formaldehyde (65 ml), and acetic acid (1 drop) is stirred for 20–30 min at 120–140 °C. The white mass obtained is broken into small pieces and washed with water/ethanol and then with ethanol in order to remove nonpolymerized material. After drying at 60 °C, 46.2 g of dry polymer was obtained. For further investigations the polymer is ground to a particle size of about 200 mesh and equilibrated

[*] Prof. Dr. R. Kinne [**], Dr. J.-T. Lin
Max-Planck-Institut für Biophysik
Heinrich-Hoffmann-Strasse 7, D-6000 Frankfurt 71 (Germany)

[**] Present address: Yeshiva University, Albert Einstein College of Medicine 1300 Morris Park Avenue, Bronx, N. Y. 10461 (USA)

[***] This work was supported by the Deutsche Forschungsgemeinschaft. — Based on a lecture delivered at the XIth International Congress of Biochemistry in Toronto on July 10, 1979.

with the appropriate buffer. After transfer to a chromatography column, the polymer was washed with water or buffer solution until no absorption was observed at 256 nm in the eluate. The protein mixture was then applied.

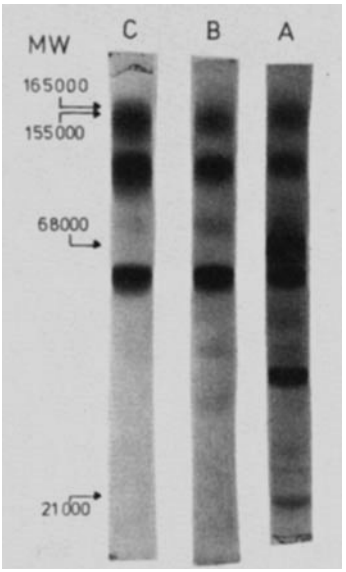


Fig. 2. Protein pattern of the fractions obtained from the crude Jack bean extract (Fig. 1b). A, crude extract; B, fraction eluted by D-glucose; C, commercially available Concanavalin A (Pharmacia, Tübingen). The protein pattern was determined by polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate (SDS). Polyacrylamide concentration 8%.

Binding of lectins: The binding was determined by incubation of the polymer (10 mg) with increasing concentrations of the lectins (0.13 mg/ml–2.6 mg/ml) in ammonium acetate (0.1 mol/l, pH 6.5) for 2 h at 22 °C. After the incubation, the polymer was sedimented and the protein content of the supernatant was determined. Bovine serum albumin was used as control for unspecific adsorption; this adsorption was negligibly small.

Received: May 22, 1979;
supplemented: July 27, 1979 and
April 8, 1980 [Z 492 IE]
German version: Angew Chem. 92, 547 (1980)

[1] *de Koninck*, Justus Liebigs Ann. Chem. *15*, 258 (1835).
[2] *G. Zemplén, R. Bognar*, Ber. Dtsch. Chem. Ges. *75*, 1040 (1942).
[3] *R. Kinne*, Curr. Top. Membr. Transp. *8*, 209 (1976); *R. Kinne, H. Murer, E. Kinne-Saffran, M. Thees, G. Sachs*, J. Membr. Biol. *21*, 375 (1975); *A. Klip, S. Grinstein, G. Semenza, ibid 51*, 47 (1979).
[4] *M. Dubois, K. A. Giles, J. K. Hamilton, P. A. Rebers, F. Smith*, Anal. Chem. *28*, 350 (1956).
[5] *H.-G. Elias*, Makromoleküle. Hüthig & Wepf, Basel 1972, pp. 714ff, 733ff.

Collision Induced Fragmentation of Alkylideneammonium Ions[**]

By *Hans J. Veith*[*]

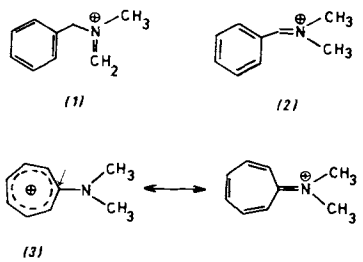
Alkylideneammonium ions play a special role in organic synthesis and as natural products (cf. [1a]). We report here on a mass spectrometric method (FD-CA) with which, in addition to their molecular weights, structural details of alkylideneammonium salts can be determined.

Previously, such salts could not be investigated mass spectrometrically since the ionic structure does not remain intact on transfer of the salt into the gas phase (cf. [1b]). With the field desorption (FD) method, however, alkylideneammonium ions can be generated intact in the gas phase from the corresponding salts. While the masses of the cations can thus be determined directly, and the occurrence of cluster ions permits determination of the molecular weights of the salts, no structural details are obtained from the FD-mass spectrum, since the field-desorbed alkylideneammonium ions do not decompose within the mass spectrometric time scale owing to the low excitation energy[2].

A possibility of producing fragmentation is offered by the collisional activation (CA) method. The highly accelerated ions collide inelastically with a neutral target gas, thereby experiencing an excitation separated in space and time from the actual ion-formation process, which leads to fragments of the ions to be investigated (cf. [3]). These fragment ions are generated in the first field-free region of a double-focusing mass spectrometer and recorded with a linked-scan device[4].

The FD-CA mass spectra of the three isomeric alkylideneammonium ions *(1)*—*(3)* (Fig. 1), generated by field desorption from the tetrafluoroborates[5], differ primarily in the intensity ratios of the main fragmentations. The ion *(1)* decomposes, predominantly by heterolysis of the N—C_{benzyl} bond, into a $C_7H_7^{\oplus}$ ion ($m/e = 91$). This charge transfer from the N atom to the aromatic ring is also observed in ion *(2)*, but the formation of the $C_7H_7^{\oplus}$ ions from *(2)* and from *(3)* is associated with a hydrogen migration. Apparently, less energy is required for the elimination of *N*-methylmethyleneamine from *(1)* than in the case of the ions *(2)* and *(3)* since the proportion of competing decompositions in *(2)* and *(3)* increases considerably. In the CA spectrum of *(2)* the $[M^{\oplus} - CH_4]$ ion ($m/e = 118$) reaches *ca.* 60% of the intensity of the $C_7H_7^{\oplus}$ ion and appears as base peak in the spectrum of the ion *(3)*.

The *N,N*-dimethylaminotropylium structure, both in the case of ion *(3)* as well as partially after isomerization of *(2)*, is proven by the occurrence of more intense signals at $m/e = 90$ and 89 in comparison to the CA spectrum of *(1)*. The formation of these ions can be explained in terms of homolysis of the C—N bond and *N,N*-dimethylamine elimination, respectively. As in the case of phenylalkyl-substituted ammonium ions[4] the elimination of 52 mass units ($m/e = 82$) is observed with ions *(1)* and *(2)* and of 26 mass units ($m/e = 108$) with ion *(3)*. Despite the low signal intensity these fragments provide information about the charge localization. Positively charged aromatic systems eliminate one molecule of acetylene, both as is well-known under electron-impact as well as under CA conditions; uncharged benzene rings, on the other hand, directly lose two acetylene molecules in the form of a neutral fragmentation under CA conditions.



(1) *(2)*

(3)

Besides its use in structural analysis, the FD-CA method opens up new entries to comparative studies on gas-phase fragmentations of alkylideneammonium ions, which are gen-

[*] Dr. H. J. Veith
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] Collision Induced Fragmentations of Field Desorbed Cations, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft; we thank Herr *M. Fischer* for help with the experiments.—Part 3: *H. J. Veith*, Adv. Mass Spectrom. *8*, in press.

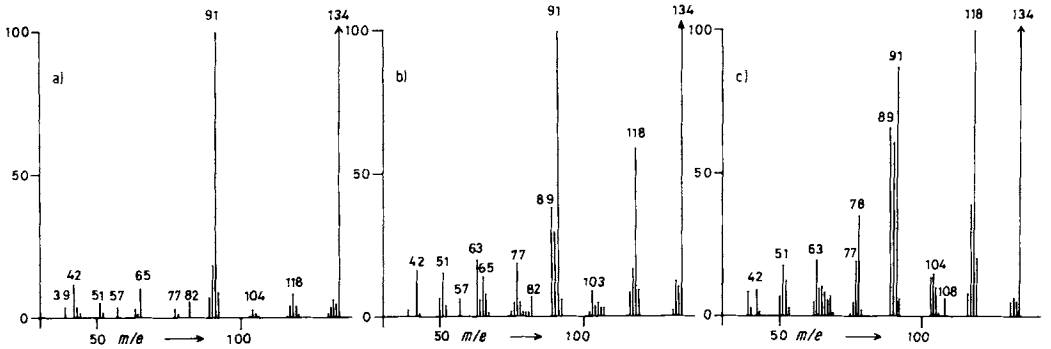
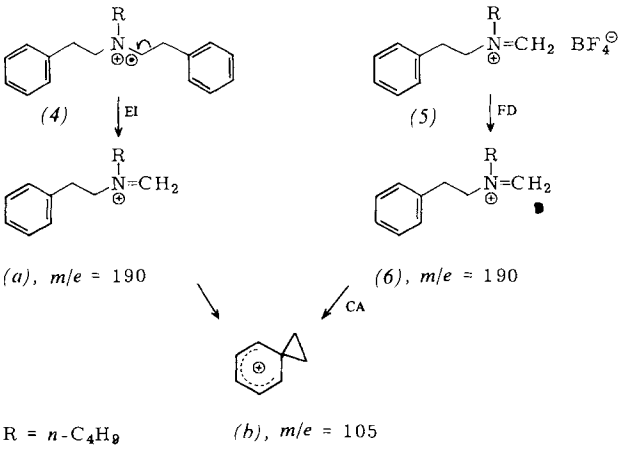


Fig. 1. FD-CA mass spectrum a) of the *N*-benzyl-*N*-methylmethyleneammonium ion *(1)*, b) of the *N,N*-dimethylbenzylideneammonium ion *(2)*, c) of the *N,N*-dimethylaminotropylium ion *(3)*.



Scheme 1. Main fragmentation of the methyleneammonium ion *a* and *(6)*, which was generated by α-cleavage in an electron-impact ionized molecular ion of *(4)* or from the tetrafluoroborate *(5)* under FD-CA conditions.

erated from the molecular ions of alkylamines by α-cleavage after electron impact (EI) excitation or under FD conditions from alkylideneammonium salts.

Under EI conditions α-cleavage of the molecular ion of *N,N*-bis(β-phenylethyl)butylamine *(4)* affords the methyleneammonium ion *a* ($m/e = 190$), which, after homobenzylic heterolysis with loss of *N*-methylenebutylamine, decomposes into the ion *b* ($m/e = 105$) (cf. Scheme 1[6]). This reaction, accompanied by a charge transfer from the N atom to the benzene ring, is likewise the main reaction in the collision-induced decomposition of the ion *(6)* liberated under FD conditions from the salt *(5)*. From the intensities of the $C_7H_7^{\oplus}$ ions ($m/e = 91$) generated from *(4)* and *(6)*, which are consistent within the experimental error, it follows that the $C_7H_7^{\oplus}$ ions recorded in the EI mass spectrum of compound *(4)* are formed by secondary fragmentation from the methyleneammonium ion *a* and not, as would appear at first sight, by cleavage of a benzyl bond in the molecular ion of *(4)*. Further agreement between the EI and the FD-CA spectrum has been established for the propene and butene eliminations ($m/e = 148$ and 134, resp.), well-known in electron-impact mass spectrometry[7] (cf. Table 1).

In contrast to the electron-impact fragmentations, in the CA spectrum of *(6)* signals appear for the elimination of propane ($m/e = 146$), butane ($m/e = 132$), toluene ($m/e = 98$), and ethylbenzene ($m/e = 84$), the more intense signals being recorded for the cleavage of allyl bonds. As D-labeling experiments show, the H atom to be eliminated with the leaving

Table 1. Section of the EI mass spectrum (70 eV) of *(4)* and of the FD-CA mass spectrum of *(6)*: intensities in [%].

m/e	148	146	134	132	105	98	91	84
FD-CA-MS of *(6)*	15	49	7	16	100	31	13	10
EI-MS of *(4)* [a]	11	1	8	0.5	100	3	16	0.7

[a] The abundances are normalized to $m/e = 105 \triangleq 100\%$; $m/e = 190 \triangleq 140\%$.

group for an alkane elimination does not originate from the alkylideneammonium function. On the basis of findings with alkyl-substituted methyleneammonium ions[8], a cycloalkylmethyleneammonium structure is postulated for the ions formed in the alkane elimination. While alkane eliminations under EI conditions are only observed to a small extent—if at all—as secondary fragmentations of alkylamines, they occur as collision-induced main fragmentations in field desorbed alkylideneammonium ions. Furthermore, alkane eliminations are also recorded as collision induced main fragmentation reactions in other "closed shell" ions, *e.g.* in quaternary ammonium ions[4,9a] and in the protonated amines[9b] accessible by chemical ionization.

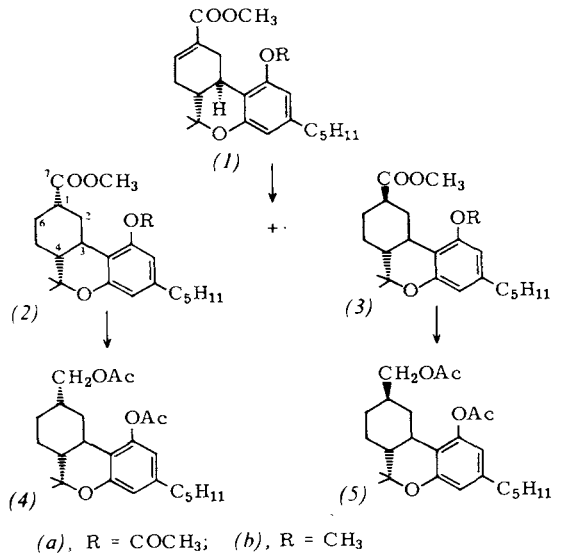
Received: October 3, 1979 [Z 493 IE]
revised: April 24, 1980
German version: Angew. Chem. *92*, 548 (1980)

[1] a) *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry. Wiley, New York 1976; b) *R. Merényi* in [1a], Part 1, p. 23.
[2] *H. J. Veith*, Org. Mass Spectrom. *11*, 629 (1976).
[3] a) *K. Levsen, H. Schwarz*, Angew. Chem. *88*, 589 (1976); Angew. Chem. Int. Ed. Engl. *15*, 509 (1976); *K. Levsen:* Fundamental Aspects of Organic Mass Spectrometry. Verlag Chemie, Weinheim 1978.
[4] *M. Fischer, H. J. Veith*, Helv. Chim. Acta *61*, 1038 (1978).
[5] The methyleneammonium salts are obtained by condensation of the corresponding *sec*-ammonium tetrafluoroborates with gaseous formaldehyde; for the preparation of *N,N*-dimethylbenzylideneammonium tetrafluoroborate see: *T. R. Keenan, N. J. Leonard*, J. Am. Chem. Soc. *93*, 6576 (1971); the preparation of *N,N*-dimethylaminotropylium tetrafluoroborate: *E. Haug, B. Föhlisch*, Chem. Ber. *104*, 2338 (1971).
[6] a) *W. J. Richter, W. Vetter*, Org. Mass Spectrom. *2*, 781 (1969); b) *P. A. Weibel, M. Hesse*, Helv. Chim. Acta *56*, 2460 (1973).
[7] a) *R. S. Gohlke, F. W. McLafferty*, Anal. Chem. *34*, 1281 (1962); b) *C. Djerassi, C. Fenselau*, J. Am. Chem. Soc. *87*, 5752 (1965).
[8] *H. J. Meyer*, Staatsexamensarbeit, Technische Hochschule Darmstadt 1979; *H. J. Veith*, unpublished.
[9] a) *H. H. Gierlich, F. W. Röllgen, F. Borchers, K. Levsen*, Org. Mass Spectrom. *12*, 387 (1977); b) *M. L. Sigsby, R. J. Day, R. G. Cooks, ibid. 14*, 556 (1979).

Base-Catalyzed Conversion of an Equatorial into an Axial Methoxycarbonyl Group Due to a 1,5-Long-Range Substituent Effect[**]

By *Raphael Mechoulam, Naftali Lander, Ilana Tamir, Zvi Ben-Zvi,* and *Yosef Kimmel*[*]

In connection with a structure/activity relationship study we needed the two isomeric diacetates *(4)* and *(5)* of 7-hydroxy-1,2,3,4,5,6-hexahydrocannabinol. They were prepared by catalytic reduction of *O*-acetyl-2,3,4,5-tetrahydrocannabinol-7-oic acid methyl ester *(1a)*[1] to the hexahydro derivatives *(2a)* and *(3a)*, which were separated by chromatography and further reduced by $LiAlH_4$ to the alcohols which on acetylation gave *(4)* and *(5)*[2]. The ethers *(2b)* and *(3b)* were prepared by hydrogenation from *(1b)*[3]. The ether *(2b)* was also prepared from the acetate *(2a)* by standard methods.



(a), R = $COCH_3$; *(b)*, R = CH_3

The esters *(2a)* and *(3a)* were separately boiled for 16 h with dry sodium methoxide in dry benzene, and the products were acetylated. We were surprised to establish that the equatorial ester *(3a)* was converted into the axial ester *(2a)*, while the latter remained unchanged under these conditions. (The stereochemical assignments are based on data given in Table 1.)

Table 1. Selected NMR data of compounds *(2a)*, *(2b)*, *(3a)*, *(3b)*, *(4)*, and *(5)* (δ values, cf. [4—6]) [a].

Cpd.	^{13}C-NMR	^{1}H-NMR			
	C-7	H-1	H-2 (eq)	H-3	H-7
(2a)	174.135 (ax)		3.18	1.77	
(2b)			3.52	1.76	
(3a)	175.496 (eq)		2.97	1.94	
(3b)			3.31	1.93	
(4)	65.535 (ax)	2.15 [b]			4.17 [c]
(5)	68.385 (eq)	1.89 [b]			3.92 [c]

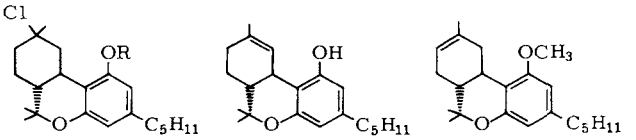
[a] 15.08 MHz ^{13}C-NMR, TMS standard; 270 MHz ^{1}H-NMR, in $CDCl_3$. [b] Determined after irradiation at the resonance frequency of the protons H-1 (in *(4)*) and H-1 (in *(5)*). [c] Octet which simplifies to a quartet with typical AB pattern on irradiation at $\delta = 2.15$ and $\delta = 1.89$; $J = 10.6 \pm 0.2$ Hz.

[*] Prof. Mechoulam, Dr. N. Lander, Dr. I. Tamir, Dr. Z. Ben-Zvi, Y. Kimmel
Dept. of Natural Products, Hebrew University
Pharmacy School, Jerusalem (Israel)

[**] We thank the US National Institute of Drug Abuse for financial support.

Harvey et al.[2] have shown that the methoxycarbonyl group in *(2a)* is axial. We were able to confirm this result and to assign the configuration of C-7 for *(2a)*, *(2b)*, *(3a)*, *(3b)*, *(4)*, and *(5)* on the basis of further NMR data (Table 1). The two protons H-7 are not equivalent in *(4)* and *(5)*.

In contrast to the *O*-acetyl compound *(2a)* (with axial ester group), which does not undergo rearrangement, the corresponding *O*-methyl compound *(2b)* forms the isomer *(3b)* (with equatorial ester group) under the same basic conditions *(vide supra)*; *(3b)* is stable under these conditions. The unusual conversion of the equatorial methoxycarbonyl group in *(3a)* into an axial one in *(2a)* seems to depend on the presence of the potential phenolate ion situated five carbon atoms away from the methoxycarbonyl group.



(6), R = H
(8), R = CH_3

(7) *(9)*

Another cannabinoid reaction likewise influenced by the free phenol group is the dehydrochlorination of 1-chlorohexahydrocannabinol *(6)* by strong bases to give *(7)*[7]. With potassium *tert*-pentyl oxide the yield is essentially quantitative. However, reaction of the ether *(8)* with the same base gives exclusively *(9)*, an isomer of *(7)*.

Received: January 11, 1980 [Z 494 IE]
German version: Angew. Chem. *92*, 577 (1980)

[1] *R. Mechoulam, Z. Ben-Zvi, S. Agurell, I. M. Nilsson, J. L. G. Nilsson, H. Edery, Y. Grunfeld,* Experientia *29*, 1193 (1973).
[2] Compounds *(2a)*, *(3a)*, *(4)*, and *(5)* were independently prepared by *D. J. Harvey, B. R. Martin, W. D. M. Paton,* J. Pharm. Pharmacol. *29*, 495 (1977), from *(1a)* supplied by us.
[3] *J. L. G. Nilsson, I. M. Nilsson, S. Agurell, Z. Ben-Zvi, R. Mechoulam.* Acta Pharm. Suec. *9*, 215 (1972).
[4] *G. W. Buchanan, J. B. Stothers,* Chem. Commun. *1967*, 1250; *G. W. Buchanan, J. B. Stothers, S. T. Wu,* Can. J. Chem. *47*, 3113 (1969).
[5] *M. Gordon, S. H. Grover, J. B. Stothers,* Can. J. Chem. *51*, 2092 (1973); *J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith, J. D. Roberts,* J. Am. Chem. Soc. *92*, 7108 (1970).
[6] *H. Booth* in *J. W. Emsly, J. Feeney, L. H. Sutcliff:* Progress in N.M.R. Spectroscopy. Vol. 5. Pergamon, Oxford 1969, p. 149.
[7] *K. E. Fahrenholtz, M. Lurie, R. W. Kierstead,* J. Am. Chem. Soc. *89*, 5934 (1967), footnote 28; *R. Mechoulam, P. Braun, Y. Gaoni, ibid. 89*, 4552 (1967); *T. Petrzilka, W. Haefliger, C. Sikemeier,* Helv. Chim. Acta *52*, 719 (1969).

1,4-Dihydro-1,4-bis(dicyanomethylene)triptycenes. Synthesis and Intramolecular Charge-Transfer Interaction[**]

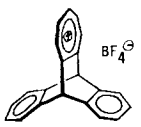
By *Kimiaki Yamamura, Tomoo Nakazawa,* and *Ichiro Murata*[*]

Recently we reported evidence for a new type of intramolecular charge-transfer (CT) interaction between the nonpa-

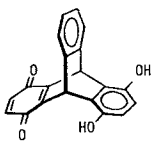
[*] Prof. Dr. K. Yamamura
Department of Chemistry, College of General Education
Kobe University, Nada-ku, Kobe 657 (Japan)
Prof. Dr. T. Nakazawa, Prof. Dr. I. Murata [†]
Department of Chemistry, Faculty of Science, Osaka University, Toyonaka, Osaka 560 (Japan)
[†] Author to whom correspondence should be addressed.

[**] This work was supported by a Grant-in-Aid for Scientific Research (No. 343007) from the Ministry of Education, Japan.

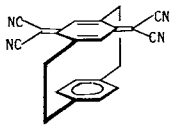
rallel donor and acceptor in a rigid spatial arrangement in *(1)*[1]. Evidence for similar CT interaction has also been reported for a triptycene quinhydrone *(2)* by *Iwamura* and *Makino*[2].



(1)



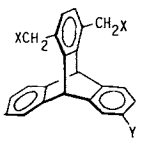
(2)



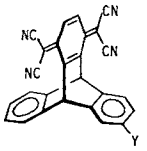
(3)

In contrast to the rich and varied chemistry and physics displayed by *inter*molecular electron donor-acceptor complexes of tetracyanoquinodimethane (TCNQ)[3], the chemistry of *intra*molecular versions of these complexes has only recently begun to develop. These studies by *Misumi et al.*[4] and *Staab et al.*[5], however, have been concerned only with the cyclophane type compounds such as *(3)* and its derivatives. We now report on the intramolecular CT interaction between TCNQ and remote benzene moieties in triptycene type compounds *(7a)* and *(7b)*.

1,4-Dimethyltriptycene *(4a)*[6], on bromination with *N*-bromosuccinimide [$(PhCO)_2O_2$, benzene, reflux 3 h] gave 1,4-bis(bromomethyl)triptycene *(5a)*[7] [colorless plates, m.p. 200—202 °C, 74%] which was cyanated with potassium cyanide in dimethyl sulfoxide [110 °C, 4 h] to the biscyanomethyl derivative *(6a)*[7] [colorless prisms, m.p. 284—286 °C, 60%]. Conversion of *(6a)* into the desired TCNQ type compound *(7a)* could be accomplished according to the well-known Wheland-Martin procedure[8] for TCNQ synthesis, *i.e. (6a)* was treated with sodium methoxide in benzene and dimethyl carbonate under reflux for 3 h and the resulting methanol was distilled off azeotropically with benzene. At room temperature cyanogen bromide was distilled with dry nitrogen into the reaction mixture which was then refluxed for 1 h. Chromatographic workup [Wako gel C-200] with a 1:1 mixture of benzene and hexane afforded *(7a)* as red microcrystals in 5% yield.



(4a), X = Y = H
(4b), X = H, Y = OCH_3
(5a), X = Br, Y = H
(5b), X = Br, Y = OCH_3
(6a), X = CN, Y = H
(6b), X = CN, Y = OCH_3



(7a), Y = H
(7b), Y = OCH_3

The methoxy derivative *(7b)* was prepared as green microcrystals starting from *(4b)*, readily available from 1,4-dimethylanthracene and 3-methoxybenzyne [generated *in situ* from 2-bromo-3-iodoanisole and magnesium].

The structures of *(7a)* and *(7b)* were confirmed primarily by their spectroscopic properties (Table 1). In the ^{1}H-NMR spectra the bridgehead protons appear at very low field [$\delta = 6.84$ for *(7a)* and 6.76 for *(7b)*] due to the close proximity of the cyano groups to these protons.

The electronic spectra of *(7a)* and *(7b)* along with those of TCNQ itself and the cyclophane *(3)* are shown in Figure 1. The new absorption bands of *(7a)* and *(7b)*, not shown by either component alone, are expectedly observed in the visible; at the same time the wavelength of the absorption maximum of *(7b)* is much longer than that of *(7a)* owing to the increased π-basicity of the anisole ring. In sharp contrast to the cyclophane *(3)*[9], these long wavelength absorption maxima

Table 1. Selected physical properties of *(7a)* and *(7b)*.

Cpd.	M.p. [°C] (dec.)	UV/VIS λ_{max} nm (log ε) [a]	^{1}H-NMR (δ-values) [b]
(7a)	>300	409 (4.66) 535 (3.40)	7.56, 7.13 (AA'BB', 8H), 7.34 (s, 2H), 6.84 (s, 2H)
(7b)	>300	411 (4.66) 584 (3.02)	7.52, 7.12 (AA'BB', 4H), 7.40 (d, 1H, $J = 8.0$ Hz), 7.34 (s, 2H), 7.14 (d, 1H, $J = 2.5$ Hz), 6.76 (s, 2H), 6.60 (dd, 1H, $J = 8.0$, 2.5 Hz), 3.75 (s, 3H)

[a] In CH_2Cl_2. [b] In CD_2Cl_2 for *(7a)*, in $CDCl_3$ for *(7b)*.

of *(7a)* and *(7b)* are strongly solvent dependent and exhibit a blue shift with increasing polarity of the solvent [*(7a)*: $\lambda_{max} = 535$ nm in CH_2Cl_2; $\lambda_{max} = 505$ nm in CH_3CN; *(7b)*: $\lambda_{max} = 584$ nm in CH_2Cl_2; $\lambda_{max} = 544$ nm in CH_3CN][10]. These observations suggested that the bands observed in the long wavelength region are to be assigned to CT transitions between benzene rings and the remote TCNQ moiety. As can be seen from Figure 1, the apparent CT interaction in *(7a)* is stronger than that of the [2.2]paracyclophane *(3)*[4a].

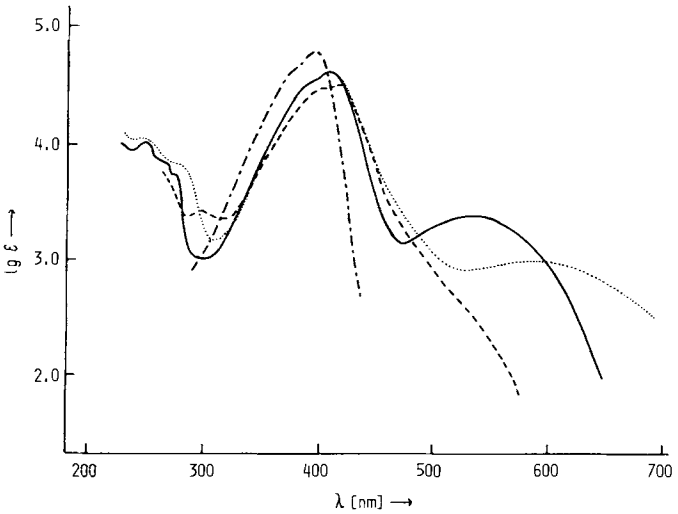


Fig. 1. UV and visible spectra of *(7a)* (—), *(7b)* (···), TCNQ (— · — · —), and *(3)* (– – –) in dichloromethane.

Thus the absorption of *(7a)* at 535 nm is almost eight times stronger than that of *(3)*. These results should provide information about the dependence of the intramolecular CT band on the mutual orientation of the donor and acceptor units.

Received: October 30, 1979 [Z 495a IE]
German version: Angew. Chem. 92, 565 (1980)

CAS Registry numbers:
(3), 62309-33-5; *(4a)*, 17417-17-3; *(4b)*, 74143-53-6; *(5a)*, 74143-54-7; *(6a)*, 74128-83-9; *(7a)*, 73524-84-2; *(7b)*, 73524-85-3; 1,4-dimethylanthracene, 781-92-0; 3-methoxydihydrobenzene, 2161-90-2; 2-bromo-3-iodoanisole, 74128-84-0; TCNQ, 1518-16-7

[1] *T. Nakazawa, I. Murata*, J. Am. Chem. Soc. 99, 1996 (1977); see also *D. N. Butler, I. Gupta*, Can. J. Chem. 56, 80 (1978); *T. Nakazawa, N. Abe, K. Kubo, I. Murata*, Tetrahedron Lett. *1979*, 4995.
[2] *H. Iwamura, K. Makino*, J. Chem. Soc. Chem. Commun. *1978*, 720.
[3] Cf. *A. F. Garito, A. J. Heeger*, Acc. Chem. Res. 7, 232 (1974).
[4] a) *M. Yoshida, H. Tatemitsu, Y. Sakata, S. Misumi*, Tetrahedron Lett. *1976*, 3821; b) *M. Yoshida, Y. Tochiaki, H. Tatemitsu, Y. Sakata, S. Misumi*, Chem. Lett. *1978*, 829; c) *H. Tatemitsu, B. Natsume, M. Yoshida, Y. Sakata, S. Misumi*, Tetrahedron Lett. *1978*, 3459.
[5] *H. A. Staab, H.-E. Henke*, Tetrahedron Lett. *1978*, 1955.
[6] *T. H. Regan, J. B. Miller*, J. Org. Chem. *32*, 2789 (1967).
[7] Elemental analyses and ^{1}H-NMR spectra are in agreement with the structures given.

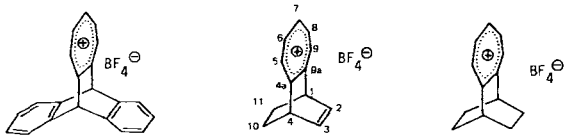
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0544 $ 02.50/0

[8] *R. C. Wheland, E. L. Martin*, J. Org. Chem. *40*, 3101 (1975).
[9] The electronic spectrum of the cyclophane *(3)* showed no solvent dependence; *S. Misumi*, personal communication.
[10] The anomalous high-energy shifts on increasing the solvent polarity for *(7a)* and *(7b)* have not been completely elucidated.

Synthesis and Intramolecular Charge-Transfer Interaction in 1,4-Dihydro-1,4-ethanobenzotropylium Tetrafluoroborate[**]

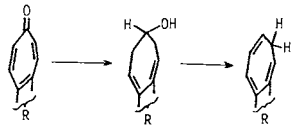
By *Tomoo Nakazawa, Yoshihide Niimoto, Keiji Kubo,* and *Ichiro Murata*[*]

We have previously reported strong intramolecular charge-transfer (CT) interactions between the tropylium unit and remote benzene rings in *(1)* despite the minimized overlap of the orbital systems of both donor and acceptor[1]. In principle, olefins should conceivably be able to replace the aromatic hydrocarbon moiety as donor. Thus, the title compound *(2a)* seems to be a reasonable candidate for examination of intramolecular remote π-π interaction. This communication describes the synthesis and properties of *(2a)* together with those of the dihydro analog *(2b)* as a reference compound.



(1) *(2a)* *(2b)*

Reduction of the bridged tropone *(3a)*[2] [$NaBH_4$ in aq. CH_3OH, at room temp.] gave the dienol *(4a)*[3], colorless needles, m.p. 90.5—91.5 °C, in 65% yield. Compound *(4a)* was converted into its mesylate [CH_3SO_2Cl and Et_3N in CH_2Cl_2] which (without isolation) was subjected to elimination with 1,5-diazabicyclo[5.4.0]undec-5-ene in CH_2Cl_2 to give the tropylidene *(5a)*[3] in 77% yield. Subsequent hydride abstraction with trityl tetrafluoroborate afforded, in 57% yield, the salt *(2a)*[3] as colorless needles, m.p. 116—117 °C (dec.). The dihydro derivative *(2b)*[3], colorless leaflets, m.p. 130.5 °C (dec.), was prepared in the same manner starting from *(3b)*[2].



(3) *(4)* *(5)*

a, R =  *b*, R = 

The structural assignment of *(2a)* and *(2b)* was based on spectral data (Table 1). As a consequence of the strong interaction in an excited state, *(2a)* exhibits characteristic absorptions, absent from the saturated reference compound *(2b)*[4] (Fig. 1). The spectrum of *(2a)* in acetonitrile exhibits *inter alia* a new absorption maximum at 325 nm which is shifted to 334 nm upon changing the solvent to less polar dichloromethane[5], suggesting a CT interaction between the tropylium ring and the remote ethylene π-system[6].

In order to examine the effect of the electronic interaction on the ground state stability of the tropylium unit we have determined pK_{R^+} and the reduction potentials of *(2a)* and *(2b)* which are also shown in Table 1. The tropylium is con-

Table 1. Comparison of physical properties of *(2a)* and *(2b)* with those of tropylium tetrafluoroborate.

Cpd.	UV λ_{max} [nm] (log ε) in CH_2Cl_2	UV λ_{max} [nm] (log ε) in CH_3CN	^{1}H-NMR in CD_2Cl_2 δ values	^{13}C-NMR in CD_3CN δ values	pK_{R^+} [e]	$E_{1/2}$ [V *vs* SCE] [f]
(2a)	236 (4.58)	230.7 (4.65)	1.55—2.05 (m, H-10, 11)	24.0 (C-10, 11)	8.4_7	-0.44_1
	279.4 (3.78)	276 (3.77)	4.80 (m, H-1, 4)	48.4 (C-1, 4)		
	334 (3.14)	325 (3.15)	6.76 (m, H-2, 3)	134.9 (C-2, 3)		
			9.06 (m, $C_7H_5^{\oplus}$)	174.8 (C-4a, 9a)		
				149.5 (C-5, 9)		
				152.5 (C-6, 8)		
				150.8 (C-7)		
(2b)	230.3 (4.57)	225 (4.64)	1.41—1.66 (m, H-2, 3, 10, 11 syn)	24.5 (C-2, 3, 10, 11)	8.8_2	-0.45_5
	285 (3.70)	284 (3.68)	2.06—2.30 (m, H-2, 3, 10, 11 anti)	42.5 (C-1, 4)		
				176.6 (C-4a, 9a)		
	300 (3.66)	296.5 (3.64) sh	3.82 (m, H-1, 4)	151.5 (C-5, 9)		
			9.04 (m, $C_7H_5^{\oplus}$)	152.2 (C-6, 8)		
				151.2 (C-7) [c]		
Tropylium $BF_4^{\ominus}$	217		9.30 in CH_3CN [b]	155.4 [d]	4.7_0	-0.24_8
	280 [a]					

[a] *J. Feitlson*, J. Chem. Phys. *43*, 2511 (1965); *A. Julg*, J. Chim. Phys. *62*, 1372 (1965). [b] *G. Fraenkel, R. E. Carter, A. McLachlan, J. J. Richards*, J. Am. Chem. Soc. *82*, 5846 (1960); *K. M. Harmon, A. B. Harmon, B. C. Thompson, ibid. 89*, 5309 (1967); *R. W. Hurray, M. L. Kaplan*, Tetrahedron Lett. *1967*, 1307. [c] *K. Okamoto*, unpublished data. We thank Prof. *K. Okamoto* for informing us of his data. [d] *H. Spiesecke, W. G. Schneider*, Tetrahedron Lett. *1961*, 468. [e] Measured spectrophotometrically in 20% aq. CH_3CN. [f] Measured in CH_3CN by polarography using tetraethylammonium perchlorate as supporting electrolyte at 25 °C.

[*] Prof. Dr. T. Nakazawa, Y. Niimoto, K. Kubo, Prof. Dr. I. Murata [*]
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)
[*] Author to whom correspondence should be addressed.

[**] This work was supported in part by a Grant-in-Aid for Scientific Research (No. 343007) from the Ministry of Education, Japan. We thank Prof. *S. Ikeda, T. Ozeki* and *K. Yokoi* of this department for measurement of the reduction potentials.

siderably more stable in *(2a)* and *(2b)*, corresponding to the increase in reduction potentials (decrease in electron affinity) when compared with the parent tropylium ion. The remarkably high pK_{R^+} values and reduction potentials of *(2a)* and *(2b)* appear to be due to an electron donating inductive effect of the bridging alkyl group[7]. At first glance, the apparent CT interaction observed in the UV spectrum of *(2a)* would seem to stabilize the tropylium unit. Interestingly, however,

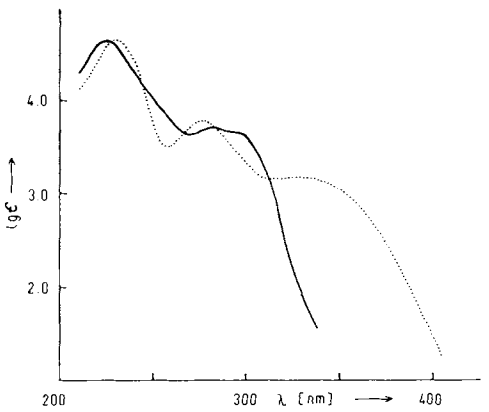


Fig. 1. UV spectra of *(2a)* (····) and *(2b)* (—) in CH_3CN.

the pK_{R^+} value of *(2a)* is found to be less than that of *(2b)*, albeit by only 0.35 pK units. This trend is also reflected in the slight decrease in the reduction potential of *(2a)* as compared with that of *(2b)*[8]. This indicates that the CT interaction between the tropylium ring and the remote ethylene π-system is more favorable in the excited state than in the ground state of *(2a)*.

Received: April 15, 1980 [Z 495b IE]
German version: Angew. Chem. *92*, 566 (1980)

CAS Registry numbers:
(2a), 73701-19-6; *(2b)*, 73701-21-0; *(3a)*, 67074-21-9; *(3b)*, 67074-23-1; *(4a)*, 74128-85-1; *(4a)*·mesylate, 74128-86-2; *(5a)*, 74128-87-3; tropylium tetrafluoroborate, 27081-10-3

[1] *T. Nakazawa, I. Murata*, J. Am. Chem. Soc. *99*, 1996 (1977); see also *D. N. Butler, I. Gupta*, Can. J. Chem. *56*, 80 (1978); *T. Nakazawa, N. Abe, K. Kubo, I. Murata*, Tetrahedron Lett. *1979*, 4995.

[2] *T. Nakazawa, Y. Niimoto, I. Murata*, Tetrahedron Lett. *1978*, 569.

[3] Elemental analyses and ^{1}H-NMR spectra are in agreement with the structures given.

[4] *G. Hohlneicher, R. Kiessling, H. C. Jutz, P. A. Straub*, Ber. Bunsenges. Phys. Chem. *70*, 60 (1966); *P. Schuster, D. Vedrilla, O. E. Polansky*, Monatsh. Chem. *100*, 1 (1969).

[5] *E. Kosower*, J. Am. Chem. Soc. *80*, 3253 (1958); *K. Dimroth, C. Reichardt, T. Siepmann, F. Bohlmann*, Justus Liebigs Ann. Chem. *661*, 1 (1963); *C. Reichardt, K. Dimroth*, Fortschr. Chem. Forsch. *11*, 1 (1968); *M. Feldmann, B. G. Graves*, J. Phys. Chem. *70*, 955 (1966).

[6] The CT-band of *(2a)* is also observed in its MCD spectrum and is confirmed by modified CNDO/2 calculations. *M. Hatano* and *A. Tajiri*, to be published.

[7] It has been observed that the reduction potential of the tropylium ion increases with increasing methyl substitution; see *K. Takeuchi, Y. Yokomichi, T. Kurosaki, Y. Kimura, K. Komatsu, K. Okamoto*, Abstracts M33, The 29th Symposium on Organic Reaction Mechanisms, Osaka, Japan, October 4–7, 1978.

[8] This fact could be interpreted by considering the difference in inductive effect between the ethano- and the etheno-bridges of *(2b)* and *(2a)*, respectively. The stabilization of the tropylium unit *(2a)* by electron supply from the remote ethylene π-orbital would not be significant in the ground state of this molecule. Cf. *H. Iwamura, K. Makino*, J. Chem. Soc. Chem. Commun. *1978*, 720; *K. Yamamura, T. Nakazawa, I. Murata*, Angew. Chem. *92*, 565 (1980); Angew. Chem. Int. Ed. Engl. *19*, 543 (1980).

L-Gulose or D-*gluco*-Hexodialdose from D-Glucurono-6,3-lactone by Controlled Reductions[**]

By *Wilhelm V. Dahlhoff, Peter Idelmann*, and *Roland Köster*[*]

The reduction of *O*-ethylboron-protected -onic and uronic acid lactones with ethyldiboranes(6)[***] is well suited for the preparation of aldoses and dialdoses. In some cases, by incorporating monofunctional *O*-(diethylboryl)-[1a,2] or difunctional *O*-(ethylboranediyl)-[1d] protecting groups, the reactions can also be directed, so that various pure end products become accessible in high yield from the same starting material.

We obtained highly pure L-gulose *(3)* by reduction of the free β-D-glucurono-6,3-lactone *(1)* with ethyl-hydro-boranes(3)[***]. The lactone *(1)* is converted in a single step at ≈50 °C with diethyl-hydro-borane(3) (molar ration ≤1:5) into an *O*-ethylboron-protected α/β-gulofuranose *(2)*, from which the anhydrous solid L-gulose *(3)* can be liberated without loss by treatment with methanol/ethylene glycol (Scheme 1).

However, if the non-reduced compound *(4)* is initially prepared from *(1)* with the aid of various *O*-(ethylboranediyl) reagents *e.g.* triethylboroxin[1d] or triethylborane/ethyldiboranes(6)[1c] the treatment of the product with ethyldiboranes(6) gives an essentially quantitative yield of an equimolar mixture of ethylboron-protected D-*gluco*-hexodialdose *(5)* and D-glucose *(6)*. Compound *(5)* can easily be separated completely from *(6)* and transformed quantitatively by methanol into pure anhydrous D-*gluco*-hexodialdose *(7)* (Scheme 1).

The chemical analyses [C, H, B values, ethane number[1a], hydride number[1d]] and spectroscopic data [IR, MS, ^{1}H-, ^{13}C-NMR] of *(2)* to *(7)* confirm their composition, structure, and purity.

Hitherto, L-gulose *(3)* was known only as a hydrate syrup; the older method of preparation from *(1)* led to impure *(3)* in *ca.* 10% yield. Likewise, *(7)* was accessible from *(1)* in only moderate yields (≲22%)[3].—With the new *O*-ethylborane method, *(3)*[3,6] and *(7)*[3,4] can be prepared in pure form considerably more simply and in better yields than previously.

Procedure

(2): To a solution of ethyldiboranes(6) (23.4 g, 335 mmol >BH, 14‰ $H^{\ominus}$) in tetrahydrofuran heated to 45 °C is added 11.3 g (64.2 mmol) of *(1)* within 3.5 h from a swivel-mounted side arm. An increase in temperature (to 50—60 °C; exothermic reaction!) is accompanied by evolution of H_2 (≈4.2 Nl). Ethene is passed (≈30 min) into the colorless, clear solution (trapping by excess >BH) at ≈50 °C. On evaporating the solution down at ≤80 °C (bath)/10^{-1} torr, 20.4 g (98%) of *(2)* is obtained as a colorless syrup; $[\alpha]_D^{20} = +24.7$ (c=7.4, $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ=5.65 ($J_{1,2}$<1 Hz; H^1, β-*(2)*), 5.74 ($J_{1,2}$=5 Hz (H^1, α-*(2)*); α:β≈38:62 (after 1 h).

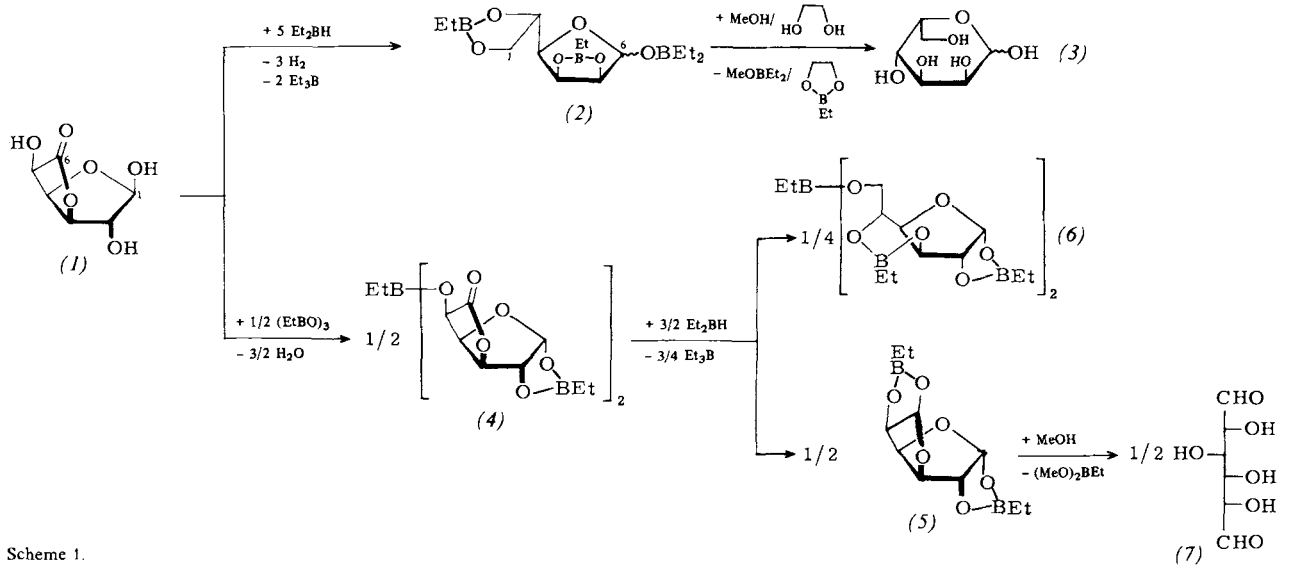
(3): Methanol (≈100 ml) is added dropwise to 12.9 g (39.8 mmol) of *(2)* with continuous removal of $MeOBEt_2$/MeOH from the mixture by distillation. After subsequent further evaporation at 10^{-1} torr the residue is treated with 15 ml of 1,2-ethanediol and once again evaporated down (≤80 °C (bath)/10^{-3} torr). The boron-free residue is treated with

[*] Prof. Dr. R. Köster, Dr. W. V. Dahlhoff, Dipl.-Chem. P. Idelmann
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim an der Ruhr (Germany)

[**] Organoboron Monosaccharides. Part 6 (Part of a planned dissertation by *P. Idelmann*, Universität Bochum, 1980).—Parts 1—5: [1a—e].

[***] Ethyldiboranes(6) or ethyl-hydro-boranes(3) mentioned in the text and the Et_3BH denoted in Scheme 1 are actually equilibrium mixtures with the overall composition of "tetraethyldiborane(6)"; cf. *R. Köster* and P. Binger, Inorg. Synth. XV, 141 (1974).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0546 $ 02.50/0



Scheme 1.

≈ 20 ml ethanol and then distilled at 10^{-3} torr to remove all volatiles. The glassy *(3)* thus obtained (7.2 g, 100%) can be ground to a white powder, which softens at 60—80 °C and gives a clear melt at 80 °C: $[\alpha]_D^{22} = +23.3$ ($c = 1.6$, H_2O); calc. and obs. 2.8% $H^{\oplus}$[1a]. Solid *(3)* can be precipitated from ethanol with diethyl ether.—Hitherto, *(3)* has only been isolated as a syrup: $[\alpha]_D^{23} = +20$ ($c = 13.6$, H_2O)[5]; syrupy *(3)* contains 1.2 mol of H_2O per mol (determination of ethane number[1a]).

(7): Triethylboroxine (10.6 g, 63.1 mmol) is added dropwise to a stirred suspension of *(1)* (10 g, 56.8 mmol) in boiling benzene (150 ml) such that benzene/water can be continuously removed by azeotropic distillation. Finally, all readily volatile materials are removed at 10^{-2} torr. A solution of the syrupy residue [*(4)*] in toluene (50 ml) is then treated with 4.7 g (88.8 mmol ≙ BH) ethyldiboranes(6) (with 18.9‰ $H^{\ominus}$) and the mixture stirred for 24 h. After removal of all readily volatile materials (≤ 105 °C (bath)/10^{-3} torr), distillation of the partially crystalline residue [*(5)*, *(6)*] affords 7.1 g (49%) of *(5)*; b.p. 97 °C/10^{-3} torr, m.p. 85 °C; $[\alpha]_D^{22} = -13.6$ ($c = 7.1$, CCl_4).—After dissolution of *(5)* in 40 ml of heptane and addition of 30 ml of methanol, the $(MeO_2)BEt$/MeOH is azeotropically distilled off during simultaneous dropwise addition of methanol (≈ 150 ml). Concentration at 12 torr affords 4.9 g (49%) of *(7)* as anhydrous syrup, which precipitates as colorless crystals in boiling THF; m.p. 155 °C (dec.); $[\alpha]_D^{22} = +48.4$ ($c = 2.6$, H_2O).—*(7)* could hitherto not be obtained by dehydration of the monohydrate (m.p. < 100 °C); $[\alpha]_D^{22} = +49.9$ (calc.)[3].

Received: December 21, 1979 [Z 496a IE]
supplemented: April 30, 1980
German version: Angew. Chem. 92, 552 (1980)

CAS Registry numbers:
(1), 18281-92-0; *(2)*, 74143-55-8; *(3)*, 6027-89-0; *(4)*, 74143-56-9; *(5)*, 74143-57-0; *(6)*, 74143-58-1; *(7)*, 74183-86-1

[1] a) *R. Köster, K.-L. Amen, W. V. Dahlhoff*, Justus Liebigs Ann. Chem. *1975*, 752; b) *R. Köster, W. V. Dahlhoff, ibid. 1976*, 1925; c) ACS Symp. Ser. *39*, 1 (1977); d) *W. V. Dahlhoff, R. Köster*, J. Org. Chem. *42*, 3151 (1977); e) *R. Köster*, Pure Appl. Chem. *49*, 765 (1977).

[2] *R. Köster, K.-L. Amen, H. Bellut, W. Fenzl*, Angew. Chem. *83*, 805 (1971); Angew. Chem. Int. Ed. Engl. *10*, 748 (1971).

[3] *F. G. Fischer, H. Schmidt*, Chem. Ber. *93*, 658 (1960).

[4] *K. Dax, H. Weidmann*, Adv. Carbohydr. Chem. Biochem. *33*, 189 (1976).

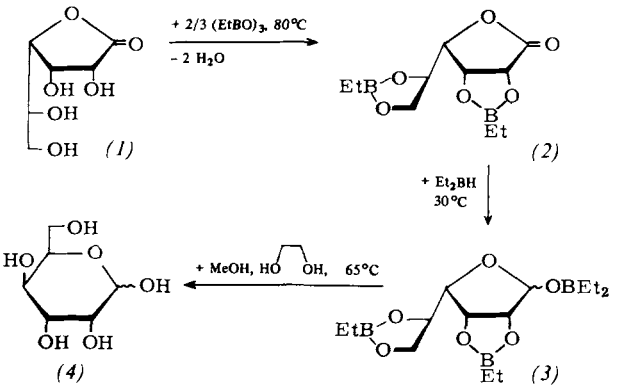
[5] *R. L. Whistler, J. N. BeMiller*, Methods Carbohydr. Chem. *1*, 137 (1962).

[6] *K. Heyns, M. Beck*, Chem. Ber. *91*, 1720 (1958); *D. K. Minster, S. M. Hecht*, J. Org. Chem. *43*, 3987 (1978); *M. E. Evans, F. W. Parrish*, Carbohydr. Res. *28*, 359 (1973).

Pure D-Gulose from D-Gulono-1,4-lactone[**]

By *Roland Köster, Peter Idelmann*, and *Wilhelm V. Dahlhoff*[*]

Like the carboxylic acid group of the *O*-ethylboron-protected D-glucurono-6,3-lactone[1], the 2,3:5,6-bis-*O*-(ethylboranediyl) derivative *(2)* of D-gulono-1,4-lactone *(1)* can also be partially reduced with ethyldiboranes(6)[***] to the aldehyde stage *(3)*. Removal of the protecting groups from *(3)* by reaction with methanol and then with glycol afforded, for the first time, pure D-gulose *(4)* from *(1)* in quantitative overall yield.



Chemical analyses [C, H, B values; B_C value[2a]; ethane number[2b]; hydride number[2c]] and spectroscopic data [IR, MS, ^1H-, ^{13}C- and ^{11}B-NMR] confirmed the composition and structure of *(2)*, *(3)* and *(4)*. Like *(4)*, *(2)* and *(3)* can also be prepared in pure form.

Previously, D-gulose *(4)* could be obtained from *(1)* or *via (1)* by reduction [*e.g.* with Na-amalgam[3]; $NaBH_4$[4]; disiamylborane[5]] only as aqueous syrup in yields of up to 50%, or contaminated with *(1)* and L-glucitol in yields of at most 80%[4]. On using tetra-*O*-benzoyl-D-gulono-1,4-lactone as starting material no *(4)* could be isolated after reduction with

[*] Prof. Dr. R. Köster, Dipl.-Chem. P. Idelmann, Dr. W. V. Dahlhoff
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim an der Ruhr (Germany)

[**] Organoboron Monosaccharides, Part 7 (Part of a planned dissertation by *P. Idelmann*, Universität Bochum, 1980).—Part 6: [1].

[***] Ethyldiboranes(6) or ethyl-hydro-boranes(3) mentioned in the text and the Et_2BH denoted in the Scheme are actually equilibrium mixtures with the overall composition of "tetraethyldiborane(6)"; cf. *R. Köster* and *P. Binger*, Inorg. Synth. XV, 141 (1974).

disiamyl-hydro-borane *(3)*[5]. The five-step synthesis of *(4)* from D-glucose is also less productive[6].

The efficiency of this new method of synthesizing *(4)* from *(1)* might be attributed to the combined reaction of *O*-ethylboranediyl protecting groups on sp^2-hybridized atoms and the ethyl-hydro-borane[***] reagent. *O*-Ethylboranediyl moieties are more easily removed than the usual difunctional protecting groups. This and the anhydrous working conditions offer additional advantages.

Experimental

(2): Triethylboroxine (43.7 g, 260.1 mmol) is added dropwise within ≈4 h at ≈90 °C (bath) to a solution of *(1)* (58 g, 325.6 mmol) in benzene (150 ml) and benzene/water azeotrope is continuously removed by distillation in a stream of inert gas (11.8 ml H_2O). All volatiles are then removed at 60 °C (bath)/10^{-3} torr. 82.8 g (100%) of white, crystalline *(2)* is obtained in >99% (GC) purity; m.p. 81 °C; $[\alpha]_D^{20} = +119.7$ ($c = 3.9$, CCl_4).

(3): Ethyldiboranes(6) [16.66‰ $H^{\ominus}$] (12.5 g, 208.3 mmol >BH) are added dropwise in 5—10 min to a stirred solution of *(2)* (46.7 g, 183.9 mmol) in toluene (150 ml) at 30—40 °C (cooling bath!). Stirring is continued for 1—2 h at 30—35 °C and ethene is then passed through the solution for 1.5 h. After removal of all volatiles *in vacuo*, 59.6 g (≈100%) of colorless, viscous *(3)* is obtained; $[\alpha]_D^{21} = -29.4$ ($c = 6.8$, CCl_4).

(4): Methanol (150 ml) is added dropwise to a solution of *(3)* (59.9 g, 183.8 mmol) in boiling methanol (50 ml) and at the same time all readily volatile compounds are removed by distillation. After removal of solvent *in vacuo* the residue is treated with 1,2-ethanediol (50 ml) and the mixture stirred for ≈1 h at 75 °C (bath) and finally distilled at 80 °C (bath)/10^{-3} torr. The glycol procedure is repeated. After addition of ethanol (50 ml) the solution is evaporated (10^{-3} torr) to complete dryness, giving 33.2 g (≈100%) of glassy, solid *(4)*, which can be crushed to a highly hygroscopic powder; flow point ≈60 °C, $[\alpha]_D^{22} = -23.2$ ($c = 2.1$, H_2O)[7].

Received: December 21, 1979 [Z 496b IE]
supplemented: April 30, 1980
German version: Angew. Chem. *92*, 553 (1980)

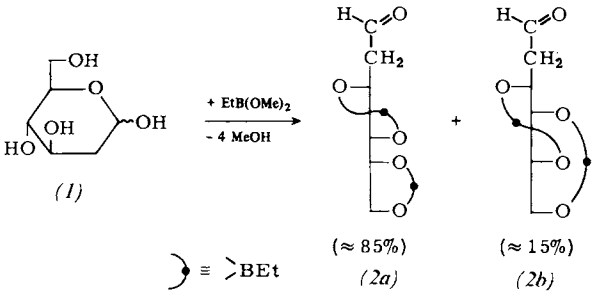
[1] *W. V. Dahlhoff, P. Idelmann, R. Köster*, Angew. Chem. *92*, 552 (1980); Angew. Chem. Int. Ed. Engl. *19*, 546 (1980).
[2] a) *R. Köster, Y. Morita*, Justus Liebigs Ann. Chem. *704*, 70 (1965); b) *R. Köster, K.-L. Amen, W. V. Dahlhoff, ibid. 1975*, 752; c) *W. V. Dahlhoff, R. Köster*, J. Org. Chem. *42*, 3151 (1977).
[3] *H. S. Isbell*, Methods Carbohydr. Chem. *1*, 135 (1962).
[4] *R. K. Hulyalkar*, Can. J. Chem. *44*, 1594 (1966); *L. M. Lerner, B. D. Kohn, P. Kohn*, J. Org. Chem. *33*, 1780 (1968).
[5] *P. Kohn, R. H. Samaratino, L. M. Lerner*, J. Am. Chem. Soc. *87*, 5475 (1965).
[6] *W. Meyer zu Reckendorf*, Angew. Chem. *79*, 151 (1967); Angew. Chem. Int. Ed. Engl. *6*, 177 (1967); Chem. Ber. *102*, 1071 (1969).
[7] $[\alpha]_D = -20.4$; cf. *J. J. Blanksma, W. A. Van Ekenstein*, Recl. Trav. Chim. Pays Bas *27*, 1 (1908); Chem. Zentrbl. II, 1583 (1908); no $[\alpha]_D$ value is given for D-gulose in the later literature [3—6].

Simple New Method for the Synthesis of 2-Deoxy-*aldehydo*-hexoses[**]

By *Wilhelm V. Dahlhoff* and *Roland Köster*[*]

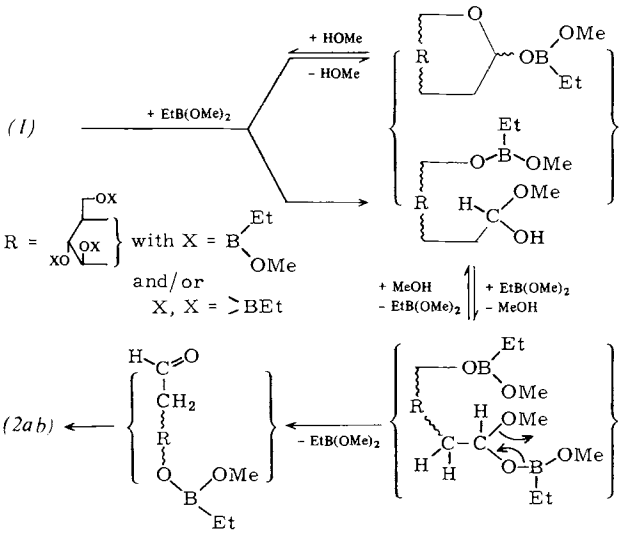
Open-chain *aldehydo*-hexoses were previously accessible from monosaccharides only *via* particularly reactive intermediates—primarily *via* the dialkyldithioacetals with mercury(II) chloride[1]. We have now discovered a preparatively very simple, novel, and direct route for the synthesis of 2-deoxy-*aldehydo*-hexoses from the free monosaccharides.

2-Deoxy-D-*arabino*-hexose [2-deoxy-D-glucose] *(1)* reacts with ethyl(dimethoxy)borane at room temperature in almost quantitative yield to give a mixture of ≈85% 2-deoxy-3,4:5,6-di-*O*-(ethylboranediyl)-*aldehydo*-D-*arabino*-hexose *(2a)* and ≈15% of the 3,5:4,6-isomer *(2b)*.



Reaction of *(1)* with ethyl(dimethoxy)borane leads initially to acetals of the methyl 2-deoxy-D-*arabino*-hexoside with intra- and intermolecular *O*-ethylboranediyl linkages. On equilibration, ethyl(dimethoxy)borane is already eliminated from these acetals at room temperature with formation of *(2b)*. Complete elimination can be achieved by removal of the borane reagent in a vacuum.

The intermediary open-chain methylacetals can be detected by ^{1}H-NMR spectroscopy by their H^1 and O^1CH_3 signals at $\delta = 4.93$ and 3.45, respectively. The characteristic ^{1}H-NMR signals of *(2ab)* are first observed as a result of elimination of $EtB(OMe)_2$ from C^1-atom during the reaction (see Table 1). No detectable amounts of *(2)* are formed on reaction of *(1)* with triethylboroxine[3] or with 1,2-diethyl-1,2-dipivaloyldiboroxane[2,3]. Thus, ethyl(dimethoxy)borane has a specific directing influence on the reaction.



The mixture *(2ab)*, which is distillable without decomposition *in vacuo*, can be stored for weeks at ≈0 °C. *(2ab)* is thus well suited for syntheses with participation of the free aldehyde function. The isomerism has no influence on most of the reactions. The protective groups can readily be removed with methanol.

Reaction of 2-deoxy-D-*lyxo*-hexose (2-deoxy-D-galactose) *(3)* with ethyl(dimethoxy)borane at room temperature leads

[*] Prof. Dr. R. Köster, Dr. W. V. Dahlhoff
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim an der Ruhr (Germany)

[**] Organoboron Monosaccharides, Part 8.—Part 7: *R. Köster, P. Idelmann, W. V. Dahlhoff*, Angew. Chem. *92*, 553 (1980); Angew. Chem. Int. Ed. Engl. *19*, 547 (1980).

initially to a mixture consisting of at least three isomeric open-chain methyl 2-deoxy-di-*O*-(ethylboranediyl)-D-*lyxo*-hexosides *(4a—c)* and only a small amount (≤10%) of 2-deoxy-di-*O*-(ethylboranediyl)-*aldehydo*-D-*lyxo*-hexoses *(5ab)*. Above ≈100 °C the ^{1}H-NMR signals for *(4a—c)* [δ = 4.9 and 5.1 (H^1), 3.50, 3.46 and 3.43 (O^1CH_3)] disappear.

(5ab) (see Table 1) can be distilled as a colorless, mobile liquid (b.p. 77 °C/10^{-3} torr), which becomes highly viscous at room temperature and finally solidifies as glassy oligomer *(6)*. On heating, *(6)* becomes mobile again and can be distilled *in vacuo* as a mixture of ≥80% 2-deoxy-3,5:4,6-di-*O*-

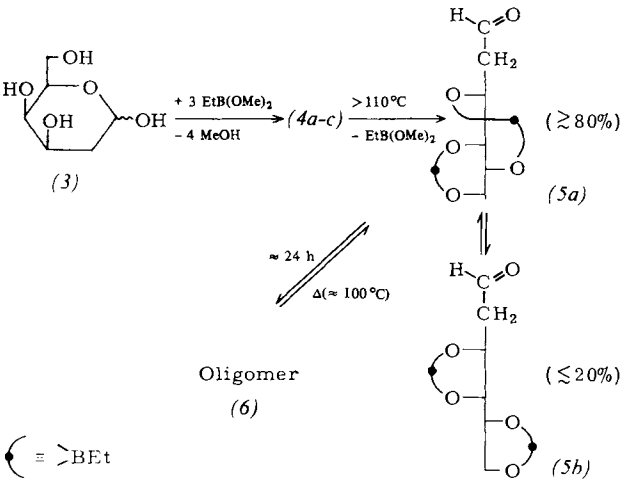


Table 1. Some spectroscopic data of the mixtures *(2ab)* and *(5ab)*.

(2ab): MS (70 eV): $m/e = 240$ ($M^{\oplus}$, B_2, <1%), 196 (B_2, 12), 141 (B_1, 65), 113 (B_1, 30), 99 (B_1, 100), 57 (B_1, 65); ^{1}H-NMR (80 MHz, $CDCl_3$): δ = 9.84 (t, $J_{1,2}$ = 1.8 Hz, H^1), 4.66 (q, $J_{2,3}$ = 6 Hz, $J_{3,4}$ = 6 Hz, H^3), 4.5—3.7 (m, H^4—H^6), 2.72 (dd, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 6 Hz, H^2), 0.9 (m, BC_2H_5); ^{11}B-NMR (neohexane): δ = 34.8 (halfwidth = 200 Hz)

(5ab): MS (70 eV): $m/e = 240$ ($M^{\oplus}$, B_2, <1%), 196 (B_2, 41), 141 (B_1, 27), 112 (B_1, 100), 99 (B_1, 75), 83 (B_1, 32), 57 (B_1, 72); ^{1}H-NMR (80 MHz, C_6D_6): δ = 9.35 (dd, $J_{1,2}$ = 2 Hz, $J_{1,2'}$ = 1.5 Hz, H^1), 4.29 (ddd, $J_{2,3}$ = 8 Hz, $J_{2',3}$ = 6 Hz, $J_{3,4}$ = 2 Hz, H^3), 3.3—3.9 (m, H^4—$H^{6'}$), 2.03 (ddd, $J_{1,2}$ = 2 Hz, $J_{2,3}$ = 8 Hz, $J_{2,2'}$ = −16.5 Hz, H^2), 1.77 (ddd, $J_{1,2}$ = 1.5 Hz, $J_{2',3}$ = 6 Hz, $J_{2,2'}$ = −16.5 Hz, $H^{2'}$), 0.95 (m, C_2H_5); ^{11}B-NMR (neohexane): δ = 31.5 (halfwidth = 200 Hz)

(ethylboranediyl)-*aldehydo*-D-*lyxo*-hexose *(5a)* and ≤20% of, presumably, the 3,4:5,6-isomer *(5b)*. As *O*-ethylboranediyl derivatives of the threitol type[4], *(5a)* and *(5b)*, in contrast to *(2a)* and *(2b)*, are in equilibrium with each other.

Experimental

(2ab): A mixture of *(1)* (5 g, 12.2 mmol) and ethyl(dimethoxy)borane (~25 ml) is heated for ≈2 h at 60—80 °C. The homogeneous mixture is finally evaporated down at 12 torr. Subsequent distillation affords 7.2 g (≈99%) *(2ab)*: b.p. ≈75 °C/10^{-3} torr; $[\alpha]_D^{20} = +14.6$ ($c = 0.7$, $CHCl_3$).

(5ab): A mixture of *(3)* (2.5 g, 15.2 mmol) and ethyl(dimethoxy)borane (10 ml) is stirred for ≈1.5 h at ≈60 °C (bath). After ≈8 min, a homogeneous phase is obtained. Removal of all readily volatile material at 12 to 10^{-3} torr and subsequent distillation of the residue (4.0 g) at 100—110 °C (bath)/10^{-3} torr for 3 h affords 3.3 g (93%) of *(5ab)*; b.p. ≈77 °C/10^{-3} torr; $[\alpha]_D^{22} = +26$ ($c = 0.7$, $CHCl_3$); 0.1 g residue.

Received: February 12, 1980 [Z 496c IE]
supplemented: April 30, 1980
German version: Angew. Chem. *92*, 553 (1980)

CAS Registry numbers:
(1), 154-17-6; *(2a)*, 74143-64-9; *(2b)*, 74143-65-0; *(3)*, 1949-89-9; *(5a)*, 74143-66-1; *(5b)*, 74143-67-2

[1] *M. L. Wolfrom, A. Thompson,* Methods Carbohydr. Chem. *2*, 427 (1963); *J. L. Barclay, A. J. Cleaver, A. B. Foster, W. G. Overend,* J. Chem. Soc. *1956*, 476; *W. Pigman, D. Horton:* Carbohydrate Chemistry and Biochemistry. 2nd edit., Vol. IA. Academic Press, New York 1972, p. 361; *J. Staněk, M. Černý, J. Kocourek, J. Pacák:* The Monosaccharides. Academic Press, New York 1963, p. 589.
[2] *R. Köster, W. V. Dahlhoff,* ACS Symp. Ser. *39*, 1 (1977).
[3] *W. V. Dahlhoff, R. Köster,* J. Org. Chem. *42*, 3151 (1977).
[4] *W. V. Dahlhoff, W. Fenzl, R. Köster,* IMEBORON IV, Salt Lake City 1979, Abstr. of Papers, p. 72.

Absolute Configuration of the Cancerostatic *S*(−)-Isophosphamide

By *Dorota A. Adamiak, Maria Gdaniec, Krzysztof Pankiewicz,* and *Wojciech J. Stec*[*]

Dedicated to Professor Jan Michalski on the occasion of his 60th birthday

Isophosphamide, 3-(2-chloroethyl)-2-[(2-chloroethyl)amino]-1,3,2-oxazaphosphorinane 2-oxide (Holoxan) *(1)*, has been found to elicit therapeutic response in human breast, ovarian and lung cancer[1]. *(1)* is chiral. In order to study the influence of configuration on the clinical significance[2] and mechanism of action of *(1)* we carried out the stereospecific synthesis of the two enantiomers[3]. In this communication we wish to describe the assignment of the absolute configuration of the levorotatory enantiomer of *(1)*, $[\alpha]_D^{20} = -39.4°$ ($c = 5.0$, MeOH). (−)-*(1)* crystallizes from diethyl ether in the orthorhombic space group $P2_12_12_1$ with $a = 5.144(1)$, $b = 12.655(3)$ and $c = 19.004(4)$ Å; $Z = 4$. The structure was solved by usual methods[4]; in the refinement the coordinates and temperature factors were varied, both for the model (x, y, z) and the enantiomorph ($\bar{x}$, $\bar{y}$, $\bar{z}$) with proper inclusion of anomalous scattering contributions from Cl and P atoms. Final weighted discrepancy indices ($R_w = [\sum w(|F_{obs}| - |F_{cal}|)^2 / \sum w|F_{obs}|^2]^{1/2}$) are 7.9% for (x, y, z) and 7.7% for ($\bar{x}$, $\bar{y}$, $\bar{z}$). On the basis of *Hamilton*'s $\mathcal{R}$-factor ratio test[5], the model (x, y, z) can be excluded at a significance level <0.005. Thus (−)-*(1)* is *S*-configurated[6] (Fig. 1).

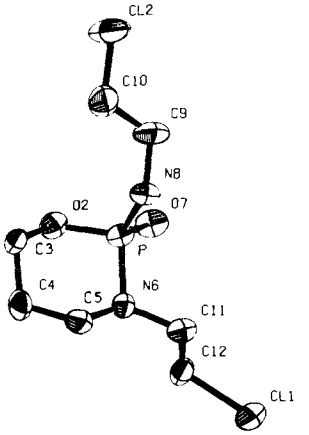


Fig. 1. Molecular structure of *S*(−)-*(1)* (ORTEP plot) showing thermal ellipsoids of the atoms at the 20% probability level.

[*] Prof. Dr. W. J. Stec [+], Dr. K. Pankiewicz
Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies
PL-90-362 Lodz (Poland)
Dr. A. D. Adamiak, Dr. M. Gdaniec
Institute of Chemistry, Adam Mickiewicz University
PL-60-780 Poznan (Poland)
[+] Author to whom correspondence should be addressed.

The six-membered ring has a chair conformation; the substituent O7 is equatorial, while in the racemate structure it is axial[7]. The P—N bonds have partial double bond character; the hybridization of N6 is found to lie between sp^2 and sp^3. The molecules in the crystal are linked *via* only one 2.79 Å-long hydrogen bond between atoms N8 and O7.

Received: December 4, 1979 [Z 497 IE]
German version: Angew. Chem. 92, 578 (1980)

CAS Registry number:
S-(1), 66849-33-0

[1] *P. J. Creaven, L. M. Allen, M. H. Cohen, R. L. Nelson*, Cancer Treat. Rep. *60*, 445 (1976); *G. Falkson, H. C. Falkson, ibid. 60*, 955 (1976).

[2] All investigations so far reported were performed with racemic *(1)* only.

[3] *R. W. Kinas, K. Pankiewicz, W. J. Stec, P. B. Farmer, A. B. Foster, M. Jarman*, Bull. Acad. Polon. Sci. Ser. Sci. Chim. *24*, 39 (1978).

[4] Syntex-P2$_1$ four-circle diffractometer with graphite monochromator, $Cu_{K\alpha}$ radiation, $\theta-2\theta$ scan, 655 reflections with $I \leq 1.96\sigma(I)$, corrections for geometric and absorption factors, solution with standard Patterson and Fourier heavy atom methods.

[5] *W. C. Hamilton*, Acta Crystallogr. *18*, 502 (1965).

[6] The absolute configuration R was assigned for (+)-*(1)* by means of its stereospecific transformation to the intermediate obtained also from *S*(−)-cyclophosphamide; *K. Pankiewicz, R. Kinas, W. J. Stec, A. B. Foster, M. Jarman, J. M. S. Van Maanen*, J. Am. Chem. Soc., in press.

[7] *H. A. Brassfield, R. A. Jacobson, J. G. Verkade*, J. Am. Chem. Soc. *97*, 4143 (1975); *A. Perales, S. Garcia-Blanco*, Acta Crystallogr. *B 33*, 1935 (1977).

Vesicles with a Monolayer, Redox-Active Membrane

By *Ehrenfried Baumgartner* and *Jürgen-Hinrich Fuhrhop*[*]

The first monolayer membranes made of ammonium amphiphiles with two charged end groups, flexible polymethylene chain, and rigid central unit were recently synthesized by *Kunitake et al.*[1]. These membranes form vesicles only on addition of large amounts of cholesterol. We now report a similar, but much simpler membrane which forms stable vesicles without additives and also contains redox-active terminal groups.

The monomethylbipyridinium ion *(1)* was prepared in 70% yield from bipyridine by reaction with dimethyl sulfate in $CHCl_3$ and treated with *N,N'*-(β-bromoethyl)dicarboxamides *(2a—c)* in *n*-butanol. The tetracations *(3a—c)* were obtained in 60—70% yield. Compound *(3a)* could be isolated as the crystalline tetrachloride; *(3b, c)* are amorphous but chromatographically homogeneous, and their spectroscopic data (quantitative UV, ^{1}H-NMR in CD_3OD, IR) are in accord with the structures given. *(3a)* and *(3b)* are readily soluble in water (≥100 mg/ml) and have not yet been further investigated. *(3c)* was only modestly soluble in water (≤1 mg/ml) and gave milky suspensions from which solids slowly deposited.

Sonification of a suspension containing about 10 mg of *(3c)*/ml at 50 °C (Ultrasonics W 18 SF, frequency 20 kHz, *ca.* 100 watt) gave clear colorless solutions in which hydrophobic dyes such as protoporphyrin dimethyl ester, magnesium protoporphyrin dipotassium salt, and magnesium octaethylporphyrin dissolved at concentrations up to about 10^{-4} M. On chromatography of such solutions, *e.g.* with the dipotassium salt on Sephadex G 25, the red dye migrates as a uniform zone. It does not migrate in alkaline solution without addition of *(3c)*. The colorless solution of *(3c)* was studied by electron microscopy without fractionation after sonification. After staining with uranyl acetate, spherical vesicles having typical diameters of about 100—600 Å could be detected at 40000× magnification.

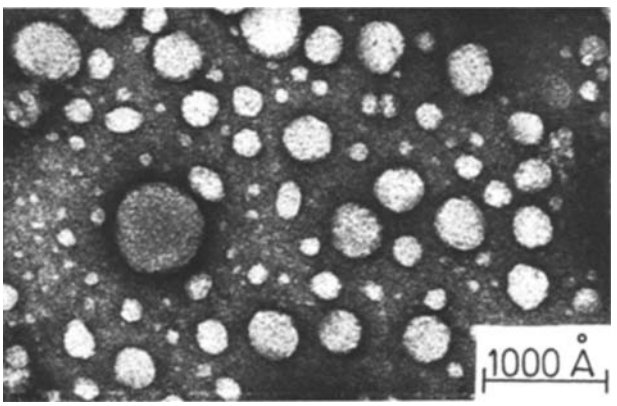
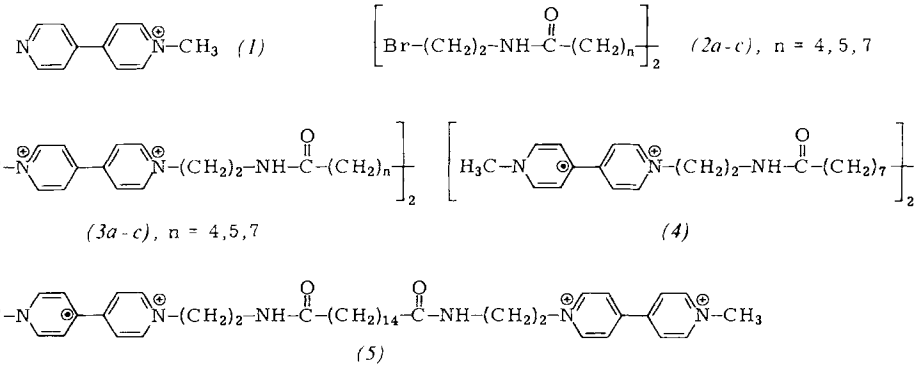


Fig. 1. Electron micrograph of the vesicles (stained with uranyl acetate).

These vesicles are relative large. Comparison with analogous dimolecular membrane particles of lecithin[2] and of synthetic material[3] suggests that the vesicles contain several membranes. The monolayer cholesterol-containing membrane obtained by *Kunitake*, however, forms single-walled vesicles[1]. We could answer this structural question by a simple chemical experiment, *viz.* by reducing an aqueous solution of *(3c)* with sodium dithionite before and after sonification, to give the viologen radical *(4)*.

Since the dithionite ions cannot penetrate the hydrophobic vesicle membrane, only the bipyridinium layer facing the external aqueous medium is reduced. We found that in the case of the clear vesicle solution exactly 50% of the bipyridinium units are reduced [formation of *(5)*], while 100% reduction to *(4)* is observed in the emulsion. Deviations from the expected extinction[4] did not exceed ±5% in several independent experiments. Hence it can be concluded that the vesicles described are single walled, for only 25% reduction of the bipyridinium "heads" would be possible for double-walled vesicles. Attempts to reduce the internal layer of the vesicles by



[*] Prof. Dr. J.-H. Fuhrhop, Dipl.-Chem. E. Baumgartner
Institut für Organische Chemie der Freien Universität
Takustrasse 3, D-1000 Berlin 33 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0550 $ 02.50/0

sonifying the emulsion of *(3c)* in the presence of dithionite have so far failed because the viologen radicals *(4)* decompose under the influence of ultrasonics.

The ^{1}H-NMR spectra of the vesicles of *(3c)* and the ESR spectra of the radical vesicles of *(5)* showed only slight signal broadening compared to those of non-aggregated analogous molecules. We therefore believe that these novel synthetic vesicles are particularly well suited for the study of effects originating from substances dissolved in the membrane. Moreover, electrons and protons can probably be transferred from the aqueous phase *via* the redox-active surface into the hydrophobic interior of the membrane; this effect could be utilized to drive energy-consuming processes.

Received: January 25, 1980 [Z 498 IE]
German version: Angew. Chem. *92*, 564 (1980)

CAS Registry numbers:
(1) methyl sulfate, 35022-69-6; *(2a)*, 74128-71-5; *(2b)*, 74128-72-6; *(2c)*, 74128-73-7; *(3a)* tetrachloride, 74128-74-8; *(3b)* tetrabromide, 74128-75-9; *(3c)* tetrabromide, 74128-76-0; *(4)* dibromide, 74143-52-5; *(5)* tribromide, 74128-77-1

[1] *Y. Okahata, T. Kunitake*, J. Am. Chem. Soc. *101*, 5231 (1979).
[2] *D. Papahadjopoulos, W. J. Vail, K. Jacobson, G. Poste*, Biochim. Biophys. Acta *394*, 483 (1975).
[3] *T. Kunitake, Y. Okahata*, J. Am. Chem. Soc. 99, 3860 (1977).
[4] *E. M. Kosower, J. L. Cotter*, J. Am. Chem. Soc. *86*, 5524 (1964).

New Dinuclear Iridium(II) Complexes Arising by Oxidative Addition of I_2 to $[Ir_2(\mu\text{-}StBu)_2(CO)_2L_2]$[**]

By *Jean-Jacques Bonnet, Philippe Kalck,* and *René Poilblanc*[*]

The mechanisms of oxidative addition reactions of small molecules to mononuclear d^8 transition metal complexes are of current interest[1]. In some cases, an observed free radical process[2] has been interpreted in terms of d^7 labile intermediate species. Carrying on our investigations on the reactivity of dinuclear bridged d^8 metal complexes[3,4], we have studied the oxidative addition of halogens. This paper deals with the general preparation of dinuclear iridium(II) complexes by reaction of iridium(I) compounds with iodine. Only very few iridium(II) compounds are known[5].

$$[Ir_2(\mu\text{-}StBu)_2(CO)_2L_2] + I_2 \rightarrow [Ir_2(\mu\text{-}StBu)_2(CO)_2L_2I_2]$$
(1)—(4) *(5)—(8)*

(1) and *(5)*, L = CO; *(2)* and *(6)*, L = $P(OMe)_3$
(3) and *(7)*, L = PMe_2Ph; *(4)* and *(8)*, L = PMe_3

The complexes *(1)—(4)*[6] react readily at room temperature with one mole of iodine to give compounds of types *(5)—(8)*. All these complexes were obtained as crystals in high yield from toluene/hexane solutions. Microanalytical data and molecular weights are consistent with the above quoted molecular formula.

The infrared spectrum of *(5)* (Table 1) exhibits two systems with three ν_{CO} bands each, which suggests the presence of two isomers. Each group of three bands is characteristic of C_{2v} symmetry. Since $[Fe_2(\mu\text{-}SMe)_2(CO)_4(PR_3)_2]$, where the two phosphane ligands are in apical position[7], also gives a pattern of three ν_{CO} bands, it may be concluded that the iodine atoms of *(5)* are in apical position as well, and that the isomerism is due to different relative positions of the *tert*-butyl groups. Comparison with the $^{13}C\{^1H\}$-NMR spectrum of *(1)* shows *(5b)* to be the *syn-endo* isomer while *(5a)* is the *anti* isomer. The same mixture of isomers (*(5a)* ≈ 15% and *(5b)* ≈ 85%) is obtained, irrespective of the conditions of synthesis (*i.e.* low or high temperature, UV irradiation).

The complexes *(2)* and *(3)* give only the *cis-anti* isomers *(6a)* and *(7a)*. However, starting from *(4)*, which was found to be *cis* both in the solid state and in solution[6], two isomers are detected. Slow crystallization at low temperature from toluene/hexane allows the separation of pure *(8a)* (red crystals); *(8b)* is obtained together with small amounts of *(8a)*. The infrared spectrum of *(8a)* contains two ν_{CO} bands; the $^{31}P\{^1H\}$-NMR spectrum shows just one signal, indicative of a symmetric molecule containing two equivalent phosphorus atoms. As no phosphorus-phosphorus coupling was observed, and by analogy with complex *(5)*, we attribute the apical positions to iodine atoms. This situation differs substantially from that of the complex $[Ir_2(\mu\text{-}StBu)_2(CO)_2(PMe_3)_2H_2]$[3] where the two phosphane ligands are in apical position, leading to a large J_{PP} coupling constant. Moreover, the $^{13}C\{^1H\}$-NMR spectrum indicates *(8a)* to have *cis-anti* geometry. Indeed, as shown for *(5a)* and *(5b)*, the shifts of quaternary carbons are characteristic of the *endo* and *exo* positions.

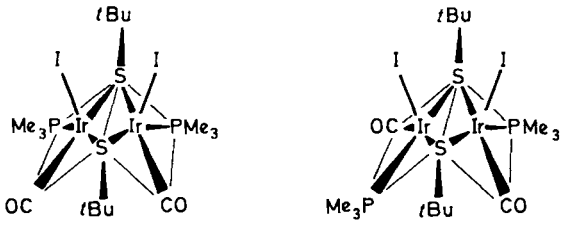
Table 1. Selected spectroscopic data of complexes *(5a)*, *(5b)*, *(8a)*, and *(8b)*.

Complex	IR [a] ν(CO) [cm^{-1}]	^{1}H-NMR	$^{13}C\{^1H\}$-NMR δ values [c]	$^{31}P\{^1H\}$-NMR	Structure
(5a)	2099 vs	1.65 [b]	164.09 (CO), 162.30 (CO),		*anti*
	2078 s	1.64 [b]	60.76 (*exo*-C—S), 52.23 (*endo*-C—S),		
	2046 vs	1.58	34.78 (*exo*-CH_3), 33.78 (*endo*-CH_3)		
(5b)	2092 w	1.65 [b]	165.48 (CO)		*syn-*
	2069 vw	1.64 [b]	54.29 (C—S)		*endo*
	2038 w		33.78 (CH_3)		
(8a)	1995 vs	2.06 (d, P—CH_2, $^2J_{PH}$ = 11.0 Hz)	172.29 (CO, J_{PC} = 13.0 Hz), 56.70 (*exo*-C—S),	−44.1	*cis-*
	1970 m	1.65 (*t*Bu)	49.30 (*endo*-C—S), 33.93 (*exo*-CH_3),		*anti*
		1.52 (*t*Bu)	33.28 (*endo*-CH_3), 20.04 (P—CH_3, J_{PC} = 40.8 Hz)		
(8b)	2008 vs	2.20 (d, P—CH_3, $^2J_{PH}$ = 10.8 Hz)	172.18 (CO), 168.54 (CO),	−64.8 (s)	*trans-*
	1977 m	2.12 (d, P—CH_3, $^2J_{PH}$ = 11.3 Hz)	57.55 (*exo*-C—S), 52.99 (*endo*-C—S),	−37.1 (s)	*anti*
		1.56 (*t*Bu)	34.04 (*exo*-CH_3), 32.81 (*endo*-CH_3),		
		1.52 (*t*Bu)	21.89 (d, P—CH_3, J_{PC} = 37.0 Hz),		
			20.27 (d, P—CH_3, J_{PC} = 40.7 Hz)		

[a] *(5a)/(5b)* in hexadecane, *(8a)* and *(8b)* in CsBr. [b] *(5a)* or *(5b)*. [c] For comparison in the case of *(5a)* and *(5b)*: *(1)*, δ = 174.25 (CO), 49.87 (C—S), 33.94 (CH_3).

[*] Prof. J. J. Bonnet, Dr. Ph. Kalck, Prof. R. Poilblanc
Laboratoire de Chimie de Coordination du CNRS associé à l'Université Paul Sabatier
205 route de Narbonne, F-31400 Toulouse (France)

[**] This work was supported by the Centre National de la Recherche Scientifique.



(8a) *(8b)*

The data for isomer *(8b)* (Table 1) are consistent with a *trans-anti* geometry. In order to explain the diamagnetism observed for complexes *(5)—(8)*, a metal-metal bond is required.

A full X-ray structure determination was undertaken on a single crystal of *(7a)*. Its structure (Fig. 1) is reminiscent of that found for *(2)*[3] concerning the relative positions of the various ligands. The metal-metal distance in *(7a)* is 2.703 Å, as against 3.216 Å found for *(2)*.

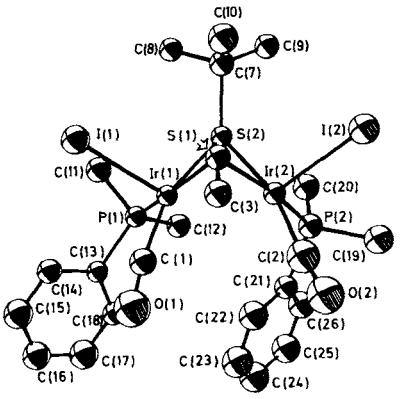


Fig. 1. Crystal structure of compound *(7a)*; isotropic model, $R = 7\%$.

As no interconversion was observed at room temperature between isomers *(8a)* and *(8b)*, the question of the mechanism of the oxidative addition to the *cis*-configurated complex *(4)* is of interest. Indeed the addition of small molecules to rhodium thiolato-bridged dinuclear complexes was found to occur on *a single* metal center[4]. Similarly the addition of H_2 to complexes *(2)—(4)* was rationalized in terms of a mono-addition to only one metal center followed by the migration of one hydrogen atom[3]. Since the addition of galvinoxyl retards the reaction, a radical process could be involved for the addition of iodine.

Received: October 29, 1980 [Z 499 IE]
German version: Angew. Chem. *92*, 572 (1980)

CAS Registry numbers:
(1), 63312-27-6; *(2)*, 63292-76-2; *(3)*, 74183-89-4; *(4)*, 63292-79-5; *(5a)*, 74144-12-0; *(5b)*, 74183-90-7; *(6a)*, 74144-13-1; *(7a)*, 74144-14-2; *(8a)*, 74144-15-3; *(8b)*, 74183-91-8; I_2, 7553-56-2

[1] *A. J. Deeming*, MTP Int. Rev. Sci. Inorg. Chem. Ser. 1. Vol. 9. Butterworths. London 1972, p. 117.

[2] *J. S. Bradley, D. E. Connor, D. Dolphin, J. A. Labinger, J. A. Osborn*, J. Am. Chem. Soc. *94*, 4043 (1972); *J. A. Labinger, A. V. Kramer, J. A. Osborn, ibid. 95*, 7908 (1973).

[3] *J. J. Bonnet, A. Thorez, A. Maisonnat, J. Galy, R. Poilblanc*, J. Am. Chem. Soc. *101*, 5940 (1979).

[4] *A. Mayanza, J. J. Bonnet, J. Galy, Ph. Kalck, R. Poilblanc*, J. Chem. Res. (*S*) *1980*, 146; (*M*) *1980*, 2101.

[5] *F. G. Moers, J. A. N. de Jong, P. M. H. Beaumont*, J. Inorg. Nucl. Chem. *35*, 1915 (1973); *M. Angoletta, P. L. Bellon, M. Manassero, M. Sansoni*, J. Organomet. Chem. *81*, C40 (1974); *R. Mason, K. M. Thomas, H. D. Empsall, S. R. Fletcher, P. N. Heys, E. M. Hyde, C. E. Jones, B. L. Shaw*, J. Chem. Soc. Chem. Commun. *1974*, 612; *A. Arânes, F. Morazzoni, T. Napoletano*, J. Chem. Soc. Dalton Trans. *1975*, 2039; *G. Pilloni, G. Schiavon, G. Zotti, S. Zecchin*, J. Organomet. Chem. *134*, 305 (1977); *M. Angoletta, L. Malatesta, G. Caglio*, J. Chem. Soc. Dalton Trans. *1977*, 2131.

[6] *D. de Montauzon, Ph. Kalck, R. Poilblanc*, J. Organomet. Chem. *186*, 121 (1980).

[7] *J. A. de Beer, R. J. Haines, R. Greatex, N. N. Greenwood*, J. Chem. Soc. *A 1971*, 3271.

A Novel Proton-Ordered, Two-Dimensional Cross-linking of Water Molecules in Pyridine Trihydrate

By *Dietrich Mootz* and *Hans-Georg Wussow*[*]

Dedicated to Professor George A. Jeffrey on the occasion of his 65th birthday

Pyridine and water form an addition compound in the solid state, which was hitherto regarded as a dihydrate[1]. By reinvestigation of the melting diagram of pyridine-water and a complete crystal structure determination we have now been able to characterize this compound[2] as a trihydrate, whose structure is determined in an unusual way by hydrogen bonds.

Pyridine trihydrate melts incongruently at $-29.5\,^{\circ}C$ with decomposition into liquid phase and ice. Single crystals obtained from solutions with *ca.* 40 mol-% pyridine show the orthorhombic space group Pbca with eight $C_5H_5N \cdot 3H_2O$ formula units in the unit cell and, at $-50\,^{\circ}C$, the lattice constants $a = 1244.6(3)$, $b = 1783.2(6)$, $c = 679.1(2)$ pm. The structure determination (932 significant reflections, $R = 0.078$) led to ordered positions for all atoms. The water molecules are cross-linked two-dimensionally by five independent hydrogen bonds with O...O distances of 274.7 to 284.0 pm with formation of annelated four-, five-, and six-membered rings in the ratio 1:2:1 (Fig. 1[3]). One proton on each atom O(1) does not participate in this crosslinking, but makes, alternately from both sides of the water layer, a hydrogen bond to the N atom of a pyridine molecule (O...N 279.6 pm). In this way, the pyridine molecules are enclosed between successive water layers at a distance *b*/2.

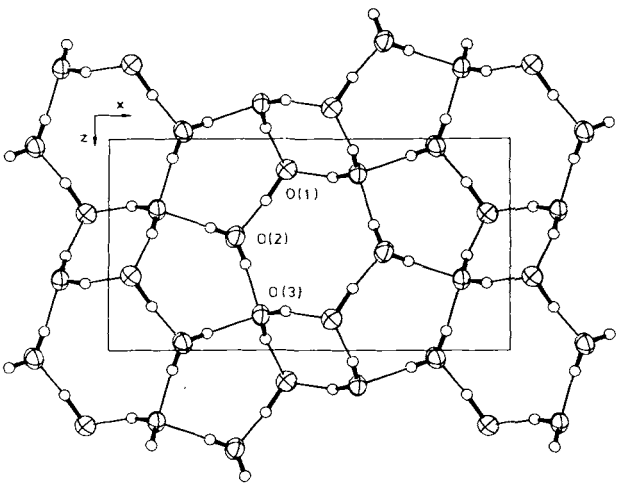


Fig. 1. Two-dimensional cross-linking of the water molecules in pyridine-water (1/3) by hydrogen bonds.

The geometry of the enclosure and the cross-linking of the water molecules are thus fundamentally different from that in the three-dimensional polyhedric clathrate and semicla-

[*] Prof. Dr. D. Mootz, Dipl.-Chem. H.-G. Wussow
Institut für Anorganische Chemie und Strukturchemie der Universität Universitätsstrasse 1, D-4000 Düsseldorf (Germany)

thrate hydrates[4] (*inter alia*, gas hydrates, higher hydrates of alkylamines), even though the rings occurring in the water structures and in limited regions also their annelation are common structural elements.—Two-dimensional water structures have also been observed in the hexahydrates of piperazine[5] and pinacol[6], but in both cases only with five-membered rings, disordered protons and more extensive cross-linking through the difunctional organic molecule.

Received: February 22, 1980 [Z 500 IE]
German version: Angew. Chem. 92, 559 (1980)

[1] *M. Ewert*, Bull. Soc. Chim. Belg. *46*, 90 (1937).
[2] We have recently also been able to determine the crystal structure of pyridine. It is unexpectedly complicated, having four independent molecules in general positions (space group $Pna2_1$, $z = 16$).
[3] *C. K. Johnson*, Zeichenprogramm OR TEP II, ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tenn. (1976).
[4] *G. A. Jeffrey, R. K. McMullan*, Prog. Inorg. Chem. *8*, 43 (1967); *G. A. Jeffrey*, Acc. Chem. Res. *2*, 344 (1969).
[5] *D. Schwarzenbach*, J. Chem. Phys. *48*, 4134 (1968).
[6] *H. S. Kim, G. A. Jeffrey*, J. Chem. Phys. *53*, 3610 (1970).

A New Variant of the Amphoterism of Tin(II) Hydroxide: $Sn(OH)_2$ as Stannio Complex Ligand[**]

By *Wolf-Walther du Mont* and *Brigitte Neudert*[*]

Tin(II) hydroxide is a colorless, highly associated compound of unknown structure[1] which decomposes on dissolution or fusion. Attempts to precipitate tin(II) hydroxide from aqueous solutions do not give $Sn(OH)_2$ but rather basic Sn^{II} derivatives whose compositions only approximate to SnO_2H_2, such as "$3\,SnO \cdot H_2O$". Structural features of such compounds are Sn—O(H)—Sn and Sn—O—Sn bridges, as well as pyramidal SnO_3 and SnO_4 units at tin(II)[1,2]. The amphoterism of "$Sn(OH)_2$" (in aqueous medium: acceptor and donor of OH^-) has long been known. So far there has been no evidence for basic properties of tin(II) hydroxide arising not from OH groups but from the metal itself as a weak Lewis base. If it were possible to involve the 5s-electron pair of tin in coordination with metal acceptors without significantly perturbing the tin-oxygen bridge, then $Sn(OH)_2$ would appear of interest as a non-toxic polymeric carrier material for transition metal catalysts.

We have now prepared the first such complexes in which transition metal acceptors ML_n are indeed fixed to tin(II) hydroxide by coordinative Sn—M bonds. Thus the lone pair at tin, which is frequently stereochemically active in SnO and its derivatives[2a,3], can be utilized for tin-transition metal coordination.

$$M(CO)_5SnCl_2 \cdot THF + 2\,R_3SnOH \rightarrow 2\,R_3SnCl + THF + M(CO)_5Sn(OH)_2 \quad (2)$$

(1a), M = Cr R = C_6H_5
(1b), M = W R = CH_3

Like *Zuckerman*'s synthesis of $Sn(OH)_2$, our preparation of $Sn(OH)_2$ metal complexes utilizes chloride/hydroxide exchange with triphenyl- or trimethyl-tin hydroxide: the $SnCl_2$-metal complexes *(1)* react with R_3SnOH in toluene at room temperature within a few days to form pentacarbonyl(dihydroxystannio)chromium(0) *(2a)* and -tungsten(0) *(2b)* which can be isolated in 50—75% yield as yellow and colorless powders, respectively.

The physical properties of the $Sn(OH)_2$-metal complexes are remarkably similar to those of tin(II) hydroxide: the new compounds *(2)* are not volatile and cannot be melted without decomposition (decomposition above about 150 °C); they are sparingly soluble in water, alcohols, and inert organic solvents. The tin-transition metal coordination is confirmed by well-resolved doublet signals in the ^{119m}Sn Mössbauer spectra (Table 1); the values of the isomer shifts are characteristically lowered relative to those of $Sn(OH)_2$ by withdrawal of 5s electrons into Sn—Cr or Sn—W bonds[4], with the quadrupole splitting being increased.

In contrast to $Sn(OH)_2$, the complexes *(2)* are sufficiently soluble in tetrahydrofuran (THF) to permit recording of NMR spectra. The ^{119}Sn-NMR spectra each show one signal (Table 1); that of *(2b)* is shifted upfield by about 200 ppm relative to that of *(2a)*[5]. THF adducts of the stannio complexes are present in these solutions, as also revealed by the changed CO stretching frequencies. The frequency of the ν(CO) bands of the solid, base-free but associated (by tin-oxygen bridging) $Sn(OH)_2$ metal complexes (Table 1) shows the inorganic polymer $Sn(OH)_2$ to be a ligand with donor/acceptor properties resembling those of conventional phosphane or phosphite ligands.

Table 1. Spectroscopic data of the $Sn(OH)_2$-metal complexes *(2)* [a].

	^{119m}Sn-Mössbauer [b]		^{119}Sn-NMR [c]	IR [d]	
	I.S. (δ)	Q.S. (Δ)	δ	ν(OH)	ν(CO)
(2a)	1.95	2.72	+ 9.5	3505 (br)	2072 s, 2000 sh, 1950 vs
(2b)	1.98	2.76	−198	3530 (br)	2088 s, 2000 sh, 1940 vs (br)
$Sn(OH)_2$ [1]	2.83	2.20	—	3390 (br)	—

[a] The composition of the compounds was confirmed by elemental analysis. [b] δ and Δ values in mm s^{-1}; $BaSnO_3$ as standard [4]. We are grateful to Prof. *J. J. Zuckerman*, University of Oklahoma, Norman, OK. [c] Conc. solution in THF/C_6D_6; Bruker SXP, 33.55 MHz; $(CH_3)_4Sn$ as standard. [d] Nujol suspension between CsI plates, values in cm^{-1}.

Procedure

Compound *(1b)* (1.7 g, 2.9 mmol) and trimethyltin hydroxide (1.2 g, 6.7 mmol) are stirred in toluene (25 ml) and THF (2 ml) for 3 d. After removal of solvent, washing of the residue with toluene and dichloromethane, and drying at 0.1 mbar, compound *(2a)* (0.7 to 1.1 g, 50—75%) is obtained as a colorless powder that does not melt below 200 °C. The compound dissolves in THF to give a yellow solution.

Received: November 8, 1979 [Z 501a IE]
German version: Angew. Chem. 92, 561 (1980)

[*] Priv.-Doz. Dr. W.-W. du Mont, B. Neudert
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] Reactions of Coordinated Carbene Analogues. Part 5. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 4: *W.-W. du Mont*, Z. Anorg. Allg. Chem. *450*, 57 (1979).

[1] *W. D. Honnick, J. J. Zuckerman*, Inorg. Chem. *15*, 3034 (1976); and references cited therein.
[2] a) *P. G. Harrison*, Coord. Chem. Rev. *20*, 1 (1976); b) *R. A. Howie, W. Moser*, Nature (London) *219*, 372 (1968).

[3] *R. M. Braun, R. Hoppe*, Angew. Chem. *90*, 475 (1978); Angew. Chem. Int. Ed. Engl. *17*, 449 (1978).
[4] *W.-W. du Mont, J. L. Lefferts, J. J. Zuckerman*, J. Organomet. Chem. *166*, 347 (1979).
[5] This shift difference is also found in the ylide complexes $M(CO)_5$—$SnCl_2$—B (M = Cr, W; B = THF, PR_3): *W.-W. du Mont, H.-J. Kroth*, Z. Naturforsch. *35b*, 700 (1980); *W.-W. du Mont*, Chemiedozententagung Darmstadt 1979, Abstract B 57.

Bis(di-*tert*-butylphosphino)tellurium(II): A Derivative of Phosphinous Anhydride Exhibiting Umpolung[**]

By *Wolf-Walther du Mont*[*]

Formation of phosphane chalcogenides R_3PX (X = O, S, Se, Te) from phosphanes is generally regarded as a P^{III}/P^{V} redox reaction[1]. We have found phosphane tellurides to be exceptions insofar as they behave like kinetically labile tellurium complexes in the presence of an excess of phosphane[2]. All known R_3PTe/PR_3 systems display fast tellurium transfer reactions ("fluxional redox systems") on the ^1H- and ^{31}P-NMR time scale, even at room temperature[2,3] [eq. (1)]. However, if tellurium is correspondingly transferred from tri-*n*-butylphosphane telluride to di-*tert*-butyl(trimethylsilyl)phosphane *(1a)*, then tellurium transfer to silylphosphane is followed immediately by insertion of tellurium into the phosphorus-silicon bond [eq. (2)]. Elemental tellurium reacts similarly, with insertion into the P—Si, P—Ge, and P—Sn bonds of the phosphanes *(1a)*—*(1e)* [eq. (3)].

$$R_3P{=}Te + R'_3P \rightleftharpoons R'_3P{=}Te + R_3P \quad (1)$$

(R, R' = Alkyl, dialkylamino, in some cases aryl)

$$n\mathrm{Bu_3P{=}Te} + \underset{(1a)}{t\mathrm{Bu_2(Me_3Si)P}} \rightleftharpoons \left[t\mathrm{Bu_2P}\begin{matrix}\diagup\!\!=\mathrm{Te}\\ \diagdown\ \ \mathrm{SiMe_3}\end{matrix}\right] + n\mathrm{Bu_3P} \quad (2)$$

$$\downarrow$$

$$t\mathrm{Bu_2P{-}Te{-}SiMe_3}\ \ (2a)$$

$$t\mathrm{Bu_2P{-}EMe_3} + \mathrm{Te} \longrightarrow t\mathrm{Bu_2P{-}Te{-}EMe_3} \quad (3)$$

(1) → *(2a)*, E = Si; *(2b)*, E = Ge; *(2c)*, E = Sn

The silyl-, germyl-, and stannyl-phosphane tellurides $R_2(Me_3E)P{=}Te$ expected as intermediates in the essentially quantitative formation of the new silyl, germyl, and stannyl tellurophosphinites *(2a)*—*(2c)* according to eq. (2) and (3) are not sufficiently long-lived to permit detection in the ^{31}P-NMR spectra of the reaction mixtures[4]. In contrast, the insertion products *(2)* with the new structural unit R_2P—Te—ER_3 have been unequivocally characterized by ^1H-, ^{31}P-, and ^{119}Sn-NMR spectra (Table 1). These compounds cannot be prepared pure because the rapid formation of *(2)* is followed within a few hours by redistribution equilibria [eq. (4)]; hence *(2)* is always accompained by the known bis(trimethylelement)tellurides *(3)* and the new "tellurophosphinous anhydride" *(4)* in the isolated products.

The remarkable formation tendency of *(4)*, the first tellurium compound substituted only with R_2P groups, in equilibrium with *(2)* and *(3)* and the thermal stability (formation of R_4P_2 only on UV irradiation) suggested synthesis according to eq. (5): The product, obtained in 80% yield in toluene, crystallizes from pentane as pale-yellow needles, m.p. 77 °C[5]. Its ^1H- and ^{31}P-NMR spectra confirm the P—Te—P linkage in the monomeric compound (Table 1).

$$2\,(2a\text{—}c) \rightleftharpoons \underset{(3a),\ E=Si}{\underset{(3b),\ E=Ge}{\underset{(3c),\ E=Sn}{(\mathrm{Me_3E})_2\mathrm{Te}}}} + \underset{(4)}{t\mathrm{Bu_2P{-}Te{-}P}t\mathrm{Bu_2}} \quad (4)$$

$$\mathrm{Na_2Te} + 2\,t\mathrm{Bu_2PCl} \rightarrow (4) + 2\,\mathrm{NaCl} \quad (5)$$

The reaction of *(2c)* and *(4)* with protic reagents (water, alcohol) is surprising: The Te—P and Te—Si bonds of *(2a)* are smoothly cleaved, with deposition of tellurium to give not only siloxane derivatives but above all the P—H compound [di-*tert*-butylphosphane, $\delta(P) = 19.4$, $^3J(HP) = 11.4$ Hz]; in contrast, *(4)* undergoes very slow hydrolysis, and the di-*tert*-butylphosphane can likewise be detected by NMR spectroscopy. The polarity of the P—Te bond is very low (phosphorus and tellurium have very similar electronegativities), and is probably even reversed relative to the P—O, P—S, and P—Se bonds. Thus the silylphosphane *(1a)* is not necessarily oxidized on tellurium insertion according to eq. (2), but tellurium formally disproportionates in the course of formation of *(3)* and *(4)* from *(2)*, according to eq. (4)! Moreover, we no longer consider the description of phosphane tellurides $R_3P{=}Te$ as "phosphane complexes of tellurium(0)"[6] to be inappropriate.

Table 1. ^1H-, ^{31}P-, and ^{119}Sn-NMR data of compounds *(2)* and *(4)* [a].

	$\delta(H_3CE)$	$\delta(H_3CC)$	$^3J(HP)$	$\delta(^{31}P)$	$^1J(PTe)$ [b]	$\delta(^{119}Sn)$
(2a)	0.4	1.3 d	11.9	68.2	384	—
(2b)	0.7	1.4 d	11.8	68.0	382	—
(2c)	0.4	1.4 d	11.8	64.5	348	60.8 d $^2J(^{31}P^{119}Sn) = 131$ Hz
(4)	—	1.4 [c]	N = 11.5	85.5	451	—

[a] Measurements in C_6D_6 and C_6D_6/toluene, Me_4Si, 85% H_3PO_4, and Me_4Sn as standard, coupling constants in Hz; ^{31}P- and ^{119}Sn spectra are $\{^1H\}$-noise decoupled (Bruker SXP and WP 80). [b] The magnitudes of these coupling constants $^1J(^{31}P^{125}Te)$ characteristically distinguish *(2a—c)* and *(4)* from phosphane tellurides $R_3P{=}Te$ ($J = 1600$—2200 Hz). [c] $(AX_n)_2$-type multiplet.

Procedure

Sodium telluride [*ca.* 11 mmol; from Na (5.4 g, 22 mmol) and Te (16.6 g, 13 mmol)] is suspended in toluene (100 ml) and, after addition of di-*tert*-butyl(chloro)phosphane (37 g, 30 mmol) in toluene (50 ml), stirred for 12 h. Recrystallization from pentane of the crude product (*ca.* 32 g, 80%) obtained by separation and washing of the precipitate and re-

[*] Priv.-Doz. Dr. W.-W. du Mont
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

moval of toluene under reduced pressure affords *(4)* as pale yellow needles.

Received: November 14, 1979;
revised: March 14, 1980 [Z 501 b IE]
German version: Angew. Chem. *92*, 562 (1980)

[1] *G. M. Kosolapoff, H. Maier:* Organic Phosphorus Compounds. Wiley-Interscience, New York 1972.
[2] *W.-W. du Mont, H.-J. Kroth*, J. Organomet. Chem. *113*, C35 (1976).
[3] *D. H. Brown, R. J. Cross, D. Millington*, J. Organomet. Chem. *125*, 219 (1977); *D. Keat, D. G. Thompson, ibid. 141*, C 13 (1977); *O. J. Scherer, G. Schnabl*, Angew. Chem. *89*, 500 (1977); Angew. Chem. Int. Ed. Engl. *16*, 486 (1977).
[4] Detection of $R_2(Me_3E)P{=}Te$ is rendered even more difficult by rapid tellurium exchange between these compounds and a large excess of free phosphane [eq. (1) and (2)]: Only broadening of the ^{31}P-NMR signals of the phosphanes $R_2(Me_3E)P$ is observed.
[5] The composition of *(4)* has been confirmed by elemental analysis.
[6] *T. Austad, T. Rød, K. Åse, J. Songstad, A. H. Norbury*, Acta Chem. Scand. *27*, 1939 (1973).

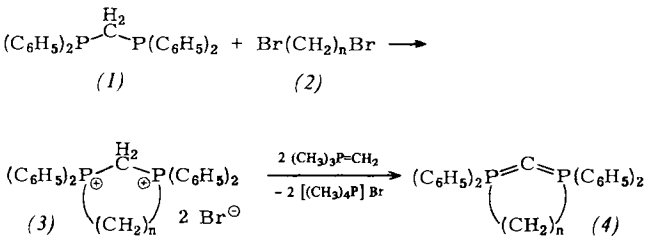
Ring-Strained Carbodiphosphoranes

By *Hubert Schmidbaur, Thomas Costa, Beatrix Milewski-Mahrla,* and *Ulrich Schubert*[*]

"Carbodiphosphoranes" R_3PCPR_3[1] are of importance in chemical synthesis[2] and as complex ligands[3]. Their highly variable molecular structures[4] and bonding[5] are topics of controversial discussion, and are closely connected with the phenomenon of triboluminescence[6].

Structural investigations on carbodiphosphoranes in the gaseous state[7] and in crystals[4] have revealed that the PCP angle can apparently fall to 121° without any great expenditure of energy[4a]. Thus it appeared possible to incorporate the P=C=P structural unit into ring systems although no examples have previously been reported.

Quaternization of methylenebis(diphenylphosphane) *(1)* with the α,ω-dihaloalkanes *(2a—c)* affords the bisphosphonium salts *(3a—c)*[8] which can readily be characterized by elemental analysis and NMR spectroscopy. Mild dehydrohalogenation of these salt precursors with methylenetrimethylphosphorane through double transylidation in tetrahydrofuran or benzene with cooling to 0—10 °C gives deep yellow solutions from which the three carbodiphosphoranes *(4a—c)* can be isolated, some of them in good yields.



(a): n = 2, *(b)*: n = 3, *(c)*: n = 4

Scheme 1

Synthesis according to Scheme 1 gives the six-membered ring *(4b)* as the sole product only for $n=3$. In the case of $n=4$, side reactions occur with skeletal rearrangement[2b,9]; however, the seven-membered ring *(4c)* can be isolated pure in *ca.* 30% yield, m.p. 127 °C (dec.). Compound *(4c)* forms yellow crystals which, unlike *(4b)*, are readily soluble in organic solvents. In the ^{13}C-NMR spectrum the C atom of the double ylide function appears at $\delta=-3.4$ as a triplet with $^1J(PC)=75.7$ Hz (in C_6D_6 rel. to TMS as int. std. at 25 °C); $\delta(CH_2)=24.0$ (s) and 35.2 (AXX') can be unequivocally assigned for the other ring carbon atoms, as can the resonance signals of the four equivalent phenyl groups. In the $^{31}P\{^1H\}$-NMR spectrum the presence of a singlet proves the equivalence of the phosphorus atoms ($\delta=-1.68$ rel. to H_3PO_4 as ext. std.). The ^1H-NMR spectrum contains only complex multiplet signals which are hardly simplified in a $\{^{31}P\}$ experiment. Mass spectrum (70 eV): $m/e=438$ (M^+). IR spectrum: $\nu(P{=}C{=}P)=1270$ and 1300 cm^{-1}.

In contrast to *(4c)*, *(4b)* shows considerable thermal lability and already decomposes at 35 °C. The mass spectrum also suggests a monomeric structure [$m/e=423$ (M^+-1)], although the poor solubility initially appeared rather puzzling. The structure was therefore elucidated by X-ray diffraction[10], and revealed an extremely unusual helical arrangement of the monomeric units in the hexagonal single crystals. Figure 1 shows one of the heterocycles in which C-5 is disordered after the fashion of a chair-boat conformation. The screw-like packing of the molecules is seen in Figure 2. Both levo- and dextro-rotatory helix packings are found in the crystalline conglomerate (space groups $P6_5$ and $P6_1$).

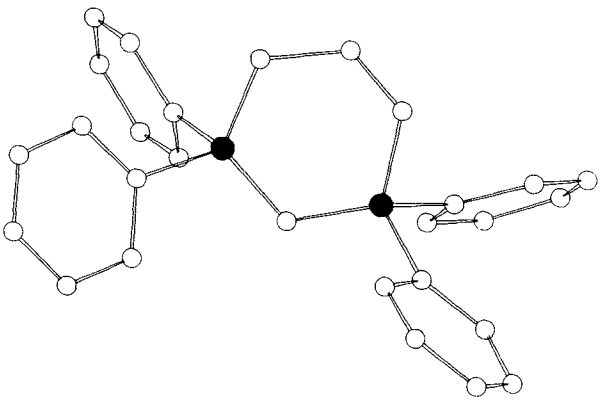


Fig. 1. Molecular structure of $(C_6H_5)_2P\text{-}C{=}P(C_6H_5)_2(CH_2)_3$ *(4b)*. The alternative position of the disordered atom C-5 has been omitted; it corresponds to a chair/boat relationship. Atomic parameters are available from the authors on request.

The P=C=P structural unit has the smallest known carbodiphosphorane angle of 117° but also equal P=C distances which lie in the expected range at 164.5 and 165.3 pm. It can be deduced from the decomposition of *(4b)* that the limit of strain of angle deformation is exceeded at ≤120°. The structure is best described by formulation as



(4b)

Compound *(4a)* is therefore expectedly even less stable and decomposes within a few hours at 20 °C. The very poorly soluble compound has so far only been characterized by means of its ^1H- and ^{31}P-NMR spectra [$\delta(P)=-22.45$ (s); $\delta(CH_2)=2.73$ ("d"), $(C_6H_5)=7.1—8.0$ (m)], mass spectrum, elemental analysis, and derivatization[11].

[*] Prof. Dr. H. Schmidbaur, Dipl.-Chem. T. Costa, Dipl.-Chem. B. Milewski-Mahrla, Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

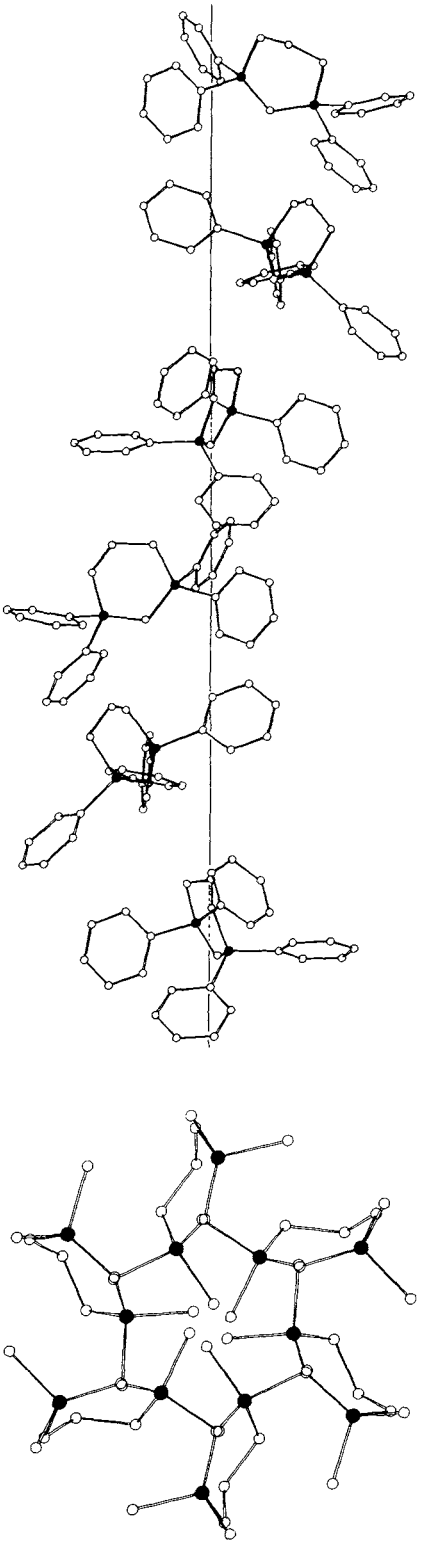


Fig. 2. a) Projection of the helical arrangement of the monomers of *(4b)* onto the *xz* plane. The disorder of C-5 is not shown.—b) Projection of the helical arrangement of the monomers onto the *xy* plane. The disorder of C-5 and the phenyl C atoms are not shown (except for C-1). The hexagonal-helical structure is immediately obvious from this figure.

Received: February 15, 1980 [Z 502 IE]
German version: Angew. Chem. *92*, 557 (1980)

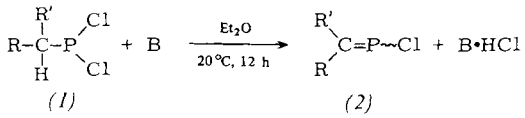
CAS Registry numbers:
(1), 2071-20-7; *(2a)*, 106-93-4; *(2b)*, 109-64-8; *(2c)*, 110-52-1; *(3a)*, 74144-31-3; *(3b)*, 74144-32-4; *(3c)*, 74144-33-5; *(4a)*, 74144-34-6; *(4b)*, 74144-35-7; *(4c)*, 74144-36-8

[1] *H. Schmidbaur*, Nachr. Chem. Tech. Lab. *27*, 620 (1979).
[2] a) *H. J. Bestmann*, Angew. Chem. *89*, 361 (1977); Angew. Chem. Int. Ed. Engl. *16*, 349 (1977); b) *R. Appel et al.*, *ibid. 88*, 340, 769 (1976); *91*, 177 (1979) and *15*, 315, 701 (1976); *18*, 169 (1979), respectively.
[3] *W. C. Kaska, D. K. Mitchell, R. F. Reichelderfer, W. D. Korte*, J. Am. Chem. Soc. *96*, 2847 (1974); *H. Schmidbaur, O. Gasser*, Angew. Chem. *88*, 542 (1976); Angew. Chem. Int. Ed. Engl. *15*, 502 (1976); *H. Schmidbaur, O. Gasser, C. Krüger, J. C. Sekutowski*, Chem. Ber. *110*, 3517 (1977).
[4] a) *H. Schmidbaur, G. Hasslberger, U. Deschler, U. Schubert, C. Kappenstein, A. Frank*, Angew. Chem. *91*, 437 (1979); Angew. Chem. Int. Ed. Engl. *18*, 408 (1979); b) *G. E. Hardy, J. I. Zink, W. C. Kaska*, J. Am. Chem. Soc. *100*, 8001 (1978); *A. T. Vincent, P. J. Wheatley*, J. Chem. Soc. Dalton Trans. *1972*, 617.
[5] *T. A. Albright, P. Hofmann, A. R. Rossi*, Z. Naturforsch. *B 35*, 343 (1980); *C. Glidewell*, J. Organomet. Chem. *159*, 23 (1978).
[6] *J. I. Zink*, Acc. Chem. Res. *11*, 289 (1978).
[7] *E. A. V. Ebsworth, T. E. Fraser, D. W. H. Rankin, O. Gasser, H. Schmidbaur*, Chem. Ber. *110*, 3508 (1977).
[8] Cf. also *G. Märkl*, Z. Naturforsch. *B 18*, 1136 (1963).
[9] *H. Schmidbaur, A. Wohlleben-Hammer*, Chem. Ber. *112*, 510 (1979); *R. Appel, G. Erbelding*, Tetrahedron Lett. *1978*, 2689.
[10] $C_{28}H_{26}P_2$; $-20\,^{\circ}C$, hexagonal, space group $P6_5$ ($Z=6$); $a=b=1034.6(5)$, $c=3679(2)$ pm, $V=3410.6\times10^6$ pm^3, $\rho_{calc}=1.24$ g/cm^3. Syntex $P2_1$/XTL, $2^{\circ}\leq2\theta\leq48^{\circ}$, $\lambda=71.069$ pm (graphite monochromator); 1054 structure factors ($F_0\geq3.90\sigma(F_0)$), $R_1=0.072$, $R_2=0.059$.
[11] *H. Schmidbaur, T. Costa, U. Deschler*, to be published.

Ph(Me$_3$Si)C=P—Cl, the First *P*-Halofunctionalized Methylenephosphane[**]

By *Rolf Appel* and *Axel Westerhaus*[*]

A few examples of acyclic phosphorus(III) compounds with coordination number 2 have recently been reported in the literature[1]. The stability of these C=P-compounds, being other than expected according to the double bond rule, was previously attributed to shielding by the bulky substituents on the carbon (*t*-Bu[1a], $SiMe_3$[2]) or phosphorus atom[1b]. That this assumption only partly applies is evidenced by the surprisingly easy preparation of the *P*-chloromethylenephosphanes *(2)*, which was accomplished by dehydrohalogenation of the α-CH acidic primary dichlorophosphanes *(1)* with tertiary amines (B).



(1) *(2)*

	R	R'	B
(a)	H	H	$N(C_2H_4)_3N$
(b)	Ph	Ph	NEt_3
(c)	Ph	$SiMe_3$	$N(C_2H_4)_3N/NEt_3$

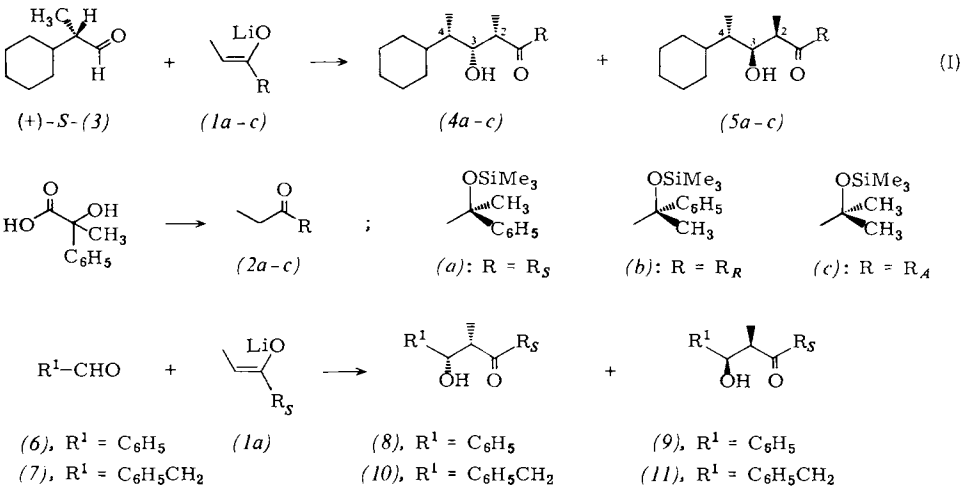
Of the new methylenephosphanes, only *(2c)* has hitherto been isolated in analytically pure form.

Chloro[phenyl(trimethylsilyl)methylene]phosphane *(2c)* is a yellow-green, distillable substance, which can be stored unchanged for several weeks in a refrigerator. Besides the correct elemental analysis and the mass spectrometrically and cryoscopically determined relative molecular mass for *(2c)*, the ^{31}P- and ^{13}C-NMR spectra unequivocally characterize the compound—and *(2a)* and *(2b)*—as methylenephosphane[3].

With *(2a)*—*(2c)* we now have ready access to valuable synthetic building blocks which can be exploited for derivatiza-

[*] Prof. Dr. R. Appel, Dipl.-Chem. A. Westerhaus
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

[**] Phosphorus-Carbon-Halogen Compounds, Part 22. Part 21: *R. Appel, G. Haubrich*, Angew. Chem. *92*, 206 (1980); Angew. Chem. Int. Ed. Engl. *19*, 213 (1980).



Scheme 1

tion at the phosphorus atom, and in the case of *(2c)* for incorporation of the P≡C triple bond by thermal elimination of trimethylchlorosilane[4].

Procedure

Chlorophenyl(trimethylsilyl)methane (72.4 g, 360 mmol) is converted with Mg (10.0 g, 400 mmol) in diethyl ether (200 ml) into the Grignard compound, which is then added dropwise slowly to an ice-cooled solution of PCl_3 (49 g, 360 mmol) in ether (150 ml). $MgCl_2$ is removed by filtration and the filtrate is evaporated down under vacuum. Fractional distillation of the residue furnishes 52.7 g (55%) of *(1c)*, b.p. 53 °C/10^{-3} torr [$^{31}P\{^1H\}$-NMR (C_6D_6): δ = 189].

A solution of *(1c)* (15.0 g, 57 mmol) in ether (200 ml) is treated with 25.3 g (220 mmol) of 1,4-diazabicyclo[2.2.2]octane and the mixture is stirred for 12 h at room temperature. The insoluble material is filtered off and washed with ether. The combined filtrates are then evaporated down under vacuum and the amine hydrochloride which precipitates is removed by filtration. After removal of solvent the residue is treated with *n*-pentane, filtered and the filtrate evaporated down and distilled: yield 7.1 g (54%) of *(2c)*, b.p. 51 °C/10^{-3} torr.

Received: February 15, 1980 [Z 503 IE]
German version: Angew. Chem. 92, 578 (1980)

[†] a) *G. Becker*, Z. Anorg. Allg. Chem. *423*, 242 (1976); b) *T. C. Klebach, R. Lourens, F. Bickelhaupt*, J. Am. Chem. Soc. *100*, 4886 (1978); c) *K. Issleib, H. Schmidt, H. Meyer*, J. Organomet. Chem. *160*, 47 (1978); d) *R. Appel, V. Barth*, Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 469 (1979).

[2] *R. Appel, J. Peters*, lecture delivered at the Int. Conf. Phosphorus Chem. Sept. 17–21, 1979 in Halle (GDR).

[3] $^{31}P\{^1H\}$-NMR (C_6D_6, 32.2 MHz, H_3PO_4 ext.): *(2a)*: δ = 235.0; *(2b)*: δ = 273.0; *(2c)*: δ = 272.0, 274.0 (*cis/trans* isomers in the ratio 1:1). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 22.6 MHz, TMS int.): *(2b)*: δ = 196.1 [d, *J*(PC) = 69.0 Hz, P=C]; *(2c)*: δ = 197.3 [d, *J*(PC) = 82.0 Hz, P=C].

[4] *R. Appel, A. Westerhaus*, unpublished.

Highly Stereoselective Aldol Condensation Using an Enantioselective Chiral Enolate[**]

By *Satoru Masamune, Sk. Asrof Ali, David L. Snitman*, and *David S. Garvey*[*]

The concept of the diastereomeric transition state is well documented[1]. Thus, in a kinetically controlled reaction which leads to the formation of new chiral centers, certain pairs of optically active substrates react to form one diastereoisomer predominantly, whereas other combinations result in inferior stereoselection. We have observed this phenomenon in an aldol condensation (Eq. 1) and have consequently developed a chiral enolate reagent which is highly enantioselective and synthetically useful. A recent report by *Heathcock et al.*[2] concerning this subject has prompted us to summarize our independent findings in preliminary form[3].

Table 1. Aldol condensation of aldehyde *(3)* with lithium enolate *(1)*.

	Aldehyde *(3)* [a]	Enolate	Structures [b] of products *(4)* and *(5)*	Combined Yields [%]	Ratio of *(4)* to *(5)*
1	(+)-*S*	*(1a)*	*(4a)*, *(5a)*	75	1:8
2	(+)-*S*	*(1b)*	*(4b)*, *(5b)*	72	1.5:1
3	(−)-*R*	*(1a)*	*(4d)*, *(5d)* [c]	75	1.5:1
4	(−)-*R*	*(1b)*	*(4e)*, *(5e)* [d]	78	1:8

[a] Prepared from optically pure 2-cyclohexylpropionic acid $LiAlH_4$ reduction and Collin's oxidation [(+)-*S*: $[\alpha]_D^{25} = +19.3$ (*c* = 1.185 C_2H_5OH); (−)-*R*: $[\alpha]_D^{25} = -18.6$ (*c* = 2.055 C_2H_5OH)] *via* methylation. (+)-*S*- and (−)-*R*-*(3)* had $[\alpha]_D^{25} = +62.8$ (*c* = 1.545 CH_2Cl_2) and −63.1 (*c* = 0.950 CH_2Cl_2), respectively. [b] The stereochemistry of the aldol products is based on the conversion of *(4)* and *(5)* through acid hydrolysis and oxidation into the corresponding 4-cyclohexyl-3-hydroxy-2-methylpentanoic acids which were compared with those obtained from 4-phenyl-3-hydroxy-2-methylpentanoic acids of known stereochemistry. [c] *(4d)*, *(5d)*: enantiomers of *(4b)*, *(5b)*. [d] *(4e)*, *(5e)*: enantiomers of *(4a)*, *(5a)*.

Initial exploratory work in this area involved the use of chiral lithium enolates *(1a)* and *(1b)* derived from *S*- and *R*-atrolactic acids, respectively. Thus, treatment of the acids[4] with 3.3 equivalents of ethyllithium provided a 65% yield of the corresponding ethyl ketones, which were in turn silylated to yield *(2a)* and *(2b)* (Scheme 1)[5]. The aldol condensation was then carried out in the usual way: after dropwise addition of aldehyde *(3)*[6] to a THF solution (−78 °C) of enolate *(1)*, generated from *(2)* with lithium diisopropylamide, the reaction mixture was stirred for 25 min and quenched with aqueous ammonium chloride for workup. The structures and yields of products *(4)* and *(5)* in each reaction are summarized in Table 1.

Two pairs (Table 1, entries 1 and 4) provided a significant stereoselection of 1:8 in sharp contrast with that (1.5:1) observed in the other cases (entries 2 and 3). Thus, only a certain pair of chiral substrates produces predominantly one of the four possible stereoisomers in an aldol condensation.

The stereochemical course of the above reaction requires some analysis. While the *Z*- or *E*-stereochemistry [only *Z* shown in *(1)*] of the enolate has been shown to be directly

[*] Prof. Dr. S. Masamune, Dr. S. A. Ali, Dr. D. L. Snitman, D. S. Garvey
Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Mass. 02139 (USA)

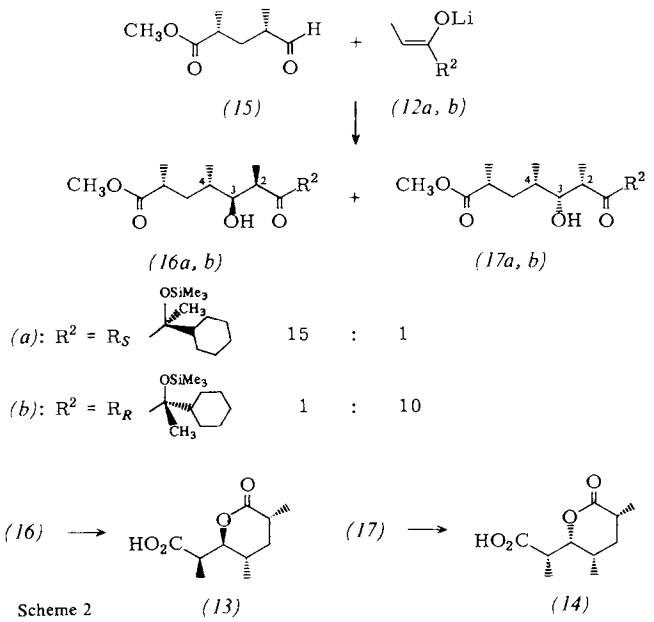
[**] This work was supported by the Sloan Research Funds (MIT), the National Institutes of Health NCI Training Grant 1T32 CA09112 and NIH AI 15403.

correlated with the *syn*- and *anti*-2,3 stereochemistry[7] of the products *(4)* and *(5)*[8], the 3,4-stereochemistry appears to depend on two factors, (a) the selectivity inherent in the reacting aldehyde commonly referred to as Cram/anti-Cram selectivity[9] and (b) the enantioselectivity arising from the chirality present in the enolate. These two selectivities were evaluated separately.

The reaction of (+)-*(3)* with the achiral reagent *(1c)* utilized earlier by *Heathcock et al.*[8c] provided a 27:73 mixture of *(4c)* and *(5c)*, showing that the selectivity inherent in aldehyde *(3)* approximates a ratio of 1:3[10]. Also, achiral aldehydes *(6)* and *(7)* were condensed with *(1a)* to afford products *(8)* and *(9)* (1:3.5 ratio in 80% yield) and *(10)* and *(11)* (1:6 in 75% yield), respectively[12]. Hence the enantioselectivity of *(1a)* can be estimated to be about 1:5. Therefore, enhanced stereoselection is only achieved when these two factors are acting in concert (entries 1 and 4).

The above results encouraged us to seek a more enantioselective chiral reagent. After investigating a variety of enolates, it was found that the hexahydro derivative *(12a)* of *(1a)*[13] demonstrated a significant increase in stereoselection (*ca.* 15:1) in the aldol condensation with phenylacetaldehyde, as compared with *(1a)*. Also, the high degree of enantioselectivity of *(12a)* or *(12b)* can counteract the normally small Cram/anti-Cram selectivity of aldehydes to the extent that *either the 3,4-anti or the 3,4-syn*[7] *aldol adduct* can now be obtained as the predominant product.

A clear demonstration of this fact is the stereoselective synthesis of both Prelog-Djerassi and *iso*-Prelog-Djerassi lactonic acid [*(13)* and *(14)*, respectively][11].



Scheme 2

As shown in Scheme 2, aldehyde *(15)*[14] was condensed with *(12a)* in THF at −78 °C to yield a mixture of *(16a)* and *(17a)* in a ratio of 15:1. Conversion of *(16a)* into (+)-*(13)* was accomplished *via* a three-step sequence[15]. In a similar fashion, the *iso*-acid *(14)* could also be obtained as the major product. Condensation of *(15)* and *(12b)* provided *(16b)* and *(17b)* in a ratio of 1:10. Thus, this new, readily available reagent can be used to control the 3,4 stereochemistry of aldol products with high diastereoselection, an achievement which has not been realized before.

Received: January 2, 1980 [Z 504 IE]
German version: Angew. Chem. 92, 573 (1980)

[1] *H. B. Kagan, J. C. Fiaud,* Top. Stereochem. *10*, 175 (1978); *J. D. Morrison, H. S. Mosher,* Asymmetric Organic Reactions. Prentice-Hall, Englewood Cliffs, N. J., 1971; *K. Mislow:* Introduction to Stereochemistry. W. A. Benjamin, New York 1966.

[2] *C. H. Heathcock, C. T. White,* J. Am. Chem. Soc. *101*, 7076 (1979); *C. H. Heathcock, M. C. Pirrung, C. T. Buse, J. P. Hagen, S. V. Young, J. E. Sohn, ibid. 101*, 7077 (1979).

[3] A lecture presented by *S. M.* at the University of Virginia on November 20, 1979 included an outline of this work.

[4] *S:* $[\alpha]_D^{25} = +36.5$ ($c = 1.525$, C_2H_5OH); *R:* $[\alpha]_D^{25} = -36.7$ ($c = 2.932$, C_2H_5OH). The reported specific rotations of the *S*- and *R*-acids are $[\alpha]_D^{10.5} = +37.7$ ($c = 3.500$, C_2H_5OH) and $[\alpha]_D^{13.8} = -37.7$ ($c = 3.354$, C_2H_5OH), respectively: *A. McKenzie, G. W. Clough,* J. Chem. Soc. *97*, 1016 (1910).

[5] Prepared by *T. Sato. (2a):* $[\alpha]_D^{25} = -125.9$ ($c = 1.290$, CH_2Cl_2); *(2b):* $[\alpha]_D^{25} = +125.5$ ($c = 1.535$, CH_2Cl_2). Both were optically pure to the limit of detection by NMR using $Eu(hfbc)_3$.

[6] *D. J. Cram, F. D. Greene,* J. Am. Chem. Soc. *75*, 6005 (1953), describe the preparation of *(3)* of unspecified optical purity.

[7] The usage of *"threo"* and *"erythro"* is often confusing. In this communication, the main chain is drawn in the zig-zag fashion, and two substituents on the same side are designed *"syn"*, and those which are not, *"anti"*.

[8] For recent examples, see for instance: a) *S. Masamune, S. Mori, D. E. Van Horn, D. W. Brooks,* Tetrahedron Lett. *1979*, 1665; *M. Hirama, S. Masamune, ibid. 1979*, 2229; b) *R. W. Hoffmann, H. J. Zeiss,* Angew. Chem. *91*, 329 (1979); Angew. Chem. Int. Ed. Engl. *18*, 306 (1979); c) *C. T. Buse, C. H. Heathcock,* J. Am. Chem. Soc. *99*, 8109 (1977).

[9] This problem has been discussed in the past in terms of several different conformations of the α-substituent (Cram, Cornforth, Krabatsos and Felkin rules). See reference [1].

[10] Somewhat surprisingly, aldehyde *(3)* prefers the "anti-Cram" approach of enolates (cf. Table 1). For an earlier example, see reference [11].

[11] *M. Hirama, D. S. Garvey, L. D.-L. Lu, S. Masamune,* Tetrahedron Lett. *1979*, 3937.

[12] Although all of compounds *(8)*—*(11)* are *syn*-2,3 stereoisomers [7], the absolute configurations of these chiral centers have not been unambiguously established.

[13] The corresponding ethyl ketones were obtained from *R*- and *S*-hexahydroatrolactic acid ($[\alpha]_D^{25} = -15.9$ ($c = 1.240$, C_2H_5OH) and $[\alpha]_D^{25} = +16.3$ ($c = 1.690$, C_2H_5OH), respectively) in the same manner as for *(2a)*.

[14] Aldehyde *(15)* was prepared from the optically pure monomethyl ester of *meso*-2,4-dimethylglutaric acid, $[\alpha]_D^{25} = -4.61$ ($c = 7.050$, $CHCl_3$).

[15] The lactonic acids *(13)* and *(14)* were formed from their corresponding aldol products by: a) lactonization with trifluoroacetic acid/methanol/dichloromethane, b) reduction with $Zn(BH_4)_2$, and c) oxidation with Jones' reagent.

Outer Sphere Electron Transfer Reactions: A Novel Linear Relationship between the Selectivity and the Normal Potential of the Reducing Agent

By *Hans-Michael Huck* and *Karl Wieghardt*[*]

In the simplest mechanism of electron transfer (ET) between two transition metal complexes (the outer-sphere mechanism) the reactants form an encounter complex in a preceding equilibrium. In the rate-determining step, the electron is transferred through the intact first coordination spheres of the two complexes; the resulting complex then decomposes to the products[1]:

$$[Ox] + [Red] \overset{K_0}{\rightleftharpoons} \{[Ox][Red]\}$$

Encounter complex

$$\downarrow k_{et}$$

$$\{[Ox^-][Red^+]\} \xrightarrow{Fast} \text{Products}$$

Successor complex

Equation (a) can then be derived for this scheme:

$$\text{rate} = \frac{k_{et} \cdot K_0 [Ox][Red]}{1 + K_0 [Red]} \qquad (a)$$

[*] Prof. Dr. K. Wieghardt, Dipl.-Chem. H. M. Huck
Institut für Anorganische Chemie der Universität
Callinstrasse 9, D-3000 Hannover 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0558 $ 02.50/0

For the one-electron reduction of the inert complexes $[Co(NH_3)_6]^{3+}$ and $[Co(NH_3)_5OH_2]^{3+}$ by the aqua complexes of Sm^{II}[2], Yb^{II}[3], U^{III}[4], Eu^{II}[5], Cr^{II}[6], V^{II}[6], and by $[Ru(NH_3)_6]^{2+}$[7] as well as by $[Cr(bpy)_3]^{2+}$[6a], eq. (a) simplifies to eq. (b) because $K_0[Red] \ll 1$.

$$\text{rate} = k[Ox][Red]; \quad k = k_{et} \cdot K_0 \tag{b}$$

Since K_0 is generally unknown, it is impossible to make any statement about the reactivity ($\log k_{et}$) of the encounter complexes.

The structures of the cations $[Co(NH_3)_6]^{3+}$ (Ox1) and $[Co(NH_3)_5OH_2]^{3+}$ (Ox2) differ only slightly; however, Ox2 is the stronger reducing agent. It therefore appears plausible to assume that for a given reducing agent y from the above series the formation constant K_0 of the encounter complexes {[Ox1],y} and {[Ox2],y} must be of the same magnitude (under otherwise identical reaction conditions). It is therefore reasonable to calculate the difference of the logarithms of the rate constants of reduction [eq. (c)].

$$\log(k_{et}^{Ox2,y} \cdot K_0) - \log(k_{et}^{Ox1,y} \cdot K_0) = \log k_{et}^{Ox2,y} - \log k_{et}^{Ox1,y} \tag{c}$$

This difference then describes the difference in reactivity between the complexes {[Ox1],y} and {[Ox2],y}; it is called the selectivity[8].

The selectivity is found to show a linear correlation with the normal potential of the reducing agent y: the more strongly reducing the action of the reducing agent, the smaller is the observed selectivity (Fig. 1):

$$\log k_{et}^{Ox2,y} - \log k_{et}^{Ox1,y} = (1.3 \pm 0.1)\, E_0^y + (2.3 \pm 0.1) \tag{d}$$

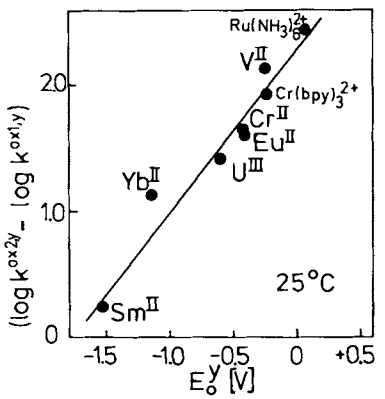


Fig. 1. Difference in the logarithms of the rate constants of reduction k [$M^{-1}s^{-1}$] of $[Co(NH_3)_6]^{3+}$ (Ox1) and of $[Co(NH_3)_5OH_2]^{3+}$ (Ox2) on reduction with the aqua ions of Sm^{II}, Eu^{II}, Yb^{II}, U^{III}, Cr^{II}, V^{II}, and by $[Ru(NH_3)_6]^{2+}$ as well as by $[Cr(bpy)_3]^{2+}$ as a function of the normal potential, E_0^y, of the reducing agent y.

The existence of a relationship such as eq. (d) appears all the more remarkable in view of the fact that the reactivities within the encounter complexes {[Ox1],y1}, {[Ox1],y2}, {[Ox1],y3}, ... *etc.* are *not* a simple function of the reduction potential of the reducing agents y1, y2, y3... For example, the outer-sphere reduction of [Ox1] and [Ox2] with $Ru(NH_3)_6^{2+}$ is about three orders of magnitude *faster* than the corresponding reaction with the stronger reducing agent $[Cr(OH_2)_6]^{2+}$. Thus the reactivity-selectivity principle[8] is not fulfilled in this case for outer-sphere ET reactions between transition metal complexes.

Received: February 1, 1980 [Z 505 IE]
German version: Angew. Chem. 92, 580 (1980)

[1] *G. M. Brown, N. Sutin*, J. Am. Chem. Soc. *101*, 883 (1979).
[2] *M. Faraggi, A. Feder*, Inorg. Chem. *12*, 236 (1973).
[3] *R. J. Christensen, J. H. Espenson, A. B. Butcher*, Inorg. Chem. *12*, 564 (1973).
[4] *J. H. Espenson, R. T. Wang*, J. Am. Chem. Soc. *93*, 380 (1971); *A. Adegite, J. F. Iyun, J. F. Ojo*, J. Chem. Soc. Dalton Trans. *1977*, 115.
[5] *J. Doyle, A. G. Sykes*, J. Chem. Soc. *A 1968*, 2836.
[6] a) *A. Zwickel, H. Taube*, J. Am. Chem. Soc. *83*, 793 (1961); b) *P. Dodel, H. Taube*, Z. Phys. Chem. (Frankfurt am Main) *44*, 92 (1965); *D. L. Toppen, R. G. Linck*, Inorg. Chem. *10*, 2635 (1971).
[7] *J. F. Endicott, H. Taube*, J. Am. Chem. Soc. *86*, 1686 (1964).
[8] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977); *A. Pross*, Adv. Phys. Org. Chem. *14*, 69 (1977).

Biscarbyne Clusters by Alkyne Cleavage: A General Reaction[**]

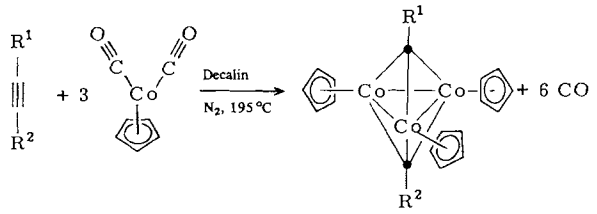
By *John R. Fritch* and *K. Peter C. Vollhardt*[*]

Surface carbyne species have recently been implicated in the H/D exchange of polymethylcycloalkanes mediated by cobalt films[1a], the isomerization of saturated hydrocarbons on iridium catalysts[1b], the interaction of acetylene and ethylene with platinum, nickel, and rhodium single crystals[1c], and the hydrogenation of carbon monoxide (Fischer-Tropsch reaction) on heterogeneous systems[1d]. We describe a *general* synthesis and preliminary physical and chemical properties of biscarbyne clusters prepared by a conceptually most simple route, the direct cleavage of alkynes. Biscarbyne clusters, particularly those derived from multiple cleavage of oligoynes, have excellent potential as, *e.g.*, suitable substrates on which to study surface-homogeneous cluster analogies[2].

We[3] have found that $(\eta^5\text{-}C_5H_5)Co(CO)_2$, which ordinarily functions as a mediator of alkyne oligomerizations to furnish catalytic and stoichiometric products (*e.g.* benzenes, and complexed cyclopentadienones and cyclobutadienes)[4] assembles a trinuclear $[(\eta^5\text{-}C_5H_5)Co]_3$ cluster which inserts into alkyne functions with remarkable ease. Thus, when a solution of diphenylacetylene and $(\eta^5\text{-}C_5H_5)Co(CO)_2$ (3 equiv.) in decalin is slowly added (syringe pump) to boiling and nitrogen flushed decalin over 24 h only 9% of the ordinarily expected cyclopentadienyl(tetraphenylcyclobutadiene)cobalt[5] is isolated on alumina chromatography. The major product (72%) is the biscarbyne cluster *(1)* (see Table 1).

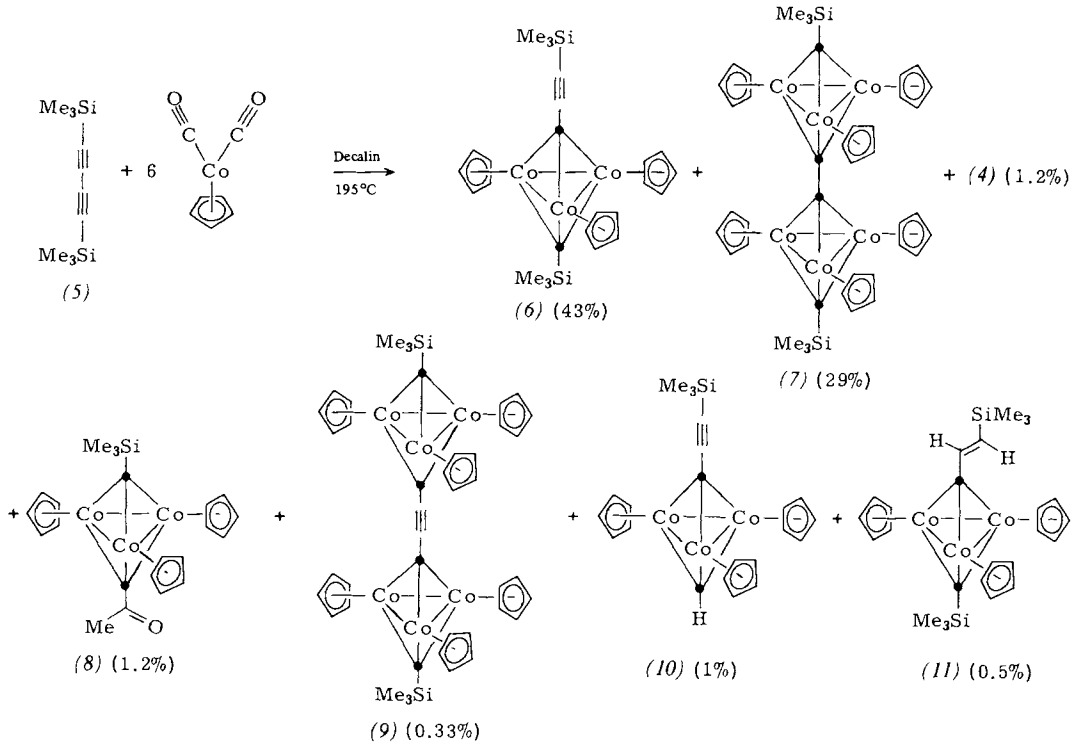
[*] Prof. Dr. K. P. C. Vollhardt, J. R. Fritch
Department of Chemistry, University of California
and the Materials and Molecular Research Division, Lawrence Berkeley Laboratory
Berkeley, California 94720 (USA)

[**] We are grateful for support by the Division of Chemical Sciences, Office of Basic Energy Sciences, U. S. Department of Energy under Contract No. W-7405-Eng-48, NSF, Chevron Research Company, Pressure Chemical Corporation, and Silar Laboratories, Inc. *K. P. C. V.* is a Fellow of the A. P. Sloan Foundation, 1976—1980, and a Camille and Henry Dreyfus Teacher-Scholar, 1978—1983; *J. R. F.* is the recipient of a Regents' Predoctoral Fellowship (1977) and a Gulf Oil Fellowship (1978).



(1), $R^1 = R^2 = C_6H_5$ (72%)
(2), $R^1 = R^2 = n\text{-}C_4H_9$ (56%)
(3), $R^1 = R^2 = CO_2CH_3$ (16%)
(4), $R^1 = Si(CH_3)_3$, $R^1 = H$ (32%)

The clusters *(2)*—*(4)* may be isolated in similar fashion. This finding is important in view of the lack of generality of the many reactions of transition metals with organic substrates. In the cleavage of trimethylsilylated alkynes, traces of

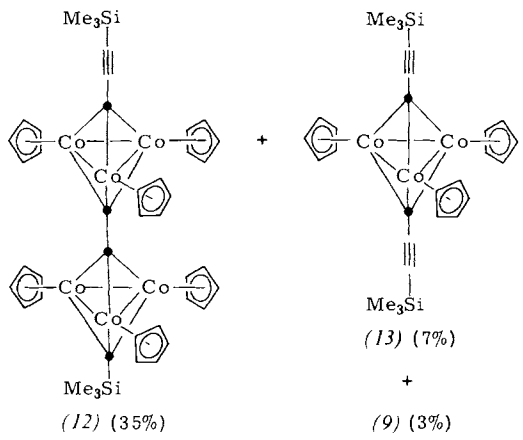


other clusters are observed which are derived from acetylide coupling and decoupling, hydrolysis, and dimerization processes. For example, complete analysis of all chromatographable products from the conversion of bis(trimethylsilyl)butadiyne *(5)* with $(\eta^5\text{-}C_5H_5)Co(CO)_2$ (molar ratio 1:6) reveals seven clusters [*(4)* and *(6)*—*(11)*]! It should be noted that the "multiple decker" sandwich *(7)* is formed despite the considerable steric crowding. Compounds *(4)* and *(9)* most likely arise *via* metathesis of *(5)* to trimethylsilylacetylene and bis(trimethylsilyl)hexatriyne (or their equivalents) in the coordination sphere of cobalt. A control experiment showed that *(7)* is an unlikely source of *(4)* *via* cleavage of the carbido bridge under the reaction conditions. Ketone *(8)* may be thought of as a hydrolysis product of *(6)* and cluster *(10)* is derived from *(6)* by protodesilylation under the reaction conditions *(vide infra)*. The formation of *(11)* points to the presence of 1,4-bis(trimethylsilyl)-1,3-butenyne in the reaction mixture, possibly derived by dimerization of trimethylsilylacetylene[6].

A similar array of products is obtained in the analogous reaction of bis(trimethylsilyl)hexatriyne, but again the major components of the reaction mixture are the singly inserted *(13)*, and the "multiple deckers" *(9)* and *(12)* (Table 1).

Treatment of *(6)* with 1% KOH/EtOH gave quantitative monodesilylation to the unstable terminal acetylene *(14)* (Table 1), whereas the action of $n\text{-}Bu_4N^{\oplus}F^{\ominus}$ in hot THF led to complete desilylation to the unsilylated analogue of *(6)*, compound *(15)* (Table 1).

The parent biscarbyne *(16)* is accessible from *(4)* by protodesilylation $C_6H_5CH_2N(CH_3)_3^{\oplus}F^{\ominus}$ (DMSO, 105 °C, 6 h, 87% yield) (Table 1). Remarkably, instant H/D exchange at the carbyne carbon is observed when *(4)* or *(16)* are exposed to CF_3CO_2D/C_6D_6 (1:1, 25 °C, deep green solution) in an NMR tube under conditions which lead to neither deutero-



(12) (35%) + *(13)* (7%) + *(9)* (3%)

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0707-0560 $ 02.50/0

Table 1. Selected physical data of compounds *(1)*—*(4)* and *(6)*—*(16)*. All new compounds gave satisfactory analytical data.

(1): purple prisms; sublimation 200 °C/10^{-3} torr; m.p. 256—257 °C; *m/e* 550 ($M^{\oplus}$ 100%), 370 (27), 247 (20), 189 (96), 124 (30); ^{1}H-NMR (CCl_4): $\delta = 8.13$ (dd, $J = 1.7$ Hz, 7.8 Hz, 4H), 7.37 (m, 6H), 4.33 (s, 15H); ^{13}C-NMR [$CDCl_3$, $Cr(acac)_3$]: $\delta = 334.6$, 167.3, 127.4, 126.7, 125.3, 85.2

(2): purple needles, m.p. 115.5—116 °C; *m/e* 510 ($M^{\oplus}$, 78%), 508 (40), 370 (100), 247 (38), 189 (87); ^{1}H-NMR (C_6D_6): $\delta = 4.97$ (t, $J = 8.0$ Hz, 4H), 4.33 (s, 15H), 2.61 (q, $J = 7.4$ Hz, 4H), 1.89 (sex, $J = 7.0$ Hz, 4H), 1.26 (t, $J = 7.0$ Hz, 6H)

(3): purple needles, m.p. 244—247 °C; *m/e* 514 ($M^{\oplus}$, 41%), 189 (100); ^{1}H-NMR (C_6D_6): $\delta = 4.49$ (s, 15H), 3.96 (s, 6H); IR ($CHCl_3$): ν_{CO} 1664 cm^{-1}

(4): purple needles, sealed capillary (N_2) sublimation at 250—310 °C, then dec.; *m/e* 470 ($M^{\oplus}$, 100%), 370 (54), 247 (28), 189 (85); ^{1}H-NMR (C_6H_6): $\delta = 18.25$ (s, 1H), 4.42 (s, 15H), 0.83 (s, 9H)

(6): [3] ^{13}C-NMR ($CDCl_3$): $\delta = 373.4$, 279.4, 127.5, 127.0, 83.9, 4.00, 0.76

(7): red-bronze crystals, dec. p. 400 °C; *m/e* 938 ($M^{\oplus}$, 22%), 749 ($M - Cp_2Co$, 12), 189 (100); ^{1}H-NMR (CS_2): $\delta = 4.63$ (s, 30H), 0.94 (s, 18H)

(8): red purple needles, dec. p. 399 °C; *m/e* 512 ($M^{\oplus}$, 19%), 370 (1), 247 (12), 189 (100); ^{1}H-NMR (CCl_4): $\delta = 4.43$ (s, 15H), 3.09 (s, 3H), 0.78 (s, 9H); IR ($CHCl_3$): ν_{CO} 1618 cm^{-1}

(9): maroon crystals, dec. p. 392 °C; *m/e* 962 ($M^{\oplus}$, 70%), 773 ($M - Cp_2Co$, 8), 189 (100); ^{1}H-NMR (CCl_4): $\delta = 4.54$ (s, 30H), 0.83 (s, 18H)

(10): red-purple flakes, m.p. 213—217 °C; *m/e* 494 ($M^{\oplus}$, 41%), 370 (14), 271 (25), 247 (49), 189 (100), 124 (22); ^{1}H-NMR (C_6D_6): $\delta = 18.60$ (s, 1H), 4.44 (s, 15H), 0.52 (s, 9H); IR ($CHCl_3$): $\nu_{C\equiv C}$ 2062 cm^{-1}

(11): purple needles, m.p. 178—180 °C; *m/e* 568 ($M^{\oplus}$, 69%), 370 (16), 247 (14), 189 (100); ^{1}H-NMR (C_6D_6): $\delta = 9.46$ (d, $J = 19.0$ Hz, 1H), 6.62 (d, $J = 19.0$ Hz, 1H), 4.35 (s, 15H), 0.78 (s, 9H), 0.44 (s, 9H)

(12): red-bronze flakes, dec. p. 393 °C; *m/e* 962 ($M^{\oplus}$, 44%), 773 ($M - Cp_2Co$, 21), 189 (100); ^{1}H-NMR ($CDCl_3$): $\delta = 4.68$ (s, 15H), 4.62 (s, 15H), 0.92 (s, 9H), 0.53 (s, 9H); IR (KBr): $\nu_{C\equiv C}$ 2069 cm^{-1}

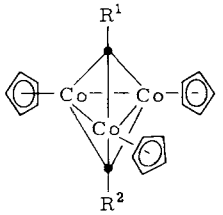
(13): purple crystals, m.p. 161.5—165 °C; *m/e* 590 ($M^{\oplus}$, 37%), 189 (100); ^{1}H-NMR (C_6D_6): $\delta = 4.38$ (s, 15H), 0.48 (s, 18H); IR ($CHCl_3$): $\nu_{C\equiv C}$ 2061 cm^{-1}

(14): purple flakes, dec. p. 102—116 °C; *m/e* 494 ($M^{\oplus}$, 32%), 189 (100); ^{1}H-NMR (C_6D_6): $\delta = 6.78$ (s, 1H), 4.45 (s, 15H), 0.79 (s, 9H); IR ($CHCl_3$): ν_{CCH} 3300 cm^{-1}, $\nu_{C\equiv C}$ 2024 cm^{-1}

(15): purple prisms, dec. p. 25 °C; *m/e* 422 ($M^{\oplus}$, 45%), 271 (17), 189 (100); ^{1}H-NMR (C_6D_6): $\delta = 18.68$ (s, 1H), 6.72 (s, 1H), 4.43 (s, 15H); IR ($CHCl_3$): ν_{CCH} 3295 cm^{-1}, $\nu_{C\equiv C}$ 2020 cm^{-1}

(16): purple crystals, sublimation 160 °C/10^{-3} torr; dec. p. 380—390 °C; *m/e* 398 ($M^{\oplus}$, 64%), 370 (42), 247 (45), 189 (100), 124 (10); ^{1}H-NMR (C_6D_6): $\delta = 18.37$ (s, 2H), 4.38 (s, 15H)

desilylation nor deuterium in corporation into the cyclopentadienyl ligands (1 h)[7]. In contrast, cluster *(1)* is inert to alcoholic HCl, but reacts with hot CF_3SO_3H to furnish benzene and toluene. On the other hand, when *(4)* is exposed to *n*-BuLi/TMEDA (THF, 25 °C, 30 min) followed by D_2O work-up unchanged *(4)* is isolated.



(14), R^1 = C≡CH, R^2 = $SiMe_3$
(15), R^1 = C≡CH, R^2 = H
(16), R^1 = R^2 = H

To test for the potential of carbyne exchange, *(1)* was heated in boiling decalin with excess (molar ratio 1:4) of di-*p*-tolylacetylene[8] for 39 d. Only traces of 1,2-diphenyl-3,4-ditolyl- and tetratolylcyclobutadiene(cyclopentadienyl)cobalt were recovered, in addition to diphenylacetylene (21%), starting cluster *(1)* (74%), and ditolylacetylene (74%). Biscarbynes may act as, or be precursors of, catalytically active species. Heating *(4)* with 1-heptene in a stainless steel bomb to 200 °C for 36 h in the presence of CO (*ca.* 27 bar) and H_2 (*ca.* 55 bar) gave 1-octanal, 1-octanol, 2-methylheptanal, and 2-methylheptanol with respective turnovers of 30, 6.8, 15.4, and 5.0 per equivalent of cobalt. Starting *(4)* was completely consumed.

The unusual spectral data of the reported biscarbynes are compiled in Table 1. They reveal the profoundly deshielding effect and the strong electron donor ability of the cluster unit[9].

Received: February 6, 1980 [Z 506 IE]
German version: Angew. Chem. *92*, 570 (1980)

CAS Registry numbers:
(1), 72271-50-2; *(2)*, 74143-41-2; *(3)*, 74143-42-3; *(4)*, 74143-43-4; *(5)*, 4526-07-2; *(6)*, 70657-46-4; *(7)*, 74143-44-5; *(8)*, 74143-45-6; *(9)*, 74127-93-8; *(10)*, 74143-46-7; *(11)*, 74127-94-9; *(12)*, 74127-95-0; *(13)*, 74127-96-1; *(14)*, 74127-97-2; *(15)*, 74127-98-3; *(16)*, 74127-99-4; diphenylacetylene, 501-65-5; dibutylacetylene, 1942-46-7; dimethyl 2-butynedioate, 762-42-5; ethynyltrimethylsilane, 1066-54-2; dicarbonyl(η^5-2,4-cyclopentadienyl)cobalt, 12078-25-0

[1] a) *F. G. Gault, J. J. Rooney*, J. Chem. Soc. Faraday Trans. I *75*, 1320 (1979); b) *F. Weisang, F. G. Gault*, J. Chem. Soc. Chem. Commun. *1979*, 519; c) *L. L. Kesmodel, L. H. Dubois, G. A. Somorjai*, J. Chem. Phys. *70*, 2180 (1979); *J. C. Hemminger, E. L. Muetterties, G. A. Somorjai*, J. Am. Chem. Soc. *101*, 62 (1979); *J. E. Demuth, H. Ibach*, Surface Sci. *78*, L238 (1978); *L. H. Dubois, D. G. Castner, G. A. Somorjai*, to be published. d) *C. Masters*, Adv. Organometal. Chem. *17*, 61 (1979); *P. Biloen, J. N. Helle, W. M. H. Sachtler*, J. Cat. *58*, 95 (1979); *J. G. Ekerdt, A. T. Bell, ibid. 58*, 170 (1979); *G. A. Somorjai*, personal communication.

[2] *E. L. Muetterties*, Science *196*, 839 (1977); Bull. Soc. Chim. Belg. *85*, 451 (1976).

[3] This communication is prompted by, and complementary to, a report of the low yield nonstoichiometric conversion of (η^5-C_5H_5)Co(alkyne)(PPh_3) into similar biscarbynes: *H. Yamazaki, Y. Wakatsuki, K. Aoki*, Chem. Lett. *1979*, 1041. For preceding work see: *J. R. Fritch, K. P. C. Vollhardt, M. R. Thompson, V. W. Day*, J. Am. Chem. Soc. *101*, 2768 (1979), and references therein.

[4] *R. S. Dickson, P. J. Fraser*, Adv. Organomet. Chem. *12*, 323 (1974); *K. P. C. Vollhardt*, Acc. Chem. Res. *10*, 1 (1977); Nachr. Chem. Tech. Lab. *25*, 584 (1977); Ann. N. Y. Acad. Sci. *333*, 241 (1980); Chem. Soc. Rev. 9, 41 (1980).

[5] *M. D. Rausch, R. A. Genetti*, J. Org. Chem. *35*, 3888 (1970).

[6] Traces of *(11)* were isolated in the synthesis of *(4)*. The homogeneous transition metal catalyzed dimerization of trimethylsilylacetylene has a precedent: *V. P. Yur'ev, G. A. Gailyumas, F. G. Yusupova, G. V. Nurtdinova, E. S. Monakhova, G. A. Tolstikov*, J. Organometal. Chem. *169*, 19 (1979).

[7] Compound *(16)* reacts with CF_3SO_3H to give green crystals of composition $(CpCo)_3(HCCH_2)^{\oplus}CF_3SO_3^{\ominus}$. We suspect this to be a ($\mu_2\eta^1$-carbene)-($\mu_3\eta^1$-carbyne) cation. An X-ray structural investigation is in progress.

[8] *A. Collet, J. Jacques*, Synthesis *1972*, 38.

[9] For the related $RC[Co(CO)_3]_3$ complexes, see: *K. M. Nicholas, M. O. Nestle, D. Seyferth* in *H. Alper:* Transition Metal Organometallics in Organic Synthesis. Academic Press, New York, N. Y., 1978. Vol. II, p. 1: *D. Seyferth*, Adv. Organometal. Chem. *14*, 97 (1976); *B. R. Penfold, B. H. Robinson*, Acc. Chem. Res. *6*, 73 (1973); *G. Pályi, F. Piacenti, L. Markó*, Inorg. Chim. Acta Rev. *4*, 109 (1970).

Gold(I)-Gold(I) Interactions. Tetrameric Gold(I) Dithioacetate

By *Olivo Piovesana* and *Pier Francesco Zanazzi*[*]

The electronic factors responsible for the geometries and stabilities of multinuclear d^{10} systems[1] are still not completely understood, particularly from the standpoint of the

[*] Prof. O. Piovesana [+]
Università di Perugia, Dipartimento di Chimica
Via Elce di Sotto 10, I-06100 Perugia (Italy)
Prof. P. F. Zanazzi
Università di Perugia, Istituto di Mineralogia e Cristallografia
Piazza Università, 06100 Perugia (Italy)
[+] Author to whom correspondence should be addressed.

degree of stabilization afforded by the interactions between the d^{10} centers (with formally closed shells)[2].

Unlike copper(I), which forms clusters with 2 to 8 metal atoms[2c], gold(I) appears to form relatively few multinuclear systems[3] in which metal atom distances are short enough to suggest some M—M bonding, and, with one possible exception[4] *(vide infra)*, all such structurally determined compounds involve either dinuclear units or mononuclear linear molecules forming polymeric gold chains or layers[3].

Here we report the facile synthesis of the air-stable gold(I) dithioacetate, which appears to be the first dithiocarboxylic acid derivative of gold, along with preliminary information on its X-ray structure. This consists of discrete tetranuclear units, $Au_4(CH_3CSS)_4$, with direct gold-gold interactions.

In the tetrameric molecule (Fig. 1) the four gold atoms are at the vertices of a rhomb. The four bridging ligands are alternately above and below the plane of the metal cluster. The molecule has approximate D_2 symmetry. The four equivalent Au—Au distances average 3.01 Å; the unique Au(2)—Au(4) distance is 3.29 Å. At an Au—Au distance of 3.01 Å, compared with those in the metal, 2.884 Å[5], and in the periphery of unbridged cluster compounds such as $[Au_6(PPh_3)_6]^{2+}$, 3.02 Å[6a], and $Au_{11}I_3[P(p\text{-}FC_6H_4)_3]_7$, 2.98 Å[6b], the metal-metal interactions are most likely to be attractive. Actually, recent MO calculations on these cluster compounds have indicated that there is a significant bonding between the peripheral gold atoms[7a]. The Au—S bond distances are normal and average 2.30 Å. The S—Au—Au and S—Au—S

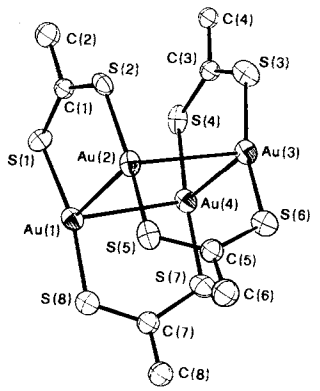


Fig. 1. Molecular structure of $Au_4(CH_3CSS)_4$ in the crystal. Space group $P\bar{1}$, $a=12.200(5)$, $b=9.728(3)$, $c=8.876(3)$ Å, $\alpha=95.32(2)°$, $\beta=110.71(3)°$, $\gamma=92.67(2)°$, $Z=2$, $\rho_{calc}=3.914$ g cm^{-3}. The intensities were measured in the $\theta-2\theta$ scan mode using monochromated Mo-K_α radiation, on a Philips PW1100 single crystal diffractometer. 3347 independent reflections were collected ($3°<\theta<25°$) of which 1828, having $I<3\sigma(I)$, were considered observed and used in the analysis. The structure was solved by direct methods and refined by a full-matrix least-squares approach (SHELX-76 program), anisotropically for the Au and S atoms, to $R=0.10$. Principal bond parameters are: Au(1)—Au(2), 2.989(3); Au(1)—Au(4), 3.003(3); Au(2)—Au(3), 3.020(3); Au(3)—Au(4), 3.022(3); Au(1)—S(1), 2.30(1); Au(1)—S(8), 2.29(1); Au(2)—S(2), 2.31(1); Au(2)—S(5), 2.32(1); Au(3)—S(3), 2.26(1); Au(3)—S(6), 2.30(1); Au(4)—S(4), 2.30(1); Au(4)—S(7), 2.30(1) Å; Au(2)—Au(1)—Au(4), 66.6(1); Au(2)—Au(3)—Au(4), 66.1(1); Au(1)—Au(2)—Au(3), 113.8(1); Au(1)—Au(4)—Au(3), 113.3(1)°.

mean angles are 94 and 193°, respectively. The deviation from linearity in the S—Au—S coordination is determined by a dihedral angle of about 16° between the planes of the ligands on opposite sides of the metal cluster.

The unstable, colorless chloro(piperidine)gold(I) is the only compound in which Au_4 units have been located[5]. Here, the unbridged, linearly co-ordinated gold atoms form a loose square cluster with an Au—Au mean distance of 3.30 Å. Whether M—M bonding interaction does or does not occur in this compound is not clearly understood[5].

The geometry of the Au_4 units and the M—M interactions in the title compound are attributable to both steric and electronic factors. Thus, interligand S—S and methyl-methyl repulsion would be severe with two alternate pairs of eclipsed ligands and interplanar separations of about 3 Å. On the other hand, there seems little to account for the deviations from linearity in the gold-sulfur coordination except some residual mutual repulsion of the ligands.

Electronic factors seem to be related to the ability of the dithioacetato ligand system to encourage d-s orbital mixing[7] on gold and to dissipate antibonding density from the plane of the cluster through its delocalized π virtual orbitals.

In a simplified bonding picture, empty ($d_{z^2}+\lambda s$) gold hybrid orbitals (directed along the S—Au—S axes) are available for the sulfur donation and filled ($d_{z^2}-\lambda s$) orbitals interact in the plane of the metal cluster. Because of the nondirectional character of the latter orbitals, the gold-gold interactions and the π interactions with the ligand system are angularly independent. The gold atoms, therefore, can move with respect to each other without sacrifice of orbital overlap and do it in order to minimize interligand repulsion.

The four in-plane hybrid atomic orbitals give rise to four cluster MOs, (one bonding, two nonbonding and one antibonding), with eight electrons and an overall antibonding effect. The extent of attractive interactions between the gold atoms should depend, therefore, on the capability of the delocalized π virtual orbitals of the tetrakis(dithiocarboxylato) framework to relieve antibonding density from the plane of the cluster.

It may be noted that d-s orbital mixing on gold and π acceptance by ligands from it have been recently found to be negligible in a large variety of mononuclear, linear gold(I) complexes[8].

Experimental

The red $Au_4(CH_3CSS)_4$ compound was prepared by heterogeneous reaction of $NaAuCl_4\cdot 2H_2O$ (1 g, 2.51 mmol) with CH_3CSSH (1 g, 10.87 mmol) in diethyl ether (50 cm^3). After the mixture stood for *ca.* 20 h at room temperature, it was filtered. The solid was recrystallized from carbon disulfide; yield *ca.* 30%, based on original gold.

Received: January 2, 1980 [Z 509 IE]
German version: Angew. Chem. *92*, 579 (1980)

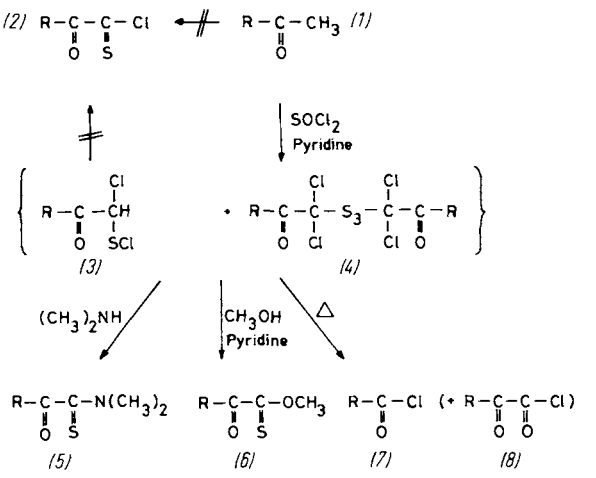
CAS Registry number:
$Au_4(CH_3CSS)_4$, 74165-53-0

[1] *J. P. Fackler, Jr.*, Prog. Inorg. Chem. *81*, 55 (1976).
[2] a) *F. J. Hollander, D. Coucouvanis*, J. Am. Chem. Soc. *99*, 6268 (1977), and references cited therein; b) *A. Avdeef, J. P. Fackler, Jr.*, Inorg. Chem. *17*, 2182 (1978); c) *P. K. Mehrotra, R. Hoffmann, ibid. 17*, 2187 (1978).
[3] *H. Schmidbaur*, Angew. Chem. *88*, 830 (1976); Angew. Chem. Int. Ed. Engl. *15*, 728 (1976); *R. J. Puddephatt:* Topics in Inorganic and General Chemistry. Vol. 16. Elsevier, Amsterdam 1978.
[4] *J. J. Guy, P. G. Jones, M. G. Mays, G. M. Sheldrick*, J. Chem. Soc. Dalton Trans. *1977*, 8.
[5] *W. D. Pearson:* Lattice Spacings and Structures of Metals and Alloys. Pergamon, London 1957.
[6] a) *P. Bellon, M. Manassero, M. Sansoni*, J. Chem. Soc. Dalton Trans. *1973*, 2423; b) *1972*, 1481.
[7] a) *D. M. P. Mingos*, J. Chem. Soc. Dalton Trans. *1976*, 1163; b) *L. E. Orgel*, J. Chem. Soc. *1958*, 4186.
[8] *P. G. Jones, A. G. Maddock, M. J. Mays, M. M. Muir, A. F. Williams*, J. Chem. Soc. Dalton Trans. *1977*, 1434.

Are α-Oxothioacyl Chlorides Formed in the Reaction of Methyl Ketones with Thionyl Chloride?[**]

By *Gunadi Adiwidjaja, Horst Günther,* and *Jürgen Voss*[*]

Oka and *Hara*[2] recently reported that they had prepared α-oxothioacyl chlorides *(2)* from methyl ketones *(1)* as well as from the α-chlorosulfenyl chlorides *(3)* formed in the same reaction. Proof of the structure of *(2)* was based merely on rather uninformative ^{1}H-NMR spectra, a C=S band at 1230 cm^{-1} (arising, however, from thionyl chloride) and a peak at $m/e = 184$ in the mass spectrum of the product mixture obtained from acetophenone *(1b)*, and its subsequent reaction to give the α-oxothioamide *(5b)*.—With exception of the oxamide derivative $R_2N—CO—CS—Cl$[3], compounds of type *(2)* have so far not been described in the literature and their existence is highly questionable (cf. [4]). We obtained other results, both on exact repetition as well as on slight modification of the procedure given in [2] (see Scheme 1).



Scheme 1.

Table 1. Primary and secondary products of the reaction of methyl ketones *(1)* with thionyl chloride.

Cpd. [a]	R	Yield [%]	M.p. [°C] B.p. [°C/torr]	^{1}H-NMR δ values	^{13}C-NMR δ values
(3a)	*t*Bu	50 [b]		1.28 (s, *t*Bu), 6.08 (s, CH)	204.5 (CO), 65.5 (CCl)
(3b)	Ph	45 [b]		6.64 (s, CH), 7.45—8.35 (m, Ph)	189.0 (CO), 65.7 (CCl)
(4a)	*t*Bu	40 [b]	72.5	1.50 (s, *t*Bu)	198.2 (CO), 94.1 (CCl_2)
(4b)	Ph	40 [b]	106	7.32—8.22 (m, Ph)	184.6 (CO), 93.8 (CCl_2)
(5a)	*t*Bu	96 [c]	40.5	1.27 (s, *t*Bu), 3.10 (s, NMe), 3.32 (s, NMe)	207.3 (CO), 198.1 (CS)
(5b)	Ph	78 [d]	84.5 [e]	3.13 (s, NMe), 3.44 (s, NMe), 7.28—7.43 (m, 3H), 7.73—7.93 (m, 2H)	188.4 (CO), 196.6 (CS)
(5c)	*p*-*t*Bu—C_6H_4	69 [d]	116	1.37 (s, *t*Bu), 3.23 (s, NMe), 3.57 (s, NMe), 7.35—8.19 (m, 4H)	
(5d)	3,5-tBu_2—C_6H_3	47 [d]	162	1.39 (s, 2*t*Bu), 3.25 (s, NMe), 3.58 (s, NMe), 7.55—7.77 (m, 3H)	
(5e)	*p*-$Me_2N—CS—CO—C_6H_4$ [f]	85	202		
(5f)	$Me_2N—CS$ [g]	5	118		
(5g)	3,5-$(Me_2N—CS—CO)_2C_6H_3$ [h]	3	226	3.25 (s, 3 NMe), 3.56 (s, 3 NMe), 8.69 (s, 3H)	184.5 (CO), 194.2 (CS)
(6a)	*t*Bu [i]	79 [d]	68—69/9	1.25 (s, *t*Bu), 4.13 (s, OMe)	203.2 (CO), 214.3 (CS)
(6b)	Ph [k]	56 [d]	86.5/0.2	4.22 (s, OMe), 7.33—7.52 (m, 3H), 7.80—7.97 (m, 2H)	187.2 (CO), 212.9 (CS)
(6c)	*p*-*t*Bu—C_6H_4	40 [d]	114/0.2	1.30 (s, *t*Bu), 4.27 (s, OMe), 7.40—7.98 (m, 4H)	
(6d)	3,5-tBu_2—C_6H_3	51 [d]	37.5—39	1.33 (s, 2 *t*Bu), 4.25 (s, OMe), 7.60—7.72 (m, 3H)	
(10a)	*t*Bu	77 [l]	77.5	1.55 (s, *t*Bu), 3.20 (s, NMe), 3.49 (s, NMe)	201.7 (NCS), 258.8 (CS)

[a] *(4a)*, *(4b)*, *(5)* and *(6)* gave correct elemental analyses. *(3c)*, *(3d)*, *(4c)*, and *(4d)* were not characterized; the mixtures obtained from *(1c)* and from *(1d)* on reaction with thionyl chloride were allowed to react directly with nucleophiles. [b] Determined NMR spectroscopically. [c] Referred to *(3a)*: [*(3a)* + *(4a)*] gave 85% *(5a)*. [d] From [*(3)* + *(4)*], referred to *(1)*. [e] M.p. (literature) 84–85 °C [2]. [f] From 1,4-diacetylbenzene. [g] From acetone. [h] From 1,3,5-triacetylbenzene. [i] λ_{max} (isooctane) = 392 (log ε = 1.68), 309 (225), 260 (3.39) s, 220 (3.94) nm; ν(CO) = 1705 cm^{-1}. [k] λ_{max} (isooctane) = 398 (log ε = 1.97), 338 (2.39), 251 (4.17), 218 (3.54) s; ν(CO) = 1665 cm^{-1}. [l] Referred to *(5a)*.

That a mixture of *(3)* and the trisulfane *(4)* is formed on reaction of *(1)* with thionyl chloride in pyridine follows from the spectroscopic data (Table 1), and especially from the ^{13}C-NMR spectra. *(4a)*, which crystallizes from the crude product at −20 °C in yields of up to 25%, was characterized, *inter alia*, by X-ray structure analysis (Fig. 1). *(4b)* could be isolated by column chromatography (SiO_2, CH_2Cl_2/CCl_4 (1:1), 5% yield).

Both the mixture [*(3)* + *(4)*] as well as pure *(4)* afford α-oxothioamides *(5)* almost quantitatively on reaction with dimethylamine. This reaction can also be carried out with other secondary aliphatic or araliphatic amines and *tert*-butylamine.

Reaction with methanol in the presence of bases affords the previously unknown α-oxothionic esters *(6)* (see Table 1), which represent a further type of esters containing adjacent C=O- and C=S-groups. In contrast to the blue α-thioxo esters R—CS—CO—OR, which tend to dimerize[5], the orange-colored isomers *(6)* are stable.

Surprisingly, we also obtained 85% 1,4-benzenebis(*N,N*-dimethyl-α-oxothioacetamide) *(5e)* from 1,4-diacetylbenzene, and even from the very complex mixtures which are formed on reaction of $SOCl_2$ with acetone or 1,3,5-triacetylbenzene we were able to isolate 5% *N,N,N',N'*-tetramethylmesoxaldithioamide *(5f)*[6] and 3% of the tristhioamide *(5g)*, respectively, in analytically pure form by column chromatography (see Table 1).—2,4,6-Tri-*tert*-butylacetophenone, on the other hand, does not give the corresponding thioamide.

The α-oxothioamides *(5)* can be sulfurized with the dimeric phosphane sulfide *(9)*[7] in good yields to the red to green-

[*] Prof. Dr. J. Voss, Dipl.-Chem. H. Günther
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
Dr. G. Adiwidjaja
Mineralogisch-Petrographisches Institut der Universität
Hamburg (Germany)

[**] Activated Thiocarboxylic Esters, Part 7. This work was supported by the Deutsche Forschungsgemeinschaft (Project Vo 180/5) and the Fonds der Chemischen Industrie. We thank Chemischen Werken Hüls for supplying us with 1,3,5-triacetylbenzene.—Part 6: [1].

ish black α-thioxothioamides *(10)*, a class of substances of which only one example has hitherto been reported[8].

The mixture of *(3)* and *(4)*, which is also readily accessible in larger quantities, is thus a valuable starting material for products which presumably would be formed from the still unknown *(2)*.

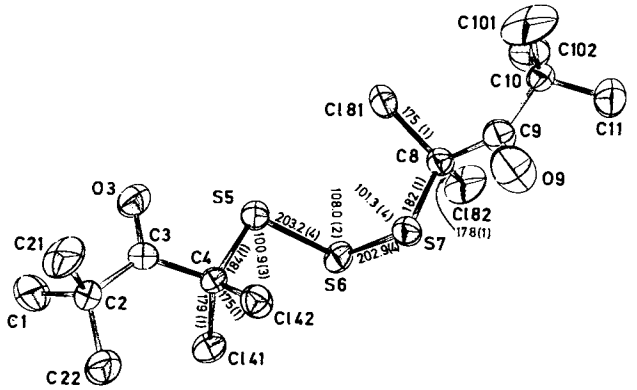
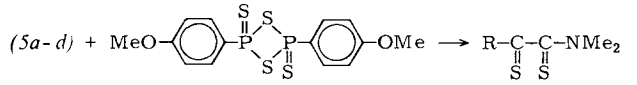


Fig. 1. Molecular structure of the trisulfane *(4a)* in the crystal (ORTEP diagram); vibration ellipsoids with 30% probability. – Space group $P2_12_12_1$, $a = 2655.6$, $b = 1173.5$, $c = 629.1 \pm 0.1$ pm, $Z = 4$, $\rho = 1.48$ g cm^{-3}. The intensities of the reflections were measured with an automated single crystal diffractometer Syntex P_{2_1} ($Cu_{K\alpha}$ radiation) and corrected in the usual way. The crystal structure was determined on the basis of 1584 symmetric independent structure amplitudes by the direct method using the computer program MULTAN and refined to $R = 6.8\%$ ($R_w = 6.1\%$).

On heating (distillation) [*(3)* + *(4)*] one obtains acyl chlorides *(7)* and *(8b)*, but not the pure α-chlorosulfenyl chlorides *(3)*, and under no circumstances *(2)*[2]. Recent reports of *Pizey* and *Symeonides*[9], in which only pivaloyl chloride *(7a)*, *i.e.* the thermolysis product of [*(3a)* + *(4a)*], could be obtained on reaction of pinacolone with thionyl chloride, are to



(9) *(10a-d)*

be seen in this light. The surprisingly uniform thermolysis, however, is preparatively not without interest, for it leads practically in one step from methyl ketones to acyl chlorides in acceptable yields.

Experimental

(5a): A solution of *(4a)* (4.32 g, 10 mmol) in ether (50 ml) is added dropwise at −80 °C to a stirred solution of $(CH_3)_2NH$ (4.5 g, 100 mmol) in ether (50 ml). After warming to room temperature, the reaction mixture is poured into 500 ml of water, neutralized with dil. HCl, the ether removed, the aqueous phase extracted with $CHCl_3$, the organic phases washed with water, dried with Na_2SO_4 and evaporated to dryness. Recrystallization of the residue from hexane affords pale yellow crystals of *(5a)*.—*(5b—d)* are synthesized analogously from [*(3)* + *(4)*].

(6a): The mixture [*(3a)* + *(4a)*] obtained from *(1a)* (5 g, 50 mmol) is dissolved in 100 ml methanol and treated dropwise with stirring at 0 °C with 27.7 ml (20.2 g = 200 mmol) of triethylamine. The mixture is diluted with 300 ml water, neutralized with dil. HCl, extracted with ether, washed with water, dried with Na_2SO_4 and evaporated down. The residue is dissolved in $CHCl_3$, filtered over a layer of SiO_2, and distilled in a vacuum; *(6a)* is an orange-yellow oil.

(10a): A solution of *(5a)* (5 g, 28.9 mmol) in toluene (60 ml) is treated with 6.5 g (15.9 mmol) of *(9)* and the mixture heated under reflux for 3 h. After cooling, the mixture is poured into 500 ml water, extracted with ether (3 × 150 ml), the combined ether phases washed twice with water, dried with Na_2SO_4, and evaporated down. The red, crystalline residue is dissolved in $CHCl_3$ and filtered over a layer of SiO_2. *(10a)* forms luminous carmine-red crystals.

Distillation of [*(3a)* + *(4a)*] at normal pressure affords *(7a)* in 50% yield [based on *(1a)*].—[*(3b)* + *(4b)*] gives a mixture of *(7b)* (36% yield) and *(8b)* (15% yield).

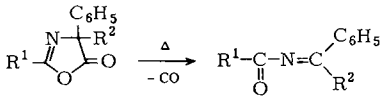
Received: May 14, 1979 [Z 507 IE]
supplemented: February 25, 1980
German version: Angew. Chem. *92*, 559 (1980)

[1] *J. Voss, H. Günther*, Synthesis *1978*, 849.
[2] *K. Oka, S. Hara*, Tetrahedron Lett. *1976*, 2783.
[3] *W. G. Phillips, K. W. Ratts*, J. Org. Chem. *37*, 1526 (1972).
[4] *G. Seybold*, Angew. Chem. *87*, 710 (1975); Angew. Chem. Int. Ed. Engl. *14*, 703 (1975).
[5] *K. Thimm, J. Voss*, Tetrahedron Lett. *1975*, 537; *P. Metzner, J. Vialle, A. Vibet*, Tetrahedron *34*, 2289 (1978).
[6] *E. Campaigne, G. Skowronski, R. A. Forsch, J. C. Beckman*, Synth. Commun. *6*, 387 (1976), have obtained *(5a)* *via* another more complicated route.
[7] *B. S. Pedersen, S. Scheibye, N. H. Nilsson, S.-O. Lawesson*, Bull. Soc. Chim. Belg. *87*, 223 (1978).
[8] *P. A. Barrett*, J. Chem. Soc. *1957*, 2056.
[9] *J. S. Pizey, K. Symeonides*, Phosphorus Sulfur *8*, 1 (1980).

Acylated Ketenimines and Allenes from Oxazol-5(4*H*)-ones and Furan-2(3*H*)-ones[**]

By *Hans-Michael Berstermann, Raymond Harder, Hans-Wilhelm Winter*, and *Curt Wentrup*[*]

Flash vacuum pyrolysis of 4-substituted isoxazol-5(4*H*)-ones results in the elimination of CO_2 and formation of acetylenes, isocyanides, or related compounds[1]. Oxazol-5(2*H*)-ones thermally extrude CO_2 with formation of nitrile ylides[2a], whereas both CO_2- and CO-elimination from oxazol-5(4*H*)-ones is known[2b]. We now report that oxazol-5(4*H*)-ones *(1)* and *(3)* and furan-2(3*H*)-ones *(5)* extrude CO only. The reaction of *(5)* constitutes a useful synthesis of propadienyl ketones *(6)*.



(1) *(2)*

(a), $R^1 = R^2 = C_6H_5$; *(b)*, $R^1 = p\text{-}CH_3C_6H_4$, $R^2 = C_6H_5$; *(c)*, $R^1 = C_6H_5$, $R^2 = H$

The oxazol-5(4*H*)-ones *(1)* were prepared by standard methods[3] and subjected to flash pyrolysis[4] at 500—900 °C/*ca.* 10^{-4} torr. Over this temperature range, the only products,

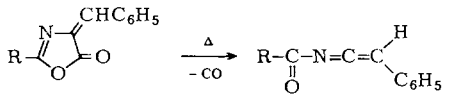
[*] Prof. Dr. C. Wentrup, Dipl.-Chem. H.-M. Berstermann, Dipl.-Chem. H.-W. Winter
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg (Germany)
Dr. R. Harder
Institut de Chimie Organique de l'Université
CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie and abstracted in part from the diploma thesis of *H.-M. Berstermann*, Marburg 1979, and the doctoral thesis of *R. Harder*, Lausanne 1976.

formed virtually quantitatively (95—99% at 600 °C), were the *N*-alkylideneamides *(2)*.

This simple reaction offers certain advantages over the normal procedure for the preparation of aroylated imines *(2)*. For example, *(2b)* was prepared for the purpose of comparison in 20% yield from *p*-toluyl chloride and benzophenone imine; the latter is obtained in 80% yield from phenylmagnesium bromide and benzonitrile.

An analogous CO extrusion from the azlactones *(3)* would give rise to the ketenimines *(4)*. Indirect evidence for the formation of *(4a)* was obtained previously by pyrolysis of *(3a)*[5]. We have now secured direct IR spectroscopic evidence for the formation of *(4)* by pyrolysis of *(3)* at 600 °C/*ca.* 10^{-4}

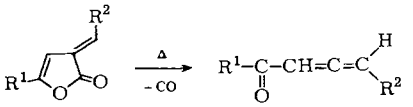


(3) *(4)*

(a), R = C_6H_5; *(b)*, R = CH_3

torr in an apparatus equipped with a 10-cm quartz pyrolysis tube and collecting the products on a turnable KBr disc cooled to *ca.* −196 °C. On infrared monitoring of the pyrolyses of *(3a)* and *(3b)*, sharp absorptions ascribed to *(4)* were observed at 2019 cm^{-1}, the region typical[6] for ketenimines.

The above results prompted an examination of the pyrolysis of 3-arylmethylidenefuran-2(3*H*)-ones *(5)* which, by analogy, should yield the propadienyl ketones *(6)*. The compounds *(5)* (see Table) are easily prepared by condensation of the appropriate 5-substituted furan-2(3*H*)-one with aromatic aldehydes[7], and were shown by ^{1}H-NMR spectroscopy to exist in the *E*-form[8]. The compounds *(5)* were pyrolyzed at 700 °C/*ca.* 10^{-4} torr, the products isolated on a cold



(5) *(6)*

finger cooled with liquid N_2, and then purified by layer chromatography on SiO_2. The allenes *(6)* were characterized by their IR absorptions (see Table 1), ^{1}H-NMR and mass spectra, and by ^{13}C-NMR resonances near $\delta = 215$ ppm (=C=), and near $\delta = 190$ (CO). All the allenes *(6)* are unstable at room temperature, the furoylallenes *(6c)* and *(6f)* so much so that they could not be isolated in substance.

Compound *(6a)* was the only member of this series previously known; it had been obtained[9] together with an isomeric alkyne. In our work, no evidence (IR spectroscopy) has been obtained for the production of alkynes isomeric with *(6a—f)*. This, together with the sensitivity of compounds *(6)*, testifies to the mildness of flash vacuum pyrolysis as a preparative method.

Experimental

(2b): *(1b)* [m.p. 135 °C] was prepared in 69% yield from benzilic acid and *p*-tolunitrile adapting the method reported[3] for *(1a)*. The pyrolysis of *(1b)* (250 mg) at 600 °C/10^{-4} torr (25 × 2 cm quartz pyrolysis tube) gave 200 mg (95%) of *(2b)*, m.p. 152 °C after recrystallization from EtOH. ^{1}H-NMR (CCl_4): $\delta = 2.4$ (s, 3H), 7.1 (d, $J = 8$ Hz, 2H), 7.2—7.6 (m, 10H), 7.7 (d, $J = 8$ Hz, 2H) ppm; IR (KBr): 1660 (C=O), 1630 (C=N) cm^{-1}.

(6): *(5a)* (500 mg) was pyrolyzed at 700 °C/10^{-4} torr by sublimation from a flask held at 145—150 °C. The pyrolyzate was collected on a cold finger at −196 °C, rapidly dissolved in $CHCl_3$, and chromatographed on a 20 cm SiO_2 plate (0.5 mm thickness), eluting with toluene. The compound having $R_f \approx 0.1$ was extracted with acetone and identified as *(6a)* (see Table 1).—*(6b, d, e)* were prepared in a similar manner and isolated by layer chromatography; *(6c, f)* dimerized under these conditions.

Received: November 5, 1979 [Z 508a IE]
German version: Angew. Chem. *92*, 555 (1980)

CAS Registry numbers:
(1a), 61365-94-4; *(1b)*, 74143-79-6; *(1c)*, 28687-81-2; *(2a)*, 1585-45-1; *(2b)*, 74143-80-9; *(2c)*, 10374-29-5; *(3a)*, 842-74-0; *(3b)*, 881-90-3; *(4a)*, 74165-57-4; *(4b)*, 74143-81-0; *(5a)*, 53949-11-4; *(5b)*, 70041-48-4; *(5c)*, 74143-82-1; *(5d)*, 74143-83-2; *(5e)*, 74143-84-3; *(5f)*, 74143-85-4; *(6a)*, 74143-86-5; *(6b)*, 74143-87-6; *(6c)*, 74143-88-7; *(6d)*, 74143-89-8; *(6e)*, 74143-90-1; *(6f)*, 74143-91-2

[1] See *C. Wentrup, B. Gerecht, H. Briehl*, Angew. Chem. *91*, 503 (1979); Angew. Chem. Int. Ed. Engl. *18*, 467 (1979), and references therein.
[2] a) *G. Höfle, W. Steglich*, Chem. Ber. *104*, 1408 (1971); *W. Steglich, P. Gruber, H.-U. Heininger, F. Kneidl, ibid. 104*, 3816 (1871); *H.-M. Berstemann, K.-P. Netsch, C. Wentrup*, Chem. Commun. *1980*, 503; b) *P. Gruber, L. Müller, W. Steglich*, Chem. Ber. *106*, 2863 (1973); *S. Götze, W. Steglich, ibid. 109*, 2327 (1976); *M. R. Johnson, L. R. Sousa*, J. Org. Chem. *42*, 2439 (1977).
[3] *F. R. Japp, A. Findley*, J. Chem. Soc. *75*, 1027 (1899); *C. W. Bird*, J. Org. Chem. *27*, 4091 (1962).
[4] See *C. Wentrup*, Chimia *31*, 258 (1977).
[5] *C. Wentrup, W. Reichen*, Helv. Chim. Acta *59*, 2615 (1976).
[6] *C. L. Stevens, J. C. French*, J. Am. Chem. Soc. *76*, 4398 (1954); *R. B. Woodward, R. A. Olofson*, Tetrahedron Suppl. 7, 415 (1966); *S. Stankovsky, S. Kovac*, Chem. Zvesti *28*, 234 (1974).

Table 1. Flash vacuum pyrolysis of furanones *(5)* at 700 °C/*ca.* 10^{-4} torr. Compounds *(5)* were sublimed into the apparatus at about 10 °C below their melting points; *(5d)* was distilled into the apparatus at 50—60 °C.

Cpd.	R^1	R^2	*(5)*, m.p. [°C]	*(6)*, yield [%]	*(6)*, $\nu_{C=C=C}$ [cm^{-1}]
a	C_6H_5	C_6H_5	154—155	50	1935 [a]
b	C_6H_5	*p*-CH_3O—C_6H_4	171—172.5	45	1935 [b]
c	C_6H_5	2-Furyl	117—119	[c]	1930
d	CH_3	C_6H_5	Oil	85	1928 [d]
e	CH_3	*p*-CH_3O—C_6H_4	97—98	80	1935
f	CH_3	2-Furyl	77—78.5	[c]	1940

[a] IR (film): 3000 w, 1935 s, 1650 s, 1595 m, 1448 m, 1395 m, 1272 s, 1210 s cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 6.60$ (d, $J_{HC=C=CH} = 6.5$ Hz, 1H), 6.73 (d, $J_{HC=C=CH} = 6.5$ Hz, 1H), 7.2—8.0 (m, 10H); ^{13}C-NMR ($CDCl_3$): $\delta = 97.2$, 98.1, 127.1, 127.8, 128.0, 128.4, 128.6, 130.9, 132.5, 137.1, 190.1, 215.4. [b] ^{1}H-NMR ($CDCl_3$): $\delta = 3.74$ (s, 3H), 6.52 (d, $J = 6.5$ Hz, 1H), 6.65 (d, $J = 6.5$ Hz, 1H), 6.81 (d, $J = 8.7$ Hz, 2H), 7.17 (d, $J = 8.7$ Hz, 2H), 7.1—7.9 (m, 5H). [c] Not isolable in substance; yields of *(6c)* and *(6f)* in solution: 50 and 80%, respectively. [d] ^{1}H-NMR ($CDCl_3$): $\delta = 2.2$ (s, 3H), 3.7 (s, 3H), 6.03 (d, $J = 6.3$ Hz, 1H), 6.51 (d, $J = 6.3$ Hz, 1H), 6.80 (d, $J = 8.8$ Hz, 2H), 7.74 (d, $J = 8.8$ Hz, 2H).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0707-0565 $ 02.50/0*

[7] *J. Thiele*, Liebigs Ann. Chem. *306*, 142 (1899); *J. Thiele, R. Tischbein, E. Lossow, ibid. 319*, 180 (1901); *F. W. Schueler, C. Hanna*, J. Am. Chem. Soc. *73*, 3528 (1951); *R. Filler, E. J. Piasek, H. A. Leipold*, Org. Synth. *43*, 3 (1963).

[8] The *E*-configuration of *(5a)* was demonstrated by *A. Maquestiau, Y. van Haverbeke, R. N. Muller*, Bull. Soc. Chim. Belg. *83*, 259 (1974). The *E*-configuration of *(5d–f)* is demonstrated by a relatively large coupling of *ca.* 0.7 Hz between the CH_3 group and the exocyclic proton. *E.g.* for *(5e)* the ^{1}H NMR spectrum in $CDCl_3$ shows an ABX_3 system for the methylidene proton (A), the ring proton H-4 (B), and the methyl group at C-5 (X_3): $\delta = 2.18$ (X_3), 6.24 (B), 7.21 (A); $J_{AB} = 0.9$, $J_{AX} = 0.7$, $J_{BX} = 1.2$ Hz (based on computer simulation and spin decoupling experiments). The remaining signals in *(5e)* were at $\delta = 3.84$ (s, 3H (OCH_3)), 6.92 (d, $J = 8.8$ Hz, 2H (arom.)), 7.49 (d, $J = 8.8$ Hz, 2H (arom.)).

[9] *T. L. Gilchrist, D. P. Pearson*, J. Chem. Soc. Perkin I *1976*, 989.

Cyclic Carbodiimides in Nitrene Rearrangements[**]

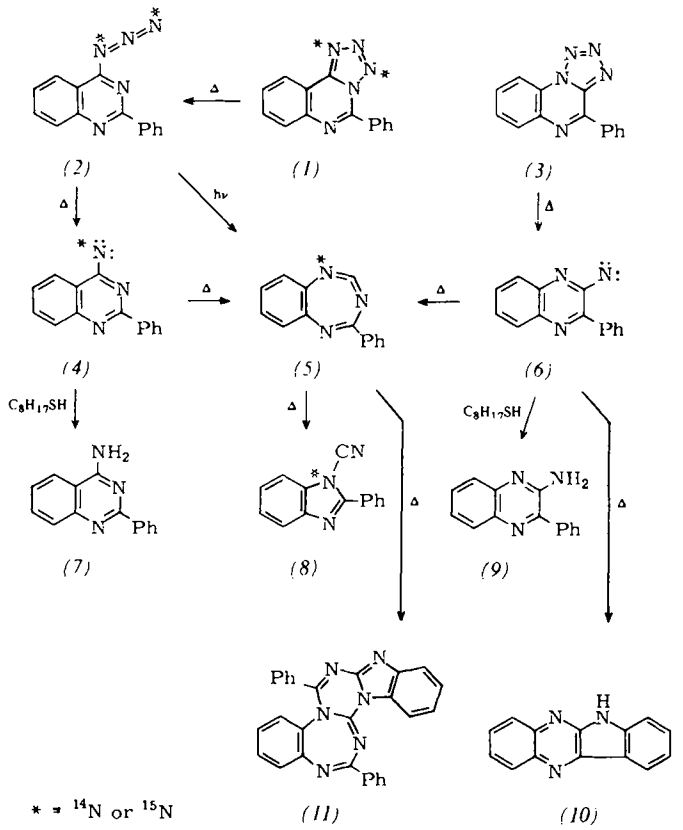
By *Curt Wentrup, Célestin Thétaz, Enrico Tagliaferri, Hans Jörg Lindner, Brigitte Kitschke, Hans-Wilhelm Winter,* and *Hans Peter Reisenauer*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In the course of our studies on the rearrangements of heterocyclic nitrenes it became necessary to postulate cyclic carbodiimides as key intermediates in some reactions[2]. However, no such intermediate had ever been directly observed. We now wish to report conclusive chemical evidence as well as the direct spectroscopic observation of a cyclic carbodiimide in reactions of this type.

The tetrazolo[1.5-*c*]quinazoline *(1)* exists exclusively as a tetrazole in the solid state[3], but sublimation of *(1)* at 100 °C/10^{-4} torr and subsequent condensation of the vapor on a KBr disc at −196 °C afforded the azide *(2)*, characterized by intense IR absorptions at 2150, 2120, 1620, 1570, and 1370 cm^{-1}. The solid azide was transformed back into the tetrazole *(1)* on warming to *ca.* −40 °C. It can thus be asserted that a gas-phase thermolysis of *(1)* will give initially the azide *(2)*[4].

Flash vacuum thermolysis of *(1)* at temperatures above 300 °C/10^{-3} torr gave 2-phenylbenzimidazole-1-carbonitrile *(8)* in quantitative yield[5]. The same product was obtained in 92% yield together with 8% of indolo[2,3-*b*]quinoxaline[5] *(10)* by thermolysis of tetrazolo[1,5-*a*]quinoxaline *(3)* at 380 °C/10^{-3} torr. In the case of *(3)*, only weak bands due to the corresponding azide were observable by IR spectroscopy at −196 °C, following thermolyses near the temperature where the reaction *(3)*→*(8)* takes place (300–400 °C).



Ring contraction to *(8)* also occurred by thermolysis of either *(1)* or *(3)* in benzene solution in a sealed tube at 160–180 °C (59 and 88%, respectively). In addition, the solution thermolyses of *(1)* and *(3)* in various solvents always afforded a yellow dimer in variable yield (*e.g.* 57% from *(1)* in cyclohexane at 180 °C for 72 h; 25% from *(3)* in mesitylene at 165 °C for 240 h). The infrared, ^{13}C-NMR, and mass spectra of the dimers obtained from *(1)* and *(3)* were identical, and the structure *(11)*, possessing the novel imidazo[1,2-*a*][1,3,5]triazino[6,5-*a*][1,3,5]triazepine ring system, was determined by X-ray crystallography[6]. The solution thermolyses also afforded the amines *(7)* and *(9)*, respectively, which are the products expected from hydrogen abstraction by the triplet ground state nitrenes *(4)* and *(6)*. The best yields of amines were obtained by decomposition of *(1)* and *(3)* in a 1:1 mixture of octanethiol and mesitylene at 150 °C for 16 h, giving 10% of *(7)*, and 20% of *(9)*, respectively. It was established that no *(9)* was formed from *(1)*, and no *(7)* from *(3)*. An interconversion of the nitrenes *(4)* and *(6)* is therefore excluded.

When *(1)* was labeled with ^{15}N (90 atom-% ^{15}N[3]), a subsequent flash vacuum thermolysis gave *(8) labeled exclusively in the ring*, as shown by hydrolysis to 1-[^{15}N]-2-phenylbenzimidazole. A direct ring contraction *(4)*→*(8)* is therefore excluded[7].

Since *(1)* did not give any *(9)* or *(10)*, the reaction *(4)*→*(6)*→*(8)* is also excluded. The only reasonable precursor for *(8)* and *(11)* is therefore the cyclic carbodiimide *(5)*. When starting from the quinoxaline *(3)*, a direct ring contraction *(6)*→*(8)* cannot be excluded, but since the same dimer *(11)* is obtained, the nitrene *(6)* must isomerize at least in part to *(5)*. The presence of the triazepine ring in *(11)* indicates that this is a rearrangement product of an initially formed carbodiimide dimer.

Proof for the formation of the cyclic carbodiimide *(5)* was obtained by photolysis of the azide *(2)*, matrix-isolated in Ar

[*] Prof. Dr. C. Wentrup [†], Dipl.-Chem. H.-W. Winter
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)
Dr. C. Thétaz, Dipl.-Chem. E. Tagliaferri
Institut de Chimie Organique de l'Université
CH-1005 Lausanne (Switzerland)
Prof. Dr. H. J. Lindner, B. Kitschke
Institut für Organische Chemie der Technischen Hochschule
D-6100 Darmstadt (Germany)
Dr. H. P. Reisenauer, Institut für Organische Chemie der Universität
D-6300 Giessen (Germany)

[†] To whom correspondence should be addressed. This work was initiated at the Universite de Lausanne.

[**] Hetarylnitrenes, Part 7. Financial support by the Schweizerischer Nationalfonds (1972–1977), the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie (1977–1979) is gratefully acknowledged. We are indebted to Prof. *G. Maier* (Giessen) for the use of his matrix photolysis equipment. This work is taken in part from the Doctoral Thesis of *C. Thétaz* (Lausanne, 1977) and the Diploma Thesis of *E. Tagliaferri* (Lausanne, 1976), and was presented in part by *E. Tagliaferri* and *C. Wentrup*, Autumn Meeting of the Swiss Chemical Society, Bern, October 8, 1977.—Part 6: [1].

at 10 K [$\lambda > 375$ nm]. The azide absorptions disappeared rapidly, and were replaced by intense carbodiimide absorptions at 2010 and 1610 cm^{-1}. The carbodiimide was stable at 10 K, but the bands disappeared irreversibly on warming of the matrix.

The ring expansion of other arylnitrenes and -carbenes has been described elsewhere[2, 8]. However, this is the first time that a common intermediate—the seven-membered ring carbodiimide *(5)*—has been shown to be involved in the gas phase, in solution, and in a matrix.

Received: January 25, 1980;
revised: May 20, 1980 [Z 508b IE]
German version: Angew. Chem. 92, 556 (1980)

CAS Registry numbers:
(1), 6499-41-8; *(2)*, 63399-59-7; *(3)*, 74144-28-8; *(5)*, 74144-29-9; *(7)*, 1022-44-2; *(8)*, 55810-22-5; *(9)*, 33488-29-8; *(10)*, 243-59-4; *(11)*, 74144-30-2

[1] *R. Harder, C. Wentrup*, J. Am. Chem. Soc. *98*, 1259 (1976).
[2] *C. Wentrup* in *R. A. Abramovitch*: Reactive Intermediates. Vol. 1, Chapter 4, Plenum Press, London 1980, pp. 263—319 (submitted in August, 1977).
[3] *C. Wentrup, C. Thétaz*, Helv. Chim. Acta *59*, 256 (1976); *C. Thétaz, F. W. Wehrli, C. Wentrup, ibid. 59*, 259 (1976).
[4] We have observed the valence tautomeric azides and diazo-compounds generated from several tetrazolo- and triazolo-azines and -diazines in a similar manner; *H.-W. Winter, C. Wentrup*, unpublished results.
[5] *(8)*, m.p. 110 °C, IR (KBr): $\nu_{C=N}$ 2200 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.3—8.3; mass spectrum, *m/e* 220 ([*M* + 1]$^+$, 17.7%), 219 (*M*$^+$, 100), 218 ([*M* − 1]$^+$, 13.4). *(10)* was identified by comparison with an authentic sample; *G. M. Badger, P. J. Nelson*, J. Chem. Soc. *1962*, 3926.
[6] *(11)* crystallized from $CHCl_3$ with one molecule of crystal solvent, $C_{28}H_{18}N_6 \cdot CHCl_3$, m.p. 257- 258 °C; space group $P\bar{1}$, $Z = 2$. Crystal data: $a = 1218.0(1)$, $b = 986.0(1)$, $c = 1259.0(1)$ pm; $\alpha = 100.70(5)$, $\beta = 110.73(5)$, $\gamma = 95.66(5)°$. 3039 reflections were measured with $Cu_{K\alpha}$ radiation on a two-circle diffractometer. 2242 symmetry independent reflections with $|F| \geq 2\sigma_F$ were used for the determination of the structure, which was refined to $R = 0.103$. The triazepine ring has a pronounced boat form, N(1) being quasi-pyramidal.
[7] When the thermolysis of ^{15}N-labeled *(1)* to *(8)* was carried out in solution, $\geq 78\%$ of the label was found in the benzimidazole ring; thus $\leq 22\%$ of direct ring contraction. *(4)* → *(8)* may take place under these conditions. Direct ring contraction in pyridylnitrenes has been described [1].
[8] *O. L. Chapman, J.-P. Le Roux*, J. Am. Chem. Soc. *100*, 282 (1978); *O. L. Chapman, R. S. Sheridan, ibid. 101*, 3690 (1979).

cis-/trans-Tris-[2.1.1]-σ-homobenzenes; Synthesis and Stereochemistry of $[_\sigma 2 + _\sigma 2 + _\sigma 2]$-Cycloreversions[**]

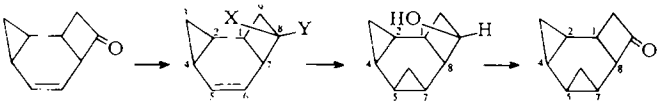
By *Horst Prinzbach, Hans-Peter Schal, Dieter Hunkler*, and *Hans Fritz*[*]

Dedicated to Professor Wolfgang Lüttke on the occasion of his 60th birthday

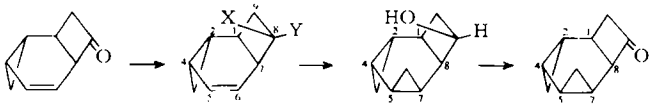
The *cis-/trans*-isomers of tris-[1.1.1]-σ-homobenzenes differ in their tendency to undergo $[_\sigma 2 + _\sigma 2 + _\sigma 2]$ cycloreversions. This—preparatively exploitable—differentiation is determined stereoelectronically and should increasingly alter in favor of the *trans* compounds in transition states with more than nine ring members. Thus, for the tris-[2.1.1]-, tris-[2.2.1]- and tris-[2.2.2]-skeletons[1] it could be expected, with overall increasing activation barriers, that the *trans*-compounds also increasingly undergo $[_\sigma 2 + _\sigma 2 + _\sigma 2]$ cycloreversions[2]. However, it was questionable whether "trishomoaromatic" stabilization in the stereoisomeric ten-, eleven-, and twelve-membered transition states would be sufficient to favor the "internal" cycloreversion process over the "external" competing reactions.

For our initial thermolysis studies on tris-[2.1.1] systems we synthesized the *cis-/trans*-isomeric tris-[2.1.1]-ketones *(5)* and *(10)* from the bis-[2.1]-ketones *(1)* and *(6)*[3], respectively. The CO function in *(1)* and *(6)* should sterically facilitate homologization and retard the Cope reaction typical for the corresponding 1,4,7-cyclodecatriene in the expected thermolysis products *(12)* and *(14)*. The ketone *(5)* is also of interest as potential precursor for the still unknown *cis*-tris-[1.1.1] skeletal unit.

The cyclopropanation of *(1)* and *(6)* meets with the usual difficulties[4]. Satisfactory—though not always completely reproducible—results could only be achieved after reduction to the respective *endo*-alcohols *(2)* and *(7)*. Reaction of *(1)* with $NaBH_4$ or diisobutylaluminum hydride (DIBAH) afforded *(2)* and *(3)* in the ratio 6:1 and 10:1, respectively (total yield

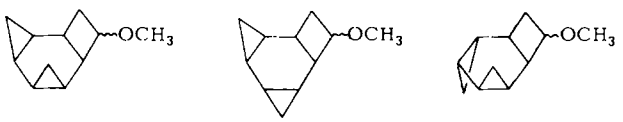


(1) *(2)*, X = OH, Y = H; *(3)*, X = H, Y = OH *(4)* *(5)*



(6) *(7)*, X = OH, Y = H; *(8)*, X = H, Y = OH *(9)* *(10)*

of 94% in each case). Almost pure *(7)* [< 5% *(8)*, total *ca.* 90%] was obtained on reaction of *(6)* with $NaBH_4$. On subjecting *(2)* to a modified Conia procedure[5], a mixture of alcohols and their methyl ethers is obtained in *ca.* 50—60% yield which have to be separated by preparative layer chromatography (CH_2Cl_2/SiO_2). The main product (40%) is the *endo*-[2.1.1]-alcohol *(4)*; the methyl ethers *(4a)* and *(4b)* could also be identified. *(7)* is cyclopropanated in comparable yield (50—60%) on the side of the OH-group to give *(9)* and the side product *(4c)*. After oxidation with pyridinium chlorochromate (CH_2Cl_2, 20 °C), the colorless oily ketones *(5)* and *(10)* (^{1}H-NMR data, see Table 1) are each obtained in *ca.* 60% yield.

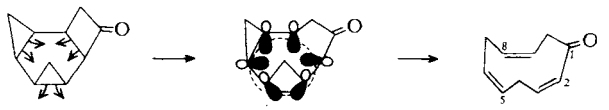


(4a) *(4b)* *(4c)*

The *cis*-ketone *(5)* is stable in CCl_4 solution up to *ca.* 120 °C; at higher temperatures ($t_{1/2}$(150 °C) = 40 min) it is converted quantitatively (TLC, GC, ^{1}H-NMR) into the conformationally flexible *Z,Z,Z*-2,5,8-cyclodecatrien-1-one *(12)*. This uniform behavior is also observed on gas phase pyrolysis (350 °C; quartz tube)[6] (no products such as ketenes or cyclooctatriene[2] resulting from the cleavage of "external" bonds). Calculations based on kinetic data measured (^{1}H-NMR) between 135 and 160 °C in degassed samples and evaluated according to the first order rate law gave the parameters $E_a = 140 \pm 2$ kJ mol^{-1} ($\log A = 13.8$) and $\Delta H^{\neq} = 137 \pm 2$ kJ mol^{-1} ($\Delta S^{\neq} = 8 \pm 3$ JK^{-1})[7]. The unifor-

[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. H.-P. Schal, Dr. D. Hunkler, Prof. Dr. H. Fritz
Lehrstuhl für Organische Chemie der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

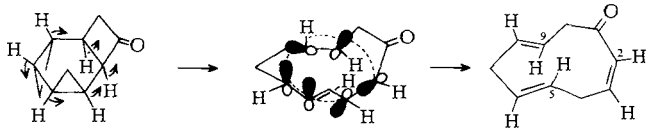
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *H. Mäder*, BASF, for carrying out numerous GC/MS measurements.



(5) (11) (12)

mity and ease of the conversion *(5)*→*(12)* leave no doubt of a cooperative orbital involvement [*(11)*]; the difference in the kinetic data compared to those estimated for the *cis*-tris-[1.1.1] skeletal moiety ($E_a = 100$—126 kJ·mol^{-1})[8a] reflects not only the reduced H/H transannular strain in the educt but also the lower bent-bond character of the four-membered ring.

(10) is kinetically very much more stable than *(5)*: in solution (CCl_4) there is still no recognizable change (^{1}H-NMR) after 2 h at 200 °C. At 300 °C (gas phase) and 50% conversion (GC/MS and ^{1}H-NMR analysis), *Z,E,E*-trienone *(14)* and *(12)* (88% and 5%, respectively) are formed, together with at least two further trace components which do not occur in the thermolysis of *(5)*[9]. At 350 °C and 75% conversion the ratio *(14)*:*(12)* changes to 77:8 (it is still unclear whether *(14)* isomerizes to *(12)*). Since the two remaining 2,5,8-cyclodecatrien-1-ones arising from "forbidden" routes should be more



(10) (13) (14)

stable than *(14)* opening of one bond disrotatorily and of two bonds conrotatorily in *(10)* is most likely exclusive rather than only highly selective. The *Z,E,E*-configuration of *(14)*, which is unusual in ten-membered rings, leads to high steric strain and conformational hindrance (see Table 1). That 5-H/9-H shows a high chemical shift (Table 1) in spite of mutual compression, may be due to anisotropic influences, as are evident in the conformation formulated here. Under these steric conditions the "trishomoaromatic" transition state *(13)* (C-2/C-4 disrotatory, C-1/C8 and C-5/C7 conrotatory) has preference. For this variant of the "symmetry allowed" $[_\omega 2 + _\sigma 2 + _\sigma 2]$ cycloreversion a very efficient overlapping between the six potential sp^2 centers can actually be seen in the model—although later on the reaction coordinate than in the case of *(5)*→*(12)*. *(10)* isomerizes more readily than the *trans*-tris-[1.1.1] skeletal moiety studied by *de Meijere et al.*[8b]; this observation is in agreement with the prediction based on a concerted process. However, the threefold disrotation formulated for *(10)*[8] and other *trans*-tris-[1.1.1] skeletal units[10] is questionable. Together with *(5)*→*(12)*, the transformation *(10)*→*(14)* can be regarded as a particularly impressive example for the preference of cooperative processes in tris-σ-homobenzene skeletons. This preference goes so far that even cyclobutane rings participate in trishomoconjugated systems[11]. Hence the ketones *(5)* and *(10)* or their derivatives, *e.g.* the alcohols *(4)* and *(9)* are potential precursors (σ route) for the hitherto undetectable ten-membered trishomotropylium ions.

Received: November 28, 1979 [Z 510 IE]
German version: Angew. Chem. *92*, 575 (1980)

[1] *G. McMullen, G. Sedelmeier, R. Hildebrand, H. Fritz, H. Prinzbach*, Tetrahedron Lett. *1979*, 3847; and references cited therein.

[2] Example: Other than in the case of the *cis-/trans*-isomeric bis-[2.1] compounds *(1)* and *(6)*, in the homologous bis-[2.2] compounds the thermal $[_\pi 2 + _\pi 2 + _\pi 2]$-cycloreversion is just as likely in the *trans*-isomer.

[3] *H. Prinzbach, H.-P. Schal, D. Hunkler*, Tetrahedron Lett. *1978*, 2195; *H. Prinzbach*, Chimia *33*, 332 (1979); *H.-P. Schal*, Dissertation, Universität Freiburg.

[4] *H. Prinzbach, H.-P. Böhm, S. Kagabu, V. Wessely, H. Vera Rivera*, Tetrahedron Lett. *1978*, 1243, and references cited therein.

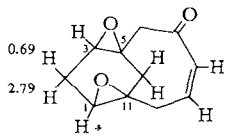
[5] *J. M. Denis, C. Girard, J. M. Conia*, Synthesis *1972*, 549.

[6] *R. Schwesinger, H. Fritz, H. Prinzbach*, Chem. Ber. *112*, 3318 (1979); and references cited therein; we thank Dr. *G. McMullen* for carrying out the gas-phase experiments.

[7] For comparison: cyclobutanone decomposes on gas-phase pyrolysis (353 ± 20 °C; $\log A = 14.53$, $E_a = 217$ kJ·mol^{-1}) with comparable α(C—C)- and β(C—C)-homolysis into ketene and ethylene; *M. N. Das, F. Kern, T. D. Coyle, W. D. Walters*, J. Am. Chem. Soc. *76*, 6271 (1954); *S. W. Benson, H. E. O'Neal*, Nat. Stand. Ref. Data Ser. Nat. Bur. Stand. *21*, 283 (1970).

[8] a) *J. Spanget-Larsen, R. Gleiter*, Angew. Chem. *90*, 461 (1978); Angew. Chem. Int. Ed. Engl. *17*, 441 (1978), and references cited therein; b) *W. Spielmann, D. Kaufmann, A. de Meijere, ibid. 90*, 470 (1978) and *17*, 440 (1978), and references cited therein.

[9] On hydrogenation, *(12)* and *(14)* give cyclodecanone. The steric relationships were mainly derived from the ^{1}H-NMR data (Table 1). The *Z,E,E*-configuration of *(14)* also follows from epoxidation experiments (*m*-chloroperbenzoic acid, CH_2Cl_2, 0 °C, 2 h). *Inter alia* the *syn*-diepoxide *(15)* is isolated, whose structure is confirmed by ^{1}H-NMR analysis (360 MHz, 60 °C).

(15) 

$J_{1,11} \simeq J_{3,5} \simeq 2.5$ Hz

[10] *H. Prinzbach, H. Fritz, H. Hagemann, D. Hunkler, S. Kagabu, G. Philipposian*, Chem. Ber. *107*, 1971 (1974).

[11] *R. C. Haddon*, Tetrahedron Lett. *1974*, 4303, and references cited therein.

Table 1. ^{1}H-NMR-Data ($CDCl_3$).

	δ values										*J* [Hz]
	1-H	2-H	3-H	4-H	5-H	6-H	7-H	8-H	9-H	10-H	
(2)	2.68	1.18	0.51 0.81	1.18	6.33	5.58	2.98	4.17	1.65 2.47		$J_{1,2} = 7$—8, $J_{4,5} = J_{6,7} = 3.5$, $J_{7,8} = 7.5$, $J_{8,9n} = 6.5$, $J_{8,9x} = 7.0$
(3)	2.54	1.36	0.05 1.00	1.30	6.21	5.70	2.82	3.69	2.31 2.24		$J_{1,2} = 6.5$, $J_{4,5} = 5$, $J_{6,7} = 5.5$, $J_{7,8} = 7$, $J_{8,9n} = J_{8,9x} = 7$—8
(4)	2.45	0.60	−0.13 0.44	1.20	1.39	−0.04 0.65	0.65	2.92	4.29	1.20 2.29	$J_{1,2} = 9$, $J_{4,5} = 7.5$, $J_{7,8} = 9$, $J_{9,10n} \approx J_{9,10x} \approx 8$
(5)	2.59	1.17	−0.60 0.33	1.48	1.23	−0.16 0.6	0.6	3.65		2.48 3.20	$J_{1,2} = 9$, $J_{4,5} \approx 9$, $J_{7,8} = 10$
(7)	2.41	1.15	0.31 0.90	1.24	6.34	5.31	2.75	4.16	1.80 2.52		$J_{1,2} \leq 1$, $J_{4,5} = 5$, $J_{6,7} = 3.0$, $J_{7,8} = 7.5$, $J_{8,9n} \approx 9$, $J_{8,9x} \approx 7$
(9)	2.12	0.64	−0.08 0.55	1.18	1.18	−0.49 0.91	0.73	2.80	4.75	1.53 2.39	$J_{1,2} \approx 0$, $J_{4,5} \approx 1$, $J_{7,8} = 8$, $J_{9,10n} \approx J_{9,10x} \approx 8$
(10)	2.57	0.85	−0.01 0.76	1.25	1.19	0.08 0.71	0.9	3.42		2.58 3.11	$J_{1,2} = 0$, $J_{4,5} \approx 1$, $J_{7,8} = 9$
(12)		5.8	5.9	3.13	5.5	5.60	2.83	5.55	5.36	3.29	$J_{2,3} = 12$, $J_{5,6} = 11$, $J_{8,9} = 11$
(14) [a]		6.19	5.90	2.92	5.04	5.52	2.77	5.87	5.21	3.1	$J_{2,3} = 12.5$, $J_{2,4} = 1.5$, $J_{3,4} = 7$, $J_{4,5} = 7$, $J_{5,6} = 16.5$, $J_{6,7} = 7$, $J_{7,8} = 7$, $J_{8,9} = 16.5$, $J_{9,10} = 7$

[a] 60 °C; in particular, the 4-H-, 10-H-signals are greatly broadened at *ca.* 25 °C.

Ligand-Property Control in the Nickel(0)/Butadiene/P-Ligand Catalytic System: Dominance of "Steric" Factors in the Control of Oligomer Distribution[**]

By *Paul Heimbach, Joachim Kluth, Hartmut Schenkluhn,* and *Bruno Weimann*[*]

The control of isomeric distribution in the cyclooligomerization of butadiene on nickel-ligand catalysts can be attributed to several mutually independent ligand-association processes[1]. This finding permits the study of the control of individual association processes by ligand properties and hence comparison of the results obtained with various model complexes. We illustrate such an analysis in the present report of control of the degree of oligomerization (details of the control of cyclodimer distribution will be found in [2]).

Table 1. Experimental data on ligand-property control in the nickel(0)/P-ligand/butadiene (1:1:170) catalytic system, $[Ni]_0 = 34$ mmol/l (40 mmol/l at $-78\,^{\circ}C$); $T = 60\,^{\circ}C$, $t = 48$ h, butadiene conversion >95%; see [1a] for experimental procedure. *c*-DIM = cyclodimer, *c*-TRIM = cyclotrimer; $Z = 100 \times c\text{-TRIM}/(c\text{-DIM} + c\text{-TRIM})$.

Ligand L_i	χ [cm^{-1}]	θ [°]	*c*-DIM [%] [a]	*c*-TRIM [%] [a]	Z_{exp}	Z_{calc}
$PtBu(iPr)_2$	2.0	167	45.8	49.6	52	46
$P(iPr)_3$	3.1	160	68.8	23.6	26	32
$P(nPr)_3$	4.9	139	73.9	12.9	15	18
PEt_3	5.6	132	64.5	29.0	31	22
$PPhEt_2$	7.9	136	85.3	12.6	13	17
$PPhMe_2$	9.2	122	66.8	23.5	26	34
$P(PhCH_2)_3$	10.3	160	74.0	23.2	24	7
PPh_2Et	10.6	140	84.1	13.1	13	14
PPh_3	12.9	145	85.0	14.8	15	12
$PPh_2(OEt)$	15.5	133	88.8	5.9	6	14
$PPh(O\text{-}nBu)_2$	17.3	118	56.6	40.5	42	37
$PPh(OEt)_2$	18.3	116	50.8	40.4	44	41
$PPh_2(OPh)$	18.5	139	87.8	12.1	12	9
$P(O\text{-}nBu)_3$	19.5	112	48.6	49.1	50	51
$P(O\text{-}iPr)_3$	19.8	130	70.2	22.1	24	15
$P(OMe)_3$	23.4	107	38.0	59.8	59	63
$PPh(OPh)_2$	23.7	129	89.8	11.1	11	14
$P(O\text{-}o\text{-}Tol)_3$ [b]	28.0	141	97.6	1.4	2	2
$P(O\text{-}o\text{-}Biph)_3$ [c]	28.9	152	97.7	1.5	2	5
$P(OPh)_3$	29.2	128	87.4	12.2	12	11

[a] Remainder: unknown and open-chain butadiene oligomers. [b] Tol = tolyl. [c] Biph = biphenylyl.

In order to obtain quantitative information about the (ligand-property dependent) control of the degree of oligomerization (see Table 1) at constant $[L]_0/[Ni]_0$ ratio of unity, the amount of trimer was examined by multilinear regression analysis[3]. The ligand properties were characterized by the "steric" parameter θ and the "electronic" parameter χ[4]. Figure 1 reproduces the correlation found. Each ligand $L_i(\theta_i, \chi_i)$ is characterized by a point in the xy plane; the amount of trimer Z is plotted in the z direction. According to this analysis the influence of the "steric" parameter θ predominates:

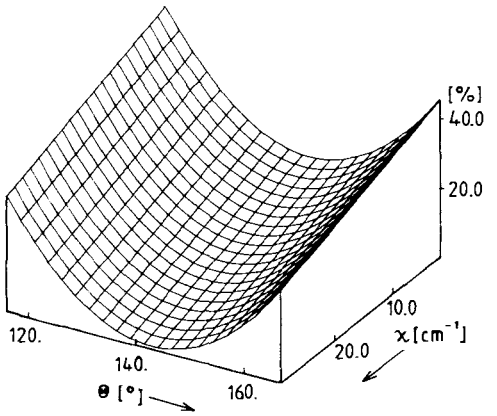


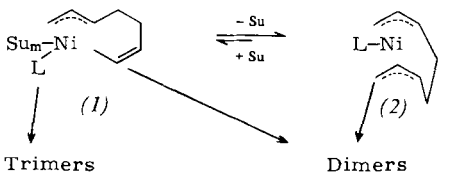
Fig. 1. Surface representation of the amount of cyclododecatriene in the butadiene cyclooligomers as function of "electronic" χ and "steric" θ ligand parameters

$$Z_{calc} = 946.8 - 0.67\,\chi - 12.968\,\theta + 0.454 \cdot 10^{-1}\,\theta^2$$

$S = 5.47$; $MR = 0.9606$; σ (estimated) = 4.5; extent of control 25% "electronic", 75% "steric".

75% of the overall control induced by the chosen P-ligands is "steric" in character. Thus both small and large cone angles θ of the P-ligands favor cyclotrimerization of butadiene.

According to studies on ligand concentration control maps of 11 representative P-ligands[1,5], an octadienediyl(ligand)nickel(II) complex is responsible for control of the degree of oligomerization at a $[L]_0/[Ni]_0$ ratio of unity at constant nickel concentration of 34 mmol/l. Depending upon the ligand, the π,σ-bisallyl form *(1)* (L = tricyclohexylphosphane[6a]) or the π,π-bisallyl form *(2)* (L = triphenylphosphane[6b], tri(2-biphenylyl) phosphite[6c]) is preferentially formed. Only the π,σ form can associate with a further substrate molecule and react to form butadiene trimers.



Su = Butadiene, L = P–Ligand, m = 0 or 1

Increasing donor character (decreasing χ value) or bulkiness of the P-ligand ($\theta > 150°$) favors formation of *(1)*. Thus trimer formation should increase with such ligands. Moreover, it should also be considered that for steric reasons association of the substrate to form *(1)* is all the easier the smaller the cone angle of the P-ligand ($\theta < 140°$); association should be more difficult at large angles.

There are accordingly two opposing effects to be expected for the control of the degree of cyclooligomerization, in agreement with the minimum found in the proportion of steric control. The electronic ligand effect, however, is uniform and probably essentially reflects the $\pi,\sigma/\pi,\pi$-equilibrium of the precursor complexes (thermodynamic selectivity).

Received: September 13, 1979;
supplemented: February 4, 1980 [Z 511a IE]
German version: Angew. Chem. *92*, 567 (1980)

[*] Prof. Dr. P. Heimbach [†], Dipl.-Chem. J. Kluth, Dr. H. Schenkluhn [†]
Universität Essen-Gesamthochschule
Fachbereich 8—Chemie, Organische Chemie I
Postfach 6843, D-4300 Essen 1 (Germany)
and Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr (Germany)
Dr. B. Weimann
Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr (Germany)
[†] To whom correspondence should be addressed.

[**] Control of Metal-Catalyzed Reactions, Part 10.—Part 9: *P. Heimbach, J. Kluth, H. Schenkluhn* in *B. Pullman:* Catalysis in Chemistry and Biochemistry: Theory and Experiment. Vol. 12. D. Reidel, Dordrecht 1979, p. 227.

[1] a) *F. Brille, J. Kluth, H. Schenkluhn*, J. Mol. Catal. *5*, 27 (1979); b) *F. Brille, P. Heimbach, J. Kluth, H. Schenkluhn*, Angew. Chem. *91*, 428 (1979); Angew. Chem. Int. Ed. Engl. *18*, 400 (1979); c) *A. Sisak, H. Schenkluhn, P. Heimbach*, Acta Chim. Acad. Sci. Hung. *103*, 377 (1980); d) *P. Heimbach, H. Schenkluhn*, Top. Curr. Chem. *92*, 45 (1980).

[2] *P. Heimbach, J. Kluth, H. Schenkluhn, B. Weimann*, Angew. Chem. *92*, 569 (1980); Angew. Chem. Int. Ed. Engl. *19*, 570 (1980).
[3] *H. Schenkluhn, W. Scheidt, B. Weimann, M. Zähres*, Angew. Chem. *91*, 429 (1979); Angew. Chem. Int. Ed. Engl. *18*, 401 (1979); quality criteria for the optimum polynomial quotient S^2/σ^2 (S^2: variance of fit; σ^2: variance of experimental values), the multicorrelation coefficient *MR*, and a Chi^2 test.
[4] *C. A. Tolman*, Chem. Rev. *77*, 313 (1977); the "electronic" parameter χ_i of the ligand L_i is determined by IR spectroscopy *via* the induced shift of the $\nu_{CO}(A1)$ band of the $L_iNi(CO)_3$ complex, and the "steric" paramter θ_i as the corresponding apical angle.
[5] *J. Elsässer, P. Heimbach, J. Kluth, A. Sisak, H. Schenkluhn*, to be published.
[6] a) *B. Barnett, B. Büssemeier, P. Heimbach, P. W. Jolly, C. Krüger, I. Tkatchenko, G. Wilke*, Tetrahedron Lett. *1972*, 1457; b) *B. Büssemeier, P. W. Jolly, G. Wilke*, J. Am. Chem. Soc. *96*, 4726 (1974); c) *B. Büssemeier*, Dissertation, Universität Bochum 1973.

Ligand-Property Control in the Nickel(0)/Butadiene/P-Ligand Catalytic System: "Electronic" Factors in the Control of Cyclodimer Distribution[**]

By *Paul Heimbach, Joachim Kluth, Hartmut Schenkluhn*, and *Bruno Weimann*[*]

In the cyclooligomerization of butadiene on nickel-ligand catalysts the ligand-property control of the degree of oligomerization at a $[L]_0/[Ni]_0$ ratio of unity is primarily of a "steric" nature and can be interpreted by corresponding association processes[1]. We now report an analysis of the ligand-property control of cyclodimer distribution.

Under the conditions given in Table 1 the dimers vinylcyclohexene (VCH) and 1,5-cyclooctadiene (COD) predominate; Figure 1 shows the result of multilinear regression analysis[2]. (For a definition of the "electronic" and "steric" parameters χ and θ, see [1,3].) A purely "electronic" effect is found for the amount of COD in the control region

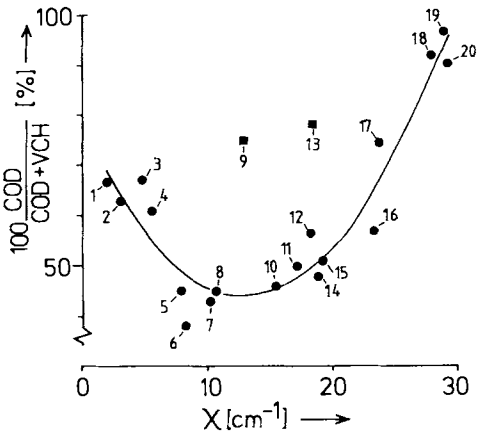


Fig. 1. Dimer distribution in the cyclooligomerization of butadiene on nickel-ligand catalysts as function of the "electronic" ligand parameter χ. (See Table 1 for numbers of experiments.)

$Z_{calc} = 79.3 - 5.43\,\chi + 0.206\,\chi^2$ (without nos. 9 and 13)

$S = 5.41$; $MR = 0.9589$; σ (estimated) $= 4.0$; extent of control: 100% "electronic" (*S*, *MR*, σ, see [1]).

Table 1. Experimental data on ligand-property control in the system nickel(0)/P-ligand/butadiene = 1:1:170, $[Ni]_0 = 34$ mmol/l, $T = 60$ °C, $t = 48$ h, butadiene conversion >95%; see [5] for experimental procedure. VCH = vinylcyclohexene, COD = 1,5-cyclooctadiene; $Z = 100 \times COD/(VCH + COD)$. The cyclodimer divinylcyclobutane, which is likewise formed, rearranges during the catalytic process to COD and VCH and can no longer be detected after 48 h[5]. The values in parentheses were not considered in the regression analysis.

No.	L_i	χ [cm^{-1}]	θ [°]	VCH [%] [a]	COD [%] [a]	Z_{exp}	Z_{calc}	$(\bar{r}_{max})_{DIM}/[Ni]_0$ [b]
1	$PtBu(iPr)_2$	2.0	167	32.1	61.6	66	69	nd
2	$P(iPr)_3$	3.1	160	33.5	56.6	63	64	nd
3	$P(nPr)_3$	4.9	139	28.4	56.4	67	58	nd
4	PEt_3	5.6	132	35.2	55.6	61	55	nd
5	$PPhEt_2$	7.9	136	53.9	44.8	45	49	nd
6	$PPhMe_2$	9.2	122	54.2	33.6	38	47	nd
7	$P(PhCH_2)_3$	10.3	160	55.1	42.1	43	45	nd
8	PPh_2Et	10.6	140	53.5	44.7	45	45	0.57 ± 0.01
9	PPh_3	12.9	145	24.4	74.4	(75)	(44)	0.89 ± 0.08
10	$PPh_2(OEt)$	15.5	133	51.9	44.2	46	45	0.95 ± 0.06
11	$PPh(O\text{-}nBu)_2$	17.3	118	48.4	48.1	50	47	nd
12	$PPh(OEt)_2$	18.3	116	41.1	45.8	53	49	nd
13	$PPh_2(OPh)$	18.5	139	20.1	75.7	(79)	(49)	3.30 ± 0.2
14	$P(O\text{-}nBu)_3$	19.5	112	47.6	49.0	51	52	nd
15	$P(O\text{-}iPr)_3$	19.8	130	46.7	43.3	48	53	0.59 ± 0.01
16	$P(OMe)_3$	23.4	107	40.4	53.9	57	65	nd
17	$PPh(OPh)_2$	23.7	129	24.5	72.7	74	66	nd
18	$P(O\text{-}o\text{-}Tol)_3$ [c]	28.0	141	7.8	91.6	92	89	5.17 ± 0.9
19	$P(O\text{-}o\text{-}Biph)_3$ [d]	28.9	152	2.5	96.7	97	94	7.49 ± 0.2
20	$P(OPh)_3$	29.2	128	8.5	90.6	91	96	4.03 ± 0.5

[a] Remainder: unknown and open-chain butadiene dimers. [b] $\bar{r}_{max}$ (maximum overall reaction rate) is defined for the conversion range of 0–95%. [c] Tol = tolyl. [d] Biph = biphenylyl.

[*] Prof. Dr. P. Heimbach [+], Dipl.-Chem. J. Kluth, Dr. H. Schenkluhn [+]
Universität Essen—Gesamthochschule,
Fachbereich 8—Chemie, Organische Chemie I
Postfach 8643, D-4300 Essen 1 (Germany)
and Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr (Germany)
Dr. B. Weimann
Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr (Germany)
[+] To whom correspondence should be addressed.

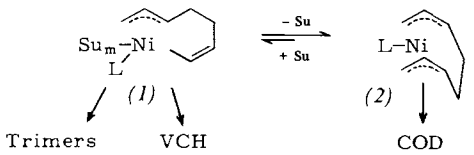
[**] Control of Metal-Catalyzed Reactions, Part 11.—Part 10: [1].

given. The correlative relation can be represented by a simple parabola (the ligands PPh_3 and PPh_2OPh are exceptions).

Octadienediyl(ligand)nickel(II) complexes are assumed as crucial catalytic intermediates for the control of the dimer distribution (see [1,4]). As expected, the pronounced steric influence of the P-ligands found in trimer formation is no longer operative in the control of dimer formation. If the ratio of cyclodimers COD and VCH were determined solely by the $\pi,\sigma/\pi,\pi$-equilibrium of the complexes *(1)* and *(2)* (thermo-

dynamic selectivity[5]), then a similar picture would result for the contribution of electronic control as for control of the degree of oligomerization (see [1]). While increasing donor character of the P-ligands (decreasing χ value) uniformly favors formation of trimers, the amount of COD in the dimeric products goes through a pronounced minimum. Hence the $\pi,\sigma/\pi,\pi$-equilibration is insufficient to explain the relationship found: a further opposing independent effect must also be considered.

Such an effect would be a ligand-induced relative activation or inhibition of the product-forming reaction step to give the dimers (kinetic selectivity[5]). In that case, the overall reaction rate of dimer formation $(\bar{v}_{max})_{DIM}$ should correlate with the corresponding product selectivity owing to the relative activation or inhibition. We therefore plotted $\log((\bar{v}_{max})_{DIM}/[Ni]_0)$[6] *versus* the product selectivity



Su = Butadiene, L = P–Ligand, m = 0 or 1

($\kappa = \log(\text{COD/VCH})$) at $[L]_0/[Ni]_0 = 1$ (Fig. 2) for a series of representative P-ligands. Remarkably, a linear relationship is found.

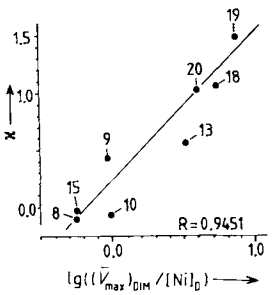


Fig. 2. Reactivity-selectivity diagram for the cyclodimers in cyclooligomerization of butadiene on nickel-ligand catalysts. (See Table 1 for numbers of experiments.)

Judging by the kinetic results (positive slope of the correlation lines in the reactivity/selectivity diagram[7]) the ligand control under discussion can be orbital-controlled. Further evidence for FMO control is seen in the nickel catalyzed cyclodimerization of piperylene to four-membered ring derivatives (symmetry-controlled metalla-ring closures)[8] and in the nickel-catalyzed 2:1 cooligomerization of butadiene with perturbed monoenes[9], in which the regiospecificity is determined *via* the electronic requirements in the LUMO of the cosubstrate (coefficient control).

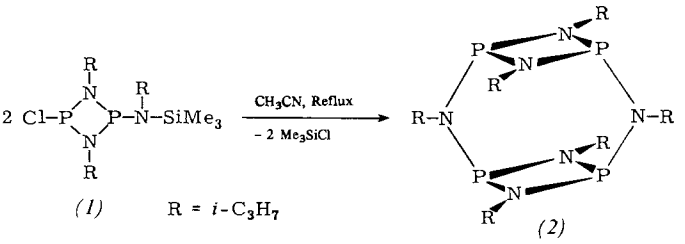
Received: September 13, 1979;
supplemented: February 4, 1980 [Z 511b IE]
German version: Angew. Chem. 92, 569 (1980)

[1] *P. Heimbach, J. Kluth, H. Schenkluhn, B. Weimann*, Angew. Chem. *92*, 567 (1980); Angew. Chem. Int. Ed. Engl. *19*, 569 (1980).
[2] *H. Schenkluhn, W. Scheidt, B. Weimann, M. Zähres*, Angew. Chem. *91*, 429 (1979); Angew. Chem. Int. Ed. Engl. *18*, 401 (1979).
[3] *C. A. Tolman*, Chem. Rev. *77*, 313 (1977).
[4] a) *B. Barnett, B. Büssemeier, P. Heimbach, P. W. Jolly, C. Krüger, J. Tkatchenko, G. Wilke*, Tetrahedron Lett. *1972*, 1457; b) *B. Büssemeier*, Dissertation, Universität Bochum 1973.
[5] *F. Brille, J. Kluth, H. Schenkluhn*, J. Mol. Catal. *5*, 27 (1979).
[6] The maximum overall reaction rate $(\bar{v}_{max})_{DIM}$ of the catalytic reaction was determined by analogy with methods of enzyme kinetics *via* the expression $-d[Su]/dt = \bar{v}_{max}[Su]^n/(K_m^n + [Su]^n)$ (Su = substrate) where n was determined by a regression analysis. A value of $n = 2$ is found for the P-ligands employed: see *P. Heimbach, J. Kluth, H. Schenkluhn* in *B. Pullman:* Catalysis in Chemistry and Biochemistry: Theory and Experiment. Vol. 12, D. Reidel, Dordrecht 1979, p. 227.
[7] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).
[8] *P. Heimbach, H. J. Hey*, Angew. Chem. *82*, 550 (1970); Angew. Chem. Int. Ed. Engl. *9*, 528 (1970).
[9] *P. Heimbach, A. Roloff, H. Schenkluhn*, Angew. Chem. *89*, 260 (1977); Angew. Chem. Int. Ed. Engl. *16*, 252 (1977).

$P_4(N\text{-}i\text{-}C_3H_7)_6$, a P_4X_6 Molecule with and without Adamantane Structure[**]

By *Otto J. Scherer, Kurt Andres, Carl Krüger, Yi-Hung Tsay,* and *Gotthelf Wolmerhäuser*[*]

Replacement of the edges of a P_4 tetrahedron by bridging groups X (O, NCH_3, *etc.*) formally affords P_4X_6 molecules which, without exception, have the adamantane-type structure[1]. The structural alternative of a P_4 rectangle doubly bridged on its short sides and singly bridged on its long sides has now been realized for the first time in the multidentate cage molecule *(2)* ("double decker"), whose design principle corresponds to that of a cryptand[2]. *(2)* was synthesized[3] by thermolysis of the diazadiphosphetidine *(1)*:



The novel tricyclic compound *(2)* forms colorless crystals which are readily soluble in benzene, ether, and dichloromethane, but sparingly soluble in pentane[4]. The ^{1}H-NMR spectrum shows the two groups of signals in the area ratio 2:1 expected for a symmetric structure [CD_2Cl_2, TMS int.; $\delta CH_3 = 1.19$ (d), $^3J(HCCH) = 6.8$ Hz (bridge), $\delta CH_3 = 1.20$ (d), $^3J(HCCH) = 6.4$ Hz (four-membered ring), $\delta CH =$ 3.82—4.22 (m)]. The singlet occurring at $\delta = 145.8$ in the $^{31}P\{^1H\}$-NMR spectrum (CD_2Cl_2, 85% H_3PO_4 ext.) is shifted downfield compared to *cis*-configurated diazadiphosphetidine derivatives (*P*-alkyl or NR_2 substituents)[5]. Compound *(2)* has a crystallographic center of symmetry (Fig. 1). The P atoms and the N atoms N1, N*1, N2, N*2 form rectangles perpendicular to each other with edges of length 2.58(1) and 3.13(1) Å (P-rectangle) and 2.23(1) and 3.07(2) Å (N-rectangle), respectively. The two $P_2(NR)_2$ four-membered rings are almost planar[6].

If *(2)* is heated in a sealed tube for several days at 156—158 °C (dry cupboard), it is converted quantitatively into the

[*] Prof. Dr. O. J. Scherer [+], Dipl.-Chem. K. Andres
Fachbereich Chemie der Universität
Postfach 3049, D-6750 Kaiserslautern (Germany)
Priv.-Doz. Dr. C. Krüger, Dr. Y.-H. Tsay, Dr. G. Wolmershäuser
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

thermodynamically more stable isomer *(3)* of known adamantane-type structure $P_4(NCH_3)_6$[7].

In contrast to *(2)*, compound *(3)* is also readily soluble in pentane, it forms colorless crystals, m.p. 264—267 °C (ready sintering above *ca.* 200 °C)[8]; ^{1}H-NMR (C_6D_6, TMS int.): $\delta CH_3 = 1.37$ (d), $^3J(HCCH) = 6.8$ Hz, $\delta CH = 3.61$ (m), $^{31}P\{^1H\}$-NMR (C_6D_6, 85% H_3PO_4 ext.): $\delta = 84.0$ (s).

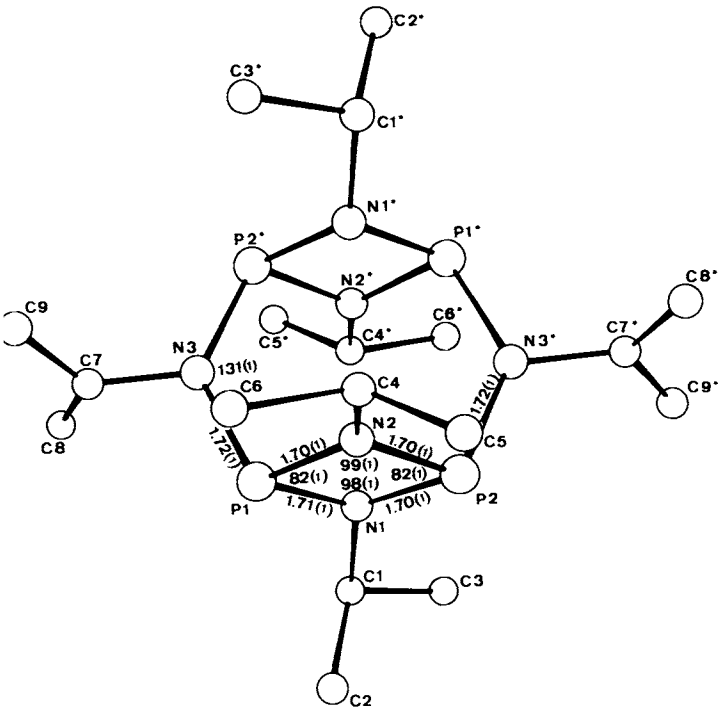
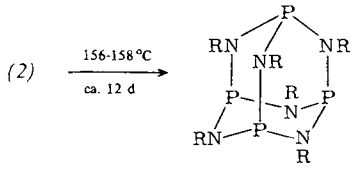


Fig. 1. Molecular structure of $P_4[NCH(CH_3)_2]_6$ *(2)* in the crystal.



(3), R = *i*-C_3H_7

Experimental

A solution of crude *(1)*[9] (14.5 g) [obtained from 11.12 g (45.0 mmol) [ClPN-*i*-C_3H_7]$_2$ *(1a)* and 45.5 mmol LiN(*i*-C_3H_7)$SiMe_3$] in 100 ml CH_3CN is heated under reflux for 15 h. After cooling to room temperature *(2)* is filtered off (G3 frit) and washed several times with CH_3CN. Filtrate and washings are again heated under reflux for 15 h; *(2)* is isolated from the solution after cooling to −45 °C, washed, and recrystallized from CH_3CN. Yield 2.6 g (25%).

Received: January 2, 1980 [Z 512 IE]
revised: May 8, 1980
German version: Angew. Chem. *92*, 563 (1980)

[1] Cf. *D. E. C. Corbridge:* The Structural Chemistry of Phosphorus. Elsevier, Amsterdam 1974, p. 421.
[2] *J.-M. Lehn*, Struct. Bonding (Berlin) *16*, 1 (1973).
[3] *(2)* is also formed in the reaction of *cis*-[ClPNR]$_2$ with *cis*-[Me_3Si(R)NPNR]$_2$ [9].
[4] Composition confirmed by C,H,N analysis, mass spectrum and cryoscopic molecular weight determination in benzene (calc. 466, obs. 443).
[5] *O. J. Scherer, G. Schnabl*, Angew. Chem. *88*, 845 (1976); Angew. Chem. Int. Ed. Engl. *15*, 772 (1976); Z. Naturforsch. *B 33*, 467 (1978); *R. Keat, A. N. Keith, A. Macphee, K. W. Muir, D. G. Thompson*, J. Chem. Soc. Chem. Commun. *1978*, 372.
[6] Crystallographic data: monoclinic, $P2_1/n$, $a = 9.81(1)$, $b = 15.973(2)$, $c = 9.980(1)$ Å, $\beta = 113.21(1)°$, $Z = 2$, $\rho_{calc} = 1.164$ g cm^{-3}; $R = 0.0984$. All molecular data are influenced by extensive disorder in the region of the isopropyl groups.
[7] *R. R. Holmes, J. A. Forstner*, J. Am. Chem. Soc. *82*, 5509 (1960).
[8] Composition confirmed by C,H,N analysis and mass spectrum [17 eV; *m/e* = 466 (100%, M^+)].
[9] *O. J. Scherer, K. Andres*, unpublished.

BOOK REVIEWS

Chemische Struktur und biologische Aktivität von Wirkstoffen. Methoden der Quantitativen Struktur-Wirkung-Analyse. By *J. K. Seydel* and *K.-J. Schaper*. Verlag Chemie, Weinheim 1979. xi, 359 pages, bound, DM 118.00.

The book justifies the claim, formulated in the preface, of being an introduction to methods and possibilities in the complex field of quantitative structure-activity analysis.

A number of books professing a similar aim have appeared in the last few years, but this is the first work of this type in German and it has several advantages over its English-language predecessors. The whole subject is treated very comprehensively. The material includes an accurate description of experimental physicochemical and biological determinations,
explanatory definitions of the parameters used, with a collection of constants for more than 700 substituents in the Appendix,
an account of the historical development of the fundamental theories,
the derivation of the most important semiquantitative processes (Topliss scheme, *Darvas'* simplex method, *Bustard's* Fibonacci process),
explanations of the most common methods with statements of theoretical principles (Hansch analysis, Free-Wilson process); these are made particularly clear by numerous figures and examples,
a short outline of more recent processes (cluster, discriminants, and factor analysis, pattern recognition), with valuable hints on the formulation of appropriate computer programs,
and finally, many published examples of structure-activity relationships.

The advantages and disadvantages of the described techniques, and also their limitations, are looked at critically, in welcome contrast to the euphoria often encountered in American publications.

Study of the comprehensive review of published quantitative structure-activity analyses, which has been drawn up with remarkable industry, is greatly facilitated by the tabular presentation arranged by biological effects.

The book contains one of the most comprehensive literature collections for this field; moreover, in contrast to previous compilations, the European literature has been duly taken into account.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0707-0572 $ 02.50/0

The following critical observations may be made: In view of the confused mass of abbreviations already used in the technical literature, the introduction of new abbreviations (*e.g.* QSWB = *Q*uantitative *S*truktur-*W*irkung-*B*eziehung, for QSAR = *Q*uantitative *S*tructure *A*ctivity *R*elationship) is regrettable. The balance between the chapters does not always appear appropriate and the relevance of the described procedures for the drug chemist engaged in syntheses does not always appear to be correctly evaluated. This may be due to the fact that the book also gives an account of the relevant investigations of the Institut für Experimentelle Biologie und Medizin at Borstel, where both authors are working.

In order to promote the practical use of this book and its employment as a valuable reference work, the subject index, at the moment comprising only seven pages, should be made uniform (*e.g.* not all abbreviations are included) and substantially expanded (*e.g.* the classes of substance investigated are of interest to the chemist; so far only benzylpyridinium ions, carboxylic acid hydrazides, phenylguanines, sulfonamides, and sulfonylureas are mentioned).

The book can be recommended as required reading and/or an interesting work to all those active in the complex interdisciplinary field of research on active principles—whether drugs or plant-protection agents.

Eike Möller [NB 511 IE]

Radiotracers in Agricultural Chemistry. By *M. F. L'Annunziata.* Academic Press, New York 1979. 536 pages, bound, $ 62.00.

The special value of this book lies in its capacity as a textbook and practical manual giving both students and practical workers primarily an introduction to a broad working domain ranging from nuclear radiation and isotope decay to scintillator techniques. No more than a good third of the contents relates to problems of agricultural chemistry and to their solution by the application of radioactive-isotope techniques; two-thirds of the processes and data given could also be in a laboratory manual for radioactive procedures. To this extent, the title is unfortunately somewhat misleading.

The up-to-date nature of the literature references attached to each section must be emphasized. If, therefore, in spite of the comprehensive account given, the reader feels the need for further information, the way toward more intensive study is clearly indicated.

In the section on special problems and techniques of agricultural chemistry the emphasis is on the isolation and localization of a radioactively labeled element or its compounds. The main part—studies on soils, plants, and animals—is of somewhat smaller extent but is supplemented by about 250 literature references largely of fairly recent date. In spite of its restricted compass, the third part, which deals with autoradiography, is packed with information and contains a teaching experiment to be followed by the reader.

The Appendix (about 20% of the book) contains, *inter alia,* decay data for the most common radionuclides and references to statistical criteria of the measurement processes and to dangers, procedures for characterizing labeled substances, permissible limiting concentrations of radionuclides, and regulations for the latter's discharge into water or soil.

The author's aim, to write a classroom laboratory manual on radiotracer techniques in agricultural chemistry, has undoubtedly been achieved, but cannot be deduced from the title of the book. For the experienced practical laboratory worker many common techniques, such as Soxhlet extraction, are perhaps explained in too much detail. Surprisingly enough, the standard German-language work (*Linser* and *Kaindl:* Isotope in der Landwirtschaft) does not appear to the author to be worth mentioning.

Albert Wünsch [NB 512 IE]

German-Jewish Pioneers in Science 1900—1933. By *D. Nachmansohn.* Springer-Verlag, Berlin 1979. xx, 388 pages, bound, DM 60.00.

When in 1933 more than a thousand scientists of Jewish origin had to escape from Germany, the country lost within a few years the leading position that it had formerly been able to claim in many disciplines. This applies particularly to atomic physics, chemistry, and biochemistry, the three fields to which *David Nachmansohn* confines himself when he investigates the contribution of German Jews to modern natural science on the basis of the biographies of some important German-Jewish scientists.

An introductory chapter is devoted to the emancipation of the German Jews in the 19th century. Physics is dealt with next. Here among the Jews who had been in important positions prior to 1933, apart from *Einstein* who is deliberately excluded, one may mention in particular *Max Born, James Franck* and *Gustav Hertz,* other examples are *Otto Stern, Lise Meitner,* and *Wolfgang Pauli,* who are considered only briefly. This chapter includes little that cannot be found in the exhaustive accounts by *Armin Hermann* (Die Jahrhundertwissenschaft (1977); Die neue Physik (1979)); its real importance is that it shows how unimportant for the German scientists of the 'twenties' was the question of racial origin. It was—and this is *Nachmansohn*'s thesis—the cooperation between the Jewish and the non-Jewish scientists, almost unmarred by anti-Semitic resentment, that led to the brilliant triumphs of physics during that period.

As a biochemist, the author (who was forced to emigrate to the United States *via* France in 1933) is particularly well acquainted with the history of his own field. Chemistry and biochemistry in the early 20th century are treated exhaustively, the book being devoted mainly to the work of the Kaiser Wilhelm Institute in Berlin-Dahlem. This chapter, which with 176 pages makes up almost half the book, will prove of the greatest value for the chemist interested in the more recent history of his subject, on the one hand because of the profound knowledge of the field by the author who was an associate of *Otto Meyerhof* in Berlin until 1933, and on the other hand because of his many personal reminiscences of the scientists about whom he writes.

At the center of his considerations are the biographies of *Haber, Willstätter, Warburg, Meyerhof, Neuberg,* and *Embden.* Another, shorter chapter is devoted to representatives of the younger generation, born around 1900, who were generally only at the beginning of their careers when they were forced to emigrate: *Krebs, Ochoa, Schoenheimer,* and *Chain. Nachmansohn* has particularly studied the question of the attitude of German scientists of Jewish origin towards Judaism, and demonstrates clearly that in most cases their origin had played a minor role: they thought and felt as Germans and had substantially departed from the religious tradition of Judaism; they had often become Christians. Only the anti-Semitism of the 'twenties' and the nazi persecution made many of them turn back to Zionism, but even then Germany remained their home from which they could part only with difficulty.

What is particularly remarkable is the author's championship of the German scientists who did not emigrate in 1933. Just as he understands *Fritz Haber*'s participation in the production of poison gas in the first World War, he also defends

Werner Heisenberg against the reproach that he should have emigrated or have resisted instead of remaining in Germany and cooperating in the construction of an atomic reactor. The art of not judging human and political behavior from the point of view of the present but of understanding it in the context of its own time, which *Nachmansohn* always attempts, is an outstanding example of objective historical scholarship.

The book is directed at a wide readership, and the scientific background necessary for understanding it is explained with much didactic skill. It would be highly desirable for a German translation to appear in the near future. Many inadvertent errors could thus easily be eliminated. Most regrettably, there is no name index and only a few names appear in the subject index. More factual errors are contained particularly in the chapter on atomic physics: *Rathenau* was murdered not in July 1922 but on 24th June 1922 (p. 19). The planetary model of the atom was not a contradiction of classical Newtonian mechanics, but of Maxwell's electrodynamics (p. 35). *Johann Jakob Balmer* was not Swedish but Swiss (p. 36). *Otto Stern*'s birthplace is called Sorau (not Sohrau) and is not in Upper Silesia but in Niederlausitz (p. 39). *Sommerfeld*'s first name was not *Arthur* but *Arnold* (p. 43). *Einstein* did not die in 1956 but in 1955 (p. 78). *Strassmann* did not receive the Nobel prize (p. 136).

Andreas Kleinert [NB 513 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Lehrprogramm Biochemie I. Edited by *H. Schmidkunz* and *A. Neufahrt.* Verlag Chemie, Weinheim 1980. xii, 461 pp., sewed, DM 29.80.—ISBN 3-527-25866-3

Programmierte Prüfung. Chemie—Physik—Physikalische Chemie. Reihe: Ausbildung. Edited by *W. Klein, H. Mayer,* and *G. Reif.* Verlag Chemie, Weinheim 1980. x, 412 pp., sewed, DM 29.80.—ISBN 3-527-25848-5

The Protection of Personal and Commercial Reputation. Reihe IIC Studies, Band 3. Edited by *R. M. Kunstadt.* Verlag Chemie, Weinheim 1980. vii, 98 pp., sewed, DM 58.00.—ISBN 3-527-25697-0

The Molecular Basis of Microbial Pathogenicity. Dahlem Konferenzen. Life Sciences Research Report 16. Edited by *H. Smith, J. J. Skehel,* and *M. J. Turner.* Verlag Chemie, Weinheim 1980. 357 pp., sewed, DM 44.00.—ISBN 3-527-12018-1

Diuretika. Edited by *J. Rosenthal* and *H. Knauf.* edition medizin, im Verlag Chemie, Weinheim 1980. x, 342 pp., sewed, DM 45.00.—ISBN 3-527-15021-8

H. Staudinger, H. Mark, and K. H. Meyer—Thesen zur Größe und Struktur der Makromoleküle. By *C. Priesner,* Verlag Chemie, Weinheim 1980. x, 386 pp., bound, DM 98.00.—ISBN 3-527-25838-8

Advances in X-Ray Analysis. Vol. 23. Edited by *J. R. Rhodes, C. S. Barret, D. E. Leyden, J. B. Newkirk, P. K. Predecki,* and *C. O. Ruud.* Plenum Publishing Corporation, New York 1980. xvii, 390 pp., bound, $ 45.00.—ISBN 0-306-40435-4

Advanced Inorganic Chemistry. A Comprehensive Text. Fourth Edition. Edited by *F. A. Cotton* and *G. Wilkinson.* John Wiley & Sons, New York 1980. xvi, 1396 pp., bound, £ 17.45.—ISBN 0-471-02775-8

Organometallics in Organic Synthesis. Vol. 1: General Discussions and Organometallics of Main Group Metals in Organic Synthesis. By *Ei-ichi Negishi.* John Wiley & Sons, New York 1980. xiv, 532 pp., bound, £ 15.85.—ISBN 0-471-03193-3

Organic Syntheses. Vol. 59. Edited by *R. M. Coates.* John Wiley & Sons, New York 1980. xx, 267 pp., bound, £ 11.10.—ISBN 0-471-05963-3

Solubility Data Series. Vol. 11. Alkali Metal, Alkaline-Earth Metal and Ammonium Halides, Amide Solvents. Edited by *B. Scrosati* and *C. A. Vincent.* Pergamon Press, Oxford 1980. xx, 354 pp., bound, £ 50.00.—ISBN 0-08-023917-X

Analytical Techniques in Environmental Chemistry. Edited by *J. Albaiges.* Pergamon Press, Oxford 1980. xii, 646 pp., bound, $ 85.00.—ISBN 0-08-023809-2

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form - by photoprint, microfilm, or any other means - nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar.* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 8
August 1980
Pages 575–658

Physicochemical Principles and Applications of Supercritical Fluid Chromatography (SFC)

New analytical methods (19)

By Ulrich van Wasen, Issam Swaid, and Gerhard M. Schneider[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

In supercritical fluid chromatography (SFC) compressed gases in the region of their critical temperature are used as mobile phases. SFC has important advantages over gas chromatography (GC) for the separation of low-volatile or thermally unstable substances. Like high pressure liquid chromatography (HPLC) and gel chromatography, it is used for various special applications and preparative separations, *e.g.* in the petroleum industry and in the separation of oligomers. SFC is of great interest in fundamental research on fluid extraction and for the determination of the physicochemical properties of fluid systems. In this contribution the most important physicochemical, methodological, and instrumental principles of SFC are summarized; characteristic physicochemical applications are the determination of capacity ratios, partition coefficients, partial molar volumes, interaction second virial coefficients, and diffusion coefficients.

1. Introduction

Supercritical fluid chromatography (SFC) uses compressed gases in the critical temperature range as mobile phases. This relatively new chromatographic technique supplements well-known techniques such as gas chromatography (GC) and high pressure liquid chromatography (HPLC), and makes possible, *e.g.*, the analytical and preparative separation of thermally unstable and/or low-volatile compounds.

Klesper, Corwin, and *Turner*[1] are considered to be the discoverers of this technique: in 1962 they proposed the use of supercritical chlorofluoromethanes for the separation of some derivatives of porphyrins. Further development and extension of the method, however, were slower than might have been expected, considering its advantages. The reason for this delay could be, *inter alia*

- the rapid development of other methods, especially HPLC, on which the efforts of analytical chemists and instrument manufacturers were concentrated,
- the special operational parameters, widely unexplored and unfamiliar to chemists, as well as the technical difficulties and the high cost of SFC equipment which are, however, comparable with those of modern HPLC, as well as
- the advanced physicochemical knowledge that is necessary for an understanding of the theoretical and experimental principles of SFC.

[*] Prof. Dr. G. M. Schneider, Dipl.-Chem. I. Swaid
Lehrstuhl für Physikalische Chemie II der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)
Dr. U. van Wasen
Giulini Chemie GmbH, D-6700 Ludwigshafen (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0808-0575 $ 02.50/0*

In the mean time, SFC has found a place among chromatographic techniques, as may be seen from the increasing number of publications in this field, *e.g.* on applications in preparative separation, in the petroleum industry, and for the determination of physicochemical properties. This development was assisted by the astonishing progress of fluid extraction where supercritical gases are already used as extractants on an industrial scale.

In this contribution a survey is given in order to draw the attention of potential users to this interesting and promising method of separation.

As long ago as 1966/67, *Sie et al.*[2 5] described the use of compressed gases in chromatography. These important fundamental investigations overlap with SFC in the modern definition. The same holds for two reviews by *Giddings et al.*[6]. An interesting survey was given by *Vigdergauz* and *Semkin*[7] (see also [8,90]). In 1972 *Doran*[9] discussed the application of SFC to routine analysis. In 1973 *Bartmann* treated several aspects of this field in his thesis[10], where problems of separation theory were also considered (see also [11]). The reviews by *Gouw* and *Jentoft*[12 14] found great interest; they consider all the problems relevant to SFC (especially influence of operational parameters, apparatus, applications, *etc.*). A summary of SFC applications in practice, especially in the petroleum industry, was published in 1979 by *Snyder* and *Saunders*[15]. In 1978 *Klesper*[16] treated the most important operational parameters of SFC especially with respect to the separation of polymers. A patent has already been granted in the field of SFC[103].

Numerous citations concerning the physicochemical principles of fluid extraction that are also of interest for SFC[*] are given in some reviews[17 20].

2. Solubilities and Transport Properties in Supercritical Phases

Extensive theoretical and experimental studies have shown that highly compressed supercritical gases are able to dissolve large amounts of low-volatile substances. This pronounced solvent power is of considerable practical interest, *e.g.* in fluid extraction of caffeine (from coffee), nicotine (from tobacco), hops, spices, drugs, *etc.* A survey was provided by the Symposium on "Extraction with Supercritical Gases" held on June 5 and 6, 1978, at Essen (for contributions, see [21,22]). Three sessions at the 6th AIRAPT International High Pressure Conference, July 25—29, 1977, Boulder, Colorado, USA, and the 157th Meeting of the Electrochemical Society, May 11—16, 1980, St. Louis, Mississippi, USA, had the same main topic. (For a detailed discussion of all relevant problems see [17 25].) In this article only the most important physicochemical properties of supercritical solutions and solvents of interest for SFC are briefly reviewed.

2.1. Physicochemical Properties of Supercritical Gases

The physicochemical properties of supercritical gases will be considered for the case of carbon dioxide, which is especially important for fluid extraction and SFC. Figure 1a shows some characteristic pressure(p)–density(ρ) isotherms[26] plotted with the use of reduced variables. The compressibility κ_T

$$\kappa_T \equiv -\frac{1}{V}\cdot\left(\frac{\partial V}{\partial p}\right)_T = \frac{1}{\rho}\cdot\left(\frac{\partial \rho}{\partial p}\right)_T \qquad (1)$$

is especially large just above the critical temperature T_c (*e.g.* in the dotted region of Fig. 1a); at the critical point CP, κ_T tends to infinity. Hence a slight increase in pressure in this region causes a considerable increase in density. Since the solvent power for low-volatile substances is essentially correlated with the density (see below), this behavior is of fundamental importance for SFC, too.

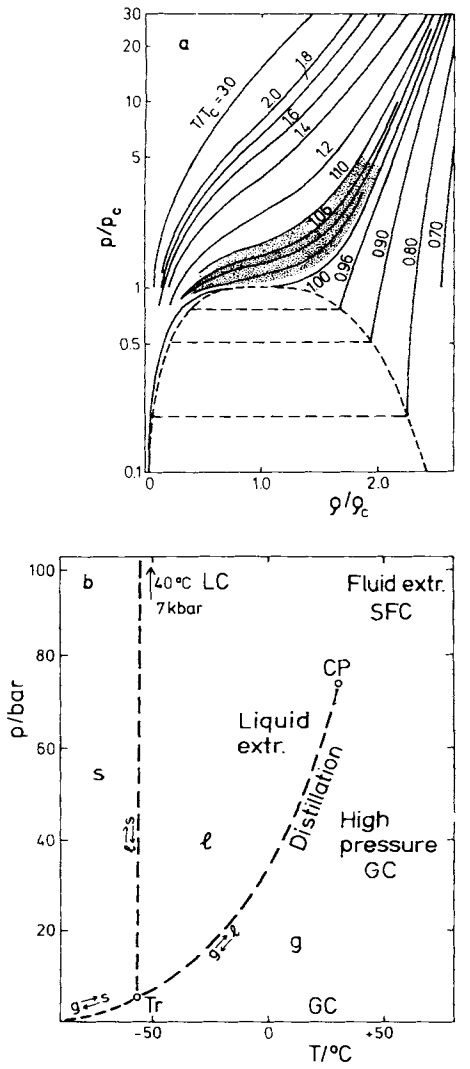


Fig. 1. Physicochemical properties of pure carbon dioxide a) $p(\rho)$ isotherms and b) $p(T)$ phase diagram (according to [26]); p = pressure, T = temperature, ρ = density, CP = critical point, p_c = critical pressure, T_c = critical temperature, ρ_c = critical density, Tr = triple point (here gls), g = gas, l = liquid, s = solid.

Figure 1b shows the $p(T)$ projection of the phase diagram of pure carbon dioxide. Here the vapor pressure curve (g⇄l) separates liquid (l) and gaseous (g) states. In Figure 1b the regions are also marked where different methods of separation (*e.g.* distillation, extraction, GC, high pressure GC, fluid extraction, SFC) can be used. The sublimation pressure

[*] For a search in the literature it might be helpful to know that the key words for SFC in the Chemical Abstracts are: chromatography, high pressure; —, supercritical; —, petroleum separation; gas chromatography, high pressure; —, supercritical; —, hyperpressure; —, dense gas; —, petroleum separation and (unfortunately) others too.

curve (g⇄s) and the melting pressure curve (l⇄s) are of no interest with regard to SFC.

Since substances are approximately in a corresponding state at their critical points, very similar reduced $p(\rho)$ diagrams as in Figure 1a are also found for other substances that can be used as extractants in fluid extraction or as mobile phases in SFC. Some of them are compiled in Table 1 (more detailed tables are found in [12, 14, 16, 47].)

Table 1. Physicochemical properties of some compounds that can be used as supercritical solvents in fluid extraction and/or mobile phases in SFC (b.p. boiling temperature at 1 atm; T_c = critical temperature; p_c = critical pressure; ρ_c = critical density; critical data of NH_3 and N_2O, and all b.p. values taken from [101], all other data from [100]; for similar compilations see [20, 16]; 1 atm = 1.013 bar).

Compound	B.p. [°C]	T_c [°C]	p_c [atm]	ρ_c [g·cm^{-3}]
CO_2	− 78.5 [a]	31.04	72.85	0.468
NH_3	− 33.35	132.4	112.5	0.235
H_2O	100.00	374.15	218.3	0.315
N_2O	− 88.56	36.5	71.7	0.45
Ethane	− 88.63	32.28	48.16	0.203
Ethene	− 103.7	9.21	49.66	0.218
Propane	− 42.1	96.67	41.94	0.217
Pentane	36.1	196.5	33.25	0.237
Chlorotrifluoromethane	− 81.2	28.9	38.7	0.579

[a] Sublimation.

For an understanding of a dynamic method of separation, such as SFC, transport properties are also important. Since in SFC the mobile phase consists of a pure supercritical gas or highly dilute solutions of the substances to be separated, it should be sufficient in most cases to discuss the transport properties of the pure supercritical gas (for details, see *e.g.*[25]). In the following only the viscosity η and the self-diffusion coefficient D_{11} will be briefly considered; characteristic values are given in Figures 2 and 16 (see [11]).

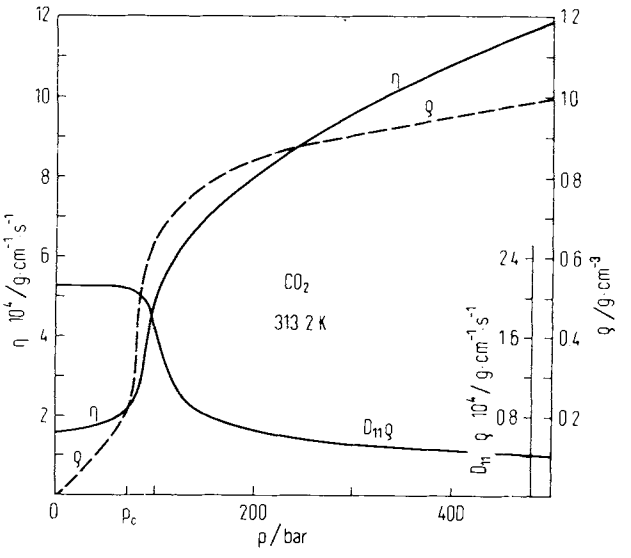


Fig. 2. Density ρ, viscosity η, and $D_{11}\cdot\rho$ of pure carbon dioxide as a function of pressure p at 40 °C (according to data from [11]); D_{11} = self-diffusion coefficient.

According to Figure 2, the viscosity of CO_2 at 40 °C (that is *ca.* 9 K above the critical temperature) remains approximately constant with increasing pressure up to the critical pressure (*i.e.*, *ca.* 70 bar) and increases significantly only at still higher pressures. Correspondingly, the product $D_{11}\times\rho$[89] is approximately constant up to the critical pressure (as predicted from the simplest approach of the kinetic theory of gases) and declines at higher pressures only. In the pressure range between p_c and *ca.* 200 bar the self-diffusion coefficients lie between 10^{-3} and 10^{-4} cm$^2\cdot$s^{-1}. It should be mentioned here that only semiquantitative information concerning diffusion processes in the mobile phase can be obtained from self-diffusion coefficients: in fact the binary diffusion coefficient D_{1i}, which can also be determined from SFC experiments, has to be considered (see Section 5.4).

Table 2. Orders of magnitude of some important physicochemical properties of supercritical fluid phases in comparison with characteristic data for liquids and dilute gases under standard conditions (NTP) (for similar compilations, see [20, 16]).

	Gas (NTP)	Supercritical fluid phase	Liquid
Density ρ [g·cm^{-3}]	10^{-3}	0.3	1
Diffusion coefficient D [cm$^2\cdot$s^{-1}]	10^{-1}	10^{-3}—10^{-4}	$<10^{-5}$
Viscosity η [g·cm$^{-1}\cdot$s^{-1}]	10^{-4}	10^{-4}—10^{-3}	10^{-2}

Table 2 compares the orders of magnitude of some important physicochemical properties of supercritical fluid solvents with characteristic values for liquids and gases (for a similar compilation see, *e.g.*, *Klesper*[16]). With respect to density (and therefore solvent power) a supercritical phase resembles a liquid more closely than a gas, whereas its viscosity is more similar to that of a NTP gas; consequently it also has a large thermal conductivity. The self-diffusion coefficients are smaller than in a NTP gas by about two to three orders of magnitude; they are, however, greater than in a normal liquid by a factor of at least 10^2. This is advantageous for the rate of equilibration and of mass transfer, as compared with liquid-liquid extraction.

2.2. Phase Equilibria in Fluid Mixtures

Of interest for SFC are highly compressed fluid mixtures of CO_2 or similar gases that can be used as mobile phases (see Table 1) predominantly with low-volatile organic compounds. The complicated phase equilibria of such mixtures have been investigated up to the critical region and at much higher pressures (*e.g.* several kbar)[17, 20, 23, 24]. For SFC applications it is an advantage that (in contrast to fluid extraction) very dilute solutions are normally present in the supercritical fluid phase. Thus it is sufficient to discuss dilute binary solutions of the substances to be separated in the extractive gas (*e.g.* CO_2), interactions between the molecules of the solutes being more or less negligible.

The different types of phase behavior of such fluid binary systems can be understood at least qualitatively from the shape of the critical curves[17, 20]. A schematic survey is given in Figure 3.

The type that is schematically represented in Figures 3a, 3c, and 3e is often found for binary mixtures of CO_2 with organic substances of medium size and polarity (*e.g.* for CO_2 + decane[27]). In Figure 3a the two-phase region liquid-gas (lg) is limited to increasing pressures by the critical curve liquid-gas; beyond the critical curve both substances 1 and 2 are miscible in all proportions. At much lower temperatures

phase separation into two liquid phases (ll) is additionally assumed; this region is normally less important for SFC experiments.

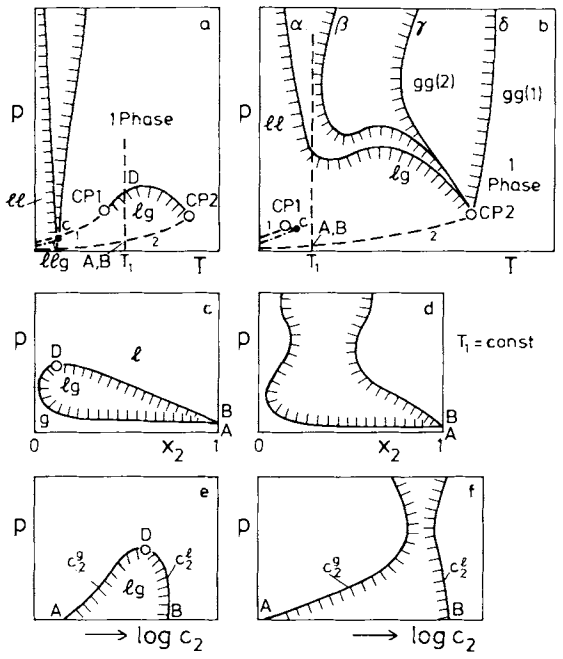


Fig. 3. Phase behavior of fluid binary systems at high pressures (schematic). a) and b) $p(T)$ projection of the phase diagram. (——) = critical curve, (- - - -) = vapor pressure curve, (— · — · —) = three-phase line llg, CP = critical point of pure component, C = critical endpoint; c) and d) $p(x_2)$ isotherm at $T = \text{const} = T_1$; e) and f) $p(\log c_2)$ isotherm at $T = \text{const} = T_1$. In b), d), f) the critical temperature of component 2 is higher and the mutual miscibility with the high-volatile component 1 lower than in a), c), d). For A, B, D see text.

Figure 3c shows a schematic $p(x)$ section for $T = \text{const} = T_1$. The lower branch between point A and the maximum D corresponds to the solubility of the low-volatile component 2 in the supercritical gas 1 whereas the upper branch between B and D represents the solubility of the supercritical gas 1 in the low-volatile liquid 2; point D is the binary critical point at the given temperature. For the pure component 2 it holds that $x_2^g = 1$ (at point A) and $x_2^l = 1$ (at point B); the densities of the gaseous and liquid phases in equilibrium, however, differ extremely, the difference being all the greater the lower the vapor pressure and hence the volatility of the pure component 2.

As a more adequate measure of composition, the concentration (here in $g \cdot cm^{-3}$) was therefore chosen instead of the mole fraction x in Figure 3e, whose abscissa is logarithmic. Here point B corresponds to the concentration of pure component 2 in the liquid phase and point A to that in the gaseous phase. On adding substance 1, c_2^g increases and c_2^l decreases with increasing pressure; at the critical point D c_2^g equals c_2^l. Figure 4 shows such a $p(\log c_2)$ isotherm for CO_2 (component 1) + decane (component 2) at 37.8 °C according to measurements by *Reamer* and *Sage*[27]. Whereas point B corresponds to a density of about 0.73 $g \cdot cm^{-3}$ and is situated somewhat below $c_2^l = 10^0$ $g \cdot cm^{-3}$, a concentration of $c_2^g \approx 3 \times 10^{-5}$ $g \cdot cm^{-3}$ for point A can be estimated from the vapor pressure of pure decane of about 0.005 bar and with the assumption of an ideal gaseous phase. The binary critical point D for the given temperature is at $p \approx 80$ bar and $c_2 \approx 8.2 \times 10^{-3}$ $g \cdot cm^{-3}$. The addition of CO_2 to pure decane thus increases the decane concentration in the gaseous phase up to point D by more than two orders of magnitude; at higher pressures decane and CO_2 are even completely miscible in all proportions.

In Figure 3b, 3d, and 3f the phase behavior is represented for binary mixtures of a high-volatile substance 1 with a substance 2 having a higher critical temperature and being less miscible with substance 1 than has been assumed in Figures 3a, 3c, and 3e. With decreasing mutual miscibility the branch of the critical curve that corresponds to liquid-liquid immiscibility (ll) in Figure 3a is shifted to higher temperatures. A superposition of the critical phenomena liquid-liquid (ll) and liquid-gas (lg) (types α and β) occurs and finally a phase behavior of type γ or δ is found; in the literature the two last types are attributed to gas-gas equilibria of the second and first kind respectively (for details see [17, 20, 23, 24]). It should additionally be mentioned that all types of phase behavior in fluid binary mixtures such as are shown in Figures 3a and 3b can be calculated in good agreement with experimental data (references are given in [28, 30, 20]).

In Figures 3d and 3f a pressure-composition isotherm is represented for case β in Figure 3b at a temperature T_1 that is situated above the critical temperature of pure component 1 (or more exactly above the temperature of the critical end point C[18]) but below the temperature minimum on the critical $p(T)$ curve in Figure 3b. In Figure 3d the right-hand branch corresponds to the solubility of 1 in 2 and the left-hand branch to that of 2 in 1; here the points A ($x_2^g = 1$) and B ($x_2^l = 1$) again coincide. A phase behavior of this type should be characteristic for typical applications of fluid extraction and SFC.

The corresponding $p(\log c_2)$ isotherm in Figure 3f is of fundamental and decisive importance. Corresponding to the very low vapor pressure of component 2, point A is situated at a very small c_2 value that increases greatly with increasing pressure (by addition of component 1). For the case shown, however, no complete mutual miscibility of the two components is obtained but the miscibility gap becomes larger again after running through a minimum width; complete mutual miscibility would only be possible at a temperature above the temperature minimum on the critical $p(T)$ curve in Figure 3b.

The relevant orders of magnitude are demonstrated in Figure 4 where the $p(\log c_2)$ isotherm at 40 °C (that is *ca.* 9 K above the critical temperature of pure CO_2) is shown for the system CO_2 (component 1) + squalane (component 2) according to measurements of *Liphard*[31] (squalane = 2,6,10,15,19,23-hexamethyltetracosane). In keeping with the density of liquid squalane of about 0.81 $g \cdot cm^{-3}$, point B is again situated somewhat below $c_2^l \approx 10^0$ $g \cdot cm^{-3}$ as was also the case for decane. Corresponding to the very low vapor pressure of squalane of only about 3×10^{-10} bar, however, point A is shifted to the very small concentration of $c_2^g \approx 5 \times 10^{-12}$ $g \cdot cm^{-3}$. Addition of CO_2 up to a pressure of 400 bar increases this concentration by about 10 orders of magnitude but without leading to complete mutual miscibility—as already mentioned above.

This increase in c_2^g is much greater than that calculated thermodynamically from the elevation of vapor pressure under the influence of the pressure of an inert gas (Poynting ef-

fect); besides, this gas is normally assumed to be insoluble in the liquid, an assumption that is only valid at vanishing inert gas pressure. This enormous increase demonstrates the specific interaction between substance 2 and the supercritical

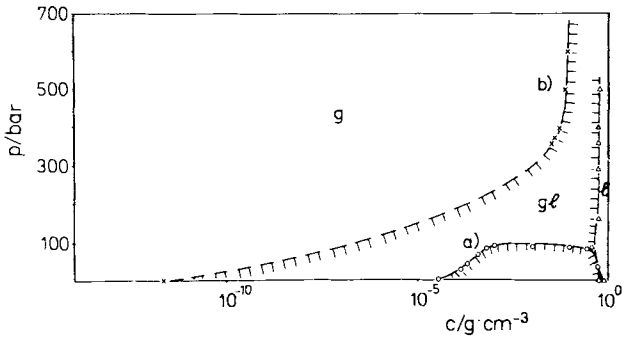


Fig. 4. $p(_{10}\log c_2)$ isotherm for a) CO_2 (component 1) + decane (component 2) at 37.8 °C (according to [27]) and b) CO_2 (component 1) + 2,6,10,15,19,23-hexamethyltetracosane (squalane; component 2) at 40 °C (according to [31]).

solvent 1, and represents the essential effect in fluid extraction and SFC. This effect has been studied by several groups[18, 20, 30, 32]. Often plots of $\log c_2^s$ *versus* density ρ at constant temperature give fairly good straight lines. In relation to SFC, this effect can also be deduced from experiments of *Stahl* and co-workers[32, 33] on the selective dissolution of low-volatile substances (especially drugs) by supercritical solvents (especially CO_2 and N_2O) and are thus related to chromatographic techniques (for a compilation, see [20, 32, 33]).

3. Apparatus

The apparatus required for SFC is similar to that for HPLC. Special features of SFC include the generation and control of the pressure, especially because of the large and highly variable compressibility of the mobile phase near the critical point and of the pressure-dependent viscosity. Until now, no fluid chromatographs are commercially available. Among the numerous chromatographs described in the literature, only those of *Karayannis et al.*[34], *Bartmann*[35, 36], *Jentoft* and *Gouw*[37], *Klesper* and *Hartmann*[38, 39], as well as the equipment of *van Wasen*[40] are mentioned (for a review, see *e.g.*[13]).

Figure 5 schematically shows the apparatus of *van Wasen*[40], which was modified by *Swaid*[41] for the measurement of diffusion coefficients (see Section 5.4). This apparatus allows fluid- as well as liquid-chromatographic investigations between room temperature and 250 °C and at pressures up to 200 bar. Detection of the eluted samples is by a UV detector. The column exit pressure can be held constant at pressures up to 200 bar by means of a special regulator.

Control of pressure and flow rate: An electrically driven duplex diaphragm pump (MP) is used to compress the mobile phase. The residual pulsations are damped by a buffer volume (P) located in an air-bath (Th_1) ($T \gg T_c$). A PI-regulator is used for pressure control. The signal of the pressure transducer (DD) at the end of the column is used to adjust the stroke of one piston of the pump, while the other piston is adjusted manually. The regulator can be connected to a programmer. The flow rate is regulated by a thermostated expansion valve (DM in Th_3) located after the detector at the end of the column; it consists of a two stage pressure reducer and a constant flow resistance (R). The pressure after the second stage is manually adjustable between 0 and 1.5 bar. The flow rate is measured by a soap bubble flowmeter (SSM) and controlled by a thermoconductivity flowmeter (SM).

The method proposed by *Klesper* and *Hartmann*[62] for control of the pressure and flow rate seems technically more complicated (for other methods of regulation of these parameters, see [13, 37, 48]).

Measurement and control of temperature: In SFC the requirements for the thermostat are very restrictive (high precision, good stability, wide temperature regime) because the experiments have to be conducted near the critical point of the mobile phase. The column of the apparatus shown in Figure 5[40] is located in a well insulated air-bath (TH_2); louvers and fans ensure temperature uniformity throughout the bath, the temperature of which is regulated using a Pt-100 sensor. The temperature of the bath is controlled by a

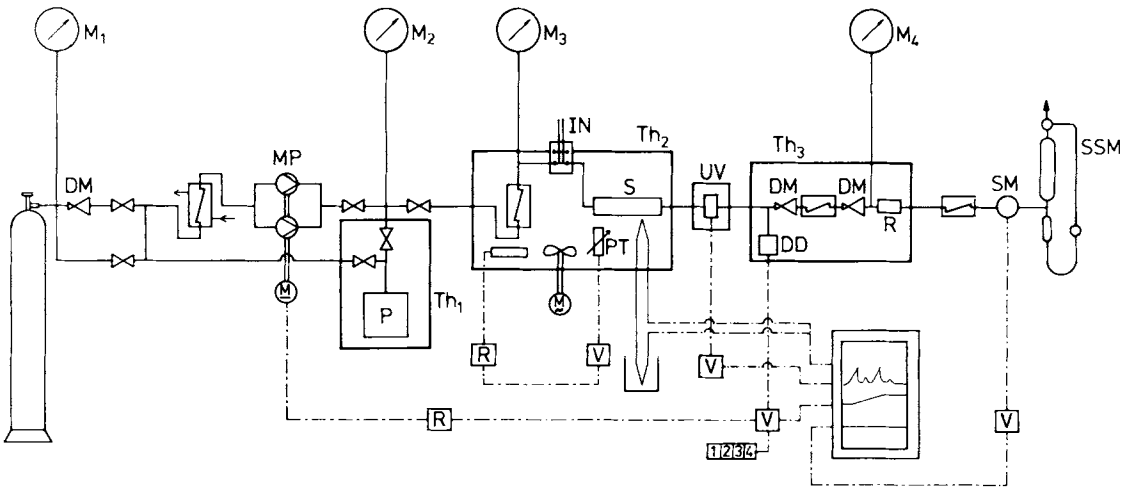


Fig. 5. Fluid chromatograph according to *van Wasen* [40] and *Swaid et al.* [41]; for comments see text. DD = pressure transducer, DM = expansion unit, IN = sample introduction, $M_{1\ldots3}$ = manometer, MP = diaphragm pump, P = buffer volume, PT = Pt-sensor, R = flow resistance, R = regulator, S = column, SM = thermoconductivity flowmeter, SSM = soap bubble flowmeter, $Th_{1\ldots3}$ = airbath, UV = UV detector, V = amplifier, 1 2 3 4 = A/D converter.

five-junction Fe-Constantan thermopile and measured by a calibrated Hg-thermometer. The mobile phase is brought to the bath temperature by passage through a tube filled with copper turnings.

Sample introduction: At low pressures (<100 bar) it is possible to inject the sample using a syringe through a septum, as is common with gas chromatographs. For pressure up to *ca.* 300 bar HPLC-introduction systems with sample loops are suitable. The most flexible introduction method, which allows the sample size to be varied, is the use of an HPLC injection system. Such an injection system was used in the apparatus shown in Figure 5. Samples of *ca.* 2 μl solution of the substance under test in CCl_4 (concentration *ca.* 3 $mg \cdot cm^{-3}$) were injected for the determination of the k_i values (see Section 5.1); 0.6 μl of the pure liquid substance were used for the determination of D_{1i} values (see Section 5.4).

Stationary phase: Adsorbents, chemically bonded phases, and molecular sieves are all used in SFC. Since the pressure drop across the column depends mainly on the geometry and the surface properties of the stationary phase, the particle size and its distribution depend on the problem to be treated. Although in many separation problems a high pressure drop is necessary to increase the efficiency of the column (see *e.g.*[16]), this is not generally the case in the determination of physicochemical properties with SFC. The conventional coated stationary phases used in GC are unsuitable for fluid chromatographic investigations, because the liquid film is easily dissolved by the supercritical mobile phase[10, 13]. Chemically bonded phases have proved to be more suitable. Adsorbents (silica gel, alumina, or molecular sieves) are generally used when the mobile phase has a relatively high critical temperature (for more specific details, see [40]).

Mobile phase: While the selectivity in GC depends on the stationary phase, in SFC and HPLC it is determined mostly by the mobile phase. The substances listed in Table 1 are used most frequently as mobile phases in SFC. Cyclohexane, benzene, ethyl acetate, tetrahydrofuran, isopropyl alcohol, and diisopropyl ether are also recommended. On the other hand, the use of halogenated alkanes, branched alkanes, ketones, and acetonitrile is limited by their thermal instability (see [47]). H_2O and NH_3 might also be used for some specific applications. The investigations carried out with the apparatus shown in Figure 5 used CO_2 and ethane as mobile phases.

Detectors: The UV detector is particularly important in SFC because most substances used as mobile phases are transparent in the UV region, while most of the medium- and high-molecular compounds usually investigated contain one or more chromophores. The investigations carried out with the apparatus shown in Figure 5 were performed using an UV detector with fixed wavelengths ($\lambda = 243$, 280 nm) and a two-beam optical system with a modified high pressure cell[40]. A UV detector developed for HPLC was also used for determination of D_{1i}; it has the following advantages: The cell has a small dead volume (8 μl) and laminar flow conditions can easily be maintained[41]. The detector cells were also thermostated to the temperatures of the mobile phase (for improvements of UV detectors in SFC, see [37, 42]).

Flame ionization detectors have been used on several occasions, but difficulties are encountered because the mobile phase must be expanded before detection (see [10, 35, 36, 43, 44, 99]). Differential refractometers attract increasing interest[47], particularly since they are more universally applicable; on the other hand, technical problems associated with the mechanical strength of the cell and the stability of the baseline must be solved. Adsorption[45, 46], scintillation[42], and thermoconductivity detectors[10] have also been used in SFC. Mass spectrometry is being used more and more widely for analysis and characterization of fractions[53].

Fraction collector: For a description and an account of the mode of operation of fraction collectors, see reference[37].

4. Analytical and Preparative Applications

Since the analytical and preparative applications have been comprehensively discussed in surveys by other authors[9, 12-16], only the most important operational parameters will be briefly described and some selected examples discussed.

4.1. Operational Parameters

The fundamental condition for the application of SFC is an adequate solubility of the substances to be investigated in the mobile phase. The most important parameters are therefore those which influence this solubility.

Pressure and temperature programs: In SFC experiments, pressures between two and three times the critical pressure and temperatures of 5 to *ca.* 40 K above the critical temperature of the mobile phase are employed. If the molecular weights of the components in the sample are distributed over a wide range (*e.g.* an oligomeric sample), then these components exhibit very different solubilities in the supercritical mobile phase. In such a case, depending upon the column conditions the components of a sample elute either incompletely (leaving the practically insoluble part on the column), or all together with a poor resolution at sufficiently high pressure and suitable temperature (regarding the pressure dependence of the height equivalent to a theoretical plate, see [2, 10]). Therefore pressure variation is essential during elution in order to obtain higher resolution and efficiency. This can be achieved by a pressure program which, for technical reasons, normally consists in a linear pressure increase with time[10, 16]. Because of the shape of the isotherms (see Fig. 1a), a large density change takes place in the region near the point of inflection and at temperatures just above the critical temperature of the mobile phase. This undesired effect can be reduced by operation at higher temperatures, as one can easily see from the form of the $p(\rho)$ isotherms at higher temperatures (Fig. 1a). Recent systematic investigations by *Klesper* and *Hartmann*[16, 39, 62], as well as by *Nieman* and *Rogers*[59], show that a slow or moderate increase in pressure with time is important for a satisfactory resolution. The best resolution possible, however, is obviously attained by a combination of pressure and temperature programs[39]. These results support the view that a continuous and gradual increase of the dissolving power of the mobile phase is important for higher resolution and that the pressure and the temperature programs should operate appropriately to this end. Particularly important is an understanding of the influence of temperature on the solubility in supercritical gases, especially at

relatively low and high pressures (in Fig. 1a these are the regions on the lower left and on the upper right).

Flow rate: The resolution is not strongly influenced by the flow rate. As a first approximation, one can assume that the thermodynamic equilibrium between the mobile and the stationary phase depends on the local values of pressure and temperature. The rate of approach to equilibrium, however, does depend on the flow rate, and low flow rates therefore improve the resolution somewhat. Furthermore, the dependence of the HETP values on the flow rate decreases with decreasing particle diameter of the stationary phase[3]. For the dependence of the HETP values on the flow rate, see [49].

Moderators: Moderators are known to increase resolution and efficiency in HPLC as well as in SFC. For example, admixture of small amounts of low-molecular alcohols such as methanol[62,96] and isopropyl alcohol[4,55,59] to a pure mobile phase (*e.g.* pentane) leads to a considerable improvement of the resolution in the separation of styrene oligomers. Whether this behavior should be attributed to the increase of the solubility in the mobile phase[102] or to a modification of the surface of the stationary phase by the moderator (see [10]) is not yet clear.

The influence of the variation in polarity of the mobile as well as of the stationary phase was systematically investigated by *Sie* and *Rijnders*[97]; they showed that an increase in the polarity of the mobile phase favors a separation of the components according to their molecular weights, while increasing polarity of the stationary phase promotes separation with respect to functional groups (so-called type separation).

4.2. Selected Examples

In the following the discussion of the operational parameters in Section 4.1 will be illustrated by selected examples.

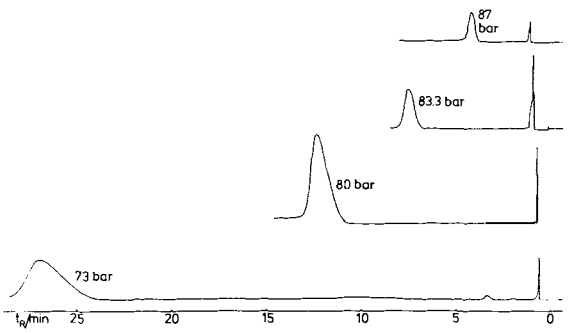


Fig. 6. Retention times t_R of hexadecane at 40 °C and several CO_2 pressures (according to [51]; see [19]). Mobile phase: 0.5 $dm^3 \cdot min^{-1}$ (NTP); stationary phase: Carbowax 400/Porasil C; column: length 2 m, internal diameter 1.4 mm; sample size: 0.2 µl.

Figure 6 demonstrates the effect of increasing the pressure of the mobile phase (here CO_2 at 40 °C, that is *ca.* 9 K above the critical temperature) on the retention time t_R of a test substance (here hexadecane) on a chemically bonded stationary phase (here Carbowax 400 on Porasil C) according to measurements by *van Wasen*[51]. At 73 bar, the peak maximum appears after *ca.* 27 min ($=t_R$); the small peak at about 3 min ($=t_0$) corresponds to an inert substance (here air). The measurements were effected with a modified flame ionization detector. With increasing pressure, t_R decreases drastically and at 87 bar it is reduced to just a few minutes.

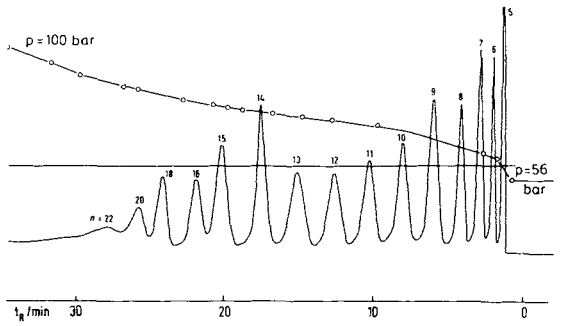


Fig. 7. SFC separation of *n*-alkanes on aluminum oxide with CO_2 at 40 °C (according to [10, 36]). Mobile phase: 1.0 $dm^3 \cdot min^{-1}$ (NTP); column: length 3 m, internal diameter 2 mm. The initial pressure of 56 bar is increased up to *ca.* 100 bar during the separation according to the pressure program given. The horizontal line gives the temperature (here 40 °C).

Figure 7 shows the separation of the *n*-alkanes from *n*-pentane to *n*-docosane also with CO_2 at 40 °C on aluminum oxide according to measurements by *Bartmann*[10,36]; here again a flame ionization detector was used. Additionally, a pressure program was used, *i.e.* the pressure increases monotonously with time by analogy with the use of a temperature program in normal GC (for details see Sections 3 and 4.1).

It is particularly remarkable that an adsorbent was used in the separation shown in Figure 7. Similar experiments using a chemically bonded stationary phase (*e.g.* Carbowax 400 on Porasil C) show a completely analogous behavior[10,36]. It follows from these findings that, in contrast to GC, the specific influence of the stationary phase is relatively small in SFC and that selectivity (as in HPLC) depends mainly on the mobile phase. Knowledge about the physicochemical state of the stationary phase in such investigations is extremely scarce, *e.g.* whether the fundamental step is a partition or an adsorption process.

An example of the separation of cyclic hydrocarbons is shown in Figure 8[10,36]. The effects are analogous to those shown in Figure 7, in spite of the fact that a chemically bonded stationary phase (Carbowax 400 on Porasil C) was used instead of an adsorbent (as in Fig. 7). During the last few years other authors have intensively studied analytical separations of hydrocarbons, especially with respect to problems in the petroleum industry (see Section 4.3).

Figure 9 shows an interesting example of a preparative separation from a paper by *Klesper* and *Hartmann*[16]. With a supercritical mobile phase consisting of 95% pentane and 5% methanol the oligomers of polystyrene up to $n=40$ are completely separated. Here the use of a moderator (5% methanol) added to the mobile phase (here pentane) in order to modify

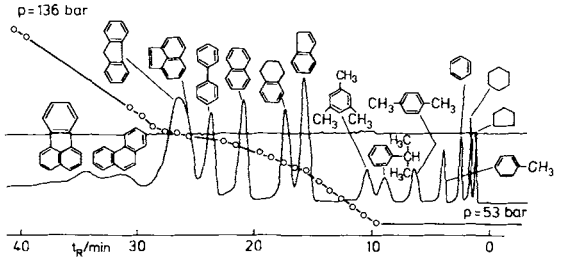


Fig. 8. SFC separation of some cyclic hydrocarbons on Carbowax 400/Porasil C with CO_2 at 40 °C (according to [10, 36]). Mobile phase: 1.0 $dm^3 \cdot min^{-1}$ (NTP); column: length 3 m, internal diameter 1.7 mm. The initial pressure of 53 bar is increased up to *ca.* 136 bar during the separation according to the pressure program given. The horizontal line gives the temperature (here 40 °C).

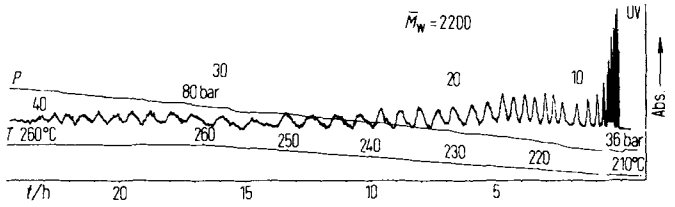


Fig. 9. SFC separation of the oligomers of styrene (up to 40 units) according to *Klesper et al.*[10,62] with combined pressure and temperature programs. Mobile phase: 95% pentane + 5% methanol, 4.2 $cm^3 \cdot min^{-1}$; stationary phase: Porasil A; column: length 6 m, internal diameter 3 mm.

its solvent properties, and a combined pressure and temperature program, are of considerable interest. Up to now few details are available regarding the joint operation of these parameters.

4.3. Literature

In the following some applications taken from the literature are cited in order to demonstrate the wide scope of SFC which is far from exhausted; especially promising preparative applications are still in an initial phase.

Up to now SFC has been applied to alkanes[10,11,36,40,54], arenes (especially polyarenes)[13,36,42,56,57], alkyl bromides[34,37], di-*n*-alkyl phthalates[50], siloxanes[58,59], polymers (especially polystyrene)[38,39,60-66], automotive exhaust gases[42,53], sulfur compounds in cigarette smoke[67], petroleum products (especially high-boiling fractions, residues, crudes)[14,15,68-70], organometal complexes, acetylacetonates, salicylaldoximes, and thenoyltrifluoroacetonates[34,37,71-73,98], as well as substances of interest for biochemistry[6].

5. Physicochemical Applications

Chromatographic experiments may afford many important physicochemical data that are often difficult to obtain by other methods, *e.g.* capacity ratios, virial coefficients, thermodynamic properties of solutions (partial molar enthalpies of solution or vaporization, activity coefficients, excess properties, *etc.*), complexation equilibrium constants, thermodynamic properties of adsorption (adsorption isotherms, enthalpies of adsorption, surface areas, *etc.*), kinetic data (*e.g.* rate constants) and diffusion coefficients (for reviews see, *e.g.*, [74-76]). Up to now the application of SFC to this field is still in its infancy. Nevertheless, very interesting physicochemical data of highly compressed fluid mixtures and pure substances can be deduced from SFC experiments.

5.1. Capacity Ratios and Partition Coefficients

The most important property in the theory of chromatographic separation processes is the capacity ratio k_i of a component i under test, given by

$$k_i \equiv \frac{c_i^{stat}}{c_i^{mob}} \cdot \frac{V^{stat}}{V^{mob}} = K_i \cdot \frac{V^{stat}}{V^{mob}} \tag{2}$$

Here c_i^{stat} and c_i^{mob} are the concentrations of component i in the stationary (stat) and the mobile (mob) phase and V^{stat} and V^{mob} the total volume of the stationary and the mobile phase in the column, respectively. V^{stat}/V^{mob} is characteristic for a given column and, to a first approximation, can be assumed constant and pressure independent. In most cases, however, the partition coefficient $K_i \equiv c_i^{stat}/c_i^{mob}$ strongly depends on the operational parameters (see Section 4.1).

Normally the capacity ratio k_i can be determined relatively easily and accurately from SFC experiments since it is related to the (total) retention time t_{Ri} of a substance i and to the retention time t_0 of an inert substance, according to

$$k_i = (t_{Ri} - t_0)/t_0 \tag{3}$$

Thus it depends linearly on t_{Ri}. Since according to equation (2) k_i is proportional to the partition coefficient K_i, equations (2) and (3) allow the calculation of thermodynamic properties (see Sections 5.3 to 5.5). Unfortunately reliable values for K_i are usually unobtainable, because V^{stat}/V^{mob} often cannot be defined exactly or can only be determined with large errors.

Here the pressure dependence of k_i is of primary interest. According to the chromatographic method different relations are found that will be shortly discussed in the following.

For liquid-liquid chromatography (LC) it can be deduced from the thermodynamics of mixtures that relation (4) holds[10,35,52]

$$\left(\frac{\partial \ln k_i}{\partial p}\right)_T = \frac{V_i^{E,\infty mob} - V_i^{E,\infty stat}}{R \cdot T} \tag{4}$$

where $V_i^{E,\infty mob}$ and $V_i^{E,\infty stat}$ are the partial molar excess volumes of component i at infinite dilution in the mobile and stationary liquid phase respectively.

At relatively low pressures, where second virial coefficients are sufficient to describe the deviations of the mobile phase from ideal behavior[2,7,54,77,78], the corresponding equation for gas-liquid partition chromatography (GC) is given by

$$\left(\frac{\partial \ln k_i}{\partial p}\right)_T = \frac{2B_{1i} - V_i^{\infty stat}}{R \cdot T} \tag{5}$$

Here B_{1i} is the interaction second virial coefficient of the mobile gas 1 and the component i under test and $V_i^{\infty stat}$ the partial molar volume of substance i in the stationary phase at infinite dilution. Thus B_{1i} data can be determined from $\ln k_i$ values as a function of pressure (see Section 5.3).

For the ranges of pressure normally relevant in SFC experiments neither a description with excess properties (as in LC) nor with virial coefficients (as in GC) will be adequate. The present discussion follows a treatment proposed by *van Wasen*[40]. In partition chromatography, eq. (2) holds for the capacity ratio k_i. For adsorption chromatography this relation can be modified to give

$$k_i = \frac{\Gamma_i}{c_i^{mob}} \cdot \frac{A_s}{V^{mob}} \tag{6}$$

where Γ_i is the surface concentration of component i and A_s the surface area of the stationary phase. This relation can be transformed to become completely analogous to eq. (2). Since pressure and temperature change neither A_s nor V^{mob}

significantly, all changes in k_i are caused by variations in the partition coefficient K_i or in Γ_i/c_i^{mob}.

In order to describe the pressure dependence of k_i thermodynamically *van Wasen* used a model originally developed by *Everett*[79] for adsorption from solutions. Here the adsorption process is assumed to be equivalent to a "chemical" equilibrium reaction according to

$$1^{mob} + \frac{1}{r} i^{stat} \rightleftarrows 1^{stat} + \frac{1}{r} i^{mob}$$

The parameter r takes into account the different spatial requirements of the molecules 1 and i on the surface of the stationary phase and is given by $r = a_i/a_1$ where a_1 and a_i are the partial molar surface areas of component 1 and i respectively. The result of a detailed treatment is

$$\left(\frac{\partial \ln k_i}{\partial p}\right)_T = \frac{V_i^{\infty,mob} - (a_i/a_1) \cdot V_{m1}^{*mob}}{R \cdot T} - \kappa_1^* \qquad (7)$$

Here $V_i^{\infty,mob}$ is the partial molar volume of component i at infinite dilution in the mobile phase, V_{m1}^{*mob} the molar volume of the pure mobile phase 1, and κ_1^* the compressibility of the pure mobile phase 1 according to equation (1). To a first approximation, one can use $r \approx (V_{mi}^{*s}/V_{m1}^{*s})^{2/3}$ for spherical molecules and $r \approx V_{mi}^{*s}/V_{m1}^{*s}$ for chain molecules (s = solid). For a corresponding relation giving the density dependence of k_i, see [40].

Figures 10 to 13 exemplify the influence of temperature and pressure, as well as of the stationary and the mobile phases, on the capacity ratio k_i of a sample i.

Figure 10 shows results for naphthalene and fluorene (component i) on deactivated silica gel (Reversed Phase, Perisorb RP-8) as stationary phase using carbon dioxide as mobile phase according to measurements by *van Wasen*[40]. Figure 10a shows $\log k_i$ for naphthalene plotted *versus* the carbon dioxide pressure p at 35, 40, and 50 °C, *i.e. ca.* 4, 9, and 19 K above the critical temperature of pure carbon dioxide. The S-shaped curves found are typical for such experiments in the supercritical region, whereas the shape at low pressures is represented in Figure 15. The pressure dependence is found to be very large: between 20 and 120 bar, k_i changes by nearly three orders of magnitude. The temperature dependence is especially interesting. The isotherms intersect at about 60 bar; at lower pressures k_i declines and at higher pressures it rises with increasing temperature, corresponding respectively to an increase or a decrease of c_i^{mob} relative to c_i^{stat}. This difference in temperature dependence can be explained from the fact that for $p \rightarrow 0$ $k_i \sim (p_i^* \cdot \lim_{x_i \rightarrow 0} f_i^{stat})^{-1}$ (where p_i^* and f_i are the vapor pressure and the activity coefficient of component i respectively; see Section 5.3). Since p_i^* (and consequently c_i^{mob}) increases with increasing temperature, k_i decreases, the temperature dependence of $\lim_{x_i \rightarrow 0} f_i^{stat}$ being normally negligible in comparison with that of p_i^*. At high pressures, however, it is no longer the vapor pressure of component i but rather the density of the supercritical solvent that is decisive for the solvent power of the mobile phase, and k_i increases with increasing temperature since the density of the mobile phase decreases with increasing temperature at constant pressure and thus c_i^{mob} declines.

The fact that the temperature dependence at higher pressures is really a density effect is demonstrated by Figure 10b

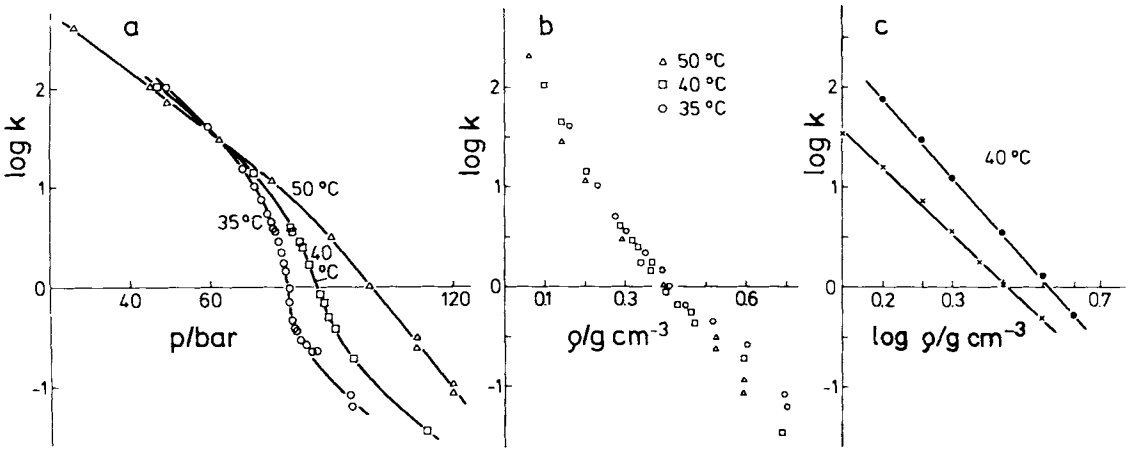


Fig. 10. Capacity ratio k as a function of pressure and temperature. $_{10}\log k$ of naphthalene on deactivated silica gel (Reversed Phase, Perisorb RP-8) at 35, 40, and 50 °C with CO_2 as mobile phase as a function of a) pressure p, b) density ρ, and c) $_{10}\log\rho$ (naphthalene (×), fluorene (•)) (according to [40]).

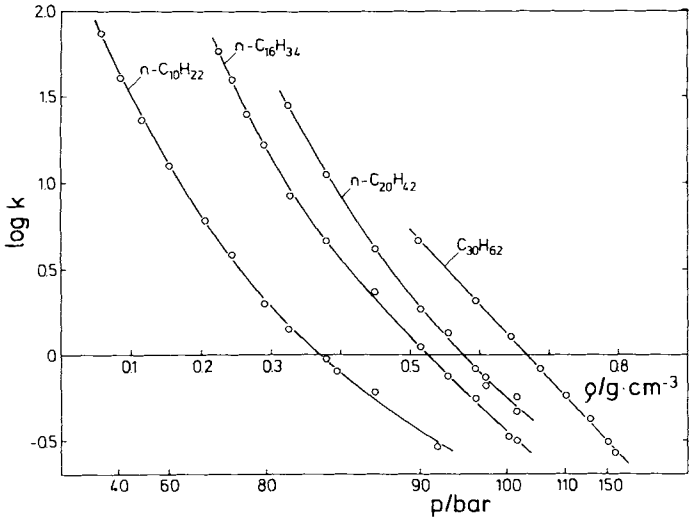


Fig. 11. Capacity ratio k for four samples. $_{10}\log k$ of decane, hexadecane, eicosane, and squalane (2,6,10,15,19,23-hexamethyltetracosane) on Carbowax 400/Porasil C (100—120 mesh) at 40 °C with CO_2 as mobile phase (0.5 $dm^3 \cdot min^{-1}$ (NTP)) as a function of density ρ and pressure p (according to [51]). Column: length 2 m, internal diameter 1.4 mm.

where $\log k_i$ is plotted against the density of pure carbon dioxide. In this diagram all isotherms coincide more or less within the limits of experimental accuracy. The plots are no longer S-shaped but only slightly curved. According to Figure 10c the curves can be further linearized by plotting $\log k_i$ *versus* $\log \rho$. Thus Figure 10 demonstrates that in the near-critical region the density of a given supercritical gas dominates its solvent power.

In Figure 11, $\log k_i$ is plotted *versus* pressure p and density ρ for decane, hexadecane, eicosane, and squalane (2,6,10,15,19,23-hexamethyltetracosane) as samples i and on Carbowax 400 (chemically bonded on Porasil C) according to measurements by *van Wasen*[51] (see Figures 10a and b). For all substances i, only slightly curved $\log k_i(\rho)$ isotherms are found that are essentially parallel. Such curves should greatly facilitate the planning of pressure programs for analytical or preparative separations.

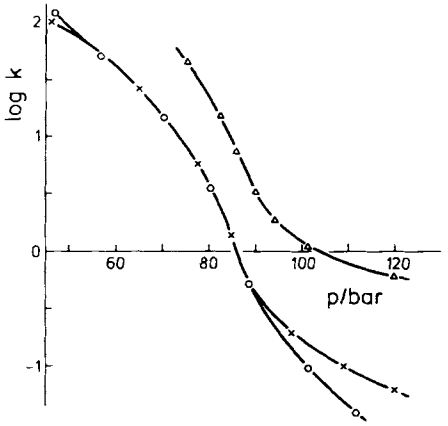


Fig. 12. Capacity ratio k for three stationary phases. $_{10}\log k$ of naphthalene on silica gel, 14 $m^2 \cdot g^{-1}$ (×), deactivated silica gel (Reversed Phase, Perisorb RP-8) (○) and silica gel, 500 $m^2 \cdot g^{-1}$ (△) at 40 °C with CO_2 as mobile phase as a function of pressure p (according to [40]).

Figure 12 shows the influence of the stationary phase. Here $\log k_i$ for naphthalene with CO_2 at 40 °C as mobile phase is plotted against pressure for three different stationary phases according to measurements by *van Wasen*[40]. For comparable surface areas the specific characteristics of the surfaces (here silica gel, 14 $m^2 \cdot g^{-1}$, or deactivated silica gel (Reversed Phase, Perisorb RP-8) with a similar surface area) have only a slight influence whereas the drastic increase in the surface area of the silica gel to 500 $m^2 \cdot g^{-1}$ is important. Corresponding to the larger A_s value, the curve is shifted to higher values of $\log k_i$; the shift, however, is smaller than would correspond to the relative increase in surface area. Thus it can again be deduced from Figure 12 that in SFC the selectivity depends primarily on the mobile phase.

Figure 13 demonstrates the influence of the mobile phase[40]. Here $\log k_i$ of naphthalene on deactivated silica gel (Reversed Phase, Perisorb RP-8) at 40 °C is plotted *versus* the density ρ (Figure 13a), *versus* the reciprocal of the molar volume $1/V_m$ (Figure 13b), which is proportional to the particle density, as well as *versus* the reduced density ρ/ρ_c (Figure 13c) for both carbon dioxide and ethane as mobile phases. The smaller capacity ratios for ethane in Figure 13a are caused by smaller Γ_i/c_i^{mob} values probably because of higher concentrations in the mobile phase ethane at the same density (here in $g \cdot cm^{-3}$). As shown in Figure 13b the distance between the curves $\log k_i(p)$ at equal values of the reciprocal molar volume (or of the particle density) becomes smaller, but the solubility in ethane remains higher. Plotting the data against reduced density (Figure 13c) changes the sequence of the curves because of the considerably smaller critical density of ethane (see Table 1).

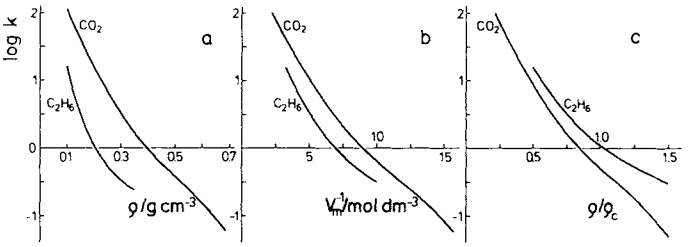


Fig. 13. Capacity ratio k for two mobile phases. $_{10}\log k$ of naphthalene on deactivated silica gel (Reversed Phase, Perisorb RP-8) at 40 °C for carbon dioxide and ethane as mobile phase respectively as a function of a) density ρ, b) reciprocal molar volume $1/V_m$, and c) reduced density ρ/ρ_c (according to [40]).

5.2. Partial Molar Volumes

Partial molar volumes in compressed fluid mixtures are difficult to determine experimentally, *e. g.* from very accurate pVT data of mixtures and of the pure components; it is even more difficult to determine the partial molar volume V_i^{∞} of a solute i at very low concentrations, *e. g.* at infinite dilution. SFC offers an elegant possibility of obtaining such experimental V_i^{∞} values; they can be deduced directly from the slopes of $\log k_i(p)$ isotherms according to equation (7).

An especially interesting application is the determination of V_i^{∞} at the critical point of the pure solvent 1; here values running to negative as well as to positive infinity are predicted by theory. In Figure 14 V_i^{∞} values of naphthalene and fluorene in CO_2 are shown that were determined by *van Wasen*[40, 80] from SFC experiments. Approaching the critical

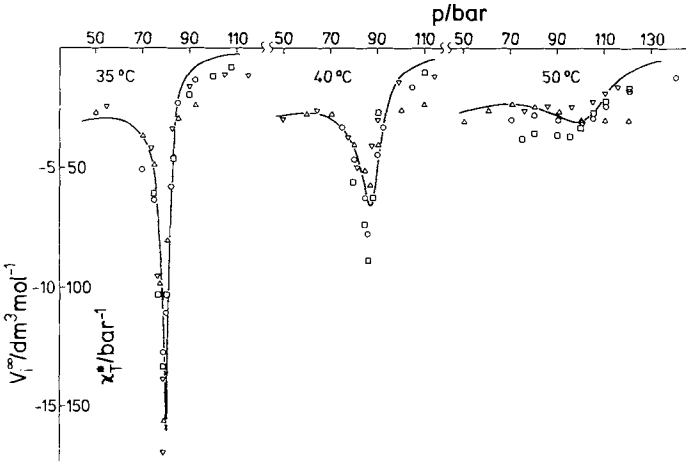


Fig. 14. Partial molar volumes V_i^{∞} (at infinite dilution) of naphthalene and fluorene in supercritical CO_2 from SFC experiments (according to [40, 80]). (▽) and (△) naphthalene, stationary phase Perisorb A and Perisorb RP-8 respectively; (□) and (○) fluorene, stationary phase Perisorb A and Perisorb RP-8, respectively; — isothermal compressibility κ_T^* of pure CO_2 (see Text).

point of pure CO_2, increasingly negative V_i^{∞} values are found; thus the experiments suggest a limiting value of V_i^{∞} tending to negative infinity. It follows from Figure 14 that, in agreement with eq. (7), no influence of the stationary phase

used in the SFC experiments can be observed. Added to this is the fact that, within the limits of experimental error, the V_i^{∞} values of the two test substances do not differ. The proportionality between V_i^{∞} and the isothermal compressibility κ_T^* of the pure solvent (here CO_2) predicted theoretically is also confirmed.

5.3. Virial Coefficients

According to equation (5) interaction second virial coefficients B_{1i} between the supercritical solvent and the solute i can be determined from the slopes of the $\log k_i(p)$ isotherms. In order to remain within the assumptions made in the derivation, the slope has to be determined at low pressures or best as the limiting slope of the curves for vanishing pressure. B_{1i} values of several systems have been determined by SFC since the mid-1960's (see [2,7,54,77,78]). Interaction second virial coefficients are of fundamental interest, *e.g.* for corrections in the determination of thermodynamic data from vapor-liquid equilibria or for theoretical predictions concerning the interaction between unlike particles.

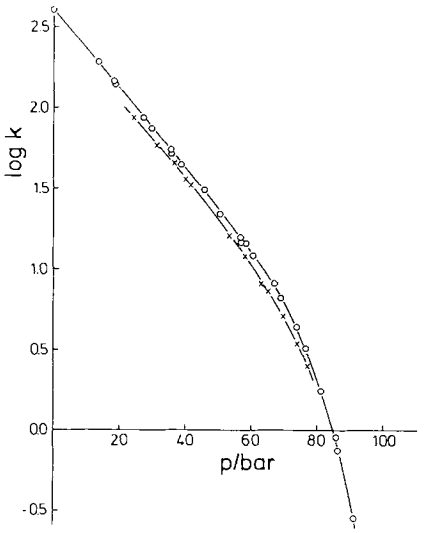


Fig. 15. Interaction second virial coefficients B_{1i} from SFC experiments with CO_2 (component 1). $_{10}\log k$ for decane (component i) on Carbowax/Porasil C (100—120 mesh) (○) and on oxydipropionitrile (OPN)/Porasil C (80—100 mesh) (×) at 40 °C with CO_2 as mobile phase (according to [51]); column: length 2 m, internal diameter 1.4 mm; flow rate of CO_2 0.5 $dm^3 \cdot min^{-1}$ (NTP). B_{1i} results from the limiting slope for $p \rightarrow 0$ (see text).

Remarkably, according to eq. (5) the slope of a $\log k_i(p)$ isotherm at sufficiently low pressures depends on the component i, the mobile phase 1, and the temperature T only and not on the stationary phase. This is also demonstrated in Figure 15 where $\log k_i$ of decane (component i) for Carbowax 400 and oxydipropionitrile (OPN) both on Porasil C with CO_2 (component 1) as mobile phase are presented according to measurements by *van Wasen*[51]. As expected, the curves exhibit the same slopes (within experimental accuracy) at low pressures. Using $V_i^{\infty stat} \approx V_{mi}^{*1}$, it follows from the limiting slope for $p \rightarrow 0$ that $B_{1i} = -635\ cm^3 \cdot mol^{-1}$ for decane and CO_2 at 40 °C; for measurements of this kind the experimental errors are about ±10%.

In contrast to the limiting slopes, the limiting values of $\log k_i$ for $p \rightarrow 0$, however, depend on the choice of the stationary phase since here k_i is proportional to $(p_i^* \cdot \lim_{x_i \rightarrow 0} f_i^{stat})^{-1}$. Thus limiting values of the activity coefficients can be calculated from the extrapolated k_i values. With increasing pressures, the $\log k_i(p)$ isotherms turn off to lower values in a characteristic manner and show the typical S-shaped curvature mentioned above (see Fig. 10a, 12).

5.4. Diffusion Coefficients

In 1960 *Giddings* and *Seager*[81], *Boheman* and *Purnell*[82], and some other groups independently developed methods for the determination of diffusion coefficients in gas mixtures by chromatographic techniques. Since then, numerous papers have been published in this field (for reviews, see [83,84,74]). Additionally, an important modification of this technique, the "peak arrest" method, has also been developed[91,92].

During such investigations *Balenoviç*, *Myers*, and *Giddings*[85] determined diffusion coefficients in compressed gases; the technique has also been extended to liquid systems[93,94]. *van Wasen*[40,86], *Swaid* and *Schneider*[41,87], and *Feist*[88] improved this technique and determined the diffusion coefficients of some organic substances in supercritical carbon dioxide at pressures up to 160 bar. Such data are of interest for mass transfer processes in SFC and fluid extraction (also on an industrial scale).

In this method the concentration profile of the eluted solute is measured at the exit of the empty column (characteristic dimensions: length *ca.* 100 m, internal diameter *ca.* 0.2 to 0.5 mm). For negligible interactions with the inner wall of the column and for $D_{eff}/\bar{U} \cdot L \leq 0.01$ an approximately symmetrical Gaussian profile is found and the variance in length units is given by

$$\sigma_i^2(z) = 2 \cdot D_{eff} \cdot t_{Ri} \tag{8}$$

For laminar flow in the column the effective diffusion coefficient D_{eff} is given by

$$D_{eff} = D_{1i} + \frac{r_0^2 \cdot \bar{U}^2}{48\, D_{1i}} \tag{9}$$

Here $\bar{U}$ is the mean linear velocity of the mobile phase, L and r_0 are the length and the inner radius of the empty column respectively, and t_{Ri} is the retention time. From the variance $\sigma_i^2(z)$ of the concentration profile, D_{eff} and then D_{1i} can be determined (see [41,87]).

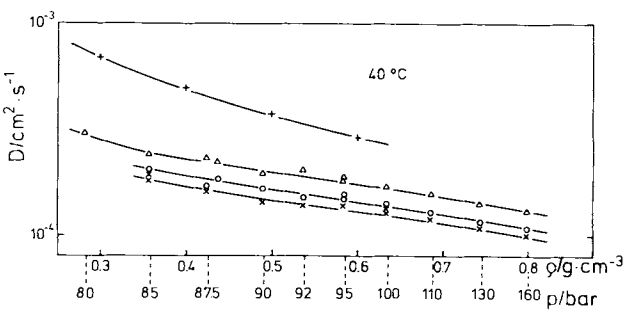


Fig. 16. Binary diffusion coefficients D_{1i} from SFC experiments with CO_2 (component 1). D_{1i} (logarithmic scale) for benzene (△), *n*-propylbenzene (○) and 1,3,5-trimethylbenzene (×) in CO_2 as a function of density ρ (according to [41, 87]); for comparison, the self-diffusion coefficient D_{11} of pure CO_2 (+) at 42 °C is plotted according to measurements of *Robb* and *Drickamer* [89].

In Figure 16 $\log D_{1i}$ for benzene, *n*-propylbenzene, and 1,3,5-trimethylbenzene in CO_2 at 40 °C is plotted against density ρ, according to measurements by *Swaid*[41, 87]; for comparison the self-diffusion coefficients D_{11} of CO_2[89] are also given. All D_{1i} values are situated between 10^{-3} and 10^{-4} $cm^2 \cdot s^{-1}$. Thus they are smaller than those of gases at normal pressure by about two or three orders of magnitude; they are, however, greater than in normal liquids by a factor of about 10^2 and are situated below the self-diffusion coefficients of pure CO_2 by one order of magnitude only. It is remarkable that *n*-propylbenzene diffuses faster in supercritical CO_2 than the isomeric 1,3,5-trimethylbenzene. Experiments for naphthalene, phenol, and caffeine gave similar results[88]. These last measurements demonstrated, however, that for even higher-molecular substances increasing interaction with the inner walls of the columns can limit the application of the method.

5.5. Miscellaneous

SFC has already been applied to the determination of molecular weight distributions, *e.g.* for polystyrenes[61] (see Figure 9). An important application of SFC could also become the study of adsorption phenomena on solid surfaces at high pressures from supercritical media[95].

6. Outlook

At present, supercritical fluid chromatography (SFC) is in a state of rapid development. Compared with gas chromatography (GC), it has important experimental advantages especially in the separation of substances with extremely low volatility or thermal stability. Like HPLC and gel chromatography, SFC is also used for special applications, *e.g.* in the petroleum industry or in the separation of oligomers. Additionally, SFC is of great interest for fundamental research concerning fluid extraction or the determination of physicochemical properties of fluid systems. These items alone indicate that the importance of SFC will increase in the future, particularly since commercial HPLC equipment should easily be modified for use in SFC.

Up to now advances in SFC have been made mainly by physicochemists or analytical chemists with physicochemical interests. For the future, studies in the following fields would appear desirable:

1) Fundamental research into the physicochemical properties of fluid pure substances and mixtures at elevated pressures (*e.g.* thermal and caloric equation of state, phase behavior, transport properties, correlation and calculation of physicochemical data).
2) Systematic investigations concerning the mobile phase (*e.g.* use of substances other than CO_2 and of mixtures, as well as choice and dosage of moderators).
3) Systematic investigations concerning the stationary phase (*e.g.* improvement of chemically bonded phases and quantitative physicochemical description of the elementary steps of separation).
4) Development of separation theory in this field (*e.g.* quantitative description of HETP, optimization of operational parameters; see [10, 11, 16]).
5) Improvement of apparatus (*e.g.* with respect to electronic control, use of density programs instead of pressure and/or temperature programs hitherto applied as well as of gradient programs for the dosing of moderators, improvement of detectors and of the experimental technique in preparative applications).

In view the significant progress made in fluid extraction (also on an industrial scale) during the last years, rapid developments may be expected in SFC in the near future.

Our own investigations reported in the present review were started in the late 1960's at the Institute of Physical Chemistry and Electrochemistry of the University of Karlsruhe. The authors are indebted to Professor E. U. Franck for his help and valuable suggestions during that time. Financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: April 28, 1980 [A 326 IE]
German version: Angew. Chem. *92*, 585 (1980)

[1] *E. Klesper, A. H. Corwin, D. A. Turner*, J. Org. Chem. *27*, 700 (1962).
[2] *S. T. Sie, W. van Beersum, G. W. A. Rijnders*, Sep. Sci. *1*, 459 (1966).
[3] *S. T. Sie, G. W. A. Rijnders*, Sep. Sci. *2*, 699 (1967).
[4] *S. T. Sie, G. W. A. Rijnders*, Sep. Sci. *2*, 729 (1967).
[5] *S. T. Sie, G. W. A. Rijnders*, Sep. Sci. *2*, 755 (1967).
[6] *J. C. Giddings, M. N. Myers, J. W. King*, J. Chromatogr. Sci. *7*, 276 (1969); *M. N. Myers, J. C. Giddings*, Prog. Sep. Purif. *3*, 133 (1970).
[7] *M. S. Vigdergauz, V. I. Semkin*, Russ. Chem. Rev. *40*, 533 (1971).
[8] *A. Przyjazny, R. Staszewski*, Chem. Anal. (Warsaw) *19*, 3 (1974).
[9] *T. Doran*, Gas Chromatogr. *9*, 133 (1972).
[10] *D. Bartmann*, Dissertation, Universität Bochum 1972.
[11] *D. Bartmann, G. M. Schneider*, J. Chromatogr. *83*, 135 (1973).
[12] *T. H. Gouw, R. E. Jentoft*, J. Chromatogr. *68*, 303 (1972).
[13] *T. H. Gouw, R. E. Jentoft*, Adv. Chromatogr. *13*, 1 (1975).
[14] *T. H. Gouw, R. E. Jentoft*, Chromatogr. Sci. *11* (Chromatogr. Pet. Anal.), 313 (1979).
[15] *L. R. Snyder, D. L. Saunders*, Chromatogr. Sci. *11* (Chromatogr. Pet. Anal.), 215 (1979).
[16] *E. Klesper*, Angew. Chem. *90*, 785 (1978); Angew. Chem. Int. Ed. Engl. *17*, 738 (1978).
[16a] *K. D. Timmerhaus, M. S. Barber:* High-Pressure Science and Technology. Sixth AIRAPT Conference. Vol. 1. Plenum Publ. Corp., New York 1979.
[17] *G. M. Schneider* in [16a], p. 506.
[18] *G. M. Schneider* in: Specialist Periodical Reports: Chemical Thermodynamics. Vol. 2. Chemical Society, London 1978, Chap. 4.
[19] *G. M. Schneider*, Angew. Chem. *90*, 762 (1978); Angew. Chem. Int. Ed. Engl. *17*, 716 (1978).
[20] *G. M. Schneider* in: Vorträge vor der Rheinisch-Westfälischen Akademie der Wissenschaften (Natur-, Ingenieur- und Wirtschaftswissenschaften). Westdeutscher Verlag, Opladen, in press.
[21] Angew. Chem. *90*, 747–802 (1978); Angew. Chem. Int. Ed. Engl. *17*, 701–754 (1978).
[22] *G. M. Schneider, E. Stahl, G. Wilke:* Extraction with Supercritical Gases. Verlag Chemie, Weinheim 1979.
[23] *J. S. Rowlinson:* Liquids and Liquid Mixtures. 2nd Edit. Butterworth, London 1969.
[24] *J. M. Prausnitz:* Molecular Thermodynamics of Fluid Phase Equilibria. Prentice Hall, Englewood Cliffs 1969.
[25] *R. C. Reid, J. M. Prausnitz, T. K. Sherwood:* The Properties of Gases and Liquids. 3rd Edit. McGraw-Hill, New York 1977.
[26] IUPAC: International Thermodynamic Tables of the Fluid State. Carbon Dioxide. Pergamon Press, Oxford 1976.
[27] *H. H. Reamer, B. H. Sage*, J. Chem. Eng. Data *8*, 508 (1963); *10*, 49 (1965).
[28] *U. Deiters*, Dissertation, Universität Bochum 1979.
[29] *J. M. M. Mendonça*, Ph. D. Thesis, Imperial College, London 1978.
[30] *S. Peter, G. Brunner*, Angew. Chem. *90*, 794 (1978); Angew. Chem. Int. Ed. Engl. *17*, 746 (1978); *S. Peter*, Ber. Bunsenges. Phys. Chem. *81*, 950 (1977).
[31] *K. G. Liphard*, Diplomarbeit, Universität Bochum 1974; *K. G. Liphard, G. M. Schneider*, J. Chem. Thermodyn. *7*, 805 (1975).
[32] *E. Stahl, W. Schilz, E. Schütz, E. Willing*, Angew. Chem. *90*, 778 (1978); Angew. Chem. Int. Ed. Engl. *17*, 731 (1978).
[33] *E. Stahl, W. Schilz*, Talanta *26*, 675 (1979).

[34] *N. M. Karayannis, A. H. Corwin, E. W. Baker, E. Klesper, J. A. Walter,* Anal. Chem. *40*, 1736 (1968).
[35] *D. Bartmann,* Diplomarbeit, Universität Karlsruhe 1969; *D. Bartmann, G. M. Schneider,* Ber. Bunsenges. Phys. Chem. *73*, 917 (1969).
[36] *D. Bartmann,* Ber. Bunsenges. Phys. Chem. *76*, 336 (1972).
[37] *R. E. Jentoft, T. H. Gouw,* Anal. Chem. *44*, 681 (1972).
[68] *E. Klesper, W. Hartmann,* J. Polym. Sci., Polym. Lett. Ed. *15*, 9 (1977).
[39] *E. Klesper, W. Hartmann,* Eur. Polym. J. *14*, 77 (1978).
[40] *U. van Wasen,* Dissertation, Universität Bochum 1978.
[41] *I. Swaid, G. M. Schneider,* Ber. Bunsenges. Phys. Chem. *83*, 969 (1979).
[42] *R. E. Jentoft, T. H. Gouw,* Anal. Chem. *48*, 2195 (1976).
[43] *O. G. Vitzthum, P. Hubert,* DBP 2127642 (1975) (Br. Pat. 1333362 (1973)).
[44] *W. Ecknig, H. J. Polster,* Chem. Tech. (Leipzig) *31*, 89 (1979).
[45] *L. J. Cashaw,* Dissertation, University of Houston, Houston, Texas 1970.
[46] *J. L. Cashaw, R. Segura, A. Zlatkis,* J. Chromatogr. Sci. *8*, 363 (1970).
[47] *W. Asche,* Dissertation, Universität Clausthal-Zellerfeld 1977; Chromatographia *11*, 411 (1978).
[48] *J. E. Conaway, E. F. Smith, L. B. Rogers,* Chem. Instrum. *8*, 167 (1977).
[49] *M. Novotny, W. Bertsch, A. Zlatkis,* J. Chromatogr. *61*, 17 (1971).
[50] *S. T. Sie, G. W. A. Rijnders,* Anal. Chim. Acta *38*, 31 (1967).
[51] *U. van Wasen,* Diplomarbeit, Universität Bochum 1974.
[52] *U. van Wasen, G. M. Schneider,* Chromatographia *8*, 274 (1975).
[53] *T. H. Gouw, R. E. Jentoft, E. J. Gallegos* in [16a], p. 583.
[54] *W. Ecknig, H. J. Polster,* Chem. Tech. (Leipzig) *31*, 245 (1979).
[55] *G. W. A. Rijnders, J. P. A. Bleumer, M. van Krevelen,* Usp. Khromatogr. *65* (1972).
[56] *K. Fuzita, I. Shimokobe, F. Nakazima,* Nippon Kagaku Kaishi *8*, 1348 (1975).
[57] *B. P. Simonian, L. B. Rogers,* J. Chromatogr. Sci. *16*, 49 (1978).
[58] *J. A. Nieman,* Dissertation, Purdue University, Lafayette, Indiana 1974.
[59] *J. A. Nieman, L. B. Rogers,* Sep. Sci. *10*, 517 (1975).
[60] *R. E. Jentoft, T. H. Gouw,* J. Polym. Sci., Polym. Lett. Ed. *7*, 811 (1969).
[61] *T. Jr. Altares,* J. Polym. Sci. *B 8*, 761 (1970).
[62] *E. Klesper, W. Hartmann,* J. Polym. Sci., Polym. Lett. Ed. *15*, 707 (1977).
[63] *J. E. Conaway,* Dissertation, University of Georgia, Athens, Georgia 1977.
[64] *W. Hartmann, E. Klesper,* J. Polym. Sci., Polym. Lett. Ed. *15*, 713 (1977).
[65] *J. E. Conaway, J. A. Graham, L. B. Rogers,* J. Chromatogr. Sci. *16*, 102 (1978).
[66] *W. Hartmann, E. Klesper* in [16a], p. 573.
[67] *W. Bertsch,* Dissertation, University of Houston, Houston, Texas 1973.
[68] *K. H. Altgelt,* Chromatogr. Sci. *11* (Chromatogr. Pet. Anal.), 287 (1979).
[69] *H. K. Altgelt, M. D. Jewell, R. De Witt, L. M. Selucky,* Chromatogr. Sci. *11*, 185 (1979).
[70] *R. Amos,* Chromatogr. Sci. *11*, (Chromatogr. Pet. Anal.), 329 (1979).
[71] *N. M. Karayannis, A. H. Corwin,* J. Chromatogr. Sci. *8*, 251 (1970).
[72] *N. M. Karayannis, A. H. Corwin,* J. Chromatogr. Sci. *47*, 247 (1970).
[73] *N. M. Karayannis, A. H. Corwin,* Anal. Biochem. *26*, 34 (1968).
[74] *R. J. Laub, R. L. Pecsok:* Physicochemical Applications of Gas Chromatography. Wiley, New York 1978.
[75] *D. C. Locke,* Int. Lab. *1975* (July/Aug.), p. 13.
[76] *H. Kelker,* Ber. Bunsenges. Phys. Chem. *72*, 187 (1973).
[77] *M. S. Vigdergauz, V. I. Semkin,* J. Chromatogr. *58*, 95 (1971).
[78] *R. B. Spertell, G. T. Chang,* J. Chromatogr. Sci. *10*, 60 (1972).
[79] *H. D. Everett,* Trans. Faraday Soc. *61*, 2478 (1965).
[80] *U. van Wasen, G. M. Schneider,* J. Phys. Chem. *84*, 229 (1980).
[81] *J. C. Giddings, S. L. Seager,* J. Chem. Phys. *33*, 1579 (1960).
[82] *J. Boheman, H. J. Purnell,* J. Chem. Soc. *1961*, 360.
[83] *T. R. Marrero, E. A. Mason,* J. Phys. Chem. Ref. Data *1*, 3 (1972).
[84] *V. R. Maynard, E. Grushka,* Adv. Chromatogr. *12*, 99 (1975).
[85] *Z. Balenović, M. N. Myers, J. C. Giddings,* J. Chem. Phys. *52*, 915 (1970).
[86] *U. van Wasen, I. Swaid, G. M. Schneider,* Ber. Bunsenges. Phys. Chem. *83*, 1130 (1979).
[87] *I. Swaid,* Diplomarbeit, Universität Bochum 1979.
[88] *R. Feist,* Diplomarbeit, Universität Bochum 1980.
[89] *W. L. Robb, H. G. Drickamer,* J. Chem. Phys. *19*, 1504 (1951).
[90] *Huang, Jun-Shung,* Hua Hsueh Tung Pao (3), 50 (1974).
[91] *C. E. Cloete, T. W. Smuts, K. De Clerk,* J. Chromatogr. *120*, 1, 17 (1976).
[92] *V. R. Chaudhary, M. G. Parande,* J. Chromatogr. *132*, 344 (1977).
[93] *A. C. Ouano,* Ind. Eng. Chem. Fundam. *11*, 268 (1972).
[94] *E. Grushka, E. J. Kikta,* J. Phys. Chem. *78*, 2297 (1974).
[95] *J. Specovius, G. H. Findenegg,* Ber. Bunsenges. Phys. Chem. *82*, 174 (1978); *84*, 690, 696 (1980).
[96] *R. E. Jentoft, T. W. Gouw,* J. Chromatogr. Sci. *8*, 138 (1970).
[97] *S. T. Sie, G. W. A. Rijnders,* Anal. Chim. Acta *38*, 31 (1967).
[98] *R. E. Jentoft, T. H. Gouw,* Anal. Chem. *44*, 681 (1972).
[99] *M. N. Myers, J. C. Giddings,* Prog. Sep. Purif. *3*, 113 (1970).
[100] *A. P. Kudchadker, G. H. Alani, B. J. Zwolinski,* Chem. Rev. *68*, 659 (1968).
[101] *R. C. Weast:* Handbook of Chemistry and Physics. 60th Edit. CRC Press, Boco Raton, Florida, 1979–80.
[102] *G. Brunner,* Habilitationsschrift, Universität Erlangen 1978.
[103] *K. Zosel,* DBP 1493190 (1964), Studiengesellschaft Kohle mbH.

Valence Changes at High Pressure in Systems Containing Lanthanoids

By A. Jayaraman[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

Pressure-induced valence change in samarium sulfide SmS is reminiscent of alchemy, for when the electronic transition has taken place, the originally dull looking substance glitters like gold. Although it is not the realization of the alchemist's dream in the true sense, the material in the new state exhibits extraordinarily interesting behavior. As a novel feature, the valence state of the samarium fluctuates between two electronic configurations at a very fast rate. The physical properties of systems containing lanthanoids can be profoundly altered by manipulating the valence state by pressure or by chemical substitution. These phenomena will be described and discussed in the present article.

1. Introduction

I intend reviewing in this paper a topic which is of great interest not only to solid state physics but also to solid state chemistry. In rare earth systems involving Ce, Sm, Eu, Yb, and Tm a change in the valence state of the lanthanoid ion can be induced by high pressure, temperature or by chemical substitution[1]. Usually, the change is from a lower to a higher valence state. The reason for this electronic transition lies in the small energy difference between the $4f^n$ and $4f^{n-1}$ electronic configurations. The valence transition usually

[*] Prof. Dr. A. Jayaraman
Bell Laboratories
Murray Hill, New Jersey 07974 (USA)

leads not to an integral valence but to an intermediate valence state. Materials of this kind generally exhibit extremely interesting properties.

The lanthanoids are predominantly trivalent due to their $4f^n 5d^1 6s^2$ outer electronic structure. On going from cerium to lutetium the inner 4f shell acquires its full complement of 14 electrons, while the number of valence electrons remains constant at 3 (4f-electrons are well localized and do not contribute to bonding). Therefore trivalency dominates the series. However, in accord with Hund's rule, near the half period and towards the end of the lanthanoid series the 5d-electron drops into the 4f-shell, giving a stable half-filled and a fully filled 4f-shell in the case of europium and ytterbium, respectively. Consequently the divalent state is a stable state for these elements. Samarium simulates Eu, and thulium simulates Yb in this respect, and are therefore also stable in the divalent state. The outer electronic structures of these divalent rate earth elements are shown along with that of Ce in Table 1.

Table 1. Outer electron configuration and potential valence state of selected lanthanoids.

Element	II	III	IV
Ce	[a]	$4f^1 5d^1 6s^2$,	$4f^0 5d^2 6s^2$
Sm	$4f^6 5d^0 6s^2$,	$4f^5 5d^1 6s^2$,	[a]
Eu	$4f^7 5d^0 6s^2$	$4f^6 5d^1 6s^2$,	[a]
Tm	$4f^{13} 5d^0 6s^2$,	$4f^{12} 5d^1 6s^2$,	[a]
Yb	$4f^{14} 5d^0 6s^2$,	$4f^{13} 5d^1 6s^2$,	[a]

[a] Non-existent.

The divalent state of Sm, Eu, Tm, and Yb should become unstable under high pressure. This can be foreseen from the fact that they have smaller ionic radii in their trivalent state and hence high pressure would favor the higher valence state. Recent high-pressure experiments on a series of lanthanoid compounds[1-3], in particular the monochalcogenides Sm, Eu, Tm, and Yb, have demonstrated the occurrence of such transformations. Moreover, not only pressure can effect this transition but also chemical substitution. A vast amount of literature has accumulated on this subject in recent years and the field of valence changes continues to be of great interest, both experimentally and theoretically[4].

The most interesting feature concerning valence transition is that the valence change is not integral but has an intermediate value. For instance in SmS, a classic substance in this regard, the valence of the high pressure phase obtained at 7 kbar is 2.7. The intermediate valence state has been variously referred to as "homogeneously mixed valence state", "fluctuating valence state", or "interconfiguration fluctuation". We will discuss the anomalous properties of this phase below.

2. Valence Change in Cerium

Historically a first-order transition in cerium at about 7 kbar was first reported in 1927[5]. Subsequent studies[6,7] established that the phase transition discovered by *Bridgman* is associated with a change in the valence state in metallic cerium, from trivalent towards the tetravalent state: this was concluded primarily from the fact that the face centered cubic *(fcc)* structure of cerium is retained while the volume decreases by about 12%. Subsequent pressure/temperature studies established the phase diagram[8] reproduced in Figure 1. The unique features of this the phase diagram are the termination of the so-called γ to α cerium phase boundary at a critical point and the shallow minimum in the melting curve. Critical termination of a phase boundary is common for vapor/liquid systems but uncommon for a solid phase boundary. The existence of a critical point for a solid-solid transition, first demonstrated in the case of cerium, would appear to characterize substances undergoing an isostructural transition. As in the case of a liquid/vapor equilibrium, there is no symmetry restriction upon a continuous transition, and hence critical points appear natural for isostructural transitions.

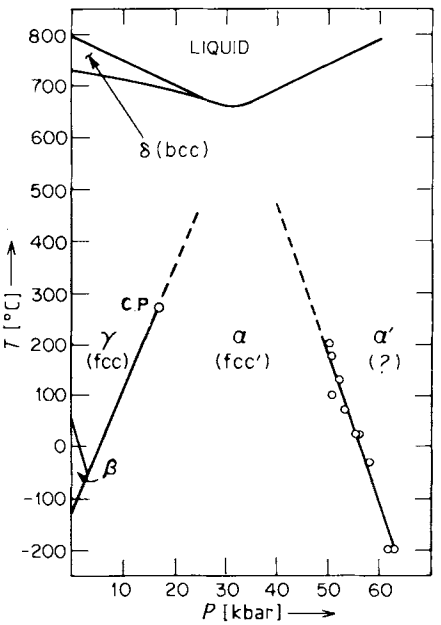


Fig. 1. Phase diagram of cerium. CP is the critical point for the γ- to α-cerium transition. β-Ce is dhcp.

The anomalous fusion behavior of cerium is again connected with valence change; the turnover in the fusion curve stems from a continuous valence change in *fcc*-cerium in the supercritical region. So far, α-cerium remains the only substance that exhibits a broad fusion curve minimum. At a pressure near 55 kbar and at room temperature, cerium is believed to undergo another isostructural transition, associated with a further change in valence towards the quadrivalent state.

3. Valence Change in Samarium Monochalcogenides

The lanthanoids and chalcogens form one-to-one compounds which all crystallize in the NaCl-type structure. A plot of their lattice parameter against atomic number is shown in Figure 2. The Sm, Eu, and Yb monochalcogenides have anomalously large lattice parameters, in the otherwise smoothly decreasing series of values. These anomalous values reflect the larger size of the divalent cation. While the compounds of the divalent metals are semiconductors, those of the trivalent ones are metallic. There is a very simple rea-

son for this: when the lanthanoid ion is divalent there is exact charge compensation and no electron is available for conduction (for instance, SmS in the ionic representation is $Sm^{2+}S^{2-}$ and the two valence electrons of Sm are taken up by the sulfur).

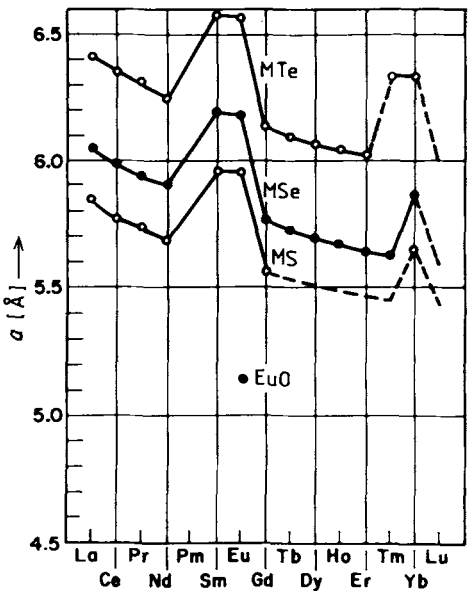


Fig. 2. Lattice parameter of lanthanoid monochalcogenides. The M^{II} monochalcogenides have anomalously large lattice parameters. Eu in EuO is divalent.

In the monochalcogenides of trivalent lanthanoids (for instance $Gd^{3+}S^{2-}+1e$) however, one electron per molecule is available for conduction (*ca.* 10^{22} electrons per cm^3). When a monochalcogenide of a divalent lanthanoid, such as SmS, is subjected to pressure it transforms according to

$$Sm^{2+}S^{2-} \rightarrow Sm^{3+}S^{2-} + 1e$$

A semiconductor-to-metallic transition results, and approximately 10^{22} electrons per cm^3 are released from the localized 4f state into the conducting 5d state. This valence change and 4f electron delocalization occur in SmS near 7000 bar. It is a spectacular phase transition reminiscent of alchemy, for the initially dull black substance suddenly glitters like gold when the transition pressure is exceeded. The material returns to its original state when the pressure is released, exhibiting a large hysteresis characteristic of a first-order transition.

The electrical conductivity of SmS abruptly increases at the transition pressure, as would be expected for a semiconductor-to-metallic transition. The resistance *vs* pressure behavior of samarium monochalcogenides is shown in Figure 3. In the case of SmSe and SmTe the semiconductor-to-metallic transition due to the valence change occurs continuously, as reflected in the ten orders of magnitude decrease in the resistivity over the 1–60 kbar region.

X-ray studies show that the NaCl-type structure is retained while the lattice contracts, resulting in a substantial change in volume. When the 4f electron is promoted to the 5d state, the outer-electronic structure of the samarium ion experiences an additional attractive force from the now unscreened nuclear change. This considerably reduces the ionic radius, and has been called an "electronic collapse", in which the crystal structure does not change but the lattice parameter simply decreases. Consequently, the compressibilities of these compounds are anomalous (see Fig. 4). The pressure-volume relationships clearly confirm the continuous nature of the valence transition in SmSe and SmTe, and a first-order phase transition in SmS.

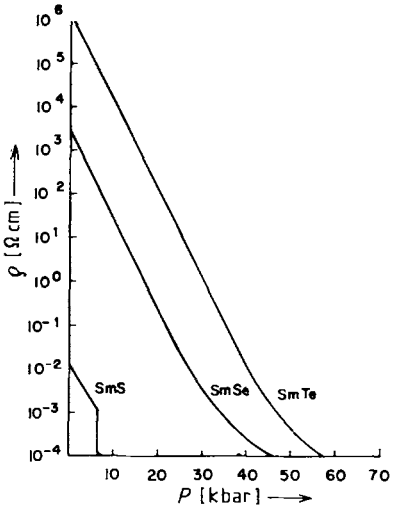


Fig. 3. Resistance *vs.* pressure data for samarium monochalcogenides. SmS undergoes a first-order transition due to valence change.

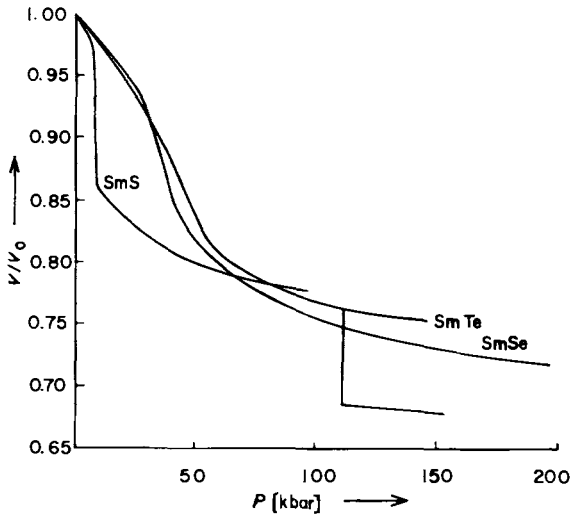


Fig. 4. Pressure-volume relationship for samarium monochalcogenides. The abrupt change in SmS is due to valence change (isostructural transition) and the abrupt change in volume for SmTe near 110 kbar is due to NaCl-CsCl transition.

It is also remarkable that the color of SmSe and SmTe turns bright copperish and metallic purple respectively. In fact, the sequence of color changes resulting from the increase in the electron concentration can be vividly seen with the latter two substances in a diamond anvil cell, which permits optical observation on the samples while they are subjected to high pressure. That the color should change with electron concentration is connected with what is known as the "plasma edge" associated with systems containing free electrons. The bright reflectivity of metals has its origin in this effect and since valence change induces the metallic state, the observed changes are to be expected. The charac-

teristic colors of the metallic chalcogenides are, however, connected with what is known as the interband contribution to the dielectric constant. Thus the change in color under pressure constitutes visible evidence of the valence transition in these divalent rare earth monochalcogenides.

It has been shown that the phase transition in SmS can also be induced by substituting a trivalent lanthanoid ion such as Gd^{III} for Sm^{II}[1,9]. The lattice parameter behavior for the substituted system $Sm_{1-x}Gd_xS$ is shown in Fig. 5. The lattice parameter varies smoothly up to $x=0.15$ and then abruptly decreases at higher gadolinium concentrations. The substance appears black up to the critical concentration, and then turns gold-like. Apparently an internal lattice pressure on Sm^{2+} arises on substitution, because the Gd^{3+} ion is much smaller than Sm^{2+}; this forces the Sm^{2+} to change its valence state.

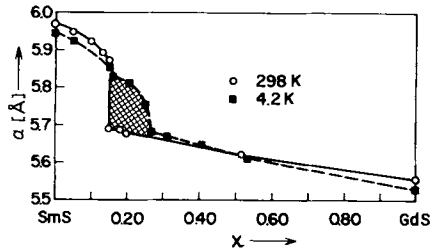


Fig. 5. Lattice parameter of $Sm_{1-x}Gd_xS$ as a function of x. The shaded region represents the composition range where the metallic phase would transform to a black phase on lowering the temperature, due to relocalization of the 4f-electron.

Thus chemical substitution can stabilize the high pressure phase at atmospheric pressure, which greatly facilitates its study. Such substitutions have been attempted for the whole lanthanoid ("Ln") series[9,10] and very interesting results have been reported for the $Sm_{1-x}Ln_x^{3+}S$ systems.

4. Intermediate Valence

As noted in Section 1, the most interesting aspect of the valence change is that an intermediate valence state is established. The lattice parameter of the collapsed SmS is found to be 5.68 Å. If the samarium had collapsed fully to the trivalent state, its lattice parameter would have decreased to 5.62 Å; this can be calculated from the known ionic radii of Sm^{3+} and S^{2-}. Thus one is led to conclude from the intermediate lattice parameter that the samarium ions have not changed their valence all the way to the Sm^{3+} state. However, the intermediate lattice parameter in itself is not sufficient proof for the intermediate valence state, for the following reason. It is possible to have in the collapsed metallic phase of SmS a mixture of Sm^{3+} and Sm^{2+} ions distributed randomly in the lattice and still observe an intermediate lattice parameter. According to *Vegard*'s law, in systems which are completely miscible with each other the lattice parameters can adopt any value intermediate between those of the pure compounds. However, confirmation that our system is not a statistically frozen mixture of Sm^{2+} and Sm^{3+} ions comes from the magnetic susceptibility behavior of the high pressure metallic phase[11] (Fig. 6). The Sm^{3+} ion should carry a local magnetic moment (angular momentum quantum number $I=5/2$) which means that one can expect strong diver-

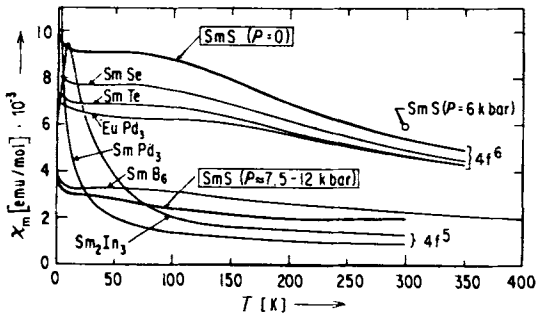


Fig. 6. Magnetic susceptibility of the high-pressure metallic phase of SmS. Other substances containing Sm^{3+} are shown for comparison. SmB_6 also exhibits behavior similar to the metallic phase of SmS. The insulating SmS phase ($P=0$) exhibits van Vleck paramagnetism.

gence in magnetic susceptibility and even magnetic ordering at low temperatures. The data in Figure 6 show neither of these to apply; in fact the susceptibility at lower temperatures is found to remain constant with temperature. This behavior is not consistent with the presence of Sm^{3+} ions, but corresponds to an intermediate valence state in which an electron fluctuates very rapidly between two electronic configurations, namely $4f^5 5d^1$ and $4f^6 5d^0$; the former is magnetic and the latter is not. Because of this rapid fluctuation the electron does not stay in the magnetically active state for sufficient length of time to contribute to the magnetic susceptibility.

In a quantum mechanical sense[12] the fluctuating valence means that the wave function of the electron is a mixture of functions having f- and d-character; the f- and d-states are hybridized:

$$\Psi = a\Psi_f + b\Psi_d$$

where a and b give the proportion of f- and d-character. The electronic band structure of such a state of affairs is represented schematically in Figure 7.

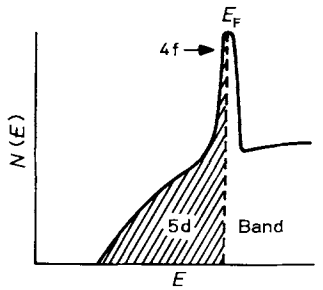


Fig. 7. In the intermediate valence phase of SmS, the Fermi level E_F is pinned at the 4f-level; the electron has both f and d character.

The Fermi level E_f is pinned to the 4f-states, and the wave function near the peak of $N(E)$ is a linear combination of f- and d-type wave functions. This picture of homogeneously mixed valence state derives support from many experimental studies on the high pressure metallic phase by X-ray photoelectron spectroscopy[13], and Mössbauer spectroscopy[14], and from measurements of transport properties[15], magnetic properties[16], bulk modulus[17], and low temperature specific heat[18]. The Debye-Waller factors for the X-ray reflections of the intermediate valence phase of SmS[19] and neutron scattering[20] studies seem to indicate that the time scale of

the fluctuation is around 10^{-12} s. The whole lattice "breathes" in unison, with the average size of the samarium ion at the lattice point corresponding to a valence of 2.7+. The picture of hybridization mentioned above may appear to be inconsistent with fluctuations between two electronic configurations, but it must be remembered these are merely two different ways of looking at the intermediate valence state.

Valence changes have also been found in the ytterbium monochalcogenides and in EuO[2]. In the Eu and Yb monochalcogenides the 4f—5d separation is far larger than for SmS and hence higher pressures are needed. These compounds are thus much more stable in the divalent state; this is to be expected because the Hund's rule stability conditions are met for Eu^{II} and Yb^{II}. The pressure-volume relationships, which provide the strongest evidence for valence change in these systems, are shown for Yb and Eu monochalcogenides in Figures 8 and 9.

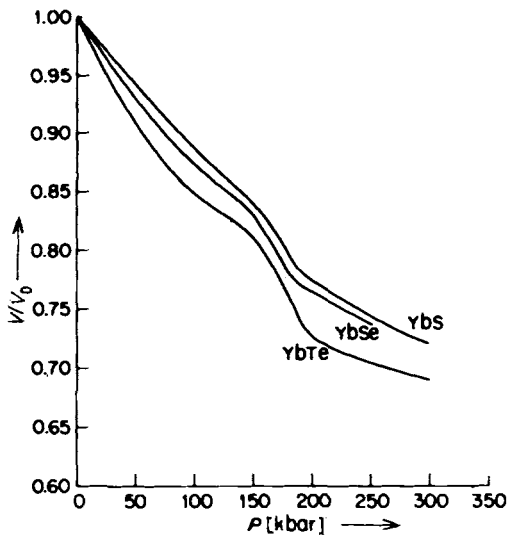


Fig. 8. Pressure-volume behavior of ytterbium monochalcogenides. The anomalies are due to valence changes.

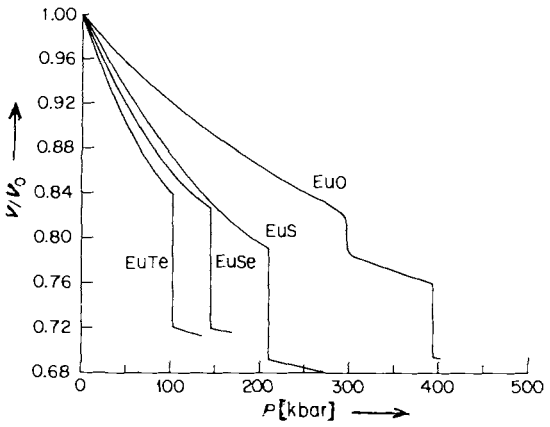


Fig. 9. Pressure-volume relationship for europium monochalcogenides. The abrupt changes in EuTe, EuSe, and EuS are due to NaCl-CsCl transition. EuO exhibits both a valence change (near 300 kbar) and NaCl-CsCl transition (near 400 kbar).

All the Yb monochalcogenides undergo a valence change which is believed to occur continuously with pressure. The color of the substance shows spectacular changes to metallic gold, copperish, and deep purple in YbS, YbSe, and YbTe respectively, which is again strong evidence for the valence change. In the case of Eu monochalcogenides, there is a competing phase transition from NaCl-type to CsCl structure. The discontinuities in Figure 9 for the Eu chalcogenides are due to the latter transition, except in the case of EuO. Only in the case of EuO does the valence change precede the NaCl-CsCl transition; this follows from the appearance of two volume discontinuities, the first of which is an isostructural transition. The homologous compounds should also exhibit the valence change at very high pressure.

5. Other Systems

Another samarium-containing system which also exhibits a valence change at high pressure will now be discussed. This compound is not as simple as the chalcogenides and has the formula Sm_4Bi_3[21]. It crystallizes in the so-called *anti*-Th_3P_4 structure, since the less electronegative samarium occupies the P sites and the more electronegative bismuth the Th sites. However, it still has a cubic structure and is easy to study by X-ray diffraction under high pressure. Charge compensation according to $3\,Sm^{2+} + 1\,Sm^{3+} + 3\,Bi^{3-}$ provides a reasonably accurate description of the compound, as confirmed by the plot of the lattice parameter[5] shown in Figure 10. The lattice constants of Sm_4Bi_3, Eu_4Bi_3, and Yb_4Bi_3 are anomalously large compared to those of the trivalent lanthanoids. In the latter the extra electron becomes a conduction electron. Thus the compounds in which the lanthanoid tends towards the divalent state are found to be semimetals with overlapping

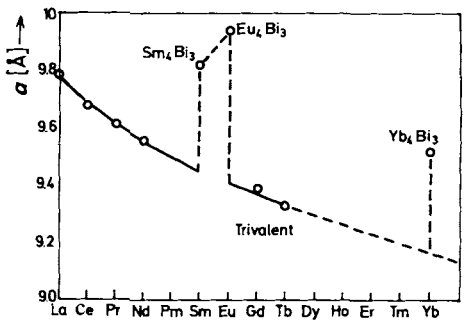


Fig. 10. Lattice parameters for the Ln_4Bi_3-type compounds. The anomalies at Ln = Sm, Eu, and Yb reflect the partial divalent nature of the lanthanoid ions.

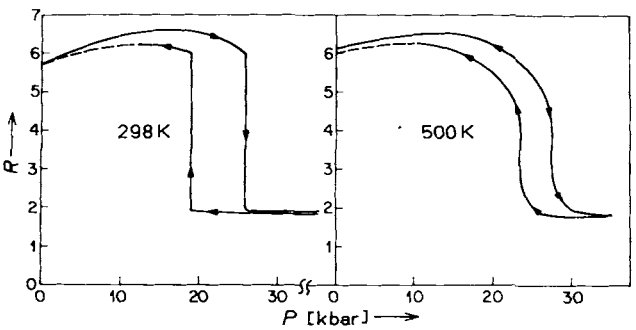


Fig. 11. Resistance (arbitrary units) *vs.* pressure data for Sm_4Bi_3. The abrupt decrease is due to the valence transition near 27 kbar. At 500 K the resistance anomaly becomes rounded. This is due to critical termination of the phase boundary at about 800 K.

valence and conduction bands. When high pressure is applied, the divalent ions may be expected to change to the higher valence state. The first of this group of compounds to be studied is Sm_4Bi_3 which shows the valence transition at about 27 kbar. Figure 11 shows the resulting sharp decrease in electrical resistivity. In Figure 12 the lattice parameter is shown as a function of pressure. An isostructural transition takes place at precisely 27 kbar with an abrupt decrease in the lattice parameter, showing the valence transition in Sm_4Bi_3 to be of first order.

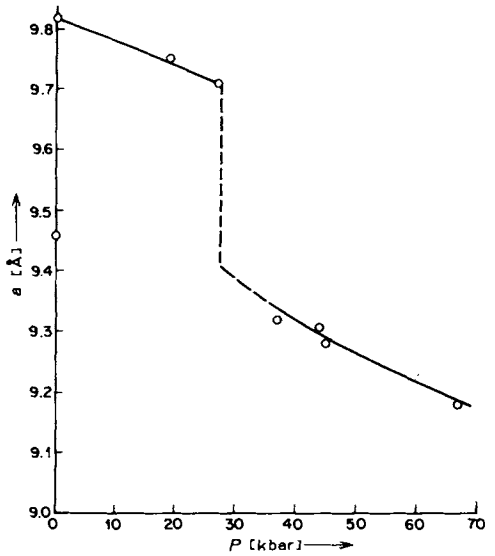


Fig. 12. Lattice parameter change under pressure for Sm_4Bi_3. The first-order valence transition is marked by an abrupt volume decrease without change of structure (isostructural transition).

The phase diagram for Sm_4Bi_3 is shown in Figure 13. Interest again centers on the critical termination of the phase boundary connected with the isostructural transition. The phase boundary in the low temperature region is connected with another subtle transition in Sm_4Bi_3, the origin of which is not clear at present.

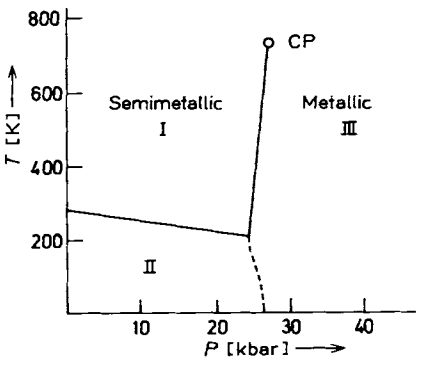


Fig. 13. Pressure/temperature diagram of Sm_4Bi_3. The I-II phase change is seen as a striking resistance decrease. The dotted line has been arbitrarily drawn as representing the II-III phase change.

Pressure studies on cerium-based systems are of much current interest, for pressure can change the valence state of cerium from Ce^{III} to Ce^{IV}, through an intermediate state[4]. There seem to be three distinct types of behavior in these systems: (i) In the trivalent state cerium carries a local magnetic moment and hence exhibits magnetic order at low temperatures; (ii) in the strongly mixed valence state the magnetism is quenched by fluctuations; and (iii) in the quadrivalent state the 4f-level is far removed from the d-band, so that it is unoccupied and the system becomes a d-band metal which may exhibit superconductivity at low temperatures[22]. Thus merely by varying the pressure we can change the system all the way from magnetism to superconductivity through an intermediate state of mixed valence. This has already been demonstrated for cerium metal.

6. Concluding Remarks

The subject of valence instabilities is at present an active field of research both from the theoretical and from the experimental point of view. Many different models and ways of looking at the so-called homogeneously mixed valence phases have been proposed, but there is still no unified picture valid for all of them. For instance, SmB_6 appears to have a hybridization gap, whereas it is not clear if SmS has a similar gap. TmSe is another system which seems to stand on a different footing. More experiments are necessary if we are to understand the homogeneously mixed valence state at the microscopic level. Homogeneously mixed valence states may have analogies in narrow d-band situations and further developments in this area are expected.

Among the potential applications of the novel state, the most obvious lies in the exploitation of the metal-semiconductor transition. Another promising application utilizes the sharp change in optical reflectivity accompanying the transition. However, such applications must await the solution of problems associated mainly with hysteresis.

From the chemical point of view, it has been suggested that the homogeneously mixed valent materials might be excellent catalysts. This most interesting aspect may turn out to be one of the most fruitful applications of fluctuating valence materials. Valency and valence changes are chemical concepts which still hold surprises in store.

I wish to thank Professor Manuel Cardona for critically reading the manuscript and the Alexander von Humboldt Foundation for the U.S. Senior Scientist award, during the term of which this paper was written at the Max-Planck-Institut für Festkörperforschung, Stuttgart.

Received: April 18, 1980 [A 329 IE]
German version: Angew. Chem. 92, 626 (1980)

[1] *A. Jayaraman, P. D. Dernier, L. Longinotti*, High Temp. High Pressures 7, 1 (1975).
[2] *A. Chatterjee, A. K. Singh, A. Jayaraman*, Phys. Rev. *B6*, 2285 (1972).
[3] *A. Jayaraman, A. K. Singh, A. Chatterjee, S. Ushadevi*, Phys. Rev. *B9*, 2513 (1974).
[4] *R. D. Parks:* Valence Instabilities and Related Narrow-Band Phenomena. Plenum Press, New York 1977.
[5] *P. W. Bridgman*, Proc. Am. Acad. Sci. *62*, 207 (1927).
[6] *A. W. Lawson, T. Y. Tang*, Phys. Rev. *76*, 301 (1949).
[7] *A. F. Schuch, J. H. Sturdivant*, J. Chem. Phys. *18*, 145 (1950).
[8] *A. Jayaraman*, Phys. Rev. *137*, A 179 (1965).
[9] *L. J. Tao, F. Holtzberg*, Phys. Rev. *B 11*, 3842 (1975).
[10] *M. Gronou, S. Methfessel*, J. Magn. Magn. Mater. 17 (1980).
[11] *M. B. Maple, D. K. Wohlleben*, Phys. Rev. Lett. *27*, 511 (1971).
[12] *C. M. Varma*, Rev. Mod. Phys. *48*, 219 (1976).

[13] *M. Campagna, G. K. Wertheim, E. Bucher*, Struct. Bonding (Berlin) *30*, 99 (1976).
[14] *J. M. D. Coey, S. K. Ghatak, M. Avignon, F. Holtzberg*, Phys. Rev. *B 14*, 3744 (1976).
[15] *T. Penney, F. Holtzberg*, Phys. Rev. Lett. *34*, 322 (1975).
[16] *B. C. Sales, D. K. Wohlleben*, Phys. Rev. Lett. *35*, 1240 (1975).
[17] *T. Penney, R. L. Melcher, F. Holtzberg, G. Güntherodt*, AIP Conf. Proc. *29*, 392 (1975).
[18] *S. von Molnar, T. Penney, F. Holtzberg*, J. Phys. (Orsay, Fr.) *37*, C4-241 (1976).
[19] *P. D. Dernier, W. Weber, L. D. Longinotti*, Phys. Rev. *B 14*, 3635 (1976).
[20] *H. A. Mook, R. M. Nicklow, T. Penney, F. Holtzberg, M. W. Shafer*, Phys. Rev. *B 18*, 2925 (1978).
[21] *A. Jayaraman, R. G. Maines, E. Bucher*, Solid State Commun. *27*, 709 (1978).
[22] *M. Croft, A. Jayaraman*, Solid State Commun. *29*, 9 (1979).

Liquid Metals and Liquid Semiconductors[**]

By Friedrich Hensel[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

Numerous liquid systems have electrical properties which resemble those of crystalline and amorphous semiconductors. The existence of "semiconducting" behavior in these liquids is mostly related to a continuous transition from a metallic to a "semiconducting" state when a thermodynamic variable such as temperature, density or concentration is changed. Changes in the nature of the chemical interaction and the associated changes in the structure of the liquid are of fundamental importance for the transition to a "semiconducting" state. This will be demonstrated for the ionic liquid CsAu, for covalent liquid selenium, and for expanded liquid metals.

1. Introduction

The discovery of noncrystalline semiconducting materials and the application of such "amorphous semiconductors" for technical purposes have stimulated an increasing interest in the electrical and physicochemical properties of electronically conducting liquids during the past 15 years. According to a proposal by *Joffe* and *Regel*[1] two classes of such liquids can be distinguished: "liquid metals" and "liquid semiconductors". At present the line of distinction between the two classes is arbitrary since generally accepted theoretical or experimental criteria are still lacking. It has become established practice to call those liquids which have electrical conductivities σ larger than 2000 $ohm^{-1}\,cm^{-1}$ metallic, since the mean free paths of the electrons calculated from σ within the framework of the free electron model[2,3] are mostly larger than the mean interatomic distance. Liquids with conductivities σ smaller than 300 $ohm^{-1}\,cm^{-1}$ are called "semiconducting"[4] because they exhibit some properties which are typical for solid crystalline and amorphous semiconductors, *e.g.* a positive temperature dependence of σ characterized by the presence of an activation energy.

The difficulty in precisely defining the boundaries between the two types of conduction is essentially related to the existence of a continuous transition from semiconducting to metallic behavior which is observed in most semiconducting liquids on changing a thermodynamic variable such as temperature, density, or composition. Conversely, it is always possible, at least in principle, to transform any metallic liquid into a semiconducting or insulating state by expansion to very low densities or by alloying with a nonmetal. Hence, a comprehensive theoretical description of semiconducting liquid systems must include not only the properties of the semiconducting range, but must also account for the properties during the course of the metal-nonmetal transformation, *i.e.* it must include a description of the electrical properties of those liquids which lie at the borderline between typical metals and typical semiconductors. Accordingly, the most appropriate experiments for the investigation of electronically conducting liquids are those which not only extend to the semiconducting and the metallic state but also embrace the transition range between the two. In Table 1 a list of groups

Table 1. List of selected liquid systems in which a metal-nonmetal transition can be induced.

Group	System	Inducing physical effect
1	Semiconducting alloys (Mg_3Bi_2, Li_3Bi, CsAu, *etc.*)	change of concentration
2	Metal-salt mixtures (Cs—CsCl, Bi—$BiCl_3$, *etc.*)	change of concentration
3	Alloys of metals with S, Se, Te (Tl_2Te, In_2Se_3, Ga_2Te_3, *etc.*)	change of concentration
4	Se, Te and their mixtures (Se_xTe_{1-x})	change of chemical structure by an increase of temperature and pressure
5	Metals (Hg, Cs, Rb, K, *etc.*)	expansion to low densities at high temperature

[*] Prof. Dr. F. Hensel
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] Lecture presented at the GDCh-meeting in Berlin, September 12, 1979.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0808-0593 $ 02.50/0*

of liquids is assembled for which semiconducting properties and a metal-nonmetal transition have been observed.

Changes in the chemical interaction and the associated structural changes of the liquid are of fundamental importance for the transition from metallic to semiconducting behavior. The best evidence for this is provided by the semiconducting liquid alloys (Table 1, Group 1). Although *e.g.* molten Li, Cs, Mg, Au, Bi, Pb and Sb are very good metallic conductors, their liquid mixtures have a relatively low conductivity at the stoichiometric compositions Li_3Bi, Li_4Pb, Mg_3Bi_2, Cs_3Sb and CsAu. At the same time the temperature dependence of the conductivity is positive. In this article, interest is focussed on the role of charge transfer in these systems, *i.e.* whether the chemical interaction is essentially ionic, as in salts. If this is the case the metal-nonmetal transition in this group would be similar to the transition observed in metal-molten salt mixtures (Table 1, Group 2), whose properties have been extensively studied by *Bredig*[5,6] and about which there are recent detailed reviews by *Nachtrieb*[7] and *Warren*[8]. We shall therefore exclude from further consideration these metal-molten salt systems as also the alloys of metals with the nonmetallic elements S, Se and Te which are listed as Group 3 in Table 1. The properties of the latter systems have also been reviewed recently[8-10]. In many respects they behave similarly to the alloys with two metallic constituents (Table 1, Group 1); here also, the conductivity has a minimum at the stoichiometric composition.

The chemical interactions in the systems mentioned above vary widely from essentially ionic to predominantly covalent depending on the differences in electronegativity of the constituent atoms, whereas in the pure liquid elemental semiconductors S, Se and Te the chemical interaction is purely covalent with a small contribution of van-der-Waals-interaction. The electronic and structural properties of selenium are especially interesting when considered over a larger temperature and pressure range. Near the melting point the properties of liquid selenium are consistent with the assumption that it consists of long polymeric chains containing up to 10^5 atoms[11,12]. However, the average chain length, the local liquid structure and the coordination number can change with increasing temperature and pressure. This continuous change in molecular structure is accompanied by a significant modification of the electronic structure: At high temperatures and pressures a continuous transformation into a liquid with conductivities approaching those in the metallic range is observed[13].

In addition to the transitions between metallic and predominantly ionic or purely covalent interaction, which will be discussed in the present article in detail for liquid CsAu and selenium, metal-nonmetal transitions in expanded fluid metals like Hg, Cs or Rb are of great theoretical and technical interest (Table 1, Group 5). Such a transition occurs in any metal at very high temperatures due to thermal expansion of the liquid to low densities[14]. As in the other systems this transition from metal to nonmetal implies that the nature of the chemical or interatomic interaction changes. A knowledge of the physicochemical mechanism of the transition is of fundamental importance, since the thermodynamic properties, as *e.g.* the free energy, the equation of state, or the specific heat of the system are determined by the interatomic interaction. This is especially important in view of the possible technical applications of liquid metals at high temperatures. In this case thermodynamic data are needed; a theoretical prediction and treatment of such data is desirable.

2. Liquid Ionic Alloys

In some liquid binary alloys of metallic constituents the conductivity passes through a minimum at well defined stoichiometric compositions. The most extensively studied system is the Cs-Au system, whose electrical conductivity σ in the concentration range between 0 and 60 atom-% Au at 600 °C is plotted in Figure 1. σ changes by almost four orders

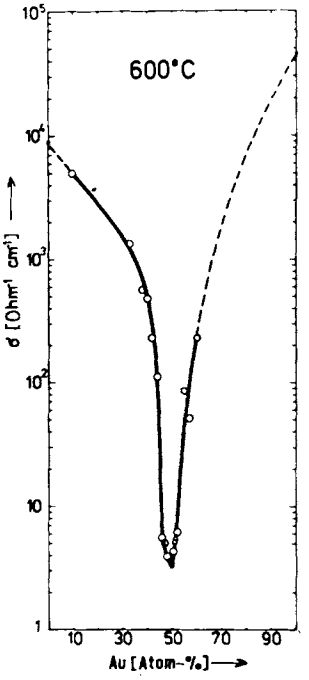


Fig. 1. Electrical conductivity σ of liquid Cs-Au mixtures as a function of the gold content at 600 °C.

of magnitude and has a pronounced minimum of 3 ohm^{-1} cm^{-1} at the stoichiometric composition CsAu. This value is of the same order of magnitude as the conductivities of molten salts; *e.g.* σ of CsCl at the melting point is about 1 ohm^{-1} cm^{-1}.

The transition to nonmetallic behavior is accompanied by a change in the temperature dependence of σ[15,16]. In Figure 2 the logarithm of the conductivity is plotted versus the reciprocal temperature. At a concentration of 44 atom-% Au, corresponding to a conductivity of about 100 ohm^{-1} cm^{-1}, the temperature dependence changes from negative to positive. The corresponding apparent activation energy E_A of the conductivity calculated according to the relationship

$$\sigma = \sigma_0 \exp(-E_A/RT) \qquad (1)$$

approaches a maximum of about 20 KJ/mol at the stoichiometric composition. It is not possible, however, to decide whether E_A is the activation energy of the diffusive motion of the ions Cs^+ and Au^- or that of thermally activated electrons, since eq. (1) is valid for both conduction mechanisms. Measurements of the optical absorption are required. Analogously to crystalline semiconductors there also exists for non-

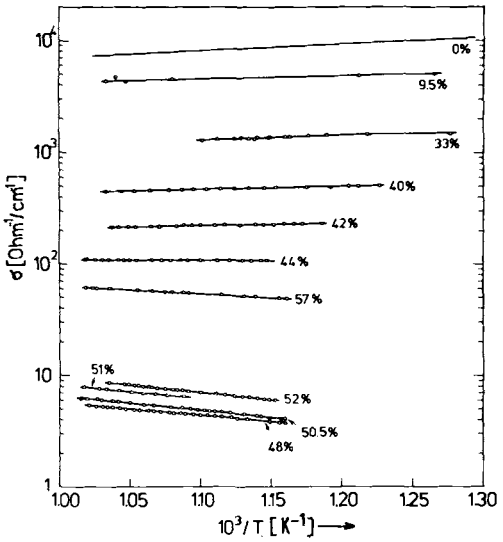


Fig. 2. Electrical conductivity σ of liquid Cs-Au mixtures as a function of the reciprocal temperature at different Au-concentrations in atom-%.

crystalline semiconducting systems a correlation between E_A for thermally activated electrons and the distance between valence- and conduction-band as derived from the optical absorption edge. However, in disordered systems—including liquids—the absorption edges are far from sharp, because there are always a few allowed states for an electron in energy ranges which are forbidden in the corresponding crystalline arrangement[4]. A schematic representation of this situation is given in Figure 3. The singularities in the electronic

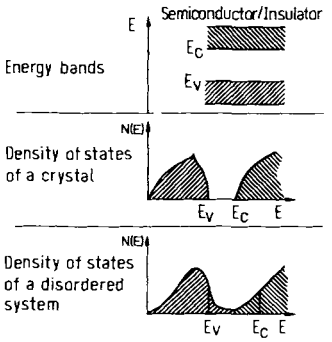


Fig. 3. A schematic representation of the energy bands and the density of states $N(E)$ as a function of the energy E of a crystalline semiconductor or insulator and a corresponding disordered semiconducting system. E_c = bottom of the conduction band, E_v = top of the valence band.

density of states $N(E)$ at the band edges are smeared out. The energy gap in the crystal [$N(E)=0$] is replaced by a minimum in $N(E)$. Figure 4 shows new results for the optical absorption edges of CsAu in the solid as well as in the liquid state[17]. The spectral dependence of the absorption coefficient $K(\omega)$ for solid CsAu (from 25 °C to 560 °C; CsAu melts at 590 °C[18]) and for liquid CsAu (626 °C) is shown as a function of the photon energy. The absorption edges of the solid phase exhibit the expected red shift which is usually observed for crystalline semiconductors or ionic insulators with increasing temperature[19]. On melting, there is an abrupt change in the position of the absorption edge of about 0.7 to 0.8 eV. The lower part of Figure 4 shows the temperature de-

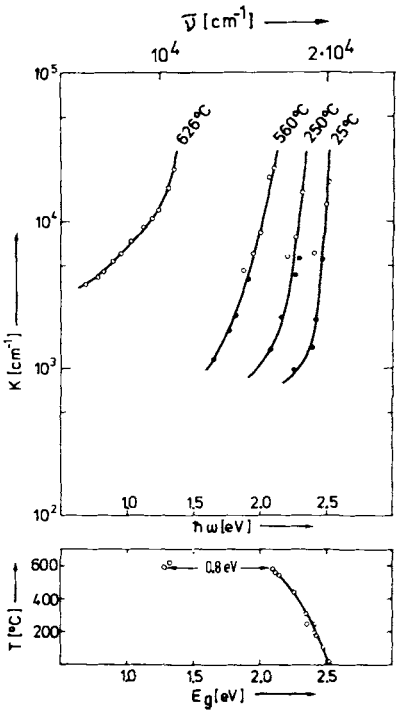


Fig. 4. Top: Optical absorption of a 100 μm-thick sample of solid or liquid CsAu as a function of the photon energy. Bottom: the temperature dependence of the position of the absorption edge. The arrow indicates the abrupt change of the position of the edge at the melting point (590 °C).

pendence of the position of the optical gap which corresponds roughly to the gap between valence- and conduction-band. It is a plot of the photon energy corresponding to $K=10^4$ cm^{-1} as a function of the temperature. There is a striking quantitative similarity between the behavior of CsAu and that of molten salts, as is demonstrated in Figure 5, where measurements of the absorption edges as a function

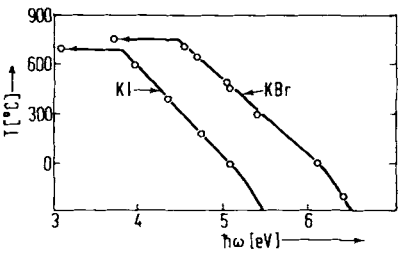


Fig. 5. Position of the absorption edge of 1 mm-thick samples of salt in the solid and liquid state. The abrupt change of the position takes place at the melting point.

of temperature are reproduced for solid and molten KI and KBr[20]. The experimental points correspond to the highest energy of light transmitted through a 0.1 cm-thick layer of the molten salt sample. The similarity between the data for CsAu and those for the molten salts is consistent with the assumption of predominantly ionic bonds in solid and liquid CsAu.

Comparison of the measured optical energy gap between valence- and conduction-band in liquid CsAu of 1.3 eV with the activation energy E_A measured for the electrical conductivity σ leads directly to the conclusion that σ is determined by ionic conduction. For a crystalline or noncrystalline intrinsic semiconductor the optical energy gap should be about

twice the activation energy for thermally activated electrons; *i.e.* one would expect an E_A-value of about 63 KJ/mol. In contrast to this the measured value of $E_A = 20$ KJ/mol is of the same order of magnitude as that observed for ion migration in salts[21]. Direct experimental evidence that liquid CsAu is entirely ionic like fully ionized salts stems from an electromigration experiment[22,23]. When electrolyzed, liquid CsAu conforms to Faraday's law. Within experimental error, one Cs^+ and one Au^- are transported to the relevant electrodes per elementary charge. Measurements of the absolute thermoelectric power also show that the contribution of electrons to the electrical transport in the liquid Cs-Au system near the stoichiometric composition is negligibly small.

Our knowledge about the electrical properties of the solid stoichiometric compound CsAu is quite poor compared to what we know about molten CsAu. The phase diagram[18] shows the existence of a congruent melting phase with a narrow range of homogeneity. It melts at 590 °C and is known to crystallize with the CsCl structure with a lattice constant of 4.263 Å[24]. The corresponding calculated molar volume of 46.63 cm^3 is 42% smaller than the volume obtained by simply adding the atomic volumes of Cs and Au. The optical energy gap at 25 °C (Fig. 4) is 2.6 eV[17,25]. On the basis of electrical conductivity σ and thermoelectric power[26,27] measurements it can be deduced that solid CsAu is always an extrinsic n-type semiconductor. Since the measured conductivity σ is always relatively large (ranging from 5 to 100 $ohm^{-1}\ cm^{-1}$) and not well reproducible, and since its temperature dependence is slightly negative (like in metals), it is suggested that a broad impurity band is formed by excess cesium which may eventually overlap with the conduction band. NMR measurements[24] show that the excess Cs is atomically dispersed in the CsAu.

Several band structure calculations have been performed for CsAu[27-29]; the results compare well with photoemission valence-band data[27,30], and they confirm the essential ionic character of the bonds in CsAu. Further support for this ionicity stems from recent Mößbauer[31] and ESCA spectroscopic measurements[32]. However, with an energy gap of 2.6 eV (at 25 °C) between conduction- and valence-band, CsAu belongs to those compounds which lie on the borderline between electronic semiconductors and ionic insulators. Consequently, CsAu shows features of both (*i.e.* electronic and ionic conductivity), as is clearly demonstrated by the behavior of the electrical conductivity at the melting point (Fig. 6). The marked change in σ on melting indicates that the electrical transport mechanism in liquid CsAu is different from that in solid CsAu. Other semiconducting substances show, in contrast to the decrease in conductivity of CsAu, a more or less large increase in σ on melting. For these semiconductors two groups must be distinguished. In the first group (Ge, Si, InSb *etc.*) the coordination number and the nature of the chemical interaction change drastically on melting. The melt becomes a metallic conductor, *i.e.* a semiconductor-metal transition accompanies the solid-liquid phase transition[33]. In the second group (Se, In_2Se_3, Ga_2Te_3 *etc.*) the coordination number changes only slightly in the melt and the short-range order of the solid persists to a large extent, *i.e.* at the melting point a transition from a solid to a liquid semiconductor occurs. In these systems the short-range order is changed only at very high temperatures and a continuous transition to metallic behavior occurs (see Section 3).

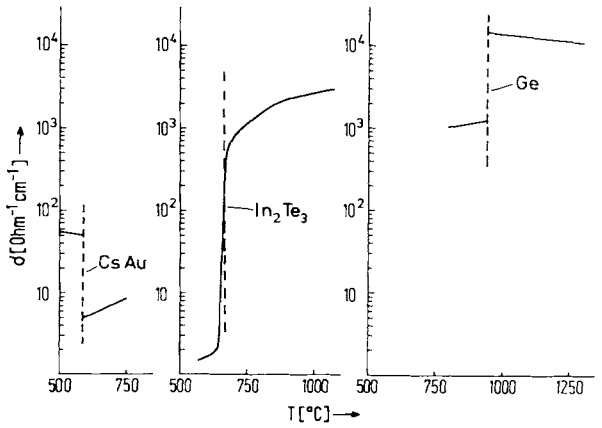


Fig. 6. Comparison of the behavior of the electrical conductivity of semiconductors at the melting point: CsAu, In_2Te_3 and Ge.

It is evident from the results presented above that CsAu does not belong to one of these two groups. It is possible for semiconductors with essentially ionic bonds and energy gaps of between 2.5 eV and 3 eV at room temperature that the solid-liquid phase transition coincides with a transition from a solid electronic semiconductor to a liquid ionic conductor. CsAu is the first example for which such a transition has been observed.

The concentration dependence of the conductivity σ in the liquid Cs-Au system (Fig. 1 and 2) establishes the occurrence of a transition from metallic to nonmetallic behavior. At σ-minimum for the stoichiometric composition CsAu the electrical transport is determined by the diffusive motion of Cs^+ and Au^-. Therefore, it seems reasonable to assume that bound states associated with the formation of Cs^+Au^- ionic assemblies remove electrons from the conduction band of cesium if the concentration is changed between pure Cs and

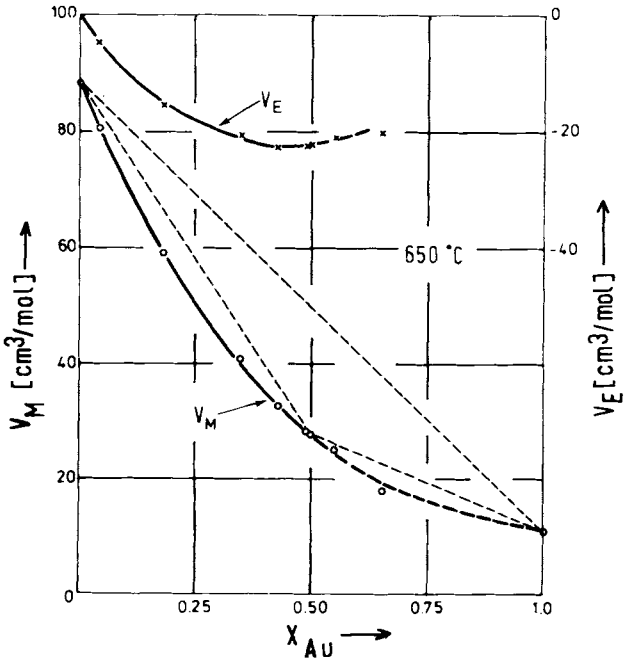


Fig. 7. Molar volume of the mixture V_M and excess volume V_E of liquid Cs-Au mixtures as a function of the mol fraction of gold.

CsAu; *i.e.* the liquid alloys over the whole concentration range—including the metallic range—are assumed to be binary mixtures of Cs^+ and Au^- and the excess metal Cs or Au. Direct evidence for the validity of this assumption comes from very recent measurements of the concentration dependence of the molar volume of the mixtures[34,35] and of the radial distribution function[35,36].

Figure 7 shows the data compiled by *Kempf* and *Schmutzler*[34] for the volume of the mixture $V_M(x)$ as a function of the mole fraction x together with those of the excess volumes V_E.

$$V_E = V_M(x) - (1-x)\,V_M(0) + x\,V_M(1) \tag{2a}$$

V_E has a broad minimum in the vicinity of the stoichiometric composition CsAu. Its unusually large negative value is comparable with the strong contraction observed on formation of CsI or CsBr from their pure constituents. Assuming that the packing fraction in the stoichiometric CsAu melt is about the same as that in molten cesium halides, *Kempf* and *Schmutzler*[34] estimated from the V_M and the well known ionic radius of Cs^+ (1.65 Å) the value $r_{Au^-} = 1.8$ Å for the Au^- ion. The resulting value for the average nearest-neighbor distance of 3.45 Å is in surprisingly good agreement with that of 3.55 Å obtained from the measured total pair distribution function[35]. Figure 8 shows the pair distribution function $g(R)$

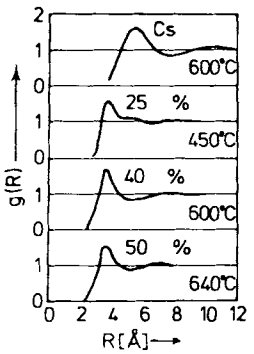


Fig. 8. Pair distribution function $g(R)$ of liquid Cs and liquid Cs-Au mixtures at different concentrations. The numbers labeled at the curves are the concentrations of Au in atom-%.

for different liquid Cs-Au mixtures which were obtained from neutron diffraction data and which are reproduced from a paper by *Martin et al.*[35]. In view of the hypothesis that an Au^- ion is formed even in very dilute solutions of Au in Cs it is especially interesting that for a Au-concentration of only 25 atom-% a first maximum is observed at 3.55 Å. At this concentration the conductivity is still higher than 10^3 ohm^{-1} cm^{-1} and in the metallic range. This is a clear indication that Cs^+ and Au^- are formed even in the diluted solutions. The attractive forces between the unlike charges and the repulsive forces between the like charges lead to short-range ordering like that which occurs in molten salts. Such ordering in dilute solutions is convincingly demonstrated by an analysis of the concentration dependence of the volume of the mixtures[34]. Figure 9 shows the partial molar volumes of Cs and Au, *i.e.*

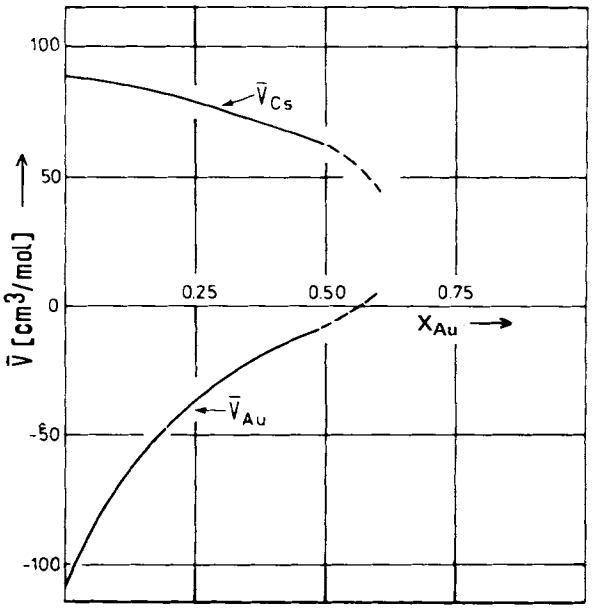


Fig. 9. Partial molar volumes $\bar{V}_{Cs}$ and $\bar{V}_{Au}$ as a function of the mol fraction of gold.

$$\bar{V}_{Cs} = V_M(x) - x\left(\frac{\partial V_M(x)}{\partial x}\right)$$

$$\bar{V}_{Au} = V_M(x) - (1-x)\left(\frac{\partial V_M(x)}{\partial x}\right) \tag{2b}$$

as a function of the mole fraction x of gold. For dilute solutions in the metallic range (*i.e.* $x<0.3$ and $\sigma>10^3$ ohm^{-1} cm^{-1}) $\bar{V}_{Cs}$ is nearly independent of the concentration and close to the value of pure liquid Cs[37], whereas $\bar{V}_{Au}$ tends to large negative values approaching -107 cm^3/mol for $x \to 0$.

The data available at present establish that liquid CsAu at the stoichiometric composition has the properties of a liquid salt. The metal-nonmetal transition in this system can be described as in the case of solutions of metals in their salts (*e.g.* Cs in CsCl[38]), *i.e.* as a solution of Cs or Au in CsAu. The concentration dependence of the electrical conductivity (Fig. 1) and of the magnetic susceptibility (Fig. 10) can be satisfactorily explained within the framework of this model[39]. The gram susceptibility shows a deep diamagnetic minimum at the stoichiometric composition CsAu. The temperature dependence near the minimum is relatively small and negative[39]. Since this is once again consistent with the assumption of predominantly ionic bonding in liquid CsAu, *Freyland* and *Steinleitner*[40], using their experimental results, and taking for the Cs^+ ion the value -36×10^{-6} cm^3 mol^{-1}[41],

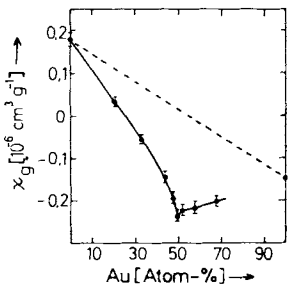


Fig. 10. Magnetic gram susceptibility, χ_g, of liquid Cs-Au mixtures as a function of the gold content.

calculated the molar diamagnetic susceptibility of the Au^- ion as -48×10^{-6} cm^3 mol^{-1}. This value is in surprisingly good agreement with the value of -50×10^{-6} cm^3 mol^{-1} obtained by extrapolation of the values for the isoelectronic sequence Bi^{+3}, Pb^{2+}, Tl^+, Au^-[41].

There is relatively little direct experimental information about the properties of the other alkali metal-gold systems. Solid LiAu and RbAu compounds crystallize, like CsAu, in the CsCl structure, whereas the structures of NaAu and KAu are complex and have not been well explored[18]. Recent experimental results for the conductivity of the liquid MAu-systems (M = alkali metal) at the stoichiometric composition are shown in Figure 11 as a function of temperature[42]. The

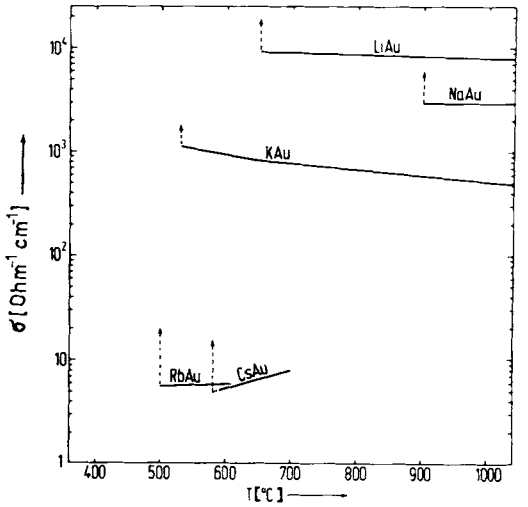


Fig. 11. Electrical conductivity σ of liquid MAu-compounds (M = alkali metal) as a function of temperature. The arrows indicate the melting temperature.

arrows indicate the melting temperature of the different compounds. The conductivities extend from values typical for ionic melts (about 5 ohm^{-1} cm^{-1}) to values for metallic melts (about 10^3 to 10^4 ohm^{-1} cm^{-1}). From the similarity of the conductivity of CsAu and RbAu it can be concluded that liquid RbAu is also an ionic conductor. In contrast to RbAu, liquid LiAu is a metallic conductor. On the other hand, the conductivity of liquid NaAu is only 3000 ohm^{-1} cm^{-1}, which represents a lower limit for metallic conductors. Liquid KAu seems to be a borderline case with properties between metallic and semiconducting behavior.

The results indicate that the transition from an ionic semiconductor to a metal lies between RbAu and NaAu. This observation is consistent with band structure calculations for the solid compounds CsAu, RbAu and LiAu[27]. The calculations show that CsAu and RbAu are semiconductors, while LiAu is a metal. The most interesting aspect of the calculation, however, is that the valence charge is centered essentially around the gold atom in all compounds. Thus LiAu is also mainly ionic despite the fact that it is a metallic and surely electronic conductor. The few data available at present demonstrate the importance of the ratio of the sizes of cations and anions. The transition from an ionic semiconductor to a metal occurs in parallel with a relatively large decrease in the size of the alkali metal atoms.

The behavior of the alkali metal-gold systems (with the exception of CsAu and perhaps RbAu) is similar to that of the well explored liquid semiconductors Li_3Bi[43-45], Mg_3Bi_2[46-49] and Li_4Pb[50-52]. Measurements of the thermodynamic properties[43,48-51] and of the liquid structure[52] indicate that the melt has an essentially ionic structure, whereas the electrical transport properties are dominated by the contribution of electrons[43,45-47]. The different behavior of CsAu, with respect to its electrical data, is essentially due to the larger energy gap between valence band and conduction band which leads to a negligibly small contribution of the electrons to the conductivity compared with the contribution of the ions, which are highly mobile in the liquid state.

3. Liquid Elemental Semiconductors

The influence of chemical interaction on the electronic structure of molten semiconductors becomes especially apparent when their behavior is studied over a wide range of temperature (cf. Fig. 6). The predominantly ionic molten CsAu retains its nonmetallic character over a wide range of temperatures. In contrast, it is characteristic of covalent semiconductors that they can be converted into an essentially metallic state by a sufficiently large increase in the temperature. It is demonstrated in Figure 6 that semiconductors such as Ge or In_2Te_3 become metallic immediately on melting while a large number of substances such as *e.g.* In_2Se_3 or Se are continuously transformed into a metallic state when the temperature is raised. The covalent structure is gradually broken down with increasing temperature, so the bonding electrons become delocalized and form an almost free "electron gas". The following treatment of the interrelation between the change in chemical structure and the semiconductor-metal transition will be mainly concerned with selenium.

The tendency of the selenium atom to bond in two-fold coordination favors formation of long helical chains (trigonal crystalline Se) or of Se_8-rings (monoclinic crystalline Se). It was long assumed that liquid selenium near its melting point also consists of a mixture of Se_8-rings and long chains[53]. However, recent investigations[54] cast doubt on the previously determined concentration of Se_8-rings[55]. In any case, the physical properties of liquid selenium—*e.g.* the unusually high viscosity of 25 poise at the melting point[56,33]—are mainly influenced by the polymeric chains. *Keezer* and *Bailey*[12] determined an average chain length of 10^5—10^6 atoms. Structural investigations by X-ray and neutron diffraction confirm the two-fold coordination in the melt[57,58]. The distance between nearest-neighbor atoms (2.38 Å)[59] is the same as in crystalline trigonal selenium. The structure of liquid selenium is, however, strongly dependent on temperature. The average chain length must decrease very rapidly with increasing temperature. For example, there is a marked decrease in the viscosity, which is only 1 cP at the normal boiling point (684.9 °C)—a value of the same order of magnitude as that of other liquids. The strong influence of temperature on the structure of liquid selenium must be accompanied by modification of its electronic structure and related electrical properties. However, an estimation of the average degree of polymerization in liquid selenium—using experimental data of the viscosity, the magnetic susceptibility and electron spin resonance[60]—shows that even at 1000 °C (the melting temperature is 217 °C) more than 90% of the atoms are still two-

fold coordinated. Since the semiconducting properties of the liquid essentially result from this twofold coordination of neighboring atoms, it is necessary to extend measurements for investigating the influence of changes in the short range order on the electronic properties to very high temperatures. The electrical conductivity[13,61,62], the absolute thermoelectric power[63,64] and the nuclear magnetic resonance[65] of liquid selenium have been measured up to supercritical temperatures and pressures. The critical pressure $p_c = 380$ bar and the critical temperature $T_c = 1590\,^{\circ}C$ have been determined[61]. Figure 12 shows the electrical conductivity σ of selenium at two pressures together with conductivity isobars of liquid tellurium[66] and of a selenium-tellurium mixture containing 50 atom-% of each component[67]. At relatively low temperatures σ markedly increases with increasing temperature, as one would expect for a semiconductor. For temperatures higher than about 1300 °C the selenium isobars flatten off and, close to the critical temperature, reach maxima with strongly pressure dependent conductivity values of almost metallic order of magnitude. In the direct vicinity of the critical point, where relatively small changes in pressure and temperature can lead to large changes in density, σ drops very rapidly with increasing temperature to values smaller than 0.1 $ohm^{-1}\,cm^{-1}$. In this region selenium can be assumed to consist mainly of Se_2 and a small amount of atomic Se. This assumption is supported by measurements of the magnetic susceptibility[68], by extrapolation of the known composition of selenium vapor at low temperatures[70], and by comparison with the optical data of supercritical sulfur vapor[69].

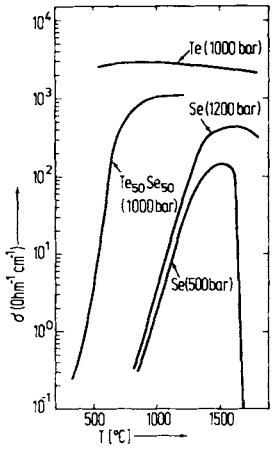


Fig. 12. Electrical conductivity σ of Se, Te and a Se-Te mixture in the molten state as a function of temperature at constant pressures.

It is obvious from Figure 12 that the conductivity isobar for the Se-Te system is very similar to the isobars for pure selenium; but the maximum is located at a lower temperature. In contrast, pure tellurium has a flat maximum with σ-values in the metallic range. There exists a direct correlation between the levels and the positions of the maxima and the bond strengths of the covalently bonded atoms in the chains which decreases in the sequence Se-Se, Se-Te[71], Te-Te. This tendency is also reflected in the structural properties of these systems[72-75]. For tellurium at the melting point an average first coordination number of three is obtained from the area under the first peak of the radial distribution function $g(R)$. This value would appear to increase rapidly with increasing temperature[73,76]. In contrast, the coordination number of selenium remains two, even up to temperatures higher than 1000 °C[74,75]. Although these numbers cannot be definitely identified with the number of bonds between an atom and its neighbor they do, however, indicate that the disorder in liquid Te is greater than in liquid Se.

The strongest indication that the transition from semiconducting to nearly metallic behavior is accompanied by a change in the local coordination number can be obtained from measurements of the thermodynamic properties. Figures 13 and 14 show the behavior of the isobaric thermal expansion coefficient α_p derived from pVT data[77,78,64] and the adiabatic compressibility β_s which was recently determined by *Yao et al.*[79] from sonic measurements. A minimum in α_p with negative values and a maximum in β_s is observed for the Se-Te mixture in the temperature range in which the conductivity σ approaches a maximum with values nearly as high as in the case of metals. Figure 13 demonstrates again the very different behavior of tellurium, which becomes metallic just above the melting point, and selenium, which tends to a metallic state at temperatures above 1300 °C. The α_p-curves have different slopes, and negative values of α_p are only observed for Te in the supercooled melt (the melting temperature is 449.5 °C). The temperature dependence of α_p of selenium fits into this picture. Figure 15[78] shows a plot of the volume of both sulfur and selenium at a fixed reduced pressure $p/p_c = 3$ as a function of the reduced temperature T/T_c. The sulfur isobar shows the behavior of normal molecu-

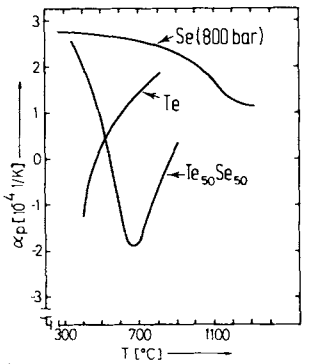


Fig. 13. Isobaric thermal expansion coefficient α_p of liquid Se, Te and $Te_{50}Se_{50}$ as a function of temperature; $\alpha_p = \frac{1}{V}\left(\frac{\partial V}{\partial T}\right)_p$.

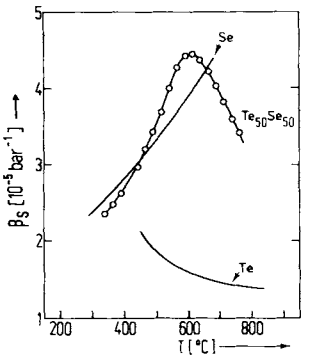


Fig. 14. Adiabatic compressibility β_s of liquid Se, Te and $Te_{50}Se_{50}$ as a function of temperature.

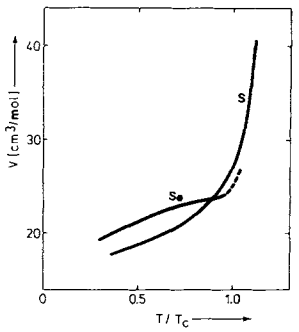


Fig. 15. Volume V of sulfur and selenium at constant supercritical reduced pressure $p/p_c = 3$ as a function of the reduced temperature T/T_c.

lar fluids with a continuous increase in volume as the critical temperature is approached, whereas the curve of selenium flattens out at a reduced temperature of about 0.8 and starts rising again in the vicinity of the critical point T_c. A plausible explanation for the anomalous minimum or maximum in α_p or β_s seems to be that the packing becomes denser with increasing temperature leading to a higher density despite the competing normal thermal expansion. The latter behavior can be compared with the abrupt metal-nonmetal transition of covalent semiconductors with diamond structure (Ge, Si and InSb) on melting, which is accompanied by an increase in the coordination number and a corresponding decrease in volume. For Se and Se-Te mixtures this metal-nonmetal transition is smeared out over a wide range of temperatures. Figure 16 gives a schematic illustration of the behavior of the volume as a function of temperature.

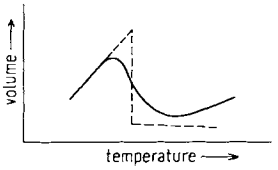


Fig. 16. Schematic illustration of the temperature dependence of the volume of a system for which the metal-nonmetal transition coincides with the liquid-solid phase transition (---, *e.g.* Ge), and for a system with a continuous transition spread over a wide temperature range (—, *e.g.* Se).

A model for the semiconductor-metal transition in liquid selenium has recently been proposed by *Warren* and *Dupree*[65]. It is mainly based on structural data, a critical analysis of the NMR data and on the assumption that the electronic structure of semiconducting polymeric selenium can be derived from the band structure of crystalline trigonal selenium. Of the six valence electrons of the selenium atom ($4s^2 4p^4$) the two 4s electrons are about 4—5 eV lower in energy than the lowest 4p-electrons and are unimportant for the electrical transport properties. Two 4p electrons form bonds to the two neighbors while the other two occupy a non-bonding state. In the condensed state (solid or liquid) the highest occupied valence band is formed by the nonbonding states (n.b.) while the empty antibonding σ^*(p) states form the conduction band (cf. Fig. 17a). The number of polymeric selenium molecules, and hence the number of neutral chain ends with unpaired electrons (C_1^0-centers), increases with increasing temperature. However, it cannot be ruled out that,

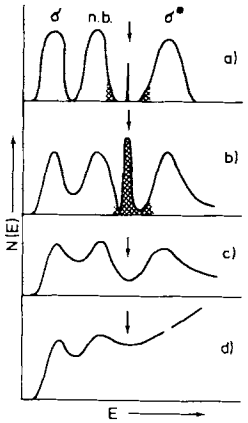


Fig. 17. Electronic structure of liquid selenium under different conditions (see text).

in liquid Se, a chain end C_1^0 reacts with the lone pair electrons of a Se-atom in an appropriate configuration to give a neutral threefold center (C_3^0-center). The existence of such stable defects has been proposed for amorphous selenium by *Mott* and *Street*[80] and by *Kastner, Adler* and *Fritsche*[81]. Calculations[82] show that the C_1^0- and C_3^0-centers lie close together in energy with a slightly lower value for C_1^0. The neutral centers introduce a narrow band of defect states in the middle between valence and conduction band (indicated by the arrows in Fig. 17) which increases with increasing temperature at the expense of the valence and conduction bands[82]. It can be expected that all bands become broader with decreasing lengths of the polymeric chains. From the behavior of the magnetic susceptibility it can be concluded[65] that the width of the band of defect states is smaller than $kT = 0.16$ eV up to 1550 °C and 400 bar. An additional increase in pressure results in a delocalization of the states between valence and conduction band (Fig. 17c). Finally, at still higher pressures the band becomes essentially metallic, similar to that of liquid Te (Fig. 17d). The validity of this model has been confirmed qualitatively by recent measurements of the optical reflectivity of liquid selenium[83] at temperatures up to 1400 °C and pressures up to 1500 bar. The characteristic features of the spectrum change only slightly with increasing temperature as long as the pressure is smaller than 500 bar, whereas application of higher pressures at temperatures above 1300 °C leads to a rapid change in the shape of the spectrum. Under high pressure it becomes very similar to that of liquid tellurium[84].

At high temperatures and slightly increased pressure the electrical, optical and structural properties of liquid selenium resemble those of liquid tellurium at its melting point. In contrast, the electrical properties of sulfur are completely different from those of selenium and tellurium over the whole liquid range. Near its melting point, sulfur is an insulator with a conductivity smaller than 10^{-12} ohm^{-1} cm^{-1}[85]. This is consistent with the large optical energy gap which can be derived from the data shown in Figure 18. It shows the absorption spectra[86] of liquid sulfur in the photon energy range from 0.5—3.5 eV (1 eV ≙ 8065.46 cm^{-1}) at temperatures between 140 °C and 1000 °C and pressures slightly higher than the vapor pressure. A continuous red shift of the edge is observed with increasing temperature. A precise analysis of the data shows that the polymerization of liquid sulfur

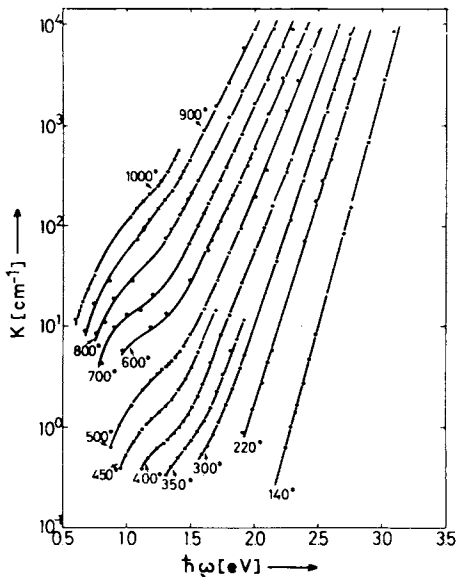


Fig. 18. Absorption spectrum of liquid sulfur as a function of temperature (in °C) at equilibrium pressure (1 eV ≙ 8065.46 cm^{-1}).

at 160 °C[87] does not affect the red shift. This result is qualitatively consistent with the fact that the number of first neighbors and their separation are virtually unchanged by the polymerization. This leads to nearly the same energy levels for both structures. However, new absorption shoulders appear in the infrared region at energies of about 1.3 eV and increase very rapidly with increasing temperatures above the polymerization temperature. From a comparison of the intensities of these absorption bands with measurements of the magnetic susceptibility[88] and of the ESR-signal[89,90] as a function of temperature it has been concluded that the absorption at 1.3 eV derives from the chains which possess unpaired electron spin states at the chain ends[86]. This conclusion is also in agreement with theoretical results obtained on the basis of the CNDO-S model[91]. Except from the appearance of the low energy band, the form of the optical absorption edge of sulfur—especially at K-values higher than 10^4 cm^{-1}—is essentially determined by a series of overlapping absorption bands which can be assigned to different species

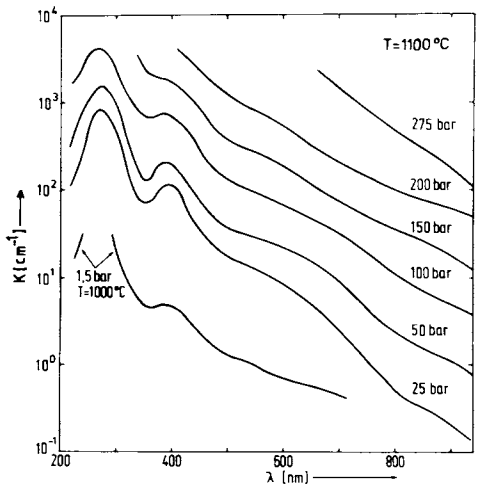


Fig. 19. Absorption spectrum of fluid sulfur at the constant supercritical temperature of 1100 °C as a function of pressure.

of sulfur, such as S_8, S_2, S_3, S_4 and probably S_6 or others[86,92,93]. Several studies on the composition of dilute sulfur vapor using different methods have established the existence of these species, and their concentration has been measured as a function of pressure and temperature[92-96]. An efficient experimental approach for explaining the spectral behavior of liquid sulfur is therefore provided by a comparison with the spectrum of the vapor, especially above the critical temperature where the density can be continuously changed over a wide range by variation of pressure. Figure 19[93] shows the behavior of the absorption coefficient as a function of the wavelength at a supercritical temperature of 1100 °C. (The critical data of sulfur are: $p_c = 205$ bar, $T_c = 1040$ °C and $\rho_c = 0.6$ g/cm^3.) A strong increase in the intensity of the S_3-band at 400 nm and of the S_4-band at 520 nm is observed with increasing pressure or density (Fig. 19). This is a clear indication that at high temperatures, liquid sulfur contains different small highly absorbing molecules besides the diradical chains detected by absorption bands at 1.3 eV[92,86,93]. Due to the logarithmic scale in Figure 19 the bands are partly smeared out to shoulders.

Recent measurements of the electrical conductivity σ of liquid sulfur over a wide range of temperature have shown that the free-radical chain-ends of the polymeric molecules give rise to carriers which determine σ[97]. Figure 20 shows a

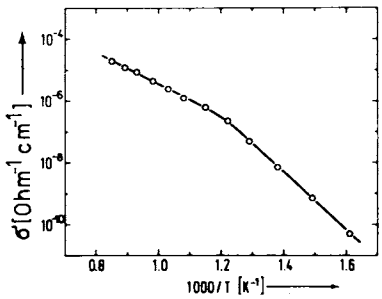


Fig. 20. Electrical conductivity σ of liquid sulfur as a function of the reciprocal temperature.

plot of the logarithm of the conductivity as a function of the reciprocal temperature [cf. eq. (1)]. The dominant feature is the relatively sharp change in the slope of the curve at about 550 °C, corresponding to activation energies of $E_A = 1.05$ eV for $T > 550$ °C and $E_A = 1.9$ eV for $T < 550$ °C. A comparison of the activation energies of the conductivity σ with the optical absorption band at 1.3 eV and the temperature dependence of the ESR signal of the free-radical chain-ends led *Edeling et al.*[97] to the conclusion that the chain-ends give rise to charge carriers which determine the form of the temperature dependence of σ in Figure 20. The inevitable presence of a very small number N_x of monovalent impurities X in liquid sulfur[98] influences the polymerization equilibrium[60]. There are two types of chain-ends. The chains are terminated by either a S—X bond or an unpaired spin[60]. The concentration of free-radical chain-ends N^* is nearly independent of X, but the average chain length decreases with increasing N_x. Under such circumstances, liquid sulfur behaves like a doped semiconductor with $(N^* + N_x)$ available defect levels and N^* acceptors[97]. The activation energy of the conductivity of such a semiconductor changes by a factor of 2 at a well defined temperature which is determined by the concentration N_x[99].

4. Metals at High Temperatures

The possible application of liquid metals at high temperatures as working fluids for technical purposes has been extensively discussed in recent years. This discussion is stimulated by the fact that liquid metals have a favorable combination of physical properties such as, *e.g.*, high latent heat of vaporization, high thermal conductivity, and high-temperature liquid range. In spite of this technological interest many fundamental physicochemical properties such as pVT-data, critical data, or specific heats, are not known with sufficient accuracy for most liquid metals at high temperatures. Reliable theoretical calculations of such data are still lacking. Experimental data relevant to properties like equation of state and critical data have to be determined at very high temperatures and relatively high pressures; the liquid range of metals extends to very high temperatures (Fig. 21). Only the critical data for Hg[100,101], Cs[102,103], Rb[103], K[104] and Na[105] have been measured with static experimental methods. *Fucke* and *Seydel*[106] have recently determined the values for Mo in a transient experiment with exploding wires.

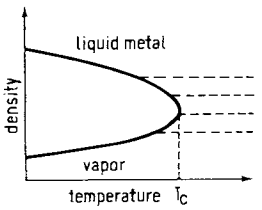


Fig. 21. Schematic illustration of the liquid-vapour equilibrium of a metal. Critical data of some metals (T_c, p_c): Hg 1490 °C, 1530 bar; Cs 1740 °C, 115 bar; Rb 1820 °C, 130 bar; K 1950 °C, 155 bar; Na 2230 °C, 250 bar; Mo 14000 °C, 5700 bar.

The main difficulty in the theoretical calculation of the properties of liquid metals, especially thermodynamic data, is the absence of an adequate interatomic-potential function for the entire liquid range. Regardless of the way in which the interatomic forces in a metal are described they must reflect the screening of the ionic charges by the electron gas and must therefore be always implicit functions of the electron density, *i.e.* of the metal density. In addition it is well known that a transition from metallic to nonmetallic, mostly semiconducting, state occurs also in a pure liquid metal, if it is continuously expanded to a low density fluid by increasing the temperature at a pressure higher than the critical pressure (*i.e.* avoiding evaporation)[14]. The transition to a nonmetallic state implies that the nature of the chemical interaction or of the interatomic forces changes; *i.e.* the description of the forces of interaction in a liquid metal must take into consideration the changes in density. This is in contrast to non-conducting liquids like argon, for which to a first approximation the thermodynamic data are usually described by reference to a single pair-potential over the whole density range from the dilute gas to the liquid.

Since the electrical properties of expanded metals in the transition range to nonmetallic behavior have already been reviewed in detail[14] we shall restrict ourselves here to only a few basic problems, *e.g.*: where in the phase diagram (Fig. 21) does the metal-nonmetal transition occur? Does a "law of corresponding states" exist for metals? How does the transition affect the thermodynamic properties and the liquid structure?

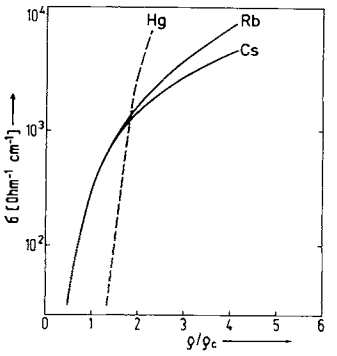


Fig. 22. Electrical conductivity σ of Hg, Cs and Rb at the supercritical, constant reduced temperature $T/T_c = 1.05$ as a function of the reduced density ρ/ρ_c.

Most measurements over a wide range of temperature—mostly up to supercritical temperatures—have been performed on the metals Hg, Cs and Rb. This is simply because these metals have the lowest critical temperatures. For Hg, extensive experimental data are available, including the electrical conductivity[100,101,107,108], the thermoelectric power[109], the Hall effect[110], the optical absorption[111] and reflection[112,113], the velocity of sound[114], the specific heat[115], the nuclear magnetic resonance[116] and the pVT-data[100,101,108]. Less data are known for the more corrosive alkali metals Cs and Rb. Up to now, the electrical conductivity[117,103,118], the thermoelectric power[117,118], the magnetic susceptibility[119,120] and the pVT-data[118,103] have been measured. The radial distribution function and thus the structure factor of Rb have recently been measured by means of neutron scattering experiments[103,120,121].

Figure 22 gives a comparison of the behavior of the conductivity of Hg[108], Cs and Rb[103] in the form of a plot of the conductivity as a function of the reduced density ρ/ρ_c at constant reduced temperature T/T_c. There is a striking difference between the two alkali metals and mercury. This is because Hg shows the characteristics of a liquid semiconductor at densities ρ smaller than 9 g/cm^3 (*i.e.* in the liquid state, $\rho_c = 5.3$ g/cm^3)[14]. The existence of an activation energy derived from eq. (1) has recently been proven for densities smaller than 9 g/cm^3[108].

By way of contrast, it is apparent from Figure 22 that the density dependence of the conductivity of Cs and Rb is very similar. The curves become identical at densities smaller than $2\rho_c$. At the density $2\rho_c$, the electron mean free path calculated with the free electron model[2] becomes equal to the mean interatomic distance. At the same time, the temperature dependence of the conductivity changes in sign from negative to positive[103]. The value of the conductivity at the critical point is about 300 ohm^{-1} cm^{-1} for both metals. This value is very close to the minimum metallic conductivity defined by *Mott* in numerous theoretical papers[122,4]. On the basis of this argument one can conclude that the metal-nonmetal transition in liquid alkali metals (a similar value of σ is observed for potassium at the critical point) coincides with the liquid-vapor phase transition.

Since the thermodynamic properties, like the electrical conductivity, are mainly determined by the density of the electron gas[2] a similar behavior of the pVT-data of Cs and

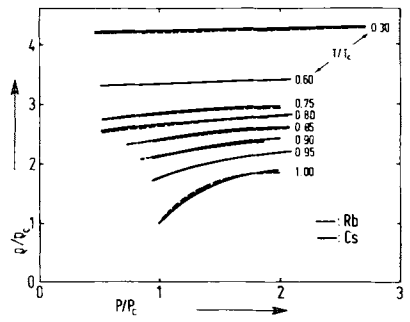


Fig. 23. Reduced diagram of the pVT data of Cs and Rb. Reduced density ρ/ρ_c as a function of the reduced pressure p/p_c at various reduced temperatures T/T_c. The isotherms for Cs and Rb at $T/T_c=0.6$ and 0.95 are indistinguishable.

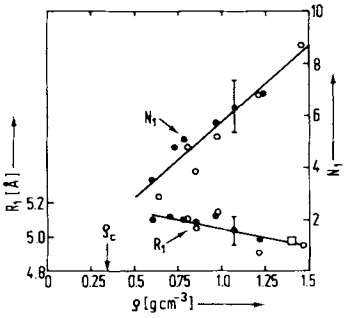


Fig. 25. Average number N_1 and mean distance R_1 of next neighbors in liquid Rb as a function of the density ρ.

Rb can be expected to occur in corresponding regions of the phase diagram according to Figure 22. This suggestion is supported by the plot in Figure 23[103]. Both metals have the same compressibility factor $z_c=p_c V_c/(RT_c)=0.22$ which is markedly different from the value $z_c=0.385$ for mercury, which is already nonmetallic at the critical point. The theoretical reasoning of this observation should lead to a "law of corresponding states" for groups of similar metals. The existence of such a law would be of considerable importance with regard to possible technical applications of liquid metals at high temperatures. In this connection a knowledge of the structure and of the isochoric thermal pressure coefficient $\gamma_v=(\partial p/\partial T)_v$ of the metals over a wide range of temperatures is of special interest. It is well known that at the melting point both quantities can be reasonably modelled[124,125] in a first approximation by hard spheres[126]. However, it must be emphasized that in a metal the diameters of the spheres will vary not only with temperature but also with density, due to the simultaneous variation in the number density of the free electrons. Figure 24 shows new measurements of the static structure factor $S(Q)$ for liquid rubidium[103,121,120,123] obtained by neutron scattering experiments. $S(Q)$ is directly related to the pair distribution function, $g(R)$, which is the probability of finding two particles of the liquid at a distance of R from each other. $g(R)$ depends only on R (see Fig. 24). The density dependence of $g(R)$ mainly reflects a linear decrease of the number of nearest neighbors, N_1, (Fig. 25) as calculated from the first peak of $g(R)$ using the formula given in the legend of Figure 24. In contrast to N_1, the nearest neighbor distance R_1, defined by the first maximum of $g(R)$, is almost constant (Fig. 25). A similar behavior is observed for the inert gases Ar and Ne[127]. From this similarity it can be assumed that the application of the hard sphere model, which provides an appropriate description of the liquid metal structure at the melting point, can be extended over a wide range of densities. A comparison between the measured structure factor $S(Q)$ and that calculated with the hard sphere model[126] is given in Figure 26. Allowing a decrease

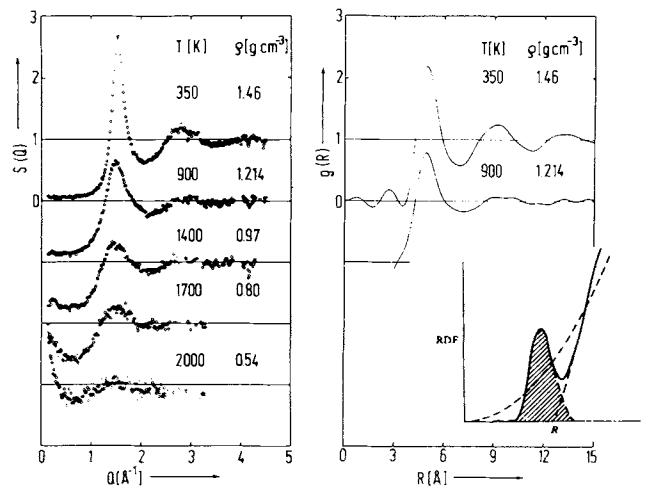


Fig. 24. Left: Static structure factor $S(Q)$ of liquid Rb as a function of temperature and density. The pair distribution function $g(R)$ (right, top) is derived from $S(Q)$ using

$$g(R)=[1+1/(2\pi n R)]\int_0^\infty [S(Q)-1)\,Q\cdot\sin(QR)]\,dQ$$

The average number of nearest neighbors is derived using $\mathrm{RDF}=4\pi R^2 g(R)$ (right, bottom)

$$N_1=2\times 4\pi\times n\int_0^{R_1} g(R)R^2\,dR$$

R_1 = position of the first peak in $G(R)$.

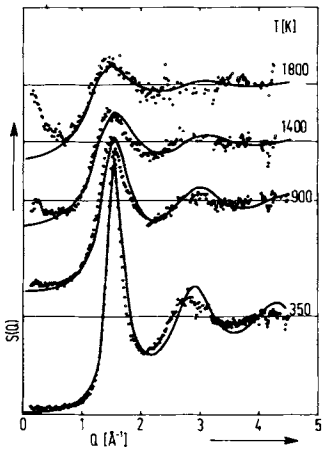


Fig. 26. Comparison between measured static structure factors $S(Q)$ (points) and those calculated with the hard sphere model (curve).

of the hard sphere diameter from 4.4 Å to 4 Å over the density range covered by the measurement yields a qualitatively satisfactory fit for $Q>0.1$ Å^{-1} over a surprisingly large density and temperature range. This observation has led to a number of attempts[103,118,130] to describe the pVT-data of liquid metals by a van-der-Waals type of theory[128]. The underlying idea is that the liquid consists of hard spheres immersed in a uniform potential which provides the cohesion that the hard-sphere system otherwise lacks. This description

is especially plausible for liquid metals, the cohesion energy of which can be attributed to the uniformly distributed gas of conduction electrons rather than to short range forces between neighboring particles. With these assumptions the pressure is given by:

$$p = p_0 - \left(\frac{\partial U}{\partial V}\right)_T = \gamma_v T - \left(\frac{\partial U}{\partial V}\right)_T \tag{3}$$

where p_0 is the hard-sphere pressure, $\gamma_v = (\partial p/\partial T)_v$ is the isochoric thermal pressure coefficient and U is the internal energy of the liquid. Figure 27 shows the γ_v-values of Rb de-

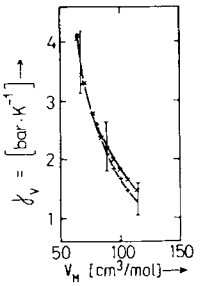


Fig. 27. Isochoric thermal pressure coefficient $\gamma_v = (\partial p/\partial T)_v$ of liquid Rb as a function of the molar volume. (×) experimental points, (+) calculated with the hard sphere model.

rived from experimental pVT-data. They are in good agreement, within experimental error, with those calculated with the hard-sphere model. The experimentally determined internal pressure $(\partial U/\partial V)_T$ is indeed to a first approximation

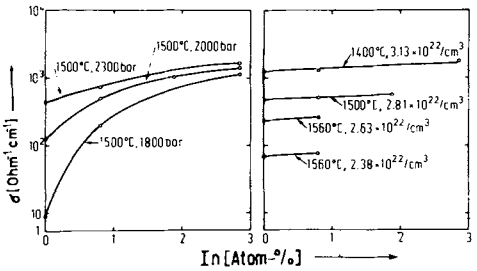


Fig. 28. Comparison of the concentration dependence of the electrical conductivity σ of dilute indium amalgams at constant pressure (left) and at constant number-density (right).

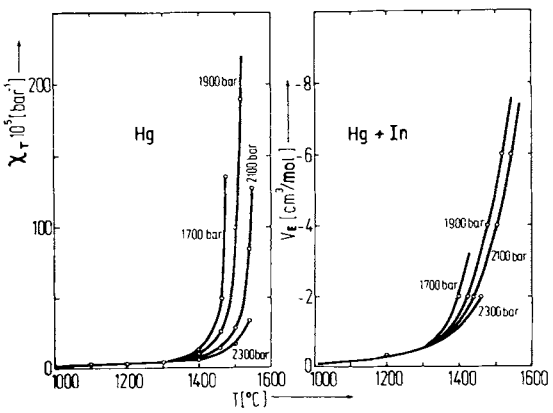


Fig. 29. Isothermal compressibility χ_T of pure Hg and excess volume V_E of In in Hg (Hg with 2.8 atom-% In) as a function of temperature at constant pressure.

only volume dependent[109, 118]. Its density dependence between the melting point density and about twice the critical density $2\rho_c$ is essentially determined by the existence of the electron gas[103]. For densities smaller than $2\rho_c$, also the electrical conductivity deviates from free-electron behavior. The experimentally observed simple dependence of the terms in eq. (3) on the volume V and temperature T is consistent with the existence of a "law of corresponding states" for the group of alkali metals.

The (divalent) metal mercury shows "semiconducting" behavior with respect to several properties at densities lower than 9 g/cm^3[14] (see Fig. 22). In this range, for example, the conductivity σ has an activation energy, and addition of a small concentration of excess electrons at constant pressure leads to marked enhancement of σ[129]. However, it has recently been demonstrated that these increases in σ have nothing to do with the "semiconducting" character of the electronic structure of Hg but are caused by the liquid and expanded state of mercury[130, 131], as is apparent from Figures 28 and 29. Figure 28 shows the effect of a few atomic percent (trivalent) indium at different constant pressures (left-hand side) or at constant number densities (right-hand side). It is obvious that the enhancement of the conductivity at constant pressure is caused by a corresponding volume contraction on alloying with In. Such a large contraction is generally observed in solvents having a very high compressibility on addition of small amounts of a solute, whose molecules exercise strong attractive forces on the molecules of the solvent[132]. The relationship between the compressibility χ_T of pure mercury and the excess volume of mixing V_E of In in Hg is demonstrated in Figure 29. Both χ_T and V_E rise quite sharply at temperatures higher than 1400 °C, *i. e.* as the density falls below the metal-nonmetal transition density of 9 g/cm^3. The transition implies a change in the nature of the interatomic interaction, and therefore anomalous behavior of the thermal properties—*e. g.* of χ_T—may generally be connected with the transition range in the electronic structure characteristic for metallic systems. It must be pointed out, however, that the transition range from a well defined liquid metal of high density to a gaseous dielectric of low density extends over a wide density range. First measurements of the dielectric behavior of gaseous Hg for densities smaller than 3.5 g/cm^3 (*i. e.* for conductivities smaller than 10^{-2} ohm^{-1} cm^{-1}) by *Hefner*[113] show a drastic increase in the refractive

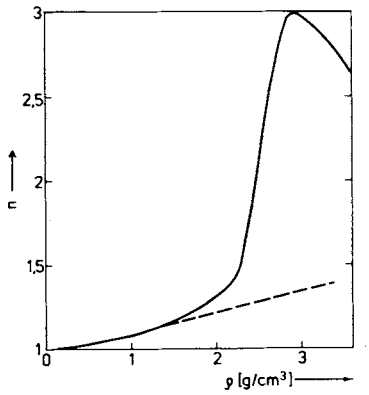


Fig. 30. Refractive index n of mercury vapour at $\lambda = 2$ μm as a function of the mercury density ρ at $T = 1530$ °C. The dotted line gives n calculated according to *Clausius-Mosotti*.

index n for densities larger than 2 g/cm^3 (Fig. 30). For comparison, Figure 30 includes a graph of the behavior of n calculated according to the Clausius-Mosotti relationship using the constant polarizability of the isolated Hg-atom. A striking upward deviation of about a factor of 2.5 from Clausius-Mosotti behavior is observed within a relatively small density range. A rapid decrease in the ionization energy[113] is expected to occur in this range due to the far-reaching polarization-forces between the neutral Hg-atoms and the ions and electrons of the slightly ionized (at 1530 °C) mercury. At the relatively low density of 3 g/cm^3 ($\rho_c = 5.3$ g/cm^3) and a temperature of 1530 °C the character of the optical properties of Hg-vapor changes abruptly within a very small and experimentally undetectable density range. This change is indicated in Figure 30 by the onset of an inflection in the refractive index curve. According to its optical data, mercury vapor above $\rho = 3$ g/cm^3 has all the properties of a solution of small metallic clusters in a solvent of a high dielectric constant. The a.c. conductivity has a maximum in the infrared spectral range which increases rapidly with increasing density[133]. In contrast, the d.c. conductivity is smaller than 10^{-1} ohm^{-1} cm^{-1} and nonmetallic. The abrupt formation of stable metal-clusters in the dense gaseous phase and particularly the mechanism of their formation and the investigation of the chemical interactions leading to their stabilization are of current interest in connection with metal-cluster complexes[134].

Received: March 27, 1980 [A 327 IE]
German version: Angew. Chem. 92, 598 (1980)

[1] *A. F. Joffe, A. R. Regel* in *A. F. Gibson:* Progress in Semiconductors. Wiley, New York 1960.
[2] *T. E. Faber:* Theory of Liquid Metals. Cambridge University Press, London 1972.
[3] *N. E. Cusack*, Rep. Prog. Phys. *26*, 361 (1963).
[4] *N. F. Mott, E. A. Davis:* Electronic Processes in Noncrystalline Materials. Clarendon Press, Oxford 1971.
[5] *M. A. Bredig, J. W. Johnson*, J. Phys. Chem. *64*, 1899 (1960).
[6] *M. A. Bredig* in *M. Blander:* Molten Salt Chemistry. Wiley, New York 1964.
[7] *N. H. Nachtrieb*, Adv. Chem. Phys. *31*, 465 (1975).
[8] *W. W. Warren*, Adv. Molten Salt Chem. *4* (1979).
[9] *M. Cutler:* Liquid Semiconductors. Academic Press, New York 1977.
[10] *J. E. Enderby* in *J. Tauc:* Amorphous and Liquid Semiconductors. Plenum Press, New York 1974.
[11] *K. Suzuki*, Ber. Bunsenges. Phys. Chem. *80*, 689 (1976).
[12] *R. U. Keezer, M. W. Bailey*, Mater. Res. Bull. *2*, 185 (1967).
[13] *H. Hoshino, R. W. Schmutzler, W. W. Warren, F. Hensel*, Phil. Mag. *33*, 255 (1976).
[14] *F. Hensel*, Angew. Chem. *86*, 459 (1974); Angew. Chem. Int. Ed. Engl. *13*, 446 (1974).
[15] *H. Hoshino, R. W. Schmutzler, F. Hensel*, Phys. Lett. *A 51*, 7 (1975).
[16] *R. W. Schmutzler, H. Hoshino, R. Fischer, F. Hensel*, Ber. Bunsenges. Phys. Chem. *80*, 113 (1976).
[17] *P. Münster, W. Freyland*, Phil. Mag. *B 39*, 93 (1979).
[18] *G. Kienast, J. Verma*, Z. Anorg. Allg. Chem. *310*, 143 (1961).
[19] *H. G. Fan*, Phys. Rev. *82*, 900 (1951).
[20] *E. Mollwo*, Z. Phys. *124*, 118 (1948).
[21] *A. Klemm* in *M. Blander:* Molten Salt Chemistry. Wiley, New York 1964.
[22] *K.-D. Krüger, R. Fischer, R. W. Schmutzler* in *R. Evans, D. A. Greenwood:* Liquid Metals 1976. Conference Series No. 30. Institute of Physics, Bristol 1977.
[23] *K.-D. Krüger, R. W. Schmutzler*, Ber. Bunsenges. Phys. Chem. *80*, 816 (1976).
[24] *G. A. Tinelli, D. F. Holcomb*, Materials Science Center, Cornell University Report No. 2935, 1977.
[25] *W. E. Spicer, A. H. Sommer, J. G. White*, Phys. Rev. *115*, 57 (1959).
[26] *F. Wooten, G. A. Condas*, Phys. Rev. *131*, 657 (1963).
[27] *H. Overhof, J. Knecht, R. Fischer, F. Hensel*, J. Phys. *F8*, 1607 (1978).
[28] *H. Overhof, R. Fischer, M. Vulli, F. Hensel*, Ber. Bunsenges. Phys. Chem. *80*, 872 (1976).
[29] *A. Hasegawa, M. Watabe*, J. Phys. *F7*, 75 (1977).
[30] *G. K. Wertheim, C. W. Bates, D. N. E. Buchanan*, Solid State Commun. *30*, 473 (1979).
[31] *G. K. Wertheim, R. L. Cohen, G. Crecelius, K. W. West, J. H. Wernick*, Phys. Rev. *B 20*, 860 (1979).
[32] *J. Knecht, R. Fischer, H. Overhof, F. Hensel*, J. Chem. Soc. Chem. Commun. *1978*, 905.
[33] *V. M. Glazov, S. N. Chizhevskaya, N. N. Glagoleva:* Liquid Semiconductors. Plenum Press, New York 1969.
[34] *A. Kempf, R. W. Schmutzler*, Ber. Bunsenges. Phys. Chem. *84*, 5 (1980).
[35] *W. Martin, P. Lamparter, S. Steeb, W. Freyland* in *E. Lüscher:* Liquid and Amorphous Metals. Nato Advanced Study Institute, 1980.
[36] *W. Martin*, Dissertation, Universität Stuttgart 1979.
[37] *P. Y. Achener*, Aerojet General Nucleonics, Report No. AGN-8195, Vol. I, 1968.
[38] *N. H. Nachtrieb*, Konferenz Physical Chemistry of Fluid Metals, Königstein 1976.
[39] *G. Steinleitner, W. Freyland*, Phys. Lett. *A 55*, 163 (1975).
[40] *W. Freyland, G. Steinleitner*, Ber. Bunsenges. Phys. Chem. *80*, 815 (1976).
[41] *A. Weiss, H. Witte:* Magnetochemie. Verlag Chemie, Weinheim 1973.
[42] *N. Nikoloso, R. W. Schmutzler, F. Hensel*, Ber. Bunsenges. Phys. Chem. *79*, 1186 (1978).
[44] *F. Hensel*, Adv. Phys. *28*, 555 (1979).
[45] *V. T. Nguyen, J. E. Enderby*, Phil. Mag. *35*, 1013 (1977).
[46] *B. R. Hochner, C. Wagner*, Acta Metall. *6*, 712 (1958).
[47] *J. E. Enderby, E. W. Collings*, J. Non-Cryst. Solids *4*, 161 (1970).
[48] *K. Hauffe, C. Wagner*, Z. Elektrochem. *46*, 160 (1940).
[49] *J. J. Egan*, Acta Metall. *7*, 560 (1959).
[50] *M. L. Saboungi, J. Marr, M. Blander*, J. Chem. Phys. *68*, 1375 (1978).
[51] *H. Ruppersberg, W. Speicher*, Z. Naturforsch. *A 31*, 47 (1976).
[52] *H. Ruppersberg, J. Egger*, J. Chem. Phys. *63*, 4095 (1975).
[53] *A. Eisenberg, A. V. Tobolsky*, J. Polym. Sci. *46*, 19 (1960).
[54] *G. Lucovsky* in *E. Gerlach, P. Grosse:* Selenium and Tellurium. Springer, Berlin 1979.
[55] *G. Briegleb*, Z. Phys. Chem. *A 144*, 321 (1929).
[56] *S. Dobinski, J. Weselowski*, Bull. Acad. Pol. Sci. Ser. *A 9* (1937).
[57] *J. Moscinski, A. Renninger, A. L. Averbach*, Phys. Lett. *A 42*, 453 (1973).
[58] *G. Tourand*, J. Phys. (Paris) *34*, 937 (1973).
[59] *M. Miscawa, K. Suzuki*, Trans. Jpn. Inst. Met. *18*, 427 (1977).
[60] *D. C. Koningsberger*, Dissertation, Eindhoven 1971.
[61] *H. Hoshino, R. W. Schmutzler, F. Hensel*, Ber. Bunsenges. Phys. Chem. *80*, 27 (1976).
[62] *V. A. Alekseev, V. G. Oveharenko, Yu. F. Ryshkov, M. V. Sadovskii*, JETP Lett. *24*, 189 (1977).
[63] *H. Hoshino, R. W. Schmutzler, F. Hensel* in *R. Evans, D. A. Greenwood:* Liquid Metals 1976. Conference Series No. 30. Institute of Physics, Bristol 1977, p. 404.
[64] *R. Fischer, R. W. Schmutzler* in *E. Gerlach, P. Grosse:* Selenium and Tellurium. Springer, Berlin 1979.
[65] *W. W. Warren, R. Dupree*, Phys. Rev. *B*, in press.
[66] *H. Endo, H. Hoshino, R. W. Schmutzler, F. Hensel* in *R. Evans, D. A. Greenwood:* Liquid Metals 1976. Conference Series No. 30. Institute of Physics, Bristol 1977, p. 404.
[67] *M. Yao, M. Misonou, K. Tamura, K. Ishida, K. Tsuji, H. Endo*, J. Phys. Soc. Jpn., in press.
[68] *W. Freyland, M. Cutler*, Trans. Faraday Soc., in press.
[69] *G. Weser, W. W. Warren, F. Hensel*, Ber. Bunsenges. Phys. Chem. *82*, 588 (1978).
[70] *H. Rau*, J. Chem. Thermodyn. *6*, 525 (1974).
[71] *P. Boolchand, P. Suromyi*, Phys. Rev. *B 7*, 57 (1973).
[72] *G. Tourand*, J. Physique *34*, 937 (1973).
[73] *G. Tourand*, Phys. Lett. *A 54*, 209 (1975).
[74] *R. Bellissent, G. Tourand*, J. Non-Cryst. Solids *35*, 1221 (1980).
[75] *M. Edeling*, Dissertation, Universität Marburg 1980.
[76] *J. E. Enderby, M. Gay*, J. Non-Cryst. Solids *35*, 1269 (1980).
[77] *H. Thurn, J. Ruska*, J. Non-Cryst. Solids *22*, 331 (1976).
[78] *R. Fischer, R. W. Schmutzler, F. Hensel*, J. Non-Cryst. Solids *35*, 1295 (1980).
[79] *M. Yao, R. Suzuki, H. Endo*, Solid State Commun., in press.
[80] *R. A. Street, N. F. Mott*, Phys. Rev. Lett. *35*, 1293 (1975).
[81] *M. Kastner, D. Adler, H. Fritzsche*, Phys. Rev. Lett. *37*, 1504 (1976).
[82] *D. Vanderbilt, J. D. Joannopoulos*, Phys. Rev. Lett. *42*, 1012 (1979).
[83] *H. P. Seyer*, Diplomarbeit, Universität Marburg 1979.
[84] *J. N. Hodgson*, Phil. Mag. *8*, 735 (1963).
[85] *B. Meyer:* Sulfur, Energy and Environment. Elsevier, New York 1977.
[86] *G. Weser, F. Hensel, W. W. Warren*, Ber. Bunsenges. Phys. Chem. *82*, 588 (1978).
[87] *A. V. Tobolsky, W. J. MacKnight:* Polymeric Sulfur and Related Polymers. Interscience, New York 1965.
[88] *J. A. Poulis, C. H. Massen, P. van der Leeden*, Trans. Faraday Soc. *58*, 474 (1962).
[89] *D. M. Gardner, G. K. Fränkel*, J. Am. Chem. Soc. *78*, 3279 (1956).
[90] *D. C. Koningsberger, T. de Neets*, Chem. Phys. Lett. *4*, 615 (1970); *14*, 453 (1972).
[91] *W. R. Salaneck*, private communication.

[92] *B. Meyer, T. V. Oommen, D. Jensen*, J. Phys. Chem. *75*, 912 (1971).
[93] *G. Weser*, Dissertation, Universität Marburg 1980.
[94] *J. Berkowitz, J. R. Marquardt*, J. Chem. Phys. *39*, 275 (1963).
[95] *D. Detry, J. Drowart, P. Goldfinger, H. Keller, H. Rickert*, Z. Phys. Chem. (Frankfurt am Main) *55*, 314 (1967).
[96] *H. Rau, T. R. N. Kutty, J. R. F. Guedes De Carvalho*, J. Chem. Thermodyn. *5*, 833 (1973).
[97] *M. Edeling, R. W. Schmutzler, F. Hensel*, Phil. Mag. *39*, 547 (1979).
[98] *B. Meyer*, Chem. Rev. *76*, 367 (1976).
[99] *N. F. Mott, R. W. Gurney:* Electronic Processes in Ionic Crystals. Clarendon Press, Oxford 1940.
[100] *F. Hensel, E. Franck*, Ber. Bunsenges. Phys. Chem. *70*, 1154 (1966).
[101] *I. K. Kikoin, A. R. Sechenkov*, Phys. Met. Metallogr. (USSR) *24*, 5 (1967).
[102] *V. S. Bhise, C. F. Bouilla*, Proc. 7th Symp. Thermophys. Prop., A. S. M. E., Gaitersburg, Md. 1977.
[103] *G. Franz*, Dissertation, Universität Marburg 1980.
[104] *W. Freyland, F. Hensel*, Ber. Bunsenges. Phys. Chem. *76*, 347 (1972).
[105] *V. S. Bhise*, Dissertation, Columbia University, New York 1976.
[106] *U. Seydel, F. Fucke*, J. Phys. *F 8*, L 157 (1978).
[107] *D. R. Postill, R. G. Ross, N. E. Cusack*, Adv. Phys. *16*, 493 (1967).
[108] *G. Schönherr, R. W. Schmutzler, F. Hensel*, Phil. Mag. *B 40*, 411 (1979).
[109] *R. W. Schmutzler, F. Hensel*, Ber. Bunsenges. Phys. Chem. *76*, 531 (1972).
[110] *U. Even, J. Jortner*, Phys. Rev. Lett. *28*, 31 (1972).
[111] *H. Uchtmann, F. Hensel*, Phys. Lett. *53A*, 239 (1975).
[112] *H. Ikezi, K. Schwarzenegger, A. L. Simons, A. L. Passner, S. L. McCall*, Phys. Rev. *B 18*, 2494 (1978).
[113] *W. Hefner*, Dissertation, Universität Marburg 1980.
[114] *M. Inutake, K. Suzuki, Frijiwaka*, Proc. 14th Int. Conf. on Phenomena in Ionized Gases, 1979.
[115] *R. W. Schmutzler*, Habilitationsschrift, Universität Marburg 1979.
[116] *V. El-Hanany, W. W. Warren*, Phys. Rev. Lett. *34*, 1276 (1975).
[117] *H. P. Pfeifer, W. Freyland, F. Hensel*, Phys. Lett. *A 43*, 111 (1973).
[118] *H. P. Pfeifer, W. Freyland, F. Hensel*, Ber. Bunsenges. Phys. Chem. *83*, 204 (1979).
[119] *W. Freyland*, Phys. Rev. *B 20*, 5104 (1979).
[120] *W. Freyland*, Habilitationsschrift, Universität Marburg 1980.
[121] *W. Freyland, F. Hensel, W. Gläser*, Ber. Bunsenges. Phys. Chem. *83*, 884 (1979).
[122] *N. F. Mott:* Metal-Insulator Transition. Taylor and Francis, London 1974.
[123] *E. Schneider, G. Franz, W. Freyland* in *E. Lüscher:* Liquid and Amorphous Metals. Nato Advanced Study Institute, 1979.
[124] *N. W. Ashcroft, J. Lekner*, Phys. Rev. *145*, 83 (1966).
[125] *M. Shimoji:* Liquid Metals. Academic Press, London 1977.
[126] *E. Thiele*, J. Chem. Phys. *39*, 474 (1963).
[127] *F. Kohler:* The Liquid State. Verlag Chemie, Weinheim 1972.
[128] *D. A. Young, B. J. Alder*, Phys. Rev. *A 3*, 364 (1971).
[129] *M. Zillgitt, R. W. Schmutzler, F. Hensel*, Phys. Lett. *A 39*, 419 (1972).
[130] *G. Schönherr*, Dissertation, Universität Marburg 1978.
[131] *U. Even, J. Magen*, J. Phys. *E 7*, 902 (1975).
[132] *J. C. Wheeler*, Ber. Bunsenges. Phys. Chem. *76*, 308 (1972).
[133] *H. Uchtmann, F. Hensel, H. Overhof*, Phil. Mag., in press.
[134] *M. J. Taylor:* Metal-To-Metal Bounded States of the Main Group Elements. Academic Press, New York 1975.

The Influence of Density and Temperature on the Properties of Pure Molten Salts

By Klaus Tödheide[*]

Dedicated to Prof. Dr. E. U. Franck at the occasion of his 60th birthday

Molten salts differ from most other types of liquids because of their high charge carrier density, which is responsible for a number of their extraordinary properties such as high ionic conductivity. Experimental and theoretical investigations during the past few years have provided information on the static and dynamic microscopic structures of this class of liquids and their relationship with the macroscopic properties. A consistent, albeit incomplete picture of the behavior of molten salts over wide ranges of temperature and density is now available including the transition from an insulator to an ionic conductor which a salt undergoes when it is compressed from vapor-like to liquid-like densities.

1. Introduction

Molten salts have been the subject of experimental and theoretical investigation for many decades. A quantitative knowledge of the equilibrium and transport properties of pure salts and of salt mixtures was necessary for the development and improvement of technical processes based on molten salts and for searching for new applications. Since the statistical treatment of liquids was not sufficiently advanced to correlate the experimental data and to interpret the results in terms of the properties of the microscopic constituents, semiempirical models were developed for this purpose[1]. The information accumulated up to about 1965 is presented in a number of books[2–5] and review articles[6–13]. Most of the data collected is contained in a handbook[14].

It is remarkable that up to that time the properties of molten salts were measured and discussed either at a fixed temperature or as a function of temperature at constant (normal) pressure. Since the density changes with temperature at constant pressure the measured temperature dependencies always included a density dependence which was neglected in the interpretation of the experimental results. The influence of density on the properties of molten salts, however, can be very important, as is demonstrated by an extreme example: liquid potassium chloride is a good ionic conductor, whereas the vapor in equilibrium with it contains nothing but uncharged particles such as molecules and associates of molecules and consequently behaves as an insulator. A transition from an insulator to an ionic conductor must therefore occur

[*] Dr. K. Tödheide
Institut für Physikalische Chemie und Elektrochemie der Universität
Postfach 6380, D-7500 Karlsruhe 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0606 $ 02.50/0

as the density is raised at constant temperature from low values to those typical for liquid phases.

To facilitate the interpretation of experimental data a clear separation of the temperature effects from those of density or volume is desirable. The separation is straight forward in the theoretical treatment of liquids by statistical or computer simulation methods, because volume and temperature can be chosen as independent variables. Experimentally it can be achieved by high-pressure investigations in combination with PVT data over the pertinent pressure and temperature ranges.

The aim of this article is to report on the progress which has been made during the past few years in the investigation of the equilibrium and transport properties and of the ionization behavior of molten salts as a function of temperature and density. Wherever possible, the results of statistical mechanical calculations, computer simulations, and experiments will be compared with one another.

2. Equilibrium Properties

2.1. Introductory Remarks

The macroscopic properties and structure of molten salts, like those of other liquids, can in principle be calculated from the properties of their microscopic constituents and the intermolecular forces, if the trajectories of all particles are followed as a function of time. The least complicated salts for such a procedure are those which are completely dissociated into monatomic ions with spherical symmetry like *e. g.* the alkali metal halides. In this case the Hamiltonian $\mathcal{H}$ of the system does not contain contributions from internal degrees of freedom and the total potential energy U_N depends only on the coordinates of the particles but not on their relative orientations:

$$\mathcal{H} = \sum_{i=1}^{N} (1/2m)|\vec{p}_i(t)|^2 + U_N(\vec{r}_1(t), \ldots, \vec{r}_N(t)) \tag{1}$$

The microscopic state of an isolated system of N such particles with mass m is completely determined by fixing the coordinate vectors $\vec{r}_i$ and the momentum vectors $\vec{p}_i$ for all particles. The time evolution of the system is described by the coupled first order differential equations (Hamilton)

$$\dot{\vec{r}}_i = \frac{\partial \mathcal{H}}{\partial \vec{p}_i}; \quad \dot{\vec{p}}_i = -\frac{\partial \mathcal{H}}{\partial \vec{r}_i}; \quad (i = 1, 2, \ldots, N) \tag{2}$$

or by the coupled second order differential equations (Newton)

$$\dot{\vec{p}}_i = m\ddot{\vec{r}}_i = -\frac{\partial \mathcal{H}}{\partial \vec{r}_i} = -\frac{\partial U_N(\vec{r}^N)}{\partial \vec{r}_i} \tag{3}$$

The potential energy can in principle be determined by solving the Schrödinger equation for all nuclei and electrons in the Born-Oppenheimer approximation[15].

However, for particle numbers of the order of 10^{23} neither the calculation of U_N nor the solution of the differential equations (2) or (3) is feasible. In order to circumvent this difficulty two different approaches have been attempted:

1. Statistical mechanics is used to calculate the macroscopic properties as far as possible by purely analytical methods as averages of microscopic properties weighted by the appropriate distribution functions[16].

2. Computer simulations are used to perform the averaging procedure numerically for systems containing 10^2 to 10^3 particles. In order to avoid the influence of the boundary of the system, which plays a very important role in the case of such small systems, periodical boundary conditions are introduced[17, 18]. The molecular dynamic method (MD) solves the equations of motion (3) and calculates time averages. The Monte Carlo method (MC) evaluates ensemble averages by producing the microstates of the system by a random number method. The probability for the microstate to be counted in the averaging procedure is chosen to be proportional to the corresponding Boltzmann factor.

The most comprehensive probability information about a system of N particles of the kind described previously is given by a distribution function $P^{(N)}(\vec{r}^N, \vec{p}^N, t)$ called probability density. Multiplied by the volume element of phase space $d\vec{r}^N d\vec{p}^N$ it yields the normalized probability of finding the system at a given time t in a microscopic state in which each of the particles $i = 1, \ldots, N$ has the coordinate vector $\vec{r}_i$ and the momentum vector $\vec{p}_i$. Because of the large number of particles this function is of no practical use. On the other hand, it contains more information than necessary for the calculation of macroscopic properties. It is thus useful to define distribution functions of lower order which are derived from $P^{(N)}$ by integrating over the coordinates and momenta of a fraction of the particles at the expense of some information being lost. At equilibrium all these distribution functions are independent of time.

2.2. Radial Distribution Function

The pair distribution function

$$f_0^{(2)}(\vec{r}_1, \vec{r}_2) = \frac{N!}{(N-2)!} \int\int P^{(N)}(\vec{r}^N, \vec{p}^N)\, d\vec{r}^{(N-2)} d\vec{p}^N \tag{4}$$

is obtained from the N particle equilibrium distribution function by integrating over all momentum vectors and $N-2$ coordinate vectors and by introducing a combinatorial factor which accounts for the indistinguishability of the particles. This function, divided by the square of the average number density $\rho = N/V$, yields

$$g_0^{(2)}(\vec{r}_1, \vec{r}_2) = f_0^{(2)}(\vec{r}_1, \vec{r}_2)/\rho^2 \tag{5}$$

For an isotropic fluid this function only depends on the distance between the two particles and is called the radial distribution function $g(r)$

$$g_0^{(2)}(\vec{r}_1, \vec{r}_2) = g(|\vec{r}_1 - \vec{r}_2|) = g(r) \tag{6}$$

The radial distribution function plays an important role in the treatment of equilibrium properties of liquids:

1. It gives the ratio of the local to the average density

$$g(r) = \rho(r)/\rho \tag{7}$$

and is therefore related to the number of particles $dN(r)$ in a spherical shell of thickness dr at a distance r from a reference particle

$$dN(r) = \rho g(r)\, 4\pi r^2\, dr \tag{8}$$

It is thus readily obtainable from computer simulations.

2. The radial distribution function can be determined from scattering experiments, *e.g.* X-ray diffraction or elastic neutron scattering.

3. Statistical mechanics demonstrates that the radial distribution function is related to the compressibility of the system by

$$\rho k T \kappa_T = 1 + 4\pi\rho \int_0^\infty [g(r) - 1] r^2\, dr \tag{9}$$

If the total potential energy can be written as the sum of effective pair potentials

$$U_N(\vec{r}^N) = \frac{1}{2} \sum_{i=1}^{N} \sum_{j \neq i} u_{ij}(r) \tag{10}$$

simple relations hold between the radial distribution function and the internal energy U and the pressure P of the system

$$U = \frac{3}{2} N k T + 2\pi N \rho \int_0^\infty u(r) g(r) r^2\, dr \tag{11}$$

$$P = \rho k T - \frac{2}{3}\pi\rho^2 \int_0^\infty \frac{du(r)}{dr} g(r) r^3\, dr \tag{12}$$

For calculation of the thermodynamic properties of the system it suffices then to know the effective pair potential and the radial distribution function as a function of temperature and density.

The utility of effective pair potentials for molten alkali metal halides has been discussed extensively by *Woodcock*[19] and by *Sangster* and *Dixon*[20]. If the difference in ionic sizes is not too large the Born-Mayer-Huggins potential

$$u_{ij}(r) = \frac{z_i z_j e^2}{4\pi\varepsilon_0 r} + B_{ij} \exp(-A_{ij} r) - C_{ij} r^{-6} - D_{ij} r^{-8} \tag{13}$$

has proven to be useful, although improvements are desirable in some cases. It does not contain a term which accounts for the polarizability of the ions. $z_i e$ is the charge of an ion. The parameters A, B, C, and D can be determined from the properties of the corresponding crystalline salts[20–23].

For molten salts two complications arise as compared with simple liquids (*e.g.* argon):

1. Since ions with positive and negative charge are present in the melt at least three different partial radial distribution functions $g_{++}(r)$, $g_{+-}(r)$, and $g_{--}(r)$ are needed for the description of even the simplest molten salts.

2. The Coulomb term in the pair potential [eq. (13)] which stems from the charge of the ions is long-ranged compared to the other terms and therefore complicates the statistical treatment as well as the computer simulations.

2.2.1. Experimental Determination of Radial Distribution Functions

The arrangement of particles in melts, like their positions in crystals, can be extracted from diffraction patterns. Elastic neutron scattering is particularly well suited for the determination of radial distribution functions in molten salts. Since neutrons are scattered from nuclei the positions of the nuclei are directly reflected by the distribution of the scattered intensity. In addition the scattering behavior of a melt may be varied drastically by isotopic substitution without changing the structure of the melt.

From the intensity scattered into a scattering angle 2θ one obtains, after application of corrections for background, multiple, and incoherent scattering and suitable normalization, a scattering function $I(Q)$ which is related to the partial structure factors $S_{\alpha\beta}(Q)$ ($\alpha, \beta = +, -$) of a binary system[24–26] by

$$I(Q) = N[x_+ f_+^2 S_{++}(Q) + x_- f_-^2 S_{--}(Q) + f_+ f_- S_{+-}(Q)] \tag{14}$$

where $Q = (4\pi/\lambda)\sin\theta$; λ is the wavelength of the neutrons, f_α is the average scattering length and x_α the mole fraction of the ions of type α. The partial structure factors are connected with the partial radial distribution functions through a Fourier transformation:

$$S_{\alpha\beta}(Q) = \delta_{\alpha\beta} + \frac{8\pi x_\alpha x_\beta \rho}{x_\alpha + x_\beta} \int_0^\infty [g_{\alpha\beta}(r) - 1] \frac{\sin Q r}{Q \cdot r} r^2\, dr \tag{15}$$

where $\delta_{\alpha\beta}$ is the Kronecker symbol. If an isotopic substitution is carried out for the anions in the melt, f_- in eq. (14) is changed but the $S_{\alpha\beta}$ remain unaltered. Thus the three partial structure factors of a binary melt can be derived from the elastic neutron scattering patterns of three different, suitably chosen isotopic mixtures. From the structure factors the partial radial distribution functions are calculated by inverting eq. (15).

A favorable candidate for an isotopic substitution is chlorine, because the coherent scattering lengths of ^{35}Cl and ^{37}Cl differ by almost a factor of five.

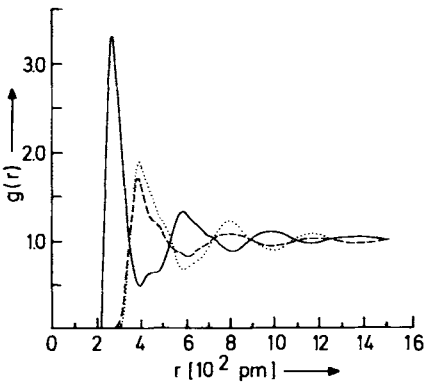


Fig. 1. Partial radial distribution functions in molten sodium chloride at 875 °C from measurements by *Edwards et al.* [29]:
———— g_{NaCl}; - - - - - - - - - - - - g_{NaNa}; · · · · · · · · · · · · · g_{ClCl}.

Measurements have been made so far on CuCl[27] KCl and CsCl[28], NaCl[29], RbCl[30], AgCl[31], and on $BaCl_2$[32]. Figure 1 shows as example the partial radial distribution functions

in molten NaCl at 875 °C and 1 atm, from which the following conclusions can be drawn:

1. The strong maximum in g_{NaCl} at 260 pm indicates that the particles are mainly surrounded by particles of opposite charge, as would be expected for an ionic melt.

2. The Na—Cl distance at the first maximum is considerably shorter than in the crystal (276 pm), although the volume increase upon melting is about 25 percent.

3. The nearest neighbor coordination number which is given by the area under the first peak of g_{NaCl} is 5.8 ± 0.1. This number is only slightly smaller than the number of nearest neighbors in the NaCl crystal.

4. g_{NaNa} and g_{ClCl} do not differ greatly. In cases where the ionic radii approach each other, *e.g.* for RbCl, g_{++} and g_{--} almost coincide.

5. The maxima of g_{NaNa} and g_{ClCl} fall on the minima of g_{NaCl} and vice versa, indicating a strong tendency towards charge compensation which is almost complete above a distance of 500 pm.

6. The number of next nearest neighbors (equal charge) is 13.0 ± 0.5.

7. The shortest distance between Na and Cl is 220 pm, between Na and Na 270 pm, and between Cl and Cl 300 pm.

8. Since g_{NaNa} and g_{ClCl} attain values different from zero at distances below that of the first minimum in g_{NaCl} a non-negligeable fraction of equally charged ions penetrates into the first coordination shell.

9. The structure of the partial radial distribution functions extends to distances above 1 nm, whereas the average radial distribution function

$$g_m(r) = (1/2)[g_{+-}(r) + 1/2(g_{++}(r) + g_{--}(r))]$$

which can be obtained from a single scattering experiment does not exhibit any structure beyond 500 pm.

The results for the other alkali metal halides show the same qualitative features. Deviations reported for KCl and CsCl[28] are most probably due to experimental errors[29].

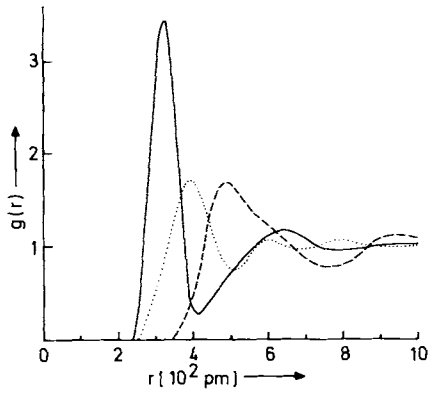


Fig. 2. Partial radial distribution functions in barium chloride at 1025 °C from measurements by *Edwards et al.* [32]:
——— g_{BaCl}; - - - - - - - - - - g_{BaBa}; ····· g_{ClCl}.

The partial radial distribution functions of $BaCl_2$[32] are shown in Figure 2. The most obvious changes with respect to the alkali metal halides are:

1. g_{BaBa} and g_{ClCl} strongly differ from each other. This is partly due to the charge difference. The comparative absence of structure in g_{ClCl} with respect to g_{BaBa} is probably linked with the higher mobility of the Cl^- ions in the melt.

2. There is substantial penetration of the chloride ions into their first coordination shell.

Elastic neutron scattering experiments on molten salts have not yet been performed at elevated pressures. Thus the influence of density on the radial distribution functions has not been established experimentally.

2.2.2. Calculation of Radial Distribution Functions by Computer Simulation

The calculation of the partial radial distribution functions can be achieved by both Monte Carlo and molecular dynamics methods. For the simulation it is necessary to split the Coulomb term in the effective pair potential into parts and to perform the Ewald summation[21,23] in order to obtain sufficiently accurate results. The major part of the results obtained so far[20,33] are for the alkali metal halides. It turns out that the Born-Mayer-Huggins potential [eq. (13)] with the constants taken from *Fumi* and *Tosi*[22,23] is superior to other effective pair potentials used for the simulations. The calculated radial distribution functions agree with the measured ones in all essential features mentioned in the preceding paragraph. The calculated first maximum of g_{+-} is usually slightly higher and is found to appear at a distance which is about 10 pm shorter than that derived from experiments. The calculations also give a slightly smaller number of nearest neighbors. This is shown for NaCl as example in Figure 3, where measurements by *Edwards et al.*[29] are compared with calculations by *Lewis et al.*[34]. The figure also demonstrates that for this salt there is no noticeable influence on the calculated radial distribution functions when the polarizability of the ions is taken into consideration by introducing a shell model[75]. For salts with a larger difference in the ionic radii (*e.g.* NaI) the influence of the polarizability starts to become evident[20]. It mainly affects g_{++}, the first peak of which is shifted towards smaller distances.

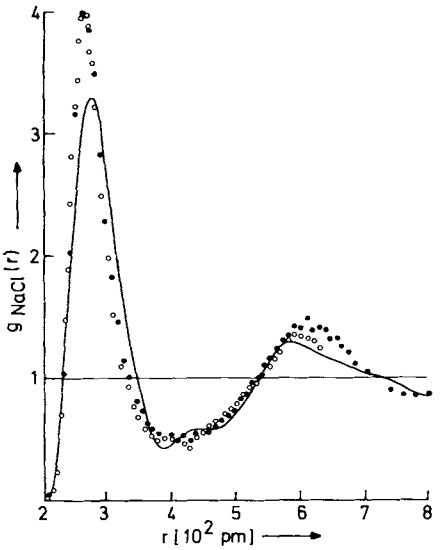


Fig. 3. Partial radial distribution function g_{NaCl} in molten sodium chloride after *Sangster* and *Dixon* [20]:
——————— measurements [29] at 1148 K;
●●●●●●●●●●●● MC calculations [34] at 1073 K;
○○○○○○○○○○○○ MD calculations accounting for the polarizabilities of the ions [75] at 1427 K.

Radial distribution functions for the alkaline earth metal halides were calculated by *Rahman et al.*[35] (BeF_2) and by *de Leeuw*[36,37] (CaF_2, $SrCl_2$). A direct comparison with experimental results is not possible, but the partial radial distribution functions calculated for $SrCl_2$ and those measured for $BaCl_2$[32] (Fig. 2) show the same characteristic features.

van Wechem[38] carried out calculations for KNO_3 assuming a disk-like shape for the nitrate ion with a radius of 230 pm and three different point charge distributions. As was expected the calculated angle-dependent distribution functions vary strongly when the charge distribution is changed. Comparison with experiment is not yet possible.

The influence of density on the radial distribution function is demonstrated in Figure 4, where the Monte Carlo results for KCl[39] are shown. Here g_{++} and g_{--} coincide within the limits of error. The characteristic quantities of the functions plotted in Figures 4a through 4c are collected in Table 1.

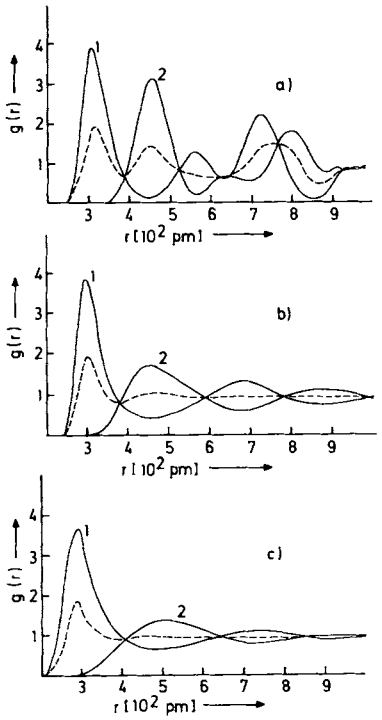


Fig. 4. Partial radial distribution functions in potassium chloride after *Woodcock* and *Singer* [39]: a) solid KCl, b) and c) molten KCl (temperatures and molar volumes, see Table 1). 1: g_{KCl}; 2: $g_{KK}=g_{ClCl}$; -------- $g_m=\frac{1}{2}g_{KCl}+g_{KK}$.

creases and the distance of closest approach d_{++} decreases markedly. An increase in the volume of the melt by a factor of two (Fig. 4, b→c) again shortens the distance r_{+-}^{max} and simultaneously diminishes the coordination number. This indicates that at the limit of very low density r_{+-}^{max} must approach as its limiting value the equilibrium distance of K and Cl in the isolated KCl molecule (267 pm) and that the coordination number n_{+-} approaches unity. Because of the higher temperature, and thus higher kinetic energy of the ions, d_{+-} decreases considerably.

This and other examples demonstrate that computer simulations offer an opportunity of calculating the structures of molten salts with spherical ions to a degree of accuracy comparable with that of experimental determinations. Furthermore, they enable calculations also in those regions of temperature and density which are inaccessible in experiments.

2.2.3. Calculation of Radial Distribution Functions by Statistical Mechanics

The analytical calculation of radial distribution functions for dense fluids from the pair potential is a difficult task. The Born-Green integrodifferential equation which links these two functions also contains the three-particle distribution function as a further unknown. For solution of the problem it is necessary to make assumptions concerning the radial distribution function or its relation to the three-particle distribution function (*e.g.* Percus-Yevick[40]). This leads to new equations relating $g(r)$ to $u(r)$ which in some cases can be solved exactly for simple potentials such as the hard sphere potential. For more realistic potentials, however, only approximate solutions can be made. Perturbation methods appear to be most successful[41]. For simple liquids (argon), systems of hard or soft spheres with temperature- and density-dependent diameters have been used as reference systems for perturbation calculations. An obvious choice as reference system for molten salts is a system of charged hard spheres. Monte Carlo simulations by *Larsen*[42] for the restrictive primitive model, in which the oppositely charged spheres have the same diameter, have shown that this system meets most of the requirements as a reference system for molten salts. The attempts made at calculating the radial distribution functions of a reference system consisting of charged spheres have been reviewed by *Gillan*[43] and *Parrinello* and *Tosi*[25]. So far, only approximative solutions of the problem are available: the mean spherical approximation (MSA)[44-46]

Table 1. Characteristic quantities for the radial distribution functions of potassium chloride shown in Fig. 4 from Monte Carlo calculations [39].

Fig.	T/K	V/cm³ mol⁻¹	Phase	d_{+-}/pm	r_{+-}^{max}/pm	r_{+-}^{min}/pm	n_{+-}	d_{++}/pm	r_{++}^{max}/pm	r_{++}^{min}/pm	n_{++}
4a	1045	41.48	solid	234	307	445	6.0	318	454	570	12.2
4b	1045	48.80	liquid	233	296	455	5.5	298	438	675	15.6
4c	2874	97.60	liquid	211	289	515	3.9	254	513	735	10.1

Upon melting (Fig. 4, a→b) the first peak in g_{+-} is shifted towards smaller distances, although the volume increases by about twenty percent. The peak is broadened and the number of nearest neighbors slightly decreases. The distance of closest approach d_{+-} remains constant. For the next nearest neighbors the distance of the first peak shortens, n_{++} in-

and the self-consistent Ornstein-Zernike approximation (SCOZA)[47,48]. Both approximations give the essential features of the radial distribution functions of the system as calculated by Monte Carlo simulation, but also show some deficiencies. The MSA, for example, gives an unphysical result in the form of negative values for $g_{+-}(r)$ at small values of r.

A purely analytical solution for a reference system on which perturbation calculations could be based for ionic melts with more realistic pair potentials has not yet been found.

2.3. Thermodynamic Properties

2.3.1. Statistical Mechanical Calculation

The calculation of the thermodynamic properties and of an equation of state for simple molten salts is in principle feasible using the methods described in Section 2.2.3. The necessary approximations, however, cause some deficiencies. The MSA leads to inconsistent results. Pressures calculated from eq. (9) differ substantially from those calculated from eq. (12). The SCOZA avoids such inconsistency by introducing four adjustable parameters, but this may lead to negative pressures under conditions where the system should be stable[49]. Because of these difficulties it is not yet possible to obtain useful thermodynamic data by purely analytical methods.

2.3.2. Computer Simulations

The development of computer simulations intended for the calculation of thermodynamic data for molten salts has been reviewed by several authors[20, 33, 50]. The majority of the calculations were carried out for alkali metal halides for temperature and volume conditions which correspond to normal pressure. The Born-Mayer-Huggins potential (13) generally affords the best agreement with experimental data. In most cases the results are not markedly improved when the polarizability of the ions is taken into account. Table 2 shows a comparison of Monte Carlo results with experimental data for KCl at its normal melting point. The excellent agreement for the molar heat capacity at constant pressure is probably fortuitous. The calculations for the internal energy are relatively accurate. As can be seen from the Table, the deviations for the properties listed generally fall outside the experimental error limits. The deviation for the pressure evaluated from the virial is exceptionally large. As *Schäfer* and *Klemm*[54] have pointed out, the virial fluctuates considerably because of the long-ranged pair potential. In order to improve the pressure calculations the statistical errors have to be reduced by enlarging the volume of the system. At constant density this requires a considerable increase in the number of particles and thus an extension of computer time.

Computer simulations offer the opportunity of analyzing the contributions of different parts of the pair potential to the magnitude of the macroscopic properties of a system. For KCl at 1045 K and a molar volume of 48.80 $cm^3\ mol^{-1}$, *Woodcock* and *Singer* calculated the following contributions (in $kJ\ mol^{-1}$) to the total potential energy of -655.5 kJ mol^{-1}: Coulomb term -724.4; repulsion K^+—K^+: 1.9; repulsion Cl^-—Cl^-: 2.6; repulsion K^+—Cl^-: 91.5; r^{-6} term: -23.7; r^{-8} term: -3.4. If the r^{-8} term, which contributes only 0.5% to the potential energy were neglected, the volume would be increased by about 5%.

In addition to the large number of simulations at normal pressure there are a few calculations for high pressures. The results of the high-pressure studies will be compared with experimental data in the next section.

Table 2. Monte Carlo results of *Woodcock* and *Singer* [39] and experimental data (cf. Ref.) for molten potassium chloride at 1045 K and 48.80 $cm^3 \cdot mol^{-1}$.

	MC	Exp.	Deviation [%]	Ref.
U/kJ mol^{-1}	−629.4	−625.5	− 0.6	[51]
P/bar	670	1.01	—	[52]
$10^6\ \kappa_T$/bar^{-1}	30.6	36.5	−16.2	[53]
$10^4\ \alpha_P$/K^{-1}	3.04	3.82	−20.4	[52]
β_V/bar K^{-1}	9.93	10.5	− 5.4	[52, 53]
C_P/$JK^{-1}\ mol^{-1}$	67.3	66.9	0.6	[51]
C_V/$JK^{-1}\ mol^{-1}$	51.7	46.9	10.2	[52]

2.3.3. Experimental Results

Thermodynamic data for molten salts at elevated pressures have exclusively been derived from *PVT* measurements which were made for the alkali metal nitrates[55-57], silver nitrate[55], some organic salts[58-60], bismuth trichloride[61], and potassium chloride[62] using various experimental techniques. At temperatures not too high above the melting temperature the density isotherms can be excellently represented by the Tait equation[64]:

$$[\rho(P)-\rho(P_0)]/\rho(P)=A\ln[(B+P)/(B+P_0)] \tag{16}$$

Here P_0 is a reference pressure (usually 1 bar), A and B are constants. The Tait equation has also been successfully used for fitting the density isotherms of other classes of liquids[65], although it gives an "unphysical" result in the limiting case of infinitely high pressure. For molten KCl the Tait equation was made an equation of state by allowing A and B to be functions of temperature. With

$$A(T)=A_0+A_1(T-T_F) \tag{17}$$

$$B(T)=B_0+B_1(T-T_F)+B_2(T-T_F)^2 \tag{18}$$

and the values for the constants given in Table 3 it is possible to fit the experimental *PVT* data for molten KCl up to 1325 K and 6 kbar with a standard deviation of 0.04%, which is one order of magnitude smaller than the experimental error (0.41%) at the highest pressure.

Table 3. Constants for the Tait equation of state with temperature dependent parameters A and B according to eqs. (16) to (18).

Constant	Value
T_F	1043.5 K
A_0	0.093619
A_1	$7.2495\times10^{-5}\ K^{-1}$
B_0	2750.5 bar
B_1	-3.8324 bar K^{-1}
B_2	3.4383×10^{-3} bar K^{-2}

The high accuracy of the *PVT* data and its analytical representation enables the calculation of other thermodynamic properties such as thermal expansion coefficient, compressibility, and internal pressure as functions of pressure and temperature for molten KCl as typical example of an ionic melt. Free energies, entropies, enthalpies, and molar heat capacities may be calculated for high pressures from their values at ordinary pressure using the well-known thermodynamic relations.

In Figure 5 the compressibility of KCl is plotted as a function of pressure for various constant temperatures. At low pressures the compressibility is substantially smaller than that of normal molecular liquids, but it becomes about the same at high pressures, thus indicating that the individual differences in the pair potentials become less important at high pressures where the compressibility is almost exclusively influenced by the repulsion forces determined by the size and shape of the particles.

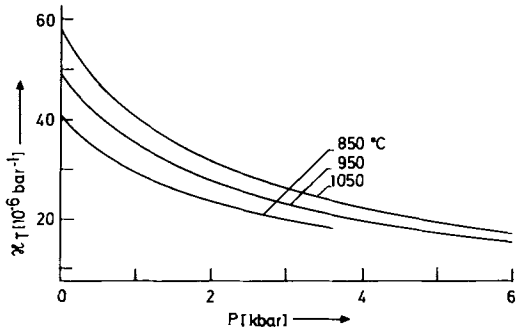


Fig. 5. Compressibility of molten potassium chloride [63].

The internal pressure of KCl at the melting point is 8.8 kbar. For molten alkali metal nitrates values of around 10 kbar were found[66], whereas the internal pressure for many simple molecular liquids lies between 2.5 and 3.5 kbar. From *PVT* measurements on molten tetraalkylammonium tetraalkylborate salts and their corresponding isoelectronic hydrocarbon-analogues it follows that the internal pressure of the salts is always higher by a factor of about 1.5 than that of the corresponding hydrocarbon[59]. For KCl, the internal pressure plotted as a function of molar volume exhibits a broad maximum which lies around 50 cm^3 mol^{-1}. It falls off slowly on the low density side of the maximum but it decreases rather steeply on the high density side. The latter feature was not found in the computer simulations[39]. From this and other observations it may be concluded that the repulsion term in the effective pair potential [eq. (13)] is too soft.

Figure 6 shows the molar heat capacity C_P of KCl at constant pressure. The values at normal pressure were calculated

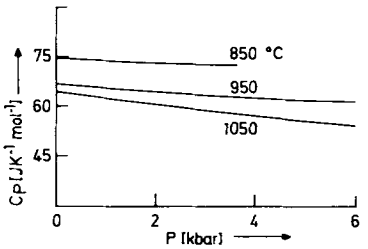


Fig. 6. Molar heat capacity of molten potassium chloride [63].

from velocity of sound measurements by *Bockris* and *Richards*[53]. C_P decreases with increasing pressure and temperature. A negative temperature dependence of C_P is unusual but was also found for $NaNO_3$ and KNO_3[67], for water[68], and for mercury[69]. The computer simulations for KCl[39] show the same trend. C_V also decreases when the temperature is raised.

The experimental results for KCl lend themselves for a comparison with computer simulation studies over broad temperature and density ranges. Table 4 shows a comparison of the *PVT* data with the best computed data. The difference between the measured densities and the values calculated by *Woodcock* and *Singer*[39], who applied the Monte Carlo method together with the Born-Mayer-Huggins potential is up to 2%. This corresponds to a pressure difference of about 850 bar. Monte Carlo calculations by *Larsen et al.*[70] show a deviation of about 4% in density. Other calculations[71–74], the results of which are not shown in the Table, deviate by as much as 15 percent in density. It appears that the Monte Carlo method used in combination with the Born-Mayer-Huggins pair potential yields results which are closer to the experimental values than those of other simulations and that the results for the thermodynamic properties in general are not improved when the polarizability of the ions is taken into account. Table 5 shows a comparison of calculated and measured values for some derived quantities. The trends in varia-

Table 4. *PVT* data for molten KCl. Comparison of computer simulation results with experimental values [63].

Ref.	T_{cal} [°C]	ρ_{cal} [g cm^{-3}]	P_{cal} [bar]	$\rho_{exp}(T_{cal}, P_{cal})$ [g cm^{-3}]	$\frac{100(\rho_{cal}-\rho_{exp})}{\rho_{exp}}$	$P_{exp}(T_{cal}, \rho_{cal})$ [bar]	$P_{cal}-P_{exp}$ [bar]
[39]	772	1.608	2820	1.635	−1.7	1967	853
	772	1.528	670	1.558	−2.0	29	641
	1033	1.528	3710	1.560	−2.0	2856	854
	1033	1.455	1440	1.465	−0.7	1260	180
	1033	1.389	(−30)	1.372	+1.3	195	−225
[70]	810	1.439	1	1.504	−4.3		
	810	1.491	810	1.544	−3.4		

Table 5. Comparison of computer simulation results [39] with experimental data [63] for molten KCl.

T [°C]	P [bar]	$10^4 \cdot \alpha_P$ [K^{-1}]		$10^6 \kappa_T$ [bar^{-1}]		β_V [bar K^{-1}]		P_i [kbar]		C_P [JK^{-1} mol^{-1}]	
cal	cal	cal	exp	cal	exp	cal	exp	cal	exp	cal	exp
772	2820	2.33	2.56	19.2	18.2	12.1	14.1	12.6	8.6	60.9	84.2
772	670	3.04	3.41	30.6	24.0	9.92	12.1	10.4	8.6	67.3	85.7
1033	3710	0.35	2.52	4.04	23.0	8.66	11.1	11.3	7.7	45.3	58.1
1033	1440	2.19	3.24	30.2	34.3	7.24	9.5	9.45	8.2	56.0	61.1
1033	(−30)	3.37	4.24	52.5	57.0	6.42	7.1	8.38	7.6	61.5	64.1

tion of the macroscopic properties thermal expansion coefficient, compressibility, thermal pressure coefficient and molar heat capacity with temperature and pressure are reproduced correctly by the simulations, but, in general, the deviations from the experimental values are larger than the experimental limits of error. The comparison thus leads to the conclusion that computer simulations do not produce results with an accuracy equal to that of careful experimental studies, even for the favorable case of a salt with spherical ions under conditions that are difficult from an experimental point of view.

Since PVT measurements on molten salts at high pressures are complicated and time consuming, it is highly desirable to have an empirical equation of state which can be used to estimate PVT data with an accuracy high enough to enable the evaluation and interpretation of other measurements. For this purpose the following equation proved to be very useful.

$$\rho(P,T)=\rho(P_0,T)/\{1-0.1\ln[1+10P\cdot\varkappa_T(P_0,T)]\} \tag{19}$$

It can be derived from eq. (16) by setting $A=0.1$ and $B(T)=0.1\,\varkappa_T^{-1}(P_0,T)$, where $\varkappa_T$ is the compressibility at normal pressure. Eq. (19) fits the measured densities of molten salts, including organic molten salts, with an accuracy of better than one percent in the pressure range up to 5 kbar. It can be assumed that it also enables the calculation of unknown PVT data with the same accuracy and that in this respect it is superior to the computer simulations.

3. Transport Properties

3.1. Statistical Treatment, Computer Simulations and Inelastic Neutron Scattering

For the statistical treatment of transport properties time-dependent distribution functions are needed which describe the dynamic behavior of the system. If the total potential energy of the system can be written as a sum of pair interactions it suffices to know the one- and two-particle functions in order to calculate macroscopic transport properties such as *e.g.* viscosity or thermal conductivity. An integrodifferential equation can be derived which contains both unknown distribution functions. In order to solve the equation, additional assumptions have to be made which can only be valid for limited ranges of the state variables. For dense, fluid phases *Rice* and *Alnatt* (cf. [28]) derived equations which enable the calculation of the transport coefficients from molecular parameters and from distribution functions. They split the pair potential into a repulsion term, which is represented by the hard sphere potential, and a soft attraction term, and then calculated the influences on the transport properties of the two parts of the potential independently. The transport coefficients calculated with the Rice-Alnatt equations deviate considerably from experimental values, even for simple liquids[28]. *Cafky* and *Babb*[76] calculated the transport coefficients of compressed gases using the Rice-Alnatt formalism. They obtained unphysical results, *e.g.* negative viscosities, when approaching liquid-like densities. Molecular dynamics calculations by *Smedley* and *Woodcock* on liquid argon and molten KCl demonstrated that cross-correlations of the forces originating from the repulsive and the attractive part of the potential are not negligible in either case and that thus one of the basic assumptions of the Rice-Alnatt theory is invalid[77].

While it is presently impossible to calculate a two-particle time-dependent distribution function by purely analytical methods or to link it with macroscopic transport properties in such a way as to give sufficiently accurate results, it is possible to establish relations between time-dependent distribution functions and physical properties of a substance which may be determined experimentally. Similarly to elastic neutron scattering, inelastic scattering enables the evaluation of a structure factor $S(\vec{Q},\omega)$ which not only depends on the transfer of momentum but also on the energy transfer $\hbar\omega$ during the scattering process. A two-particle correlation function $G(\vec{r},t)$ can be derived from the structure factor by double Fourier transformation. It is called the van Hove correlation function and measures the probability of finding a particle at $\vec{r}$ at a time t, when a particle is at $\vec{r}=0$ at $t=0$. At $t=0$ it is linked with the radial distribution function by the simple relation

$$G(\vec{r},0)=\delta(r)+\rho g(r)=G^s(\vec{r},0)+G^d(\vec{r},0) \tag{20}$$

in which the first term G^s describes the autocorrelation of single particles and the second term the cross-correlations between different particles. G^s can be obtained separately from the incoherent part of the neutron scattering.

For molten salts, three different functions $G_{\alpha\beta}(\vec{r},t)$ (α, $\beta=+,-$) are again needed for a complete description, which can only be evaluated from isotopic substitution experiments. Up to now, two inelastic neutron scattering experiments have been carried out for molten salts[78,79], both without isotopic substitution. *Price* and *Copley*[78] measured $S(\vec{Q},\omega)$ for RbBr, for which the scattering properties of the two nuclei are such that the experiment yields information on the density fluctuations in the melt. Both the scattering experiment as well as molecular dynamics calculations for this system[80] show that the density fluctuations are strongly attenuated and that they die off in very much the same way as in non-ionic systems. The limited Q-range and the limited accuracy of the experiments did not allow a calculation of $G(\vec{r},t)$. The second experiment was performed on KBr with the aim of gaining some information on charge fluctuations at high frequencies. Unfortunately, the accuracy of the experiment was insufficient for sound conclusions to be drawn.

Relations between macroscopic transport coefficients and (different) time-correlation functions of the equilibrium system can be established under the assumption that a perturbation caused by an external force is a linear function of the perturbing force and that the system responds to the perturbation in such a way as if it were generated by fluctuations in the equilibrium system (linear response theory). For the self-diffusion coefficient a relation (cf. [25])

$$D=\frac{kT}{m}\int_0^\infty Z(t)\,dt \tag{21}$$

to the normalized velocity autocorrelation function

$$Z(t)=\langle\vec{v}_i(t)\cdot\vec{v}_i(0)\rangle/\langle\vec{v}_i^2(0)\rangle \tag{22}$$

is derived in this way. The symbol $\langle\,\rangle$ denotes averaging over all the ions present as well as over different time origins.

For the specific electrical conductivity (dc) of a salt of type MX (alkali metal halides) one obtains

$$\sigma = \frac{\rho e^2}{\mu} \int_0^\infty J(t)\,\mathrm{d}t \tag{23}$$

where μ is the reduced mass of the two ions and

$$J(t) = \langle \vec{j}(t) \cdot \vec{j}(0) \rangle / \langle \vec{j}^2(0) \rangle \tag{24}$$

is the normalized autocorrelation function of the electric current

$$\vec{j}(t) = \sum_{i=1}^{N} z_i \vec{v}_i(t) \tag{25}$$

In eq. (25) the summation has to be carried out over all particles. $J(t)$ thus contains cross-correlation terms of the velocities of different particles. It can be shown that these terms are responsible for deviations from the Nernst-Einstein relation which are frequently found in the case of molten salts. For a model system of a molten salt in which the only difference between the two types of ions is the sign of their charge, this deviation may be expressed by Δ in

$$\sigma = \frac{\rho e^2}{kT}(D_+ + D_-)(1-\Delta) \tag{26}$$

Figure 7 shows the normalized autocorrelation functions of the velocity and electrical current from molecular dynamics calculations by *Hansen* and *McDonald*[80,81] for such a simple model system. The correlation functions become negative after a characteristic time interval. This means that, on average, after collisions with their neighbors the ions move in the opposite direction after this time has elapsed. For times longer than this, the correlation is lost completely. Figure 7 also shows the difference between the two functions from which $\Delta = 0.19$ is derived, a value which is almost identical with the experimental value for NaCl (0.18). *Ciccotti et al.*[83] carried out molecular dynamics calculations of transport properties using the more realistic pair potential from eq. (13). Table 6 shows their results for self-diffusion coefficients, specific conductivities, and viscosities and the good agreement with experimental data, especially for conductivity and viscosity.

Owing to the extraordinary long computing times necessary for calculation of the transport coefficients of molten salts, no temperature and density dependencies have been calculated as yet.

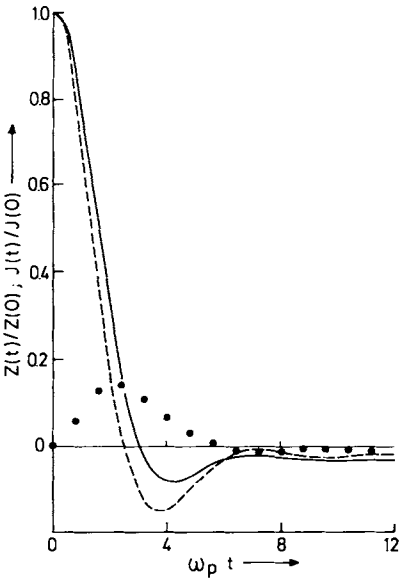


Fig. 7. Normalized autocorrelation functions of velocity (——) and of electric current (--------) and the difference between them (•••••) as function of time [81, 82]; $\omega_p^2 = 4\pi\rho e^2/m$.

3.2. Experimental Studies

For early measurements of the diffusion coefficients[84,85] and viscosities[86–88] of molten alkali metal nitrates at elevated pressures gases have been used as pressure transmitting media. During the measurements the gases dissolved in the molten salt and thus changed its properties considerably. The measured pressure dependencies of the transport coefficients depend on the type of gas and thus tell us very little about the pure salt.

Cleaver and *Herdlicka*[89] measured the interdiffusion coefficient of silver ions in molten alkali metal nitrates up to 1 kbar using a chronopotentiometric technique. The activation volume for the diffusion of silver ions increases from 5.6 cm^3 mol^{-1} in $NaNO_3$ to 13.7 cm^3 mol^{-1} in $CsNO_3$ and is thus always slightly greater than the activation volume of the molar conductivity of the respective pure solvent (cf. Table 8). It was thus concluded that the first coordination shell of the silver ions in the nitrates changes with size and polarizing power of the cations of the solvent.

The transport property of molten salts which has been studied most extensively at high pressures is the electrical conductivity. The specific conductivity of a molten salt may be written in the form

$$\sigma = \sum_i \rho_i |z_i| e \mu_i \tag{27}$$

Table 6. Comparison of transport coefficients from MD calculations [83] with experimental data [14].

Salt		T [K]	V [cm^3 mol^{-1}]	D_+ [10^{-5} cm^2 s^{-1}]	D_- [10^{-5} cm^2 s^{-1}]	σ [Ω^{-1} cm^{-1}]	η [10^{-3} kg m^{-1} s^{-1}]
LiF	cal.	1287	15.00	13.6	11.3	12.1	1.14
	exp.					9.3	
NaCl	cal.	1262	39.10	10.6	9.9	4.2	0.87
	exp.			14.0	10.1	4.2	0.83
NaI	cal.	1081	57.46	9.4	6.8	2.5	1.08
	exp.			10.5	5.9	2.7	1.01
RbCl	cal.	1119	56.48	5.0	5.2	1.81	0.99
	exp.			6.6	5.8	1.81	0.90

The summation is carried out over all types of ions i. The mobilities μ_i are not independent of each other. With $\rho_i = \nu_i \alpha \rho_0 = \nu_i \alpha N_A / V_m$, where ν_i is a stoichiometric coefficient, ρ_0 the number density of the molecules when the salt is completely undissociated, α the degree of ionization, N_A Avogadro's number, and V_m the molar volume, one obtains

$$\sigma = \sum_i \nu_i |z_i| e N_A \alpha \mu_i / V_m \tag{28}$$

From this equation it follows that the conductivity may be influenced by temperature and pressure in three ways by changing:

1. the molar volume,
2. the mobilities of the ions,
3. the degree of ionization.

In order to separate these three effects it is useful to study first of all those salts for which $\alpha = 1$, that is, which are completely dissociated into ions. This does not mean that the oppositely charged ions are greatly separated in space as in the case of dilute solutions. Here the absence of a peculiarity in the first peak of the partial radial distribution function g_{+-} at small values of r that correspond to the equilibrium distance of the ions in an isolated molecule could be used as a criterion for complete ionization. The conductivity of such salts has been studied extensively, among them the alkali metal halides[90-93], nitrates[94-99], other oxoanion salts[99-100], and a few organic salts[101,102]. Figure 8 shows as example the

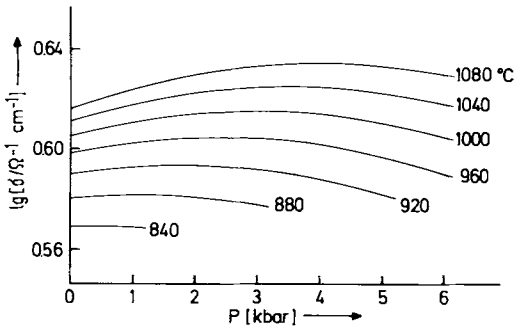


Fig. 8. Specific conductivity of molten sodium chloride [92].

specific conductivity of molten sodium chloride as a function of pressure up to 6 kbar for temperatures up to 1080 °C. At the lowest temperatures the conductivity decreases monotonously with increasing pressure. At higher temperatures it goes through a maximum which, with increasing temperature, becomes more pronounced and is shifted towards higher pressures. This behavior is caused by a superposition of the first and second of the three effects mentioned above. At lower temperature, where the density is high and the compressibility low, the pressure influence on the mobilities determines the pressure dependence of the conductivity over the whole pressure range. At high temperatures, where initially the density is lower and the compressibility higher, the influence on the molar volume is dominating, but at sufficiently high pressures the influence on the mobilities finally becomes the predominant one. Figure 9 shows the influence of the ionic sizes on the pressure dependence of the specific conductivity. Exchange of the anion in the series of sodium salts has only a small effect; the maximum is slightly shifted towards lower pressures with increasing size of the anion. In contrast, exchange of the cation in the sequence of chlorides strongly alters the pressure dependence of the conductivity. KCl still exhibits a slight maximum at the temperature chosen in Figure 9, whereas the conductivities of RbCl and CsCl fall monotonously over the whole pressure range. At still

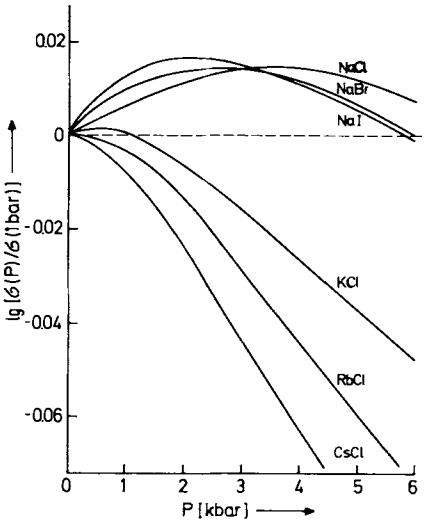


Fig. 9. Influence of the ionic sizes on the pressure dependence of the specific conductivity of molten alkali metal halides at 1040 °C [92].

higher temperatures, where measurements are not yet available, the conductivities of these salts would also show a maximum at intermediate pressures. Maxima in the conductivities when plotted against pressure were not found for the nitrates and other salts of oxoacids. These salts could only be studied over narrow temperature ranges because they start to decompose at relatively low temperatures (exception: lithium salts).

Whether the explanation given for the appearance of the maximum of the specific conductivity is correct or not can be proven by a discussion of the molar conductivity Λ, which is calculated from the specific conductivity by multiplication with the corresponding molar volume

$$\Lambda = \sigma \cdot V_m = \sum_i \nu_i |z_i| e N_A \alpha \mu_i \tag{29}$$

If $\alpha = 1$, the pressure dependence of this quantity should reflect the pressure dependence of the ionic mobility alone. Figure 10 shows the molar conductivity of NaCl as example. In fact, the maximum disappeared and the mobilities decrease monotonously over the whole pressure range.

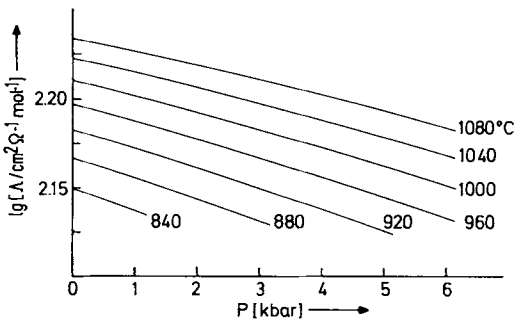


Fig. 10. Molar conductivity of molten sodium chloride [92].

Pressure and temperature dependencies of the conductivity may conveniently be expressed by the activation volume ΔV_Λ and the isobaric and isochoric activation energies, $(E_\Lambda)_P$ and $(E_\Lambda)_V$, respectively, which are defined as

$$\Delta V_\Lambda = -RT(\partial \ln \Lambda/\partial P)_T$$
$$(E_\Lambda)_P = -R(\partial \ln \Lambda/\partial(1/T))_P \quad (30)$$
$$(E_\Lambda)_V = -R(\partial \ln \Lambda/\partial(1/T))_V$$

As can be seen from the slopes of the isotherms in Figure 10, ΔV_Λ decreases with increasing temperature and is not completely independent of pressure. The activation energies increase with increasing pressure.

Table 7. Activation volume and energies for molten alkali metal halides at 1000 °C and 5 kbar [92].

	ΔV_Λ [cm³ mol⁻¹]			$(E_\Lambda)_P$ [kJ mol⁻¹]			$(E_\Lambda)_V$ [kJ mol⁻¹]		
	Cl	Br	I	Cl	Br	I	Cl	Br	I
Na	2.6	3.2	3.8	13.1	13.0	12.3	7.8	6.1	5.7
K	4.8	5.9	6.9	17.0	18.2	17.8	9.6	6.7	6.3
Rb	6.0	6.4	7.4	18.6	18.6	18.7	7.5	5.5	6.2
Cs	7.0	8.6	8.7	19.2	19.4	19.3	7.4	7.3	7.7

The activation parameters evaluated for the alkali metal halides at 1000 °C and 5 kbar are collected in Table 7. The activation volume increases with increasing ionic size. The influence of the anion is much weaker than that of the cation. The activation energies are not strongly dependent on the ionic sizes except for the lithium salts. A similar picture is obtained for the alkali metal nitrates, the activation parameters of which are listed in Table 8. Lithium nitrate has a very small activation volume and a markedly higher isochoric activation energy than the other nitrates. This is due to the small size of the lithium ions (ionic radius: 60 pm) which allows for considerable shorter distances between the oppositely charged ions, thus leading to stronger Coulombic attrac-

Table 8. Activation volume and energies for molten alkali metal nitrates at 400 °C and 1 bar [96].

	ΔV_Λ [cm³ mol⁻¹]	$(E_\Lambda)_P$ [kJ mol⁻¹]	$(E_\Lambda)_V$ [kJ mol⁻¹]	$(E_\Lambda)_V/(E_\Lambda)_P$
$LiNO_3$	0.7	15.1	14.6	0.97
$NaNO_3$	3.7	13.4	8.8	0.66
KNO_3	6.3	15.5	7.9	0.51
$RbNO_3$	7.2	16.7	7.5	0.45
$CsNO_3$ [a]	8.3	15.3	7.1	0.46

[a] At 450 °C.

tions. The last column in Table 8 gives the ratio of the isochoric to isobaric activation energy which measures the fraction of the isobaric energy of a particular melt not needed for a volume increase. For other series of completely ionized salts one finds, with a few explainable exceptions, the same dependence of the activation parameters on the ionic sizes. Thus a good estimate of the temperature and pressure dependencies of the molar conductivity seems to be feasible also for those salts for which measurements have not yet been made.

For all the salts studied so far which do not tend to form glasses, the activation volume is about 10% of the molar volume or less, whereas in solid ionic conductors (except superionic conductors) it reaches about 50% of the molar volume. If this difference were due to the volume increase upon melting, which creates the opportunity for voids of the size of the ions to be formed in the melt by thermal density fluctuations, it should be likely that a change in the charge transport mechanism is observed at very high densities, where the voids become too small to accomodate the ions. To check this, the conductivity of KCl was measured up to pressures of 50 kbar and temperatures of 1500 °C in a belt-type high-pressure apparatus[103]. Figure 11 shows the result of this investigation. The slopes of the conductivity isotherms change only slightly. There is no indication of a drastic change in the conduction mechanism, although the highest densities reached are higher than the density of crystalline KCl under normal conditions.

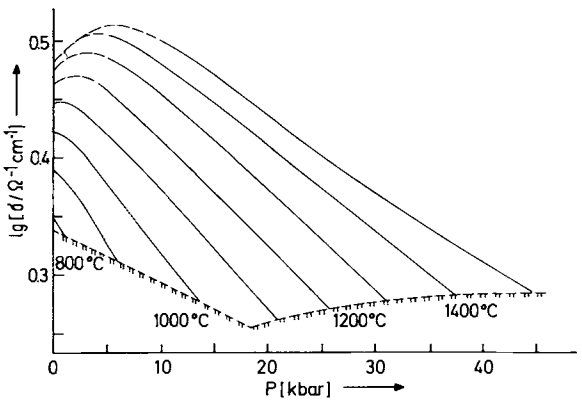


Fig. 11. Specific conductivity of molten potassium chloride up to pressures of 50 kbar [103].

Earlier measurements on the alkali metal nitrates[98] up to 50 kbar showed a change in the activation volume of the conductivity to half its low-pressure value within a pressure interval of about 5 kbar. The change was found around 20 kbar for $NaNO_3$, around 14 kbar for KNO_3 and around 9 kbar for $RbNO_3$. For $LiNO_3$ it was not observed in the pressure range covered by the experiments. The behavior found for the nitrates is most probably due to a change in the rotational motion of the nitrate ion when the density is raised.

From conductivity measurements on the lithium halides up to 1 kbar by *Cleaver et al.*[91] and to 6 kbar by *Ransford et al.*[93] it follows that for these salts not only the specific conductivity but also the molar conductivity goes through a maximum as a function of pressure, as is shown in Figure 12 for LiBr. This behavior is probably due to the high polarizing power of the lithium ions which leads to a particularly strong interaction between the lithium ion and one of the anions in its first coordination shell. When the density is increased the average distance of all the other nearest neighbors from the lithium ion decreases and this reduces the effect mentioned and makes the lithium ion more mobile. A similar effect has been found in alkali metal halide crystals which were doped with the respective lithium salt. In these crystals the lithium ion is not positioned exactly at its lattice site but is slightly shifted towards one of its neighboring anions. Upon compression of the crystal its equilibrium position moves towards the lattice site and the lithium ion simultaneously becomes more mobile[104, 105]. This observation de-

monstrates the limitation of the concept of splitting the influence of pressure on the molar conductivity into two parts, one due to a change in the ionization equilibrium and the

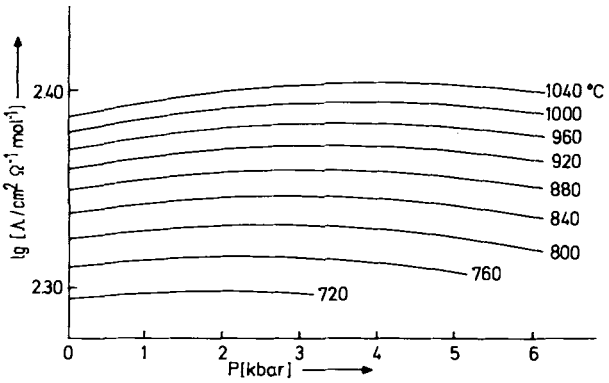


Fig. 12. Molar conductivity of molten lithium bromide [93].

other due to a change of the mobility. The model used to explain the increase of the molar conductivity of the lithium halides can be interpreted as an increase of the mobility as well as a change in the ionization equilibrium.

4. The Transition from an Insulator to an Ionic Conductor

As has been mentioned in the introduction, a salt undergoes a transition from an insulator to an ionic conductor when the density is changed from low to high values. The transition is a consequence of the increasing dissociation of the salt molecules into ions. At low temperatures the transition is discontinuous when the saturation density of the vapor is reached and the salt condenses. At supercritical temperatures, however, the transition is totally continuous. Measurements of the specific conductivity and of PVT data in this region can yield information about the ionization equilibrium as a function of density, especially at which densities the transition occurs. The most suitable salts for such an investigation are the alkali metal halides. Unfortunately, their critical temperatures are estimated to lie around 3000 K[106], too high for static high-pressure experiments. The alkali metal nitrates and other oxoanion salts start to decompose at temperatures well below their critical temperature. The first measurements in the supercritical temperature range of a molten salt have therefore been carried out on bismuth trichloride[61,107], which has a critical temperature of 905 °C and which is a reasonably good ionic conductor at its ordinary melting point ($\sigma = 0.4\ \Omega^{-1}\ cm^{-1}$). The result of this difficult experimental investigation is shown in Figure 13, where the specific conductivity of $BiCl_3$ is plotted as a function of temperature up to 1200 °C at several constant pressures up to 4 kbar. The conductivity changes by six orders of magnitude in the range covered by the measurements. Such a strong variation cannot be accounted for by the mobility effect discussed in the preceding Section. Figure 13 shows that the conductivity is extremely temperature- and pressure-dependent in the vicinity of the critical point (CP), where the density changes rapidly. The molar conductivity can be calculated from the specific conductivity and the molar volume[61] which has been measured over the same temperature and pressure ranges. It increases by five orders of magnitude when the density increases by about a factor of twenty at constant temperature, goes through a maximum and finally decreases again, since at sufficiently high densities the salt is completely ionized and the density influence on the mobility alone determines the behavior of the molar conductivity. In this range the activation volume (3.5 $cm^3\ mol^{-1}$) and the isobaric activation energy (10.9 kJ mol^{-1}) have values which are typical for completely ionized salts, whereas at low densities the isobaric activation energy can be as high as 50 kJ mol^{-1} and the activation volume has strongly negative values.

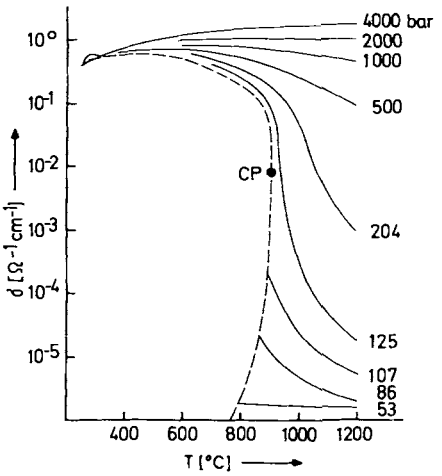


Fig. 13. Specific conductivity of bismuth trichloride in the supercritical temperature range [107].

With the reasonable assumption that the dissociation reaction is

$$2\,BiCl_3 \rightleftarrows BiCl_2^+ + BiCl_4^-$$

and with an estimate of the ionic mobilities, the degree of ionization of the salt can be estimated using eq. (29). The result is shown in Figure 14, where the degree of ionization is

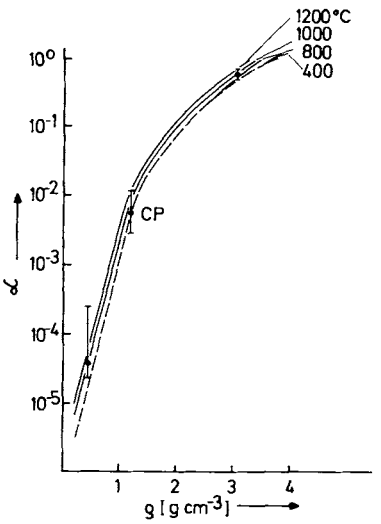


Fig. 14. Degree of dissociation of bismuth trichloride [107].

plotted as a function of density together with the respective error bars caused by the uncertainty of the mobilities. At the highest densities the degree of ionization reaches the value one, whereas at a density of 0.2 g cm^{-3} it is about 10^{-5}. The strong variation of the ionization equilibrium in favor of the ions with rising density is a consequence of the large volume shrinkage due to the dissociation reaction. The ions formed cause an electrostriction effect on the remaining molecules which are forced into the solvation shells of the ions. At constant density the degree of ionization increases only slightly with rising temperature. At the critical point (CP) only one percent of the $BiCl_3$ molecules are ionized. Bismuth trichloride is thus an essentially molecular liquid at its critical point.

The result obtained for bismuth trichloride raises the question, how the dissociation equilibrium is changed with density and at which density complete ionization ($\alpha = 1$) is reached for other salts which are either better or poorer conductors at normal pressure. As has already been mentioned no information is available for the alkali halides. However, *Buback* and *Franck* measured the electrical conductivity[108] and the density[109] of molten NH_4Cl, which may be regarded as a pseudo alkali metal halide. This salt, when heated under pressures higher than about 50 bar, melts to form an ionic melt. Its conductivity was measured along the saturation line up to 30 K below its critical temperature of 1155 K. The conductivity increases monotonously up to that temperature, contrary to that found in the case of $BiCl_3$ (Fig. 13) and other molten salts[110-112]. NH_4Cl thus appears to be an essentially ionic liquid at its critical point.

The molten mercury(II) halides are poor conductors at their normal melting points (cf. Table 9) indicating that only a small fraction of the molecules is dissociated into ions. Their conductivities were measured as a function of pressure[113-115]. They strongly increase with increasing pressure, *e.g.* by two and a half orders of magnitude in the case of $HgBr_2$ in the pressure range up to 6 kbar. The molar conductivity goes through a maximum when plotted as a function of density, like in the case of $BiCl_3$. At the point of maximum conductivity these salts are also almost completely ionized, and at still higher densities the mobility effects governs the density dependence of the molar conductivity. The maximum is found for HgI_2 at 9.5 kbar[116]. The density dependence of the molar conductivity enables an estimate of the density at which a salt is completely ionized. This density devided by the critical density is listed in Table 9 for various salts.

A behavior similar to that just discussed for the mercuric halides is also observed for a number of other molten salts which are not completely ionized at ordinary pressure, among them AlI_3, GaI_3, InI_3, BiI_3 and CdI_2 whose conductivities were measured by *Cleaver et al.*[117] up to 1 kbar. It may be suspected, therefore, that many other substances whose molecules consist of at least two different atoms with appreciably different electronegativities and which are not or only slightly ionized at ordinary conditions approach the completely ionized state as the density is increased to sufficiently high values. In fact, measurements of the conductivity of pure water up to 1000 °C and 100 kbar by *Holzapfel* and *Franck*[118] demonstrated that the ionic product of water under these conditions, where the density is about 1.6 g cm^{-3}, is by about twelve orders of magnitude higher than for liquid water under normal conditions. More than 0.1% of the H_2O molecules are ionized under the conditions quoted. Shock wave measurements[119] have shown that water reaches complete ionization at about 1.92 g cm^{-3}. Conductivity measurements on ammonia[120] indicated that this substance approaches complete ionization at a density of about 1.7 g cm^{-3}.

The examples just mentioned show that there is no qualitative difference in the ionization behavior of substances which are very dissimilar under normal conditions of pressure and temperature, *e.g.* NH_4Cl and water or typical molten salts and polar liquids. The values listed in Table 9, however, also demonstrate that much higher reduced densities and thus very high pressures are needed in order to force pure polar liquids into a completely ionized state, whereas typical molten salts may be completely ionized at densities considerably lower than their normal liquid density, which corresponds to a reduced density of about three.

Table 9. Dissociation behavior of molten salts and polar liquids: order of magnitude of the specific conductivity at normal pressure (column 2) and reduced density $\rho_r = \rho/\rho_c$ at which ionization is complete (column 3).

	$\sigma/\Omega^{-1}\,cm^{-1}$	ρ_r
NH_4Cl	1	≈ 1
$BiCl_3$	10^{-1}	3.2
HgI_2	10^{-2}	3.9
$HgBr_2$	10^{-3}	4.2
$HgCl_2$	10^{-5}	4.4
H_2O	10^{-7}	6.3
NH_3		≈ 7

5. Outlook

It is obvious that progress in the investigation of the static and dynamic properties of molten salts and their temperature and density dependencies has been rather rapid during the last few years. The computer simulation techniques have proven to be excellent mediators between theoretical and experimental studies, because they yield "exact" values for simple model systems which provide a means of testing the quality of approximations in the theoretical treatment of such systems, and, on the other hand, allow conclusions to be drawn about the applicability of effective pair potentials for more realistic ionic systems by comparing the results with experimental values. It can be assumed that the methods developed for simple molten salts will be improved and supplemented in such a way that they can also be used for more complicated molten salts and their mixtures in order to elucidate the relations between their microscopic structure and their macroscopic properties. In view of current developments regarding the use of such molten salts, not only for traditional applications but also on a large scale for batteries and fuel cells, for coal gasification and desulphurization, for scrubbing of stack gases, and for heat storage, this would constitute a great success in this field of chemistry.

Received: June 16, 1980 [A 330 IE]
German version: Angew. Chem. 92, 612 (1980)

[1] *H. Bloom, I. K. Snook,* Mod. Aspects Electrochem. 9, 159 (1974).
[2] *M. Blander:* Molten Salt Chemistry. Wiley-Interscience, New York 1964.

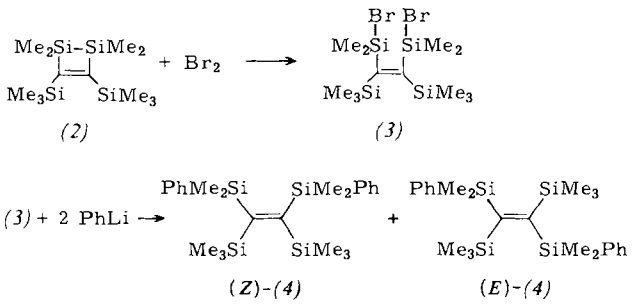
[3] *B. R. Sundheim:* Fused Salts. McGraw-Hill, New York 1964.
[4] *G. Mamantov:* Molten Salts; Characterization and Analysis. Marcel Dekker, New York 1969.
[5] *J. Lumsden:* Thermodynamics of Molten Salt Mixtures. Academic Press, New York 1966.
[6] *O. J. Kleppa,* Annu. Rev. Phys. Chem. *16*, 187 (1965).
[7] *M. Blander,* Adv. Chem. Phys. *11*, 83 (1967).
[8] *K. Luks, H. Davis,* Ind. Eng. Chem. Fundam. *6*, 194 (1967).
[9] *D. M. Gruen,* Q. Rev. Chem. Soc. *19*, 349 (1965).
[10] *W. Sundermeyer,* Angew. Chem. *77*, 241 (1965); Angew. Chem. Int. Ed. Engl. *4*, 222 (1965).
[11] *A. D. Graves, G. J. Hills, D. Inman,* Adv. Electrochem. Electrochem. Eng. *4*, 116 (1966).
[12] *R. A. Bailey, G. J. Janz,* Chem. Non-Aqueous Solvents *1*, 291 (1966).
[13] *G. J. Janz, R. D. Reeves,* Adv. Electrochem. Electrochem. Eng. *5*, 137 (1967).
[14] *G. J. Janz:* Molten Salts Handbook. Academic Press, New York 1967.
[15] *W. Kutzelnigg:* Einführung in die Theoretische Chemie, Vol. *2*. Verlag Chemie, Weinheim 1978.
[16] *J. P. Hansen, I. R. McDonald:* Theory of Simple Liquids. Academic Press, London 1976.
[17] *F. Vesely:* Computerexperimente an Flüssigkeitsmodellen. Physik Verlag, Weinheim 1978.
[18] *F. Kohler:* The Liquid State. Verlag Chemie, Weinheim 1972.
[19] *L. V. Woodcock,* J. Chem. Soc. Faraday Trans. II *70*, 1405 (1974).
[20] *M. J. L. Sangster, M. Dixon,* Adv. Phys. *25*, 247 (1976).
[21] *L. V. Woodcock,* Adv. Molten Salt Chem. *3*, 1 (1975).
[22] *F. G. Fumi, M. P. Tosi,* J. Phys. Chem. Solids *21*, 31 (1964).
[23] *M. P. Tosi, F. G. Fumi,* J. Phys. Chem. Solids *21*, 45 (1964).
[24] *J. E. Enderby, D. M. North, P. A. Egelstaff,* Philos. Mag. *14*, 961 (1966).
[25] *M. Parrinello, M. P. Tosi,* Riv. Nuovo Cimento Soc. Ital. Fis. *2*, 1 (1979).
[26] *R. A. Howe* in *C. A. Croxton:* Progress in Liquid Physics, p. 503. Wiley, New York 1978.
[27] *D. I. Page, K. Mika,* J. Phys. *C4*, 3034 (1971).
[28] *J. Y. Derrien, J. Dupuy,* J. Phys. Orsay Fr. *36*, 191 (1975).
[29] *F. G. Edwards, J. E. Enderby, R. A. Howe, D. I. Page,* J. Phys. *C8*, 3483 (1975).
[30] *E. W. J. Mitchell, P. F. J. Poncet, R. J. Stewart,* Philos. Mag. *34*, 721 (1976).
[31] *J. Y. Derrien, J. Dupuy,* Phys. Chem. Liq. *1976*, 71.
[32] *F. G. Edwards, R. A. Howe, J. E. Enderby, D. I. Page,* J. Phys. *C11*, 1053 (1978).
[33] *K. Kawamura, I. Okada,* At. Energy Rev. *16*, 209 (1978).
[34] *J. W. E. Lewis, K. Singer, L. V. Woodcock,* J. Chem. Soc. Faraday Trans. II *71*, 301 (1975).
[35] *A. Rahman, R. H. Fowler, A. H. Narten,* J. Chem. Phys. *57*, 3010 (1972).
[36] *S. W. de Leeuw,* Mol. Phys. *36*, 103 (1978).
[37] *S. W. de Leeuw,* Mol. Phys. *36*, 765 (1978).
[38] *H. van Wechem,* Thesis, Amsterdam 1976.
[39] *L. V. Woodcock, K. Singer,* Trans. Faraday Soc. *67*, 12 (1971).
[40] *J. K. Percus, G. J. Yevick,* Phys. Rev. *110*, 1 (1958).
[41] *J. A. Barker, D. Henderson,* Rev. Mod. Phys. *48*, 587 (1976).
[42] *B. Larsen,* J. Chem. Phys. *65*, 3431 (1976).
[43] *M. J. Gillan,* Phys. Chem. Liq. *8*, 121 (1978).
[44] *E. Waisman, J. L. Lebowitz,* J. Chem. Phys. *52*, 4307 (1970).
[45] *E. Waisman, J. L. Lebowitz,* J. Chem. Phys. *56*, 3086, 3093 (1972).
[46] *M. C. Abramo, C. Caccamo, G. Pizzimenti, M. Parrinello, M. P. Tosi,* J. Chem. Phys. *68*, 2889 (1978).
[47] *J. S. Høje, G. Stell,* J. Chem. Phys. *67*, 524 (1977).
[48] *B. Larsen, G. Stell, K. C. Wu,* J. Chem. Phys. *67*, 530 (1977).
[49] *B. Larsen,* J. Chem. Phys. *68*, 4511 (1978).
[50] *D. Levesque, J. J. Weis, J. P. Hansen* in *K. Binder:* Monte Carlo Methods in Statistical Physics, p. 47. Springer-Verlag, Berlin 1979.
[51] *K. K. Kelley,* U. S. Bur. Mines Bull. No. 584 (1960).
[52] *E. R. Van Artsdalen, I. S. Yaffe,* J. Phys. Chem. *59*, 118 (1955).
[53] *J. O'M. Bockris, N. E. Richards,* Proc. Roy. Soc. *A 241*, 44 (1957).
[54] *L. Schäfer, A. Klemm,* Z. Naturforsch. *A 31*, 1068 (1976).
[55] *B. B. Owens,* J. Chem. Phys. *44*, 3918 (1966).
[56] *A. F. M. Barton, G. J. Hills, D. J. Fray, J. W. Tomlinson,* High Temp. High Pressures *2*, 437 (1970).
[57] *J. E. Bannard, A. F. M. Barton,* J. Chem. Soc. Faraday Trans. I *74*, 153 (1978).
[58] *S. W. Rudich, J. E. Lind, Jr.,* J. Chem. Phys. *50*, 3035 (1969).
[59] *T. Grindley, J. E. Lind, Jr.,* J. Chem. Phys. *56*, 3602 (1972).
[60] *A. F. M. Barton, R. J. Speedy,* J. Chem. Soc. Faraday Trans. I *70*, 506 (1974).
[61] *G. Treiber, K. Tödheide,* Ber. Bunsenges. Phys. Chem. *77*, 1079 (1973).
[62] *G. Goldmann, K. Tödheide,* Z. Naturforsch. *A 31*, 656 (1976).
[63] *G. Goldmann, K. Tödheide,* Z. Naturforsch. *A 31*, 769 (1976).
[64] *P. G. Tait:* Scientific Papers, Vol. *2*, p. 334. Cambridge University Press 1898.
[65] *E. Kuss, M. Taslimi,* Chem. Ing. Tech. *42*, 1073 (1970).
[66] *J. E. Bannard,* J. Chem. Soc. Faraday Trans. I *74*, 163 (1978).
[67] *E. W. Dewing,* J. Chem. Eng. Data *20*, 221 (1975).
[68] *G. S. Kell* in *F. Franks:* Water, a Comprehensive Treatise, Vol. *1*, p. 363. Plenum Press, New York 1972.
[69] *T. B. Douglas, A. F. Ball, D. C. Ginnings,* J. Res. Nat. Bur. Stand. *46*, 334 (1951).
[70] *B. Larsen, T. Førland, K. Singer,* Mol. Phys. *26*, 1521 (1973).
[71] *D. J. Adams, I. R. McDonald,* J. Phys. *C7*, 2761 (1974).
[72] *S. Romano, I. R. McDonald,* Physica (Amsterdam) *76*, 625 (1973).
[73] *S. Romano, C. Margheritis,* Physica (Amsterdam) *77*, 557 (1974).
[74] *J. W. E. Lewis,* private communication 1974.
[75] *M. Dixon, M. J. L. Sangster,* J. Phys. *C9*, L5 (1976).
[76] *J. W. Cafky, S. E. Babb, Jr.,* J. Chem. Phys. *66*, 5137 (1977).
[77] *S. I. Smedley, L. V. Woodcock,* J. Chem. Soc. Faraday Trans. II *70*, 955 (1974).
[78] *D. L. Price, J. R. D. Copley,* Phys. Rev. *A 11*, 2124 (1975).
[79] *J. R. D. Copley, G. Dolling,* J. Phys. *C 11*, 1259 (1978).
[80] *J. R. D. Copley, A. Rahman,* Phys. Rev. *A 13*, 2276 (1976).
[81] *J. P. Hansen, I. R. McDonald,* J. Phys. *C7*, L384 (1974).
[82] *J. P. Hansen, I. R. McDonald,* Phys. Rev. *A 11*, 2111 (1975).
[83] *G. Ciccotti, G. Jacucci, I. R. McDonald,* Phys. Rev. *A 13*, 426 (1976).
[84] *S. B. Tricklebank, L. Nanis, J. O'M. Bockris,* Rev. Sci. Instrum. *35*, 807 (1964).
[85] *M. K. Nagarajan, J. O'M. Bockris,* J. Phys. Chem. *70*, 1854 (1966).
[86] *J. L. Copeland, J. B. Christie,* J. Phys. Chem. *73*, 1205 (1969).
[87] *J. L. Copeland, J. B. Christie,* J. Phys. Chem. *75*, 103 (1971).
[88] *J. L. Copeland, J. B. Christie,* J. Chem. Phys. *55*, 4925 (1971).
[89] *B. Cleaver, C. Herdlicka,* J. Chem. Soc. Faraday Trans. I *72*, 1861 (1976).
[90] *J. E. Bannard, G. J. Hills,* High Temp. High Pressures *1*, 571 (1969).
[91] *B. Cleaver, S. I. Smedley, S. N. Spencer,* J. Chem. Soc. Faraday Trans. I *68*, 1720 (1972).
[92] *R. Schamm, H. P. Vögele, W. Edelböck, K. Tödheide,* Ber. Bunsenges. Phys. Chem., in press.
[93] *H. C. Ransford, H. P. Vögele, K. Tödheide,* Ber. Bunsenges. Phys. Chem., in press.
[94] *A. F. M. Barton, B. Cleaver, G. J. Hills,* Trans. Faraday Soc. *64*, 208 (1968).
[95] *J. E. Bannard, A. F. M. Barton, G. J. Hills,* High Temp. High Pressures *3*, 65 (1971).
[96] *A. S. Quist, A. Würflinger, K. Tödheide,* Ber. Bunsenges. Phys. Chem. *76*, 652 (1972).
[97] *G. Schlichthärle, K. Tödheide, E. U. Franck,* Ber. Bunsenges. Phys. Chem. *76*, 1168 (1972).
[98] *V. Pilz, K. Tödheide,* Ber. Bunsenges. Phys. Chem. *77*, 29 (1973).
[99] *B. Cleaver,* J. Chem. Soc. Faraday Trans. I *75*, 2735 (1979).
[100] *R. Schamm, K. Tödheide,* High Temp. High Pressures *8*, 59 (1976).
[101] *A. F. M. Barton, R. J. Speedy,* J. Chem. Soc. Faraday Trans. I *70*, 506 (1974).
[102] *R. J. Speedy,* J. Chem. Soc. Faraday Trans. I *73*, 471 (1977).
[103] *R. Schamm,* Dissertation, Universität Karlsruhe 1978.
[104] *K. Thörmer, F. Lüty,* Phys. Status Solidi *B 90*, 277 (1978).
[105] *U. Holland, F. Lüty,* Phys. Rev. *B 19*, 4298 (1979).
[106] *P. J. McGonigal,* J. Phys. Chem. *67*, 1931 (1963).
[107] *G. Treiber, K. Tödheide,* Ber. Bunsenges. Phys. Chem. *77*, 540 (1973).
[108] *M. Buback, E. U. Franck,* Ber. Bunsenges. Phys. Chem. *77*, 1074 (1973).
[109] *M. Buback, E. U. Franck,* Ber. Bunsenges. Phys. Chem. *76*, 350 (1972).
[110] *L. F. Grantham, S. J. Yosim,* J. Phys. Chem. *72*, 762 (1968).
[111] *L. F. Grantham, S. J. Yosim,* J. Phys. Chem. *67*, 2506 (1963).
[112] *L. F. Grantham, S. J. Yosim,* J. Chem. Phys. *45*, 1192 (1966).
[113] *B. Cleaver, S. I. Smedley,* Trans. Faraday Soc. *67*, 1115 (1971).
[114] *J. E. Bannard, G. Treiber,* High Temp. High Pressures *5*, 177 (1973).
[115] *B. Bardoll, K. Tödheide,* Ber. Bunsenges. Phys. Chem. *79*, 490 (1975).
[116] *P. Zani,* Thesis, University of Southampton 1977.
[117] *B. Cleaver, P. N. Spencer, M. A. Quddus,* J. Chem. Soc. Faraday Trans. I *74*, 686 (1978).
[118] *W. Holzapfel, E. U. Franck,* Ber. Bunsenges. Phys. Chem. *70*, 1105 (1966).
[119] *S. D. Hamann, M. Linton,* Trans. Faraday Soc. *65*, 2186 (1969).
[120] *D. Severin,* Dissertation, Universität Karlsruhe 1971.

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Unusually Rapid *cis-trans* Isomerization of a Tetrasilylated Ethylene: Generation of Free Radicals During the Rotation[1]

By *Hideki Sakurai, Hiromi Tobita, Mitsuo Kira,* and *Yasuhiro Nakadaira*[*]

In a previous paper, we described the preparation and some properties of tetrakis(trimethylsilyl)ethylene *(1)* and related compounds including anion and cation radicals of *(1)*[2]. In this paper, we report the fast *cis-trans* isomerization of tetrasilylated ethylenes *(4)* and generation of free radicals during rotation around the double bond.



Scheme 1

(*Z*)-1,2-Bis[dimethyl(phenyl)silyl]-1,2-bis(trimethylsilyl)-ethylene (*Z*)-*(4)* was prepared according to Scheme 1 from 1,1,2,2-tetramethyl-3,4-bis(trimethylsilyl)-1,2-disila-3-cyclobutene *(2)*[3]. The reaction mixture contains almost only (*Z*)-isomer (NMR); however, after 3 h (the minimum time to separate and purify each isomer by TLC at room temperature) the ratio of (*Z*)-*(4)* to (*E*)-*(4)* was 90:10. Each isomer isomerizes to the same 60:40 (*Z*)/(*E*) mixture within 3 days at room temperature.

$$(Z)\text{-}(4) \underset{k'}{\overset{k}{\rightleftharpoons}} (E)\text{-}(4)$$

The rate constants of isomerization, k and k', were determined at 68 °C to be 3.7×10^{-4} s^{-1} and 5.6×10^{-4} s^{-1}, respectively. The activation energy is 30 kcal·mol^{-1}. The remarkably low activation energy is an indication that the olefin is very crowded.

Interestingly, *cis-trans* isomerization also takes place photochemically. Irradiation of either (*Z*)-*(4)* or (*E*)-*(4)* with a 500-W high-pressure mercury lamp for 45 min at room temperature resulted in equilibration with (*Z*)/(*E*) = 40:60. The photochemical equilibrium constant is different from the thermal one, for reasons which are still unclear.

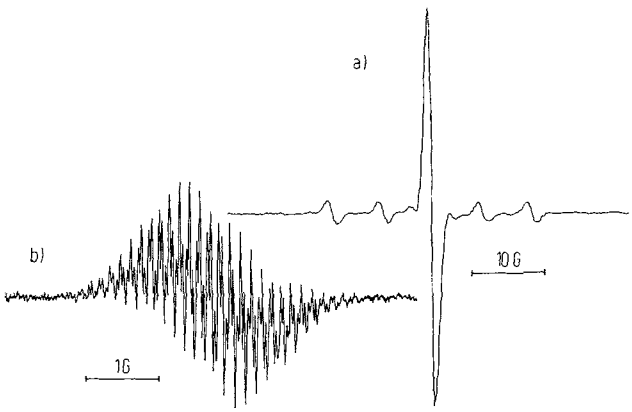


Fig. 1. ESR spectrum of *(5)*: a) Full spectrum; b) expanded spectrum of the central line.

The parent compound in the series, *viz. (1)*, shows very interesting phenomena related to the very facile isomerization of *(4)*. Thus, when *(1)* was heated neat or in decalin at about 150 °C, a strong ESR signal of the persistent radical *(5)* appeared (Fig. 1). The spectral parameters agree well with those reported previously for *(5)* by *Griller* and *Ingold*[4] (values in parentheses): $a^{29}_{Si} = 13.58$ (13.71) G, $a^{29}_{Si} = 27.75$ (27.59) G, $a_{^{13}C} = 4.8$ (4.88) G, $a_H = 1.4$ (1.35) G.

$$(Me_3Si)_2C{=}C(SiMe_3)_2 \rightleftharpoons (Me_3Si)_2\overset{\odot}{C}\text{–}\overset{\odot}{C}(SiMe_3)_2$$
(1)

$$(Me_3Si)_2\overset{\odot}{C}\text{–}\overset{\odot}{C}(SiMe_3)_2 \xrightarrow{RH} (Me_3Si)_2CH\text{–}\overset{\odot}{C}(SiMe_3)_2$$
(5)

Apparently *(1)* can abstract hydrogen during the rotation.

Received: April 2, 1980 [Z 513 IE]
German version: Angew. Chem. 92, 632 (1980)

CAS Registry numbers:
(1), 74465-53-5; *(2)*, 62346-43-4; *(3)*, 74465-54-6; *Z-(4)*, 74465-55-7; *E-(4)*, 74466-62-9; *(5)*, 53547-86-7

[*] Prof. Dr. H. Sakurai, Dipl.-Chem. H. Tobita, Dr. M. Kira, Dr. Y. Nakadaira
Department of Chemistry, Faculty of Science
Tohoku University, Sendai 980 (Japan)

[1] Chemistry of Organosilicon Compounds. Part 139.—Part 138: *H. Sakurai, K. Sasaki, A. Hosomi*, Tetrahedron Lett. *1980*, 2329.
[2] *H. Sakurai, Y. Nakadaira, M. Kira, H. Tobita*, Tetrahedron Lett., in press.
[3] *H. Sakurai, T. Kobayashi, Y. Nakadaira*, J. Organometal. Chem. *162*, C43 (1978).
[4] *D. Griller, K. U. Ingold*, J. Am. Chem. Soc. *96*, 6202 (1974).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0620 $ 02.50/0

Synthesis and Rearrangement of Azulenesulfonium Salts

By *Manfred Müller, Siegmar Braun,* and *Klaus Hafner*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Rearrangement reactions of azulenes with retention of the bicyclic system have hardly been studied so far; just a few thermally induced or acid-catalyzed isomerizations of 1-alkyl-, 1-aryl-, and 1-acylazulenes to the corresponding 2-substituted azulenes are known[1]. We have now found that *S,S*-dimethyl-4-azulenylmethylsulfonium salts of type *(3)* not only provide a facile entry to numerous 4-functionalized azulene derivatives, but also undergo a mechanistically and preparatively interesting rearrangement.

Compound *(3)* (blue platelets) can be prepared by reaction of sodium (6,8-dimethyl-4-azulenyl)methanide *(1)*[2] with dimethyldisulfane to give 6,8-dimethyl-4-(methylthiomethyl) azulene *(2)* (blue crystals) followed by methylation of *(2)*. On reaction with nucleophiles (dimethylamine, aqueous sodium acetate, sodium azide, lithium chloride or bromide), compound *(3)*—a potential umpolung product of *(1)*—affords the hitherto inaccessible compounds *(4a—e)* (blue crystals or oils, see Table 1). Reaction of *(3)* with triphenylphosphane gives the phosphonium salt *(4f)* (blue crystals) which is capable of undergoing Wittig reactions with aldehydes[3] (see Table 1).

Contrary to initial expectations, deprotonation of *(3)* with sodium methoxide (in methanol, room temperature) fails to yield the resonance-stabilized sulfonium ylide *(5a)*. Instead, a fast, and for non-benzenoid, cyclically conjugated π-electron systems previously unknown, [2.3]sigmatropic rearrangement of *(5b)*—which is presumably in equilibrium with *(5a)*—with loss of the 10π-electron system apparently takes place, giving a 78% yield of the readily isolable, stable 6,8-dimethyl-4-methylene-3a,4-dihydroazulene derivative *(6)* (yellow crystals), along with 10% of the isomeric 4,6,8-trimethyl-

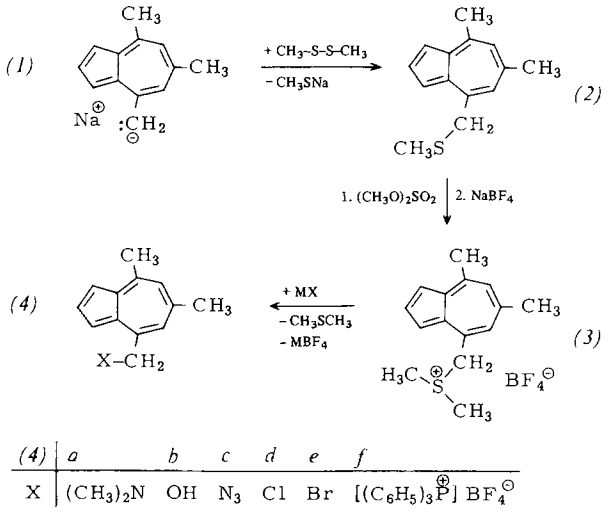
Table 1. Selected physical data of compounds *(3), (4a—f), (6), (7), (8).*

Cpd.	Yield [%]	M.p. [°C]	UV (*n*-hexane) λ [nm] (log ε)	100 MHz-^{1}H-NMR ($CDCl_3$), δ values
(2)	75	35	245 (4.42), 290 (4.73), 332 sh (3.48), 337 (3.54), 349 sh (3.61), 352 (3.64), 363 sh (3.02), 550 (2.69), 563 (2.69), 587 (2.66), 610 sh (2.66), 640 (2.28)	7.68 (t, J=4 Hz, 1 H, H-2), 7.43, 7.38 (dd, J=4 Hz, J=1.4 Hz, 2 H, H-1, 3), 7.16, 7.06 (br. s, 2 H, H-5, 7), 4.19 (s, 2 H, —CH_2—), 2.85 (s, 3 H, 8-CH_3), 2.62 (s, 3 H, 6-CH_3), 2.04 (s, 3 H, —SCH_3)
(3)	77	145 (dec.)	248 (4.39), 289 (4.65), 309 sh (3.39), 342 (3.50), 356 (3.54), 370 sh (2.74), 572 (2.69), 597 sh (2.64), 665 sh (2.20) [a]	7.88—7.71 (m, 2 H, H-2; H-1 or H-3), 7.55 (dd, J=3.8 Hz, J=2 Hz, 1 H, H-1 or H-3), 7.50, 7.38 (br. s, 2 H, H-5, 7), 5.39 (s, 2 H, —CH_2—), 3.16 (s, 6 H, —$S(CH_3)_2$), 2.93 (s, 3 H, 8-CH_3), 2.70 (s, 3 H, 6-CH_3) [b]
(4a)	81		244 (4.42), 287 sh (4.62), 290 (4.66), 304 sh (3.93), 323 sh (3.40), 330 sh (3.48), 335 (3.55), 346 sh (3.60), 350 (3.66), 360 sh (3.04), 367 sh (2.54), 387 sh (1.43), 530 sh (2.61), 548 (2.67), 566 (2.66), 589 (2.63), 613 sh (2.44), 642 (2.24), 678 sh (1.56)	7.64 (t, J=4 Hz, 1 H, H-2), 7.49, 7.30 (dd, J=4 Hz, J=1.8 Hz, 2 H, H-1, 3), 7.35, 6.98 (br. s, 2 H, H-5, 7), 3.87 (s, 2 H, —CH_2—), 2.77 (s, 3 H, 8-CH_3), 2.56 (s, 3 H, 6-CH_3), 2.27 (s, 6 H, 4-$N(CH_3)_2$)
(4b)	75	144	234 sh (4.21), 248 (4.38), 288 (4.67), 291 sh (4.66), 297 sh (4.59), 329 sh (3.51), 335 (3.59), 345 sh (3.63), 350 (3.70), 550 (2.68), 581 sh (2.63), 635 sh (2.22) [c]	7.78—7.61 (m, 1 H, H-2), 7.44—7.27 (m, 3 H), 7.13 (s, 1 H, H-5 or H-7), 5.20 (s, 2 H, —CH_2—), 4.66 (br. s, 1 H, —OH), 2.88 (s, 3 H, 8-CH_3), 2.66 (s, 3 H, 6-CH_3)
(4c)	65		246 (4.37), 286 (4.67), 290 (4.66), 307 sh (3.85), 336 (3.53), 352 (3.63), 390 sh (1.46), 538 sh (2.57), 557 (2.63), 571 (2.63), 593 (2.58), 619 sh (2.44), 650 sh (2.17), 681 sh (1.76)	7.70 (t, J=4 Hz, 1 H, H-2), 7.38, 7.32 (dd, J=4 Hz, J=1.6 Hz, 2 H, H-1, 3), 7.06 (s, 2 H, H-5, 7), 4.73 (s, 2 H, —CH_2—), 2.79 (s, 3 H, 8-CH_3), 2.57 (s, 3 H, 6-CH_3)
(4d)	75	50	215 (3.45), 247 (4.38), 288 sh (4.64), 291 (4.65), 311 sh (3.81), 330 sh (3.40), 340 sh (3.50), 343 (3.52), 353 (3.55), 394 sh (1.74), 563 sh (2.61), 575 (2.62), 595 sh (2.58), 622 sh (2.48), 653 sh (2.22), 683 sh (1.92)	7.76 (t, J=4 Hz, 1 H, H-2), 7.48, 7.42 (dd, J=4 Hz, J=1.8 Hz, 2 H, H-1, 3), 7.19, 7.13 (s, 2 H, H-5, 7), 5.06 (s, 2 H, —CH_2—), 2.87 (s, 3 H, 8-CH_3), 2.63 (s, 3 H, 6-CH_3)
(4e)	56	70	250 (4.39), 294 (4.59), 314 sh (3.86), 348 (3.50), 356 (3.50), 578 (2.65), 598 sh (2.61), 624 sh (2.53), 658 sh (2.26), 688 sh (2.01)	7.68 (t, J=3.9 Hz, 1 H, H-2), 7.50, 7.41 (dd, J=3.9 Hz, J=1.8 Hz, 2 H, H-1, 3), 7.15, 7.10 (s, 2 H, H-5, 7), 4.95 (s, 2 H, —CH_2—), 2.86 (s, 3 H, 8-CH_3), 2.61 (s, 3 H, 6-CH_3)
(4f)	89	219	227 (4.57), 251 (4.49), 279 sh (4.43), 290 (4.58), 309 sh (4.00), 341 (3.52), 356 (3.58), 566 (2.71), 600 sh (2.65), 657 sh (2.23) [a]	7.84—7.13 (m, 17 H), 6.96 (br. s, 1 H), 6.83—6.60 (m, 2 H), 5.10 (d, $J_{P,H}$=15 Hz, 2 H, —CH_2—), 2.80 (s, 3 H, 8-CH_3), 2.26 (s, 3 H, 6-CH_3)
(6)	78	< 15	219 (4.04), 261 (4.22), 290 sh (3.22), 370 (3.66)	6.77 (dd, $J_{2,3}$=5.4 Hz, $J_{1,3}$=1.4 Hz, 1 H, H-3), 6.64 (dd, $J_{2,3}$=5.4 Hz, $J_{1,2}$=2.2 Hz, 1 H, H-2), 6.44 (~t, $J\approx$1.8 Hz, 1 H, H-1), 5.90, 5.86 (br. s, 2 H, H-5, 7), 5.71, 4.72 (br. s, 2 H, =CH_2), 2.81, 2.18 (d, J=13 Hz, 2 H, —CH_2—), 2.12 (br. s, 3 H, 8-CH_3), 2.01 (s, 3 H, —SCH_3), 1.96 (br. s, 3 H, 6-CH_3) [d]
(7)	10	58	249 (4.46), 293 sh (4.69), 296 (4.70), 308 sh (3.99), 331 sh (3.47), 346 sh (3.65), 352 (3.75), 368 (3.52), 493 sh (2.64), 558 (2.69), 521 sh (2.67), 600 (2.63), 657 (2.21)	7.67 (t, J=4 Hz, 1 H, H-2), 7.51, 7.32 (dd, J=4 Hz, J=1.8 Hz, 2 H, H-1, 3), 7.17 (s, 2 H, H-5, 7), 3.95 (s, 2 H, —CH_2—), 3.12 (s, 3 H, 8-CH_3), 2.83 (br. s, 6 H, 4,6-CH_3), 2.18 (s, 3 H, —SCH_3)
(8)	45	54	247 (4.41), 292 (4.67), 296 (4.67), 301 sh (4.64), 332 sh (3.50), 345 sh (3.64), 352 (3.76), 355 sh (3.52), 369 (2.65), 563 (2.57), 600 sh (2.57), 658 (2.11)	7.55 (d, $J_{2,3}$=4 Hz, 1 H, H-2), 7.27 (d, $J_{2,3}$=4 Hz, 1 H, H-3), 6.95 (s, 2 H, H-5, 7), 4.31 (s, 2 H, —CH_2—), 3.16 (s, 3 H, 4-CH_3), 2.81 (s, 3 H, 8-CH_3), 2.55 (s, 3 H, 6-CH_3), 2.07 (s, 3 H, —SCH_3)

[a] In CH_3OH. [b] In [D_6]-acetone. [c] In dioxane. [d] 25.2 MHz-^{13}C-NMR ($CDCl_3$), δ values: 149.6 (quart. C), 144.9 (=C—H), 144.1, 132.6, 131.9 (3 quart. C), 130.5, 129.2, 126.9, 123.4 (each 1 =C—H), 111.5 (=CH_2), 62.0 (quart. C), 42.4 (—CH_2—), 27.3, 24.1, 18.4 (each 1 CH_3).

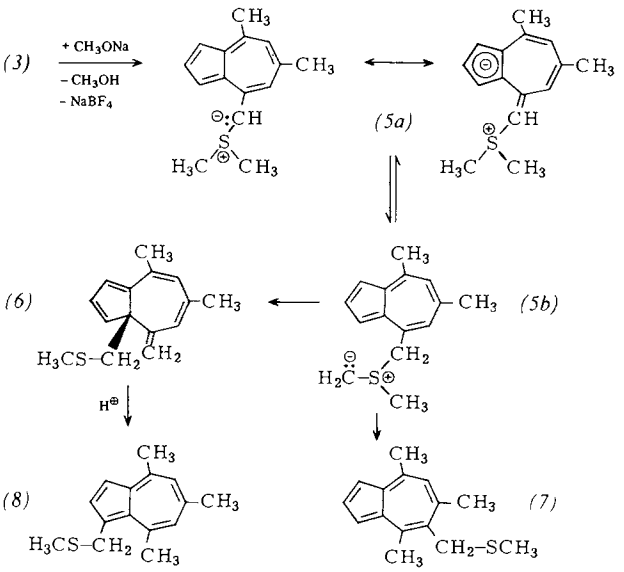
[*] Prof. Dr. K. Hafner, Dipl.-Ing. M. Müller, Dr. S. Braun
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0808-0621 $ 02.50/0*



(4)	a	b	c	d	e	f
X	$(CH_3)_2N$	OH	N_3	Cl	Br	$[(C_6H_5)_3\overset{\oplus}{P}]\ BF_4^{\ominus}$

azulene derivative *(7)* (blue needles). The structure of *(6)* was established primarily by analysis of the ^{1}H-coupled ^{13}C-NMR spectrum. Formation of compound *(6)* corresponds to that of the methylenecyclohexadiene intermediates detected in the Sommelet-Hauser rearrangement of *o,o'*-disubstituted benzyl-dimethylsulfonium and -trimethylammonium salts[4].



Unlike these intermediates, *(6)* does not undergo thermal rearrangement; however, acid-catalyzed rearrangement (1% $HClO_4$ in CH_3OH) regenerates the azulene system to give 4,6,8-trimethyl-1-(methylthiomethyl)azulene *(8)* (blue needles).

Physical data of the new compounds are compiled in Table 1.

Received: April 28, 1980 [Z 514 IE]
German version: Angew. Chem. 92, 635 (1980)

CAS Registry numbers:
(2), 74465-56-8; *(3)*, 74465-58-0; *(4a)*, 74465-59-1; *(4b)*, 74465-60-4; *(4c)*, 74465-61-5; *(4d)*, 74465-62-6; *(4e)*, 74465-63-7; *(4f)*, 74465-65-9; *(6)*, 74465-66-0; *(7)*, 74465-67-1; *(8)*, 74465-68-2

[1] *S. Kurokawa, T. Sato, T. Noguchi, K. Yano*, Bull. Chem. Soc. Jpn. *48*, 1559 (1975); *V. B. Mochalin, Yu. N. Porshner*, Usp. Khim. *46*, 1002 (1977); Russ. Chem. Rev. *46*, 530 (1977), and further references therein; *K. Hafner, W. Rieper*, unpublished.

[2] *K. Hafner, H. Pelster, H. Patzelt*, Justus Liebigs Ann. Chem. *650*, 80 (1961).

[3] *(4f)* reacts with sodium methoxide in methanol to give a bright red phosphonium ylide, which yields, *e.g.*, with benzaldehyde a chromatographically separable 1:1 mixture of *(E)*- and *(Z)*-6,8-dimethyl-4-styrylazulene (yield 69%).

[4] *G. Wittig*, Bull. Soc. Chim. Fr. *1971*, 1921; *B. M. Trost, L. S. Melvin, Jr.*: Sulfur Ylids. Organic Chemistry, Vol. 31. Academic Press, New York 1975.

Dimerization of Propylene with Catalysts Exhibiting Activities Like Highly-Active Enzymes

By *Borislav Bogdanović, Bernd Spliethoff,* and *Günther Wilke*[*]

In 1963 we discovered soluble catalysts which dimerize ethylene and propylene with high activity, even at $-20\,^{\circ}C$ at normal pressure[1]. As catalysts we have employed, *inter alia,* π-allylnickel halides in combination with Lewis acids such as $EtAlCl_2$. The dimerization of propylene can be controlled within wide limits by addition of phosphanes having different electronic and, especially, steric properties, so that dimers of various structures can be prepared at will[1]. The olefin dimerizations were performed in CH_2Cl_2 or C_6H_5Cl. We have quoted the activity of the catalysts in the dimerization of propylene at normal pressure and $-20\,^{\circ}C$ for 3—6 kg product/(g Ni·h).

In later experiments we established that the previously found, but nevertheless considerable activity was apparently exclusively determined by the reaction conditions such as stirring, cooling, and gas feed, even though relatively small amounts of catalyst were employed. As we have now found, the activity is in fact about one thousand times higher. The experiments for determining such high activities were performed as follows:

100 ml of C_6H_5Cl, 350 g (8.33 mol) of 99.8% propylene, and 0.6 g (4.72 mmol) of $EtAlCl_2$ are mixed at temperatures between -45 and $-75\,^{\circ}C$). The relatively large amount of $EtAlCl_2$ should ensure that traces of impurities are trapped (under the conditions given, $EtAlCl_2$ does not react with propylene). The vigorously stirred mixture is then treated with a solution of 0.0023 g (5 μmol) of π-$C_3H_5NiBrP(C_6H_{11})_3$ in 1 ml C_6H_5Cl (prepared by multiple dilution of aliquot amounts). A strongly exothermic reaction immediately sets in, so intensive cooling is necessary to keep the temperature of the reaction mixture constant. After 30 min the reaction is terminated by passage of gaseous NH_3, excess propylene (250—300 g) is bubbled off, and the product worked up. Table 1 lists the results of experiments at various temperatures.

Table 1. Catalytic dimerization of propylene.

T [°C]	g Product/(5 μmol cat. × 30 min)	kg Product/(g Ni·h)	mol C_3H_6/(mol Ni·h)	Turnover number/s [a]
−75	22	152	209524	60
−65	47	324	447619	130
−55	84	580	800000	230

[a] Turnover number = reaction steps at the active center; here: molecules of propylene/atom Ni (approx. values).

As expected, in the temperature range quoted the amount of product/30 min doubles on increasing the temperature by 10 °C. The composition of the products is practically independent of the temperature, in contrast to catalysts in which

[*] Prof. Dr. B. Bogdanović, Ing. (grad.) B. Spliethoff, Prof. Dr. G. Wilke
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

[**] Activity = amount of reacted substrate/(catalyst unit × unit time).

$(t\text{-}C_4H_9)P(i\text{-}C_3H_7)_2$ was employed as steering ligand[2]. In the present case we obtained, besides 10—15% of higher olefins, dimers of the following composition: 18% 4-methyl-1-pentene, 1–3% *cis*-4-methyl-2-pentene, 76% 2,3-dimethyl-1-butene, 4% 2-methyl-1-pentene, as well as traces of other isomers.

The values in Table 1 already show that the activity of the catalyst is higher by a factor of about 100 even at −55 °C than previously quoted for −20 °C. Assuming a doubling of the activity/10 °C, gives an activity of *ca.* 6000—7000 kg product/(g Ni·h) and hence the factor 1000. For a comparison with enzyme activities, appropriate experiments had to be performed at 25 °C. As experiments under pressure have shown[1b], at this temperature the catalysts are fully active, though a determination of the actual activity under pressure can be achieved only with considerable effort, owing to the limitations of the apparatus. Calculation as above gives a value of *ca.* 150×10^3 kg/(g Ni·h) and a turnover number/s of *ca.* 60000; the corresponding data for enzymes[3] are: hexokinase 100, catalase 80000, carboanhydrase 600000.

The activity of the catalyst diminishes at higher conversions, probably because of traces of impurities; nevertheless, in one experiment at −45 °C we have achieved turnover numbers of 10^6 mol propylene/mol of catalyst; on terminating the reaction the activity had fallen to about 10% of the activity during the first 30 min.

If, under otherwise identical conditions, propylene is allowed to react with a catalyst not containing phosphane, the activity is only *ca.* 1/15 of that quoted above, *i.e.* the phosphane not only exerts steering properties but also effects considerable activation. Generally, however, this catalysis would also appear to be a further example of the phenomenon already observed several times, *i.e.* that the product selectivity increases with increasing catalyst activity[4]. To our knowledge the systems described here are the most active synthetic homogeneous catalysts known to date.

Received: March 14, 1980 [Z 516 IE]
German version: Angew. Chem. *92*, 633 (1980)

CAS Registry numbers:
Propylene, 115-07-1; $EtAlCl_2$ 563-43-9; π-$C_3H_5NiBrP(C_6H_{11})_3$, 47315-25-3

[1] a) *G. Wilke*, US-Pat. 3379706 (1963), Studiengesellschaft Kohle; b) *B. Bogdanović, G. Wilke*, Brennst. Chem. *49*, 323 (1968).
[2] *G. Wilke* in *M. Tsutsui:* Fundamental Research in Homogeneous Catalysis. Vol. 3. Plenum Press, New York 1979, pp. 1 ff.
[3] *H. Winkler* in *K. Hauffe:* Katalyse. de Gruyter, Berlin 1976, p. 218.
[4] *W. Brenner, P. Heimbach, H.-J. Hey, E. W. Müller, G. Wilke*, Justus Liebigs Ann. Chem. *727*, 161 (1969), pp. 170, 171 therein.

Solubility of Nonvolatile Biochemical Substances in Compressed Carbon Dioxide[**]

By *Ziad Alwani*[*]

Industrial methods have recently been developed for the extraction of natural products with supercritical or fluid solvents at pressures of up to *ca.* 400 bar (cf. [1]). As examples might be mentioned the decaffeination of coffee, the production of hop extract, and the extraction of spices. In the construction of chemical plant for high-pressure extraction, a knowledge of parameters such as, *inter alia,* extraction rate and solubility data, is of paramount importance.

[*] Dr. Z. Alwani
Lehrstuhl für Physikalische Chemie II der Universität Bochum
Present address: Thyssen-Maschinenbau GmbH
D-5810 Witten-Annen (Germany)

[**] Based on a lecture delivered at the GDCh-Hauptversammlung in Berlin, September 12, 1979.

We have investigated the solubility of difficultly volatile biochemical substances in compressed fluid solvents using as example the model substance α-tocopheryl acetate (vitamin E acetate) in CO_2. For the measurements, a newly developed optoelectrical method[2] was used which enabled experimental determination of relatively low solubilities (for older methods see [3]).

From the clouding points of a mixture measured at various pressures and temperatures a family of $p(T)$ mixing curves was constructed for each mixture examined. The curves in Figure 1 are continuous between 20 and 50 °C and do not show any discontinuity in the neighborhood of the critical temperature of CO_2 (*ca.* 31 °C). This would indicate a continuous transition between the liquid-liquid and liquid-gas phase equilibria (for an explanation of these phenomena see [4, 5, 8]).

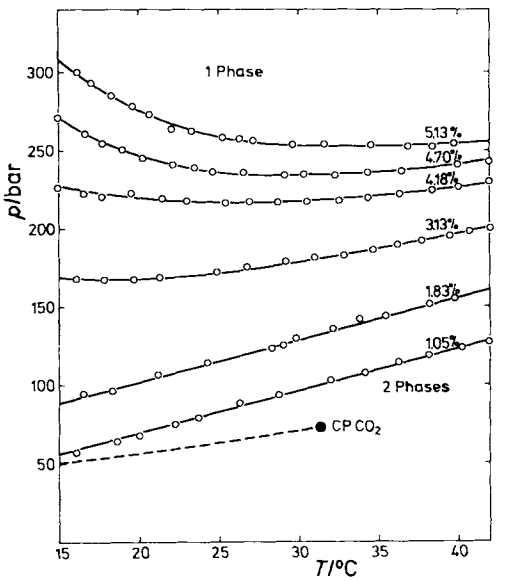


Fig. 1. $p(T)$ Curves for α-tocopheryl acetate in CO_2 at several constant concentrations [wt-%]. CP = critical point.

From the $p(T)$ curves (Fig. 1) the solubilities were determined as a function of pressure at a given temperature; sim-

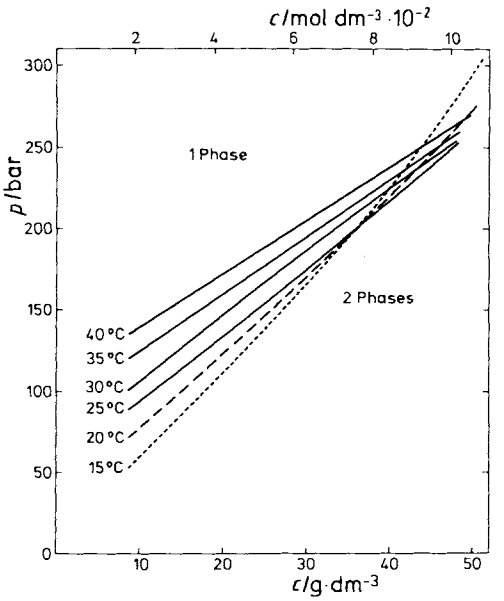


Fig. 2. $c(p)$ Curves for α-tocopheryl acetate in CO_2 at several constant temperatures.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0623 $ 02.50/0

plified additivity of the volumes of the pure substances was assumed (from the densities of CO_2[10]). According to Figure 2 the solubility increases monotonously with increasing pressure and reaches a value of *ca.* 40 $g \cdot dm^{-3}$ at 250 bar. The slopes of the curves differ only slightly above and below the critical temperature of CO_2. However, at temperatures below the critical point of CO_2, some of the curves intersect at a concentration of *ca.* 35 $g \cdot dm^{-3}$ and a pressure of *ca.* 180 bar. The systems squalane + CO_2[5] and caffeine + CO_2[9] behave similarly.

Figure 3 shows the solubility of α-tocopheryl acetate as a function of temperature at constant pressure. At constant pressures below 200 bar the solubility decreases with increasing temperature; a maximum solubility occurs at pressures above 200 bar. These curves are also continuous, *e.g.* also in the neighborhood of the critical point of CO_2.

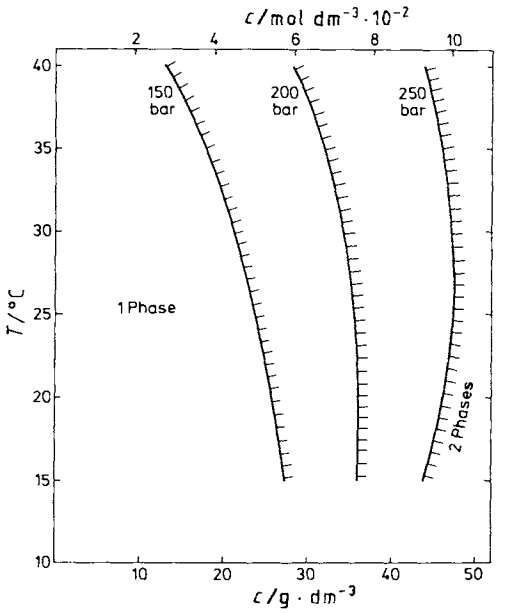


Fig. 3. $c(T)$ Curves for α-tocopheryl acetate in CO_2 at several constant pressures.

The most important findings can be summarized as follows: i) The solubility of α-tocopheryl acetate increases with increasing pressure, both in liquid as well as in supercritical CO_2. ii) Contrary to some data quoted in the literature[6, 7], the solubility of α-tocopheryl acetate changes relatively slightly when the solvent (here CO_2) is heated from subcritical to supercritical temperatures at constant pressure.—These results can be extrapolated to other nonvolatile substances and fluid solvents.

Received: March 3, 1980 [Z 517 IE]
German version: Angew. Chem. *92*, 633 (1980)

CAS Registry numbers:
CO_2, 124-38-9; α-tocopheryl acetate, 7695-91-2

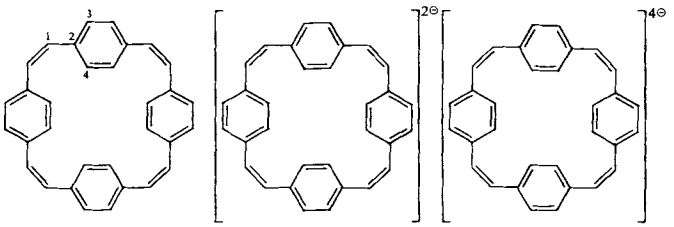
[1] *R. Eggers*, Angew. Chem. *90*, 799 (1978); Angew. Chem. Int. Ed. Engl. *17*, 751 (1978).
[2] *Z. Alwani*, Rev. Sci. Instrum. *49*, 944 (1978).
[3] *G. M. Schneider* in *B. Le Neindre, B. Vodar:* Experimental Thermodynamics. Vol. II. Butterworths, London 1975, Chapter 16, Part 2; *C. L. Young* in *M. L. McGlashan:* Specialist Periodical Reports: Chemical Thermodynamics, Vol. 2. The Chemical Society, London 1978, Chapter 3.
[4] *G. M. Schneider, Z. Alwani, W. Heim, E. U. Franck*, Chem.-Ing.-Tech. *39*, 649 (1967).
[5] *K. G. Liphard, G. M. Schneider*, J. Chem. Thermodyn. *7*, 805 (1975).
[6] *K. Zosel*, Angew. Chem. *90*, 748 (1978); Angew. Chem. Int. Ed. Engl. *17*, 702 (1978).
[7] *E. Stahl, W. Schilz, E. Schütz, E. Willing*, Angew. Chem. *90*, 778 (1978); Angew. Chem. Int. Ed. Engl. *17*, 731 (1978).
[8] *Z. Alwani, G. M. Schneider*, Ber. Bunsenges. Phys. Chem. *80*, 1310 (1976).
[9] *E. Stahl, W. Schilz*, Talanta *26*, 675 (1979).
[10] IUPAC, International Thermodynamic Tables of the Fluid State 3: Carbon Dioxide. Pergamon Press, London 1976.

Dianion and Tetraanion of [2₄]Paracyclophanetetraene—New Unusual Perimeter Systems[**]

By *Walter Huber, Klaus Müllen,* and *Olof Wennerström*[*]

The current question regarding external or internal aromaticity in polycyclic compounds like porphyrins[1] and their ions is in effect a question of whether perimeter structures with resonance stabilization can exist, and *via* which conjugation route[2]. We have found that the dianion *(2)* and the tetraanion *(3)* of [2₄]paracyclophanetetraene *(1)*[3], exhibit unusual spectroscopic properties and are novel macrocycles in which such a peripheral conjugation is present.

As electrochemical reduction of *(1)* shows, the molecule reversibly takes up two electrons at low potential[3]. On reduction with metal in a sealed NMR tube (lithium, 0.05 M solutions of *(1)* in [D_8]-tetrahydrofuran, −80 °C) a diamagnetic species is formed, which on the basis of its ^1H- and ^{13}C-NMR spectra and trapping experiments *(vide infra)* is identified as dianion *(2)* and which on prolonged contact with metal forms a new product, the tetraanion *(3)*. Both ions are stable in the absence of air, even above +60 °C.



(1) *(2)* *(3)*

Observation of the dianion, however, is possible only in the absence of the intermediary radical anions [$(1)^{\ominus}$[4], $(2)^{\ominus}$] and therefore necessitates careful monitoring of the reduction by recording the ESR and NMR spectra.

It is possible at each stage of the reduction to recover the neutral compound *(1)* as sole product by reoxidation with oxygen. Reaction of *(2)* and *(3)* with methanol affords, respectively, diprotonated and multiprotonated[5] products in which olefinic double bonds are hydrogenated.

The neutral compound *(1)* shows chemical shifts typical for aromatic and olefinic protons (see Fig. 1 and Table 1). However, owing to the drastic difference in shifts of the external (H-3) and internal (H-4) protons—both in *(2)* and in *(3)*—one must conclude that a peripheral ring current, and hence a perimeter conjugation, exists. The internal benzene protons in the dianion *(2)* absorb at $\delta = -7.07$ (!). The diamagnetic ring current in *(2)* and the paramagnetic ring cur-

[*] Prof. Dr. K. Müllen, Dr. W. Huber
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)
Dr. O. Wennerström
Department of Chemistry, University of Göteborg
Göteborg (Sweden)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. Dr. *W. Huber* thanks the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung for a grant.

rent in *(3)* evidence the ions as typical 26 $(=4n+2)\pi$- and 28 $(=4n)\pi$-perimeter systems, respectively.

Table 1. ^{1}H- and ^{13}C-chemical shifts (δ-values referred to TMS) and $^1J_{CH}$ coupling constants [Hz] of [2$_4$]paracyclophanetetraene *(1)*, its dianion *(2)*, and its tetraanion *(3)* [a]; [D$_8$]-tetrahydrofuran, $-80\,^\circ$C, ions as lithium salt. The ^{1}H-NMR signals (singlets) were assigned on the basis of the ring current effects and on the exchange-broadenings observed in the spectrum of *(2)* above $-20\,^\circ$C. The assignment of the ^{13}C-NMR signals is based on selective ^{1}H-decoupling experiments.

	Cpd.	H-1 or C-1	C-2	H-3 or C-3	H-4 or C-4	⟨δ⟩
$\delta(^1H)$	*(1)*	6.48		7.37	7.37	
	(2)	9.56		9.26	−7.07	
	(3)	2.09 [b]		4.48 [b]	12.76	
$\delta(^{13}C)$	*(1)*	129.9	136.2	129.3	129.3	131.2
	(2)	108.8	119.8	123.9	116.5	117.3
	(3)	95.9 [b]	133.3	122.4 [b]	121.6	118.3
$^1J_{CH}$	*(1)*	154		158	158	
	(2)	143		147	159	

[a] Determination of the $^1J_{CH}$ coupling constants of *(3)* is hampered by the small signal separation. [b] The assignment possibly has to be interchanged.

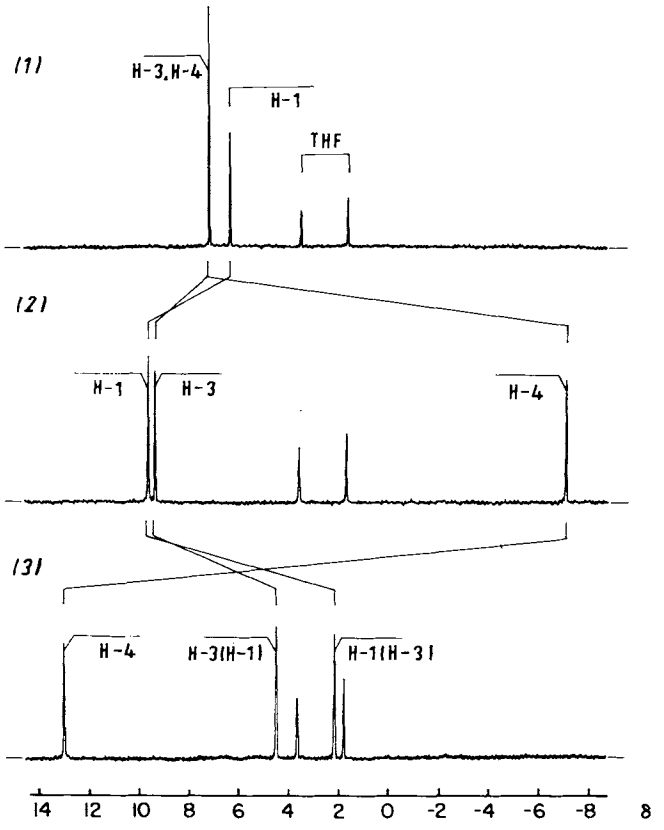


Fig. 1. ^{1}H-NMR spectra (90 MHz) of [2$_4$]paracyclophanetetraene *(1)*, its dianion *(2)*, and its tetraanion *(3)*; [D$_8$]tetrahydrofuran, $-80\,^\circ$C, ions as lithium salt.

Characteristic of the structure of the ions is the mutual approach of the π-bond orders of the formal single and double bonds. This follows from the fact that the very rapid rotation of the benzene fragments about the single bonds in the neutral compound is drastically slowed down on transition to the ions[6].

Particularly surprising from the point of view of bond theory is the fact that a perimeter conjugation extends beyond the benzene units[7]. In view of the poorly understood bonding situation in related polycycles[1,7], the question arises whether this form of conjugation differentiates between the external (C-3) or internal (C-4) loop of the benzene. Closely coupled with the solution of this problem is the knowledge of the charge distribution, which can be investigated experimentally *via* the ^{13}C-chemical shifts and/or the relevant $^1J_{CH}$-coupling constants[8].

On going from *(1)* to the dianion *(2)* the coupling constants $^1J_{CH}$ for the positions 1 and 3 diminish by *ca.* 11 Hz owing to additional π-charging. The analogous coupling constant for position 4, on the other hand, remains practically unchanged and gives no indication of the existence of an excess charge in the inner loop. That the signal of C-4 in *(2)* nevertheless experiences a pronounced upfield shift can be ascribed, in view of the topology of the present system, to the influence of the ring current on the resonance of the carbon nuclei[9]. Thus, it is also not surprising that the upfield shift of the center point of the ^{13}C-NMR signals in the transition from *(1)* to *(2)* is distinctly larger than one would expect on the basis of the usual correlation between π-charge density and chemical shift.

The aforementioned spectroscopic findings prove not only the surprising existence of a peripheral conjugation in the ionic cyclophane systems but also show that the 26 π-perimeter is preferably formed in the dianion with participation of the external loop of the benzene units.

Received: February 4, 1980 [Z 518 IE]
German version: Angew. Chem. *92*, 636 (1980)

[1] *A. Ulman, J. Manassen, F. Frolow, D. Rabinovich*, J. Am. Chem. Soc. *101*, 7055 (1979).
[2] *P. George*, Chem. Rev. *75*, 85 (1975).
[3] *B. Thulin, O. Wennerström*, Acta Chem. Scand. *B 30*, 369 (1976); *K. Ankner, B. Lamm, B. Thulin, O. Wennerström, ibid. B 32*, 155 (1978).
[4] *F. Gerson, W. Huber, O. Wennerström*, Helv. Chim. Acta *61*, 2763 (1978).
[5] That mainly the dihydro and octahydro product—apart from small amounts of the two constitutionally isomeric tetrahydro systems—are formed in the protonation of *(3)* is readily explained in terms of a series of interchanging protonation and electron transfer. *(3)* is thereby acting as reducing species.
[6] The rotation about the formal single bonds within the macrocycle, which leads to an exchange of the magnetic sites 3 and 4, cannot be frozen in *(1)*, even at $-130\,^\circ$C. While the ^{1}H-NMR spectrum of the dianion *(2)* above $-20\,^\circ$C shows an exchange broadening of the signals of H-3 and H-4 (not of H-1), indicative of the mentioned transformation of conformation, the spectrum of *(3)* shows no evidence of a dynamic process up to $+60\,^\circ$C.
[7] *H. A. Staab, F. Binnig*, Tetrahedron Lett. *1964*, 319; *R. B. DuVernet, O. Wennerström, J. Lawson, T. Otsubo, V. Boekelheide*, J. Am. Chem. Soc. *100*, 2457 (1978).
[8] *K. Müllen*, Helv. Chim. Acta *61*, 1296 (1978); *L. A. Paquette, G. D. Ewing, S. Traynor, J. M. Gardlik*, J. Am. Chem. Soc. 99, 6115 (1977).
[9] *H. O. Kalinowski, W. Lubosch, D. Seebach*, Chem. Ber. *110*, 3733 (1977); *H. Günther, H. Schmickler, H. Königshofen, K. Recker, E. Vogel*, Angew. Chem. *85*, 261 (1973); Angew. Chem. Int. Ed. Engl. *12*, 243 (1973).

Lithiated Allyl *N,N*-Dialkylcarbamates as Homoenolate Equivalents; Synthesis of Protected 4-Oxoalkanoates[**]

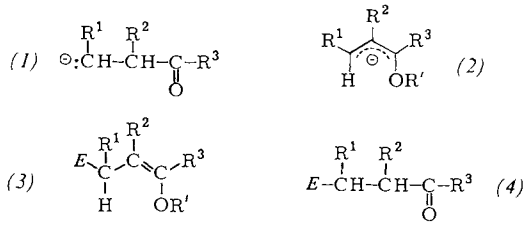
By *Dieter Hoppe, Rudolf Hanko*, and *Alfons Brönneke*[*]

Among the synthetic equivalents of the homoenolate ions *(1)* ("carbonyl-d^3 reagents"[1]), the *O*-substituted 1-hydroxyallyl anions *(2)*[2] offer the most direct preparative solution[3,4]. They are generally attacked ambidoselectively[5] by electrophiles *E* at the γ-position; the resulting enol ethers *(3)*

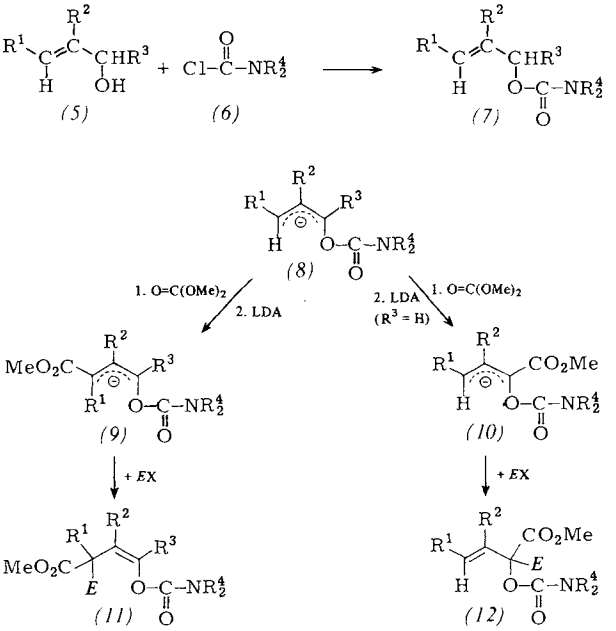
[*] Priv.-Doz. Dr. D. Hoppe, R. Hanko, A. Brönneke
Organisch-Chemisches Institut der Universität
Tammannstr. 2, D-3400 Göttingen (Germany)

[**] Metalated Nitrogen Derivatives of Carbonic Acid in Organic Synthesis, Part 18.—Part 17: *D. Hoppe, R. Follmann*, Liebigs Ann. Chem., in press.

can be hydrolyzed to the β-substituted carbonyl compounds *(4)*.

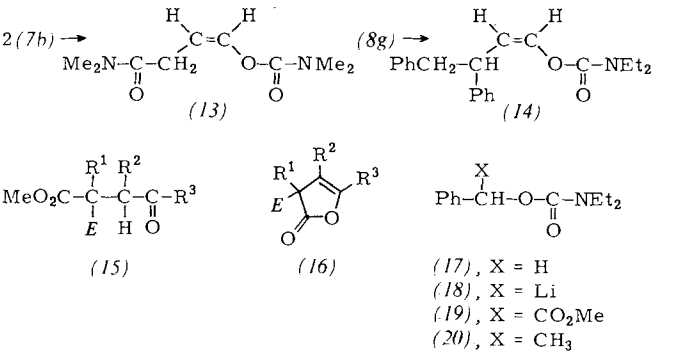


In particular, the anions *(2)* of allyl alkyl and of allyl trialkylsilyl ethers (R′ = alkyl, $SiMe_3$, or $SiEt_3$)[2] have previously been employed; however, their utility (in the absence of other electron withdrawing groups) is limited to the derivatives *(2)*, $R^1 = R^3 = H$, owing to insufficient acidity of α- and γ-substituted allyl ethers[2b]. We have now found that the presence of *N,N*-dialkylcarbamoyl groups[6] in the esters *(7)* increases the kinetic acidity of α-protons by chelation to such an extent that alkyl-substituted allyl derivatives such as *(7d)* and *(7f)* (Table 1) can also be deprotonated.



The allyl *N,N*-dialkylcarbamates *(7)*, obtained from the allyl alcohols *(5)* and the acid chlorides *(6)*, were allowed to react at −70 °C in the presence of 3 equivalents of dimethyl carbonate with 2.1 equivalents of lithium diisopropylamide (LDA) and then with an electrophile *EX*. Subsequent work-up of the reaction mixture yielded methyl *Z*-4-carbamoyloxy-3-butenoates *(11)*[7,8] together with (usually) small amounts of the isomers *(12)* (see Table 1).

Intermediates formed in the reaction sequence *(7)*→*(11)* are the allyl anions *(8)* and *(9)*, each of which react with high selectivity[5]. Only the crotyl esters *(7d)* and *N,N*-dimethylcarbamates, *e.g. (7b)*, yield substantial amounts of the α-adducts *(12)* (Table 1), *via* the anions *(10)*. As has been demonstrated with *(7c)*, the bulky *N,N*-diisopropylcarbamoyl groups effects a further increase in regioselectivity.



On metalation in the absence of a trapping agent, *(7b)* undergoes self-condensation[10] to give the butenamide *(13)*[7] (yield 40%), while the anion *(8g)* is stable at −78 °C and can be trapped as enol ester *(14)*[7] (yield 60%) with benzyl bromide.

The method described here offers a versatile entry by a one-pot process to immediate precursors of 4-oxoalkanoates *(15)* and 3-buten-4-olides *(16)*[9]. The approach demonstrated here—the protection of hydroxy groups as carbamates with concomitant enhancement of CH acidity—has also proven valuable in the generation of other α-alkoxycarbanions. For instance, reaction of the benzyl ester *(17)* proceeds *via* the lithium compound to give *(18)*, which we trapped as *(19)*[7] with dimethyl carbonate, and as *(20)*[7] with methyl iodide (yields 74 and 90%, respectively).

Table 1. Methyl 3-alkenoates *(11)* and *(12)* prepared from allyl esters *(7)*.

Educt B.p. [°C/torr]	R^1	R^2	R^3	R^4	*EX*	*t* [h]	Product	Yield [a] [%]	*(11)* : *(12)* [b] γ : α
(7a) 87—88/20	H	H	H	Et	$PhCH_2Br$	1	*(11a)*	51	95 : 5
(7b) 58—60/10	H	H	H	Me	$PhCH_2Br$	0.5	*(11b)* + *(12b)*	54 [c]	78 : 22
(7c) 82—84/10	H	H	H	*i*Pr	$PhCH_2Br$	8	*(11c)*	63	97 : <3
(7a)	H	H	H	Et	MeI	1	*(11d)*	70	95 : 5
(7d) 95—96/15	Me	H	H	Et	$PhCH_2Br$	3	*(11e)* + *(12e)*	75 [c]	47 : 53
(7e) 80—83/9	H	Me	H	Et	$PhCH_2Br$	1	*(11f)* + *(12f)*	77 [c]	85 : 15
(7f) 85—88/12	H	H	Me	Et	$PhCH_2Br$	3	*(11g)*	79	97 : <3 [d]
(7f)	H	H	Me	Et	MeI	3	*(11h)*	76	97 : <3 [d]
(7f)	H	H	Me	Et	HOAc	3	*(11i)*	65	97 : <3 [d]
(7g) 110—113/0.15	Ph	H	H	Et	—	—	—	—	—

[a] Isolated product *(11)*. [b] Determined by ^{1}H-NMR spectroscopy. [c] Yield of mixture *(12)* + *(11)*. [d] *E* in *(12)* = R^3.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0626 $ 02.50/0 Angew. Chem. Int. Ed. Engl. 19 (1980) No. 8

Procedure

The ester *(7)* is prepared by reaction of *(5)* with *(6)* (1.05 equiv.) and pyridine (1.6 equiv.) (10 h at 90 °C) under N_2 without solvent, followed by conventional aqueous-acidic and distillative workup.

Methyl Z-4-diethylcarbamoyloxy-2-methyl-3-butenoate (11d): A solution of LDA (10.5 mmol) in tetrahydrofuran (THF)/*n*-hexane (4:1) (40 ml) is treated with 1.35 g (15.0 mmol) of methanol-free dimethyl carbonate under N_2 at −78 °C; *(7a)* (0.79 g, 5.0 mmol) is then injected into the solution over 10 min *via* a CO_2-cooled tube. The mixture is stirred at −78 °C until complete consumption of *(7a)* (TLC check, $t = 1$ h) and then treated with a solution of methyl iodide (0.78 g, 5.5 mmol) in THF (3 ml). After 5 h at −78 °C, stirring is continued for 1 h at −20 °C, the mixture is neutralized with glacial acetic acid (0.90 g, 15.0 mmol) and, after removal of solvent *in vacuo*, subjected to the usual workup (with ether). The crude product is found to contain 5% *(12d)* (^{1}H-NMR: $\delta = 5.8$; 4-H_2). Chromatography on 200 g silica gel (neutral, 40—63 μm, 2.5 bar) with ether/petroleum ether (1:5) affords 0.804 g (70%) *(11d)* with $R_F = 0.50$ (1:1) [*(12d)*: 0.46]; IR (film): 1730 (O—C=O), 1715 (N—C=O), 1665 cm^{-1} (C=C); ^{1}H-NMR (CCl_4): $\delta = 6.98$ (dd, $J_{cis} = 6.5$ Hz, $^4J = 1.0$ Hz; 4-H), 4.75 (dd, $J = 6.5$ and 9 Hz; 3-H), 3.60 (s, OCH_3), 3.3 (m, 5H; NCH_2 and 2-H), 1.25 (d, $J = 7$ Hz, 2-CH_3), 1.2 (m, NCH_2CH_3).

Received: February 15, 1980 [Z 519 IE]
German version: Angew. Chem. *92*, 637 (1980)

[1] Cf. *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

[2] a) *D. A. Evans, G. C. Andrews, H. Buckwalter*, J. Am. Chem. Soc. *96*, 5560 (1974); b) *W. C. Still, T. L. Macdonald, ibid. 96*, 5561 (1974); J. Org. Chem. *41*, 3620 (1976); c) *J. Hartmann, R. Muthukrishnan, M. Schlosser*, Helv. Chim. Acta *57*, 2261 (1974); d) *W. Oppolzer, R. L. Snowden*, Tetrahedron Lett. *1976*, 4187; e) *A. P. Kozikowski, K. Isobe, ibid. 1979*, 833; f) *H. J. Reich, R. E. Olson, M. C. Clark*, J. Am. Chem. Soc. *102*, 1424 (1980), and references cited therein.

[3] Other homoenolate equivalents, cf. [1] and *D. A. Evans, J. M. Takacs, K. M. Hurst*, J. Am. Chem. Soc. *101*, 371 (1979).

[4] More recent examples cf. a) *M. Pohmakotr, K.-H. Geiss, D. Seebach*, Chem. Ber. *112*, 1420 (1979); b) *A. Hosomi, H. Hashimoto, H. Sakurai*, J. Org. Chem. *43*, 2551 (1978); c) *T. Hassel, D. Seebach*, Angew. Chem. *91*, 427 (1979); Angew. Chem. Int. Ed. Engl. *18*, 399 (1979).

[5] Cf. also *R. Gompper, H.-U. Wagner*, Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976).

[6] *D. Hoppe, L. Beckmann, R. Follmann*, Angew. Chem. *92*, 305 (1980); Angew. Chem. Int. Ed. Engl. *19*, 303 (1980).

[7] The compounds were analytically pure (C, H ±0.3%). IR and ^{1}H-NMR spectra confirm the constitution and configuration.

[8] According to the allyl coupling 3-H/4-CH_3 of 1.1—1.2 Hz, the compounds *(11g—i)* most likely have *Z*-configuration.

[9] Review: *Y. S. Rao*, Chem. Rev. *76*, 625 (1976).

[10] *Note added in proof* (July 18, 1980): metalation of esters *(7)*, $R^4 = i$Pr or Et, with *n*-butyllithium in diethyl ether and TMEDA at −78 °C provides stable solutions of anions *(8)*.

A New Preparation of 4-Aminobutyramide

By *Axel Kleemann, Wolfgang Leuchtenberger, Jürgen Martens*, and *Horst Weigel*[*]

The hydrochloride of 4-aminobutyramide *(3)* (Gabamide) is of considerable interest on account of its psychotropic properties[1]. In connection with our work on the synthesis of derivatives of natural and unnatural amino acids[2], we have now discovered a facile, productive synthesis of *(3)*: Selective hydrogenation of 3-cyanopropionamide *(2)* in the presence of hydrogen chloride affords the hydrochloride *(3)* in 71% yield.

[*] Dr. A. Kleemann, Dr. W. Leuchtenberger, Dr. J. Martens, H. Weigel
Degussa, Fachbereich Forschung Chemie
Postfach 1345, D-6450 Hanau 1 (Germany)

The synthesis of *(2)* by partial hydrolysis of succinonitrile reported in the literature[3] is unsuitable for preparative purposes, owing to the poor yield and complicated workup of the reaction mixture. We therefore sought a more favorable synthesis of *(2)* (see Table 1), and found that hydrogen cyanide cleanly adds to acrylamide *(1)* in dimethylformamide (DMF) in the presence of catalytic amounts of potassium cyanide.

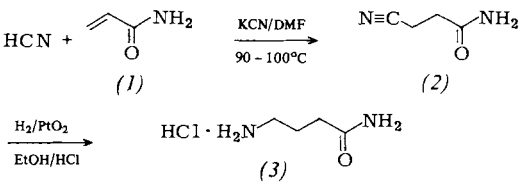


Table 1. ^{1}H-NMR data [a] of compounds *(2)* and *(3)* [b].

(2)	7.42 (br. s; 1H, —CO—NH), 6.90 (br. s; 1H, —CO—NH), 2.55 (t; 2H, —CH_2—C—N), 2.45 (t; 2H, —CH_2CON)
(3)	8.25 (s; 3H, γ-NH_3), 7.55 (br. s; 1H, —CO—NH), 6.83 (br. s; 1H, —CO—NH), 2.83 (m; 2H, —CH_2—), 2.22 (m; 2H, —CH_2—), 1.90 (m; 2H, —CH_2—)

[a] 60-MHz spectra in [D_6]-DMSO/$CDCl_3$ with TMS as internal standard; δ values. [b] *(2)* and *(3)* gave correct elemental analyses.

Our synthesis leads directly to a very clean product *(3)* (Table 1); not even the slightest traces (TLC) of butyrolactam are formed under the conditions given in the experimental section[4].

Experimental

(2): A solution of acrylamide *(1)* (71.0 g, 1 mol), dimethylformamide (100 ml), and hydrocyanic acid (27.0 g, 1 mol) is added dropwise over 1—1.5 h to a suspension of potassium cyanide (1.5 g) in dimethylformamide (50 ml) at 90 °C. The reaction is exothermic. The reaction temperature is kept at 90—100 °C. After 30 min at 95 °C, acetic acid (3 ml) is added and the reaction mixture is evaporated down at 20—30 mbar until a residue weighing 140 g is left. Addition of toluene (200 ml) and subsequent cooling to 20 °C furnishes brown crystalline *(2)* (89.1 g, 91%). Recrystallization from ethyl acetate affords pure *(2)* (72.6 g, 74%, m.p. 92—95 °C; lit. value 94 °C[3]).

(3): Compound *(2)* (19.6 g, 0.2 mol) and PtO_2 (1.5 g) are transferred to a 500 ml Hastelloy agitated autoclave containing ethanol (275 ml) and hydrogen chloride (8 g), whereupon *(2)* dissolves. After flushing with nitrogen, the mixture is hydrogenated at a hydrogen pressure of 5 bar. The reaction solution is maintained at 33 ± 3 °C. Hydrogen take-up starts immediately and is complete after 2 h. Compound *(3)* precipitates during hydrogenation. After cooling to 10—15 °C, *(3)* is washed out of the filter cake with hot methanol (100 ml). The methanolic solution of *(3)* is concentrated to 40 ml in a water-pump vacuum and stirred with ethyl acetate (100 ml). Colorless crystalline *(3)* (73%, m.p. 137—139 °C) is obtained at 20 °C.

Received: February 28, 1980 [Z 521 IE]
German version: Angew. Chem. *92*, 640 (1980)

CAS Registry numbers:
(1), 79-06-1; *(2)*, 61892-68-0; *(3)* 13031-62-4; HCN, 74-90-8

[1] *V. M. Kopelevich*, Usp. Khim. *48*, 1273 (1979).

[2] *A. Kleemann, B. Lehmann, J. Martens*, Angew. Chem. *91*, 858 (1979); Angew. Chem. Int. Ed. Engl. *18*, 797 (1979).

[3] *C. Berther*, Chem. Ber. *92*, 2616 (1959).

[4] According to ref. [3] on hydrogenation of *(2)* at 80 °C with Raney nickel as catalyst, butyrolactam is formed in 84.7% yield, and not even traces of *(3)* were present or detectable.

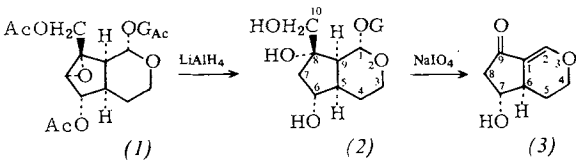
(6*R*,7*R*)-(−)-7-Hydroxy-3-oxabicyclo[4.3.0]non-1-en-9-one, A Readily Accessible and Highly Versatile Intermediate

By *Klaus Weinges, Herbert von der Eltz,* and *Dao Tran-Viet*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Starting from hexaacetyl dihydrocatalpol *(1)* we obtained the crystalline compound (6*R*,7*R*)-(−)-7-hydroxy-3-oxabicyclo[4.3.0]non-1-en-9-one *(3)*, in two reaction steps without any need for time-consuming separations. The keto enol ether *(3)* is highly reactive and is of interest as an optically active key compound, both for correlative determination of configuration of iridoid monoterpenes, and for the synthesis of natural products, especially prostanoids[1].

The starting compound *(1)* is produced almost quantitatively by acetylation and subsequent catalytic hydrogenation from catalpol, which can be isolated on a 100-g scale from a readily available drug[2]. $LiAlH_4$ reduction in tetrahydrofuran converts *(1) via* a regioselective epoxide cleavage into the amorphous product *(2)* whose constitution is established by analytical and spectroscopic studies on its crystalline heptaacetate (see Table 1). The reaction *(1)*→*(2)* can be applied to all other acetylated epoxy-iridoid glucosides (*e.g.* pentaacetyl unedoside, antirrhinoside and procumbide) and their dihydro derivatives (70—85% yield).



(1) *(2)* *(3)*

G_{Ac} = Tetraacetyl-β-D-gluco-pyranosyl G = β-D-Gluco-pyranosyl

Table 1. Some physical properties of *(2)*-heptaacetate and *(3)*.

(2)-heptaacetate: ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.80 (s; 1H, H-1), 5.27—4.80 (m; 6H, H-6, H-10, H-1′ to H-4′), 4.42 (d, ^2J = 12.5 Hz; 1H, H-10), 4.40 (d, ^2J = 12.5 Hz; 1H, H-6′), 4.12 (m; 1H, H-6′), ≈3.76 (m; 1H, H-5′), ≈3.65 (m; 2H, H-3), 2.71 (d, ^3J = 7.5 Hz; 1H, H-9), ≈2.52 (m; 1H, H-5), ≈2.40 (m; 1H, H-7), 2.28 (d, ^2J = 16.0 Hz, 1H, H-7), 2.1—2.0 (7s; 21H, CH_3CO), ≈1.6 (m; 1H, H-4), ≈1.3 (m; 1H, H-4); ^{13}C-NMR (75.46 MHz, $CDCl_3$): δ = 170.66—169.02 (6s; 7 $COCH_3$), 96.01 (d; C-1′), 93.86 (d; C-1), 88.25 (s; C-8), 77.38 (d; C-6), 73.39 (d; C-3′), 72.29 (d; C-5′), 71.42 (d; C-2′), 68.72 (d; C-4′), 65.40 (t; C-10), 62.10 (t; C-6′), 57.59 (t; C-3), 49.22 (d; C-9), 41.70 (t; C-7), 40.26 (d; C-5), 24.17 (t; C-4), 21.18—20.58 (5q; 7 CH_3CO)
(3): ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.47 (d, ^4J = 2.4 Hz; 1H, H-2), 4.40 (m, ^2J = 11.4 Hz; 1H, H-4), ≈3.96 (m; 2H, H-4, H-7), 3.03 (s; 1H, OH), 2.64 (m, ^2J = 17.3 Hz; 2H, H-6, H-8), 2.41 (m; 2H, H-5, H-8), 1.52 (m; 1H, H-5); ^{13}C-NMR (22.63 MHz, $CDCl_3$): δ = 200.66 (s; C-9), 150.71 (d; C-2), 115.92 (s; C-1), 74.82 (d; C-7), 67.26 (t; C-4), 47.95 (t; C-8), 42.18 (d; C-6), 25.62 (t; C-5); MS: *m/e* = 154 (M^+, calc. 154.0630, exp. 154.0625); 136 ($C_8H_8O_2$), 110 ($C_6H_6O_2$), 82 (C_5H_6O)

Unlike other glucosides, the iridoid glucosides also undergo cleavage of the glucoside bond on treatment with aqueous sodium periodate solution, thus yielding carboxylic acids as well as the aglycones. Compared to acid-catalyzed glucoside cleavage this method has the advantage that the aglycones can be isolated directly from the weakly alkaline solution after saturation with sodium hydrogen carbonate and do not have to be separated from the glucose. The carbon skeleton of the iridoids is, of course, only retained in this reaction if the cyclopentane ring contains no vicinal hydroxy groups. In periodate cleavage of *(2)*, water is eliminated on saturation of the reaction solution with sodium hydrogen carbonate, thus forming *(3)* instead of the aglycone (see Table 1). The configuration at C-6/7 of *(3)* is determined by that of catalpol and corresponds to the configuration at C-11/12 of prostaglandins, showing their partial synthesis from *(3)* to be possible without resolution of racemates[1].

Procedure

6,8-Dihydroxy-8-(hydroxymethyl)-1-iridanyl 1′-β-D-glucopyranoside[3] *(2)*: Hexaacetyl dihydrocatalpol *(1)* (18.4 g, 30 mmol; m.p. 155—156 °C; $[\alpha]_{589}^{20} = -69.3$ (*c* = 2 g/100 ml $CHCl_3$)) is added portionwise to a suspension of $LiAlH_4$ (7.4 g, 195 mmol) in anhydrous tetrahydrofuran (THF) (1000 ml) and heated under reflux for 4 h. The excess of $LiAlH_4$ is destroyed by addition of ethyl acetate and water. After passage of CO_2, inorganic salts are filtered off and the residue washed several times with water. The THF is removed *in vacuo* at 40 °C bath temperature and the aqueous solution heated with active charcoal (50 g) to 80 °C for 3 h. After decanting from the precipitated charcoal, the solution is treated twice more with active charcoal (2 × 50 g). TLC shows that *(2)* is no longer present in the aqueous solution. The charcoal is filtered off under suction and washed with water until no inorganic salts can be detected. After drying in air, it is extracted several times with 95% ethanol for 10 min at boiling temperature. The combined filtrates are evaporated to dryness *in vacuo*; yield 9.5 g (86%) of colorless amorphous *(2)*; $[\alpha]_{589}^{20} = -77.1$ (*c* = 1.9 g/100 ml CH_3OH).

Heptaacetate of *(2)*: P_4O_{10}-dried *(2)* (1 g) is acetylated with anhydrous pyridine (2.3 ml) and anhydrous acetic anhydride (2.9 ml) for 24 h at 50 °C. The reaction mixture is poured into ice-water and the oil precipitated is rubbed until it turns solid. The solid product is filtered off, washed with ice-water, and recrystallized from ethanol; yield 1.1 g (61%). (The mother liquor contains a hexaacetate in which one tertiary hydroxy group is not acetylated.) M.p. 100—102 °C; $[\alpha]_{589}^{20} = -61.6$ (*c* = 1 g/100 ml $CHCl_3$); $R_F = 0.31$ (mobile phase: benzene/acetone 8:2).

(3): Sodium periodate (15 g, 70 mmol) is added to a solution of *(2)* (5.5 g, 15 mmol) in water (250 ml). The solution is left to stand for 30 min at room temperature with occasional shaking. After addition of sodium hydrogen carbonate (20 g; pH = 8), the inorganic salts are filtered off and washed with water (50 ml). The filtrate is concentrated *in vacuo* at a bath temperature of 35 °C until further inorganic salts begin to precipitate. The colorless solution is extracted with ethyl acetate (5 × 100 ml), and the combined ethyl acetate extracts are dried with sodium sulfate and evaporated to dryness *in vacuo* at 35 °C bath temperature. The oil precipitated crystallizes on scratching; yield 1.8 g (78%) of *(3)*. For analysis the product is dissolved in a very small volume of cold dioxane and carbon tetrachloride is added until the onset of turbidity. Compound *(3)* crystallizes in a refrigerator; m.p. 95—97 °C; $[\alpha]_{589}^{20} = -267$ (*c* = 3 g/100 ml CH_3OH).

Received: February 27, 1980 [Z 520 IE]
German version: Angew. Chem. 92, 639 (1980)

[*] Prof. Dr. K. Weinges, Dipl.-Chem. Dipl.-Biol. H. von der Eltz, Dipl.-Chem. D. Tran-Viet
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[1] *K. Weinges et al.*, to be published.
[2] We are grateful to the Dr. W. Schwabe company, Karlsruhe, for supplying a concentrate of *ca.* 18% catalpol.
[3] We designate the hydrogenated parent of the iridoids as "iridane" and number it by analogy with the iridoids.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0628 $ 02.50/0

Vitamin B_{12} and a Vitamin B_{12} Model Compound as Catalysts of Reductive Removal of β-Haloethyl Protecting Groups from Acids[**]

By *Rolf Scheffold* and *Erik Amble*[*]

β-Haloethyl groups are used as protecting groups[2] for carboxylic acids[3a], amines[3b,c], phosphoric acids[3d], alcohols[3e], and also for aldehydes and ketones[3f]. They supplement the range of protecting groups removable by solvolysis, because they are selectively eliminated by reductive elimination according to

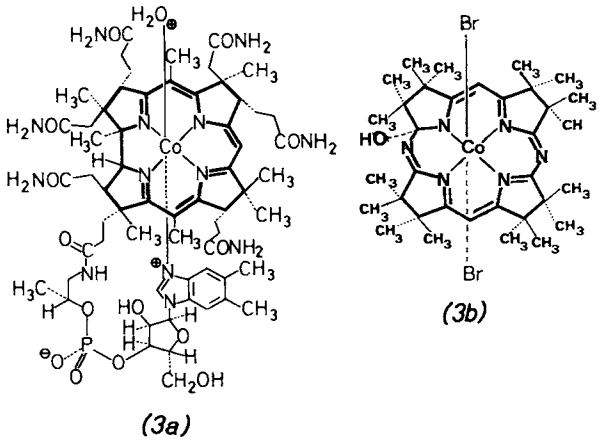
$$R{-}O{-}CH_2{-}CH_2{-}X + H^{\oplus} + 2e \rightarrow R{-}OH + CH_2{=}CH_2 + X^{\ominus}$$

Sources of electrons are metals such as zinc[4a], metal ions in low oxidation states[4b] and their complexes such as the supernucleophilic cobalt(I)-phthalocyanines[3e], and the cathode in direct[4c] or indirect[4d] electrochemical processes. The reactivity of the β-haloethyl groups decreases along the series $-CH_2CBr_3 > -CH_2CCl_3 > -CH_2CH_2I > -CH_2CH_2Br \gg -CH_2CH_2Cl$. No mild and effective elimination procedures were hitherto known[4a] for the β-chloroethyl group, which is the most stable towards bases and nucleophiles.

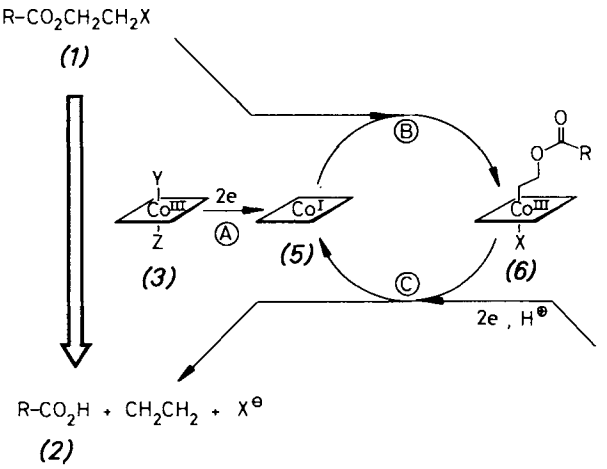
We have now found that vitamin B_{12} derivatives, *e.g.* aquocobalamin *(3a)*[5] and the readily synthesized vitamin B_{12} model compound dibromo[1-hydroxy-2,2,3,3,7,7,8,8,12,12,13,13,17,17,18,18-hexadecamethyl-10,20-diazaoctahydroporphinato]cobalt(III) *(3b)*[6], catalyze the reductive elimination of β-chloroethyl esters *(1)*, even in amounts of 10^{-3} mol. equiv. [with respect to *(1)*] under extremely mild conditions. Table 1 shows some examples of elimination catalyzed by *(3a)* or *(3b)* according to two procedures: I with zinc dust/ammonium chloride and II electrochemically at a cathode potential of -1.9 to -2.0 V[7]. The reaction conditions are mild enough not to hydrolyze even β-lactam derivatives such as *(1c)*. No reaction occurs in the absence of catalyst.

The mode of action of the catalyst is shown in Scheme 1.

$$\underset{(1)}{R{-}CO_2{-}CH_2{-}CH_2{-}X} + H^{\oplus} + 2e \longrightarrow R{-}CO_2H + CH_2{=}CH_2 + X^{\ominus}$$
$$(2)$$

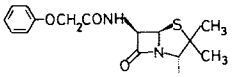


In step A, the octahedral Co^{III} complexes *(3a)* and *(3b)* are reduced at -1.5 V and at -1.2 V[8] to the catalytically active square-planar green Co^{I} complexes *(5a)* and *(5b)*, respectively. These products react in step B as nucleophiles with *(1)* to form the octahedral red Co^{III}-alkyl complexes *(6a)* and *(6b)*[8,9]. At potentials more negative than -1.7 V[7] these complexes undergo two-electron reduction according to step



Scheme 1

Table 1. Reductive cleavage of β-chloroethyl or β-bromoethyl esters *(1)* to the acids *(2)* catalyzed by aquocobalamin *(3a)* or the model compound *(3b)*. See text and procedure for routes I and II.

Reactant	R	X	Route	Reaction conditions [h/°C]	Catalyst [a]	Product	Yield [%] [b]
(1a)	C_6H_5	Cl	II	30/20	3.3% *(3a)*	*(2a)*	98
			II	30/20	none	—	0
			I	20/20	1.9% *(3a)*	*(2a)*	93
			I	30/20	none	*(2a)*	<5
(1b)	C_6H_5	Br	II	13/20	3.8% *(3b)*	*(2b)* [≡ *(2a)*]	90
(1c)		Br	II	17/1	4.0% *(3a)*	*(2c)*	95
(1d)	p-$H_3C{-}C_6H_4{-}NH$	Cl	I	15/20	1.4% *(3a)*	*(4)* [c]	96

[a] Mol-% based on 1 mol (=100%) of reactant. [b] Based on isolated material under non-optimized reaction conditions [c]. Decarboxylation occurs to give p-$H_3C{-}C_6H_4{-}NH_2$.

[*] Prof. Dr. R. Scheffold, Dr. E. Amble
Institut für Organische Chemie der Universität
Freiestrasse 3, CH-3012 Bern (Switzerland)

[**] Synthesis and Reactions of Porphinoid Metal Complexes, Part 9. This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Projekt 2.151-0.78). We are grateful to Dr. *P. Schneider*, CIBA-GEIGY AG, Basel, for supplying penicillin V and its β-haloethyl esters.—Part 8: [1].

C, and decompose to *(2)*, ethylene, and the Co^{I} complex *(5)*. If the potential required for reduction of *(6)* is maintained (electrochemically or by another reducing agent, such as zinc) the reaction continues until the substrate is completely consumed, as shown by appearance of the green color of *(5)*. We therefore call the reductive cleavage of β-haloethyl esters catalyzed by *(3)* the "traffic light reaction", since a color

change from red to green gives the go-ahead for further workup.

Procedure

Route I: β-Chloroethyl *N*-(*p*-tolyl)carbamate *(1d)* (0.53 g, 2.5 mmol), aquocobalamine *(3a)* (50 mg, 0.036 mmol), NH_4Cl (3.0 g, 56 mmol), and zinc dust (0.5 g, 7.6 mmol) [activated by 0.1 N hydrochloric acid and washing with water] in 1:1 ethanol/water (30 ml) were stirred together under argon at room temperature for 15 h. The green suspension was filtered and worked up with CH_2Cl_2: 0.26 g (96%) *p*-toluidine *(4)*, m.p. 41—43 °C.

Route II: Penicillin V β-bromoethyl ester *(1c)* (0.75 g, 1.73 mmol) and *(3a)* (95 mg, 0.07 mmol) were dissolved in 25 ml of electrolyte (0.1 N $LiClO_4$, 0.13 N NH_4ClO_4 in 4:1 ethanol/water) and electrolyzed at a stirred Hg electrode in the cathode compartment of an electrolysis cell at −1.95 V[7] and 1 °C under argon. After 17 h, the reaction solution was diluted with water (50 ml) and worked up with CH_2Cl_2: 0.57 g (95%) penicillin V *(2c)* (identified by TLC and by IR and NMR spectra).

Received: April 8, 1980 [Z 522 IE]
German version: Angew. Chem. *92*, 643 (1980)

[1] *R. Scheffold, M. Dike, S. Dike, T. Herold, L. Walder,* J. Am. Chem. Soc. *102*, 3642 (1980).

[2] *J. F. W. McOmie:* Protective Groups in Organic Chemistry. Plenum Press, London 1973, pp. 57, 204, 224.

[3] a) *R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, H. Vorbrücken,* J. Am. Chem. Soc. *88*, 852 (1966); *H. Eckert, I. Ugi,* Angew. Chem. *88*, 717 (1976); Angew. Chem. Int. Ed. Engl. *15*, 681 (1976); *B. Marinier, Y. C. Kim, J. M. Navarre,* Can. J. Chem. *51*, 208 (1973); b) *J. Grimshaw,* J. Chem. Soc. *1965*, 7136; *H. Yajima, H. Watanabe, M. Okamoto,* Chem. Pharm. Bull. *18*, 2185 (1971); c) *H. Eckert, I. Ugi,* Justus Liebigs Ann. Chem. *1979*, 278; d) *F. Eckstein,* Angew. Chem. *77*, 912 (1965); Angew. Chem. Int. Ed. Engl. *4*, 876 (1965); e) *T. B. Windholz, D. B. R. Johnston,* Tetrahedron Lett. *1967*, 2555; *R. M. Jacobson, J. W. Clader,* Synth. Commun. *9*, 57 (1979); f) *E. J. Corey, R. A. Ruder,* J. Org. Chem. *38*, 834 (1973); *E. J. Corey, E. J. Trybulski, J. W. Suggs,* Tetrahedron Lett. *1976*, 4577; *B. Bernet, A. Vasella,* Helv. Chim. Acta *62*, 1990, 2400, 2411 (1979); *J. L. Isidor, R. M. Carlson,* J. Org. Chem. *38*, 554 (1973).

[4] a) *M. Schlosser* in Houben-Weyl: Methoden der Organischen Chemie. 4th Edit. Thieme, Stuttgart 1972, Vol. V/1b, p. 204; b) *J. K. Kochi, P. E. Mocadlo,* J. Org. Chem. *30*, 1134 (1965); *T.-L. Ho,* Synthesis *1979*, 1; c) *E. Kasafirek,* Tetrahedron Lett. *1972*, 2021; *M. F. Semmelhack, G. E. Heinsohn,* J. Am. Chem. Soc. *94*, 5139 (1972); d) *C. Gosden, D. Pletcher,* J. Organomet. Chem. *186*, 401 (1980).

[5] Fluka AG, CH-9470 Buchs; *W. Friedrich:* Fermente, Hormone, Vitamine. Vol. III/2. Thieme, Stuttgart 1975, p. 33.

[6] *G. Rytz, R. Scheffold,* Helv. Chim. Acta *63*, 733 (1980).

[7] All potentials are relative to the Ag/0.01 N $AgNO_3$ reference electrode.

[8] *G. Rytz,* Dissertation, Universität Bern 1979.

[9] *G. N. Schrauzer,* Angew. Chem. *88*, 465 (1976); Angew. Chem. Int. Ed. Engl. *15*, 417 (1976); *H. Eckert, G. N. Schrauzer, I. Ugi,* Tetrahedron *31*, 1399 (1974).

Optically Active Chalcogran (2-Ethyl-1,6-dioxaspiro[4.4]nonane)[**]

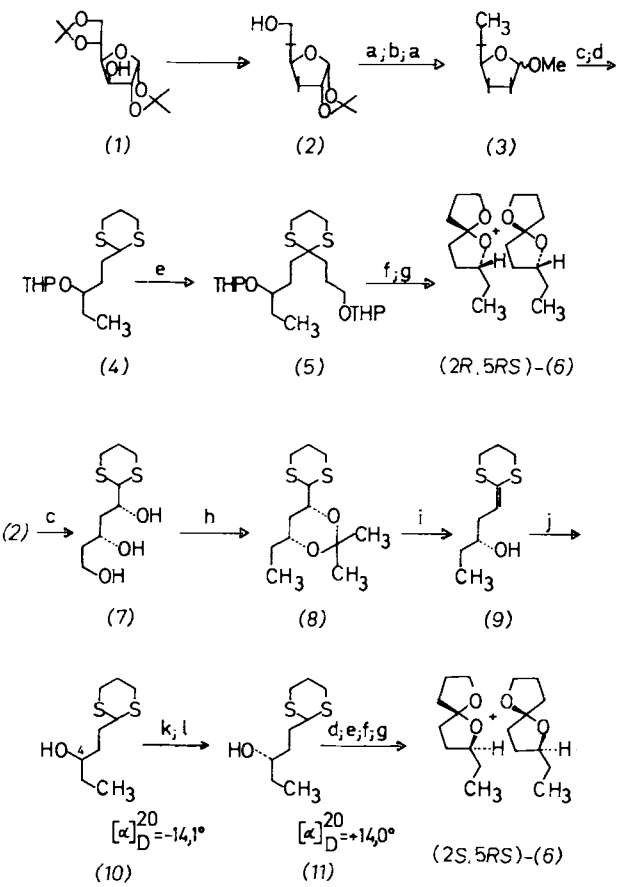
By *Hartmut Redlich* and *Wittko Francke*[*]

Chalcogran *(6)* is the aggregation pheromone of the bark beetle *Pityogenes chalcographus* (L.)[1]. Spiroketals of this type play a vital role as volatile chemical messengers in many insect species[2]. Chalcogran occurs as a mixture of diastereomers [(2*R*,5*R*) : (2*R*,5*S*), and (2*S*,5*R*) : (2*S*,5*S*), respectively, about 1:1] in the beetles.

Gas chromatograms of the volatile components of *P. chalcographus* and its sympatrically distributed relative *P. quadridens* (Htg.) cannot be distinguished[3], although the beetles are perfectly able to differentiate between the pheromone bouquets of the individual species under natural conditions. As in other bark beetles[4], a species specificity of this kind may arise from the differing chirality of the principal pheromone.

With the aim of answering this question, we have synthesized optically pure (2*R*,5*RS*)-chalcogran (2*R*,5*RS*)-*(6)* from D-glucose. Carbohydrates are in many respects ideal starting materials for the synthesis of highly pure optically active natural products. For example, use of 1,3-propanedithiol in the reaction of sugars with thiols[5] to give dithioacetals leads, with almost any sugar, to a dithiane compound which can be linked by the Corey-Seebach method[6], and thus to a wealth of readily accessible chiral synthons suitable for the preparation of chiral natural products. We have used this approach for the synthesis of the open-chain, completely protected chalcogran precursor *(5)*.

Starting from D-glucose, the 3,5-dideoxy compound *(2)*[7] and the tetradeoxy compound *(3)* can be synthesized *via* the diisopropylidene compound *(1)* (see Scheme 1). Reaction of



Scheme 1. a) In THF: NaH; CS_2; CH_3I to form xanthate. (n-Bu)$_3$SnH reduction in boiling toluene; azobisisobutyronitrile as radical chain initiator. Column chromatography. b) Methanol/HCl *ca.* 3%. Crude syrup used for further reaction. c) 1,3-Propanedithiol in $CHCl_3$/MeOH 98:2 v/v; $BF_3 \cdot Et_2O$ catalysis. d) 3,4-Dihydro-2*H*-pyran in dioxane, HOTs catalysis. e) In THF: 1.1 mol. equiv. of BuLi (−70→−20 °C); 1.5 h; $Br(CH_2)_3$—OTHP sol. in THF added dropwise at −70 °C. f) 8 mol equiv. collidine·HCl and 4 mol. equiv. HgO in 60 ml of MeOH/H_2O 2:1 v/v under reflux; *ca.* 1 h. g) $H^{\oplus}$. h) Acetone, $CuSO_4$, H_2SO_4 as catalyst, *ca.* 1 h; TsCl/pyridine; $LiAlH_4$ reduction. i) In THF: 2.2 mol. equiv. BuLi (−20 °C→RT). j) In THF: 1 mol. equiv. $LiAlH_4$, reflux. k) In THF: *(10)* and 1.1 mol. equiv. PPh_3 present; 2.2 mol. equiv. benzoic acid and 2.4 mol. equiv. diethyl azodicarboxylate added dropwise as solution in THF. l) $MeO^{\ominus}$ in MeOH.

[*] Dr. H. Redlich, Dr. W. Francke
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] Open-Chain Sugar Dithioacetals as Synthons for Natural Products, Part 1.

(3) with propanedithiol affords the open-chain optically active dithiane alcohol which, as a tetrahydropyranyl (THP) derivative *(4)*, can be linked with THP-protected 3-bromo-1-propanol by the Corey-Seebach method[6] to form the open-chain, blocked (2*R*)-chalcogran precursor *(5)*. Cleavage of the dithiane to give the ketone[8] and removal of the THP protecting groups in an acid medium lead *via* spontaneous cyclization to the desired mixture of diastereomers (2*R*,5*RS*)-*(6)* (see Scheme 1). After purification by gas chromatography, it has an optical rotation of $[\alpha]_D^{20} = +18.4$ ($c = 3.7$ in pentane)[9].

Better yields of (unprotected) *(4)* [*i.e. ca.* 70% *(10)* instead of 30% *(4)*] are obtained by the alternative reaction sequence starting from the dideoxy compound *(2)*. Compound *(2)* can be transformed directly into the open-chain thioacetal *(7)*, which in turn affords the isopropylidene compound *(8)*. Elimination with butyllithium leads to the ketene thioacetal *(9)*[10], which can be hydrogenated to *(10)*[11].

The open-chain alcohols *(10)* having (*R*) configuration at C-4 can be quantitatively converted into the benzoate with (*S*) configuration[12]. After removal of the ester group, comparison of the optical rotations [$[\alpha]_D^{20} = -14.1$ for *(10)* and $+14.0$ for *(11)*] indicates complete inversion at C-4. Compound *(11)* was transformed into (2*S*,5*RS*)-chalcogran by a reaction sequence analogous to that for (unprotected) *(4)* (see Scheme 1).

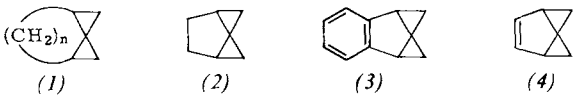
Received: September 12, 1979;
supplemented: April 17, 1980 [Z 523 IE]
German version: Angew. Chem. *92*, 640 (1980)

[1] *W. Francke, V. Heemann, B. Gerken, J. A. A. Renwick, J. P. Vité*, Naturwissenschaften *64*, 590 (1977).
[2] *W. Francke, G. Hindorf, W. Reith*, Angew. Chem. *90*, 915 (1978); Angew. Chem. Int. Ed. Engl. *17*, 892 (1978); *W. Francke, W. Reith, G. Bergström, J. Tengö*, Naturwissenschaften *67*, 199 (1980); *R. Baker, R. Herbert, Ph. E. Howse, O. T. Jones, W. Francke, W. Reith*, J. Chem. Soc. Chem. Commun. *1980*, 52.
[3] 50 m capillary with WG 11 and Marlophen 87 as stationary phases; temperature program from 60–150 °C at 3 °C/min.
[4] *E. L. Plummer, T. E. Stewart, K. Byrne, G. T. Pearce, R. M. Silverstein*, J. Chem. Ecol. *2*, 307 (1976).
[5] *E. Fischer*, Ber. Dtsch. Chem. Ges. *27*, 673 (1894).
[6] *D. Seebach*, Synthesis *1969*, 17.
[7] *D. H. R. Barton, S. W. McCombie*, J. Chem. Soc. Perkin Trans. I *1975*, 1574; *A. Zobacova, V. Hermankova, Z. Kefurtova, J. Jary*, Coll. Czech. Chem. Commun. *40*, 3505 (1975).
[8] *H. Redlich, H.-J. Neumann, H. Paulsen*, Chem. Ber. *110*, 2911 (1977).
[9] Cf. also *L. R. Smith, H. J. Williams, R. M. Silverstein*, Tetrahedron *1978*, 3231; *K. Mori, M. Sasaki, S. Tamada, T. Sugaro, S. Masuda*, Tetrahedron *35*, 1601 (1979).
[10] *T. van Es*, Carbohydr. Res. *32*, 370 (1974); *D. Horton, J. D. Wander, ibid. 13*, 33 (1970).
[11] *M. Y. H. Wong, E. R. Gray*, J. Am. Chem. Soc. *100*, 3548 (1978).
[12] *G. Grynkiewicz, H. Burzynska*, Tetrahedron *32*, 2109 (1976).

4,5-Benzotricyclo[4.1.0.0^{1,3}]hept-4-ene[**]

By *Udo H. Brinker* and *Joachim Streu*[*]

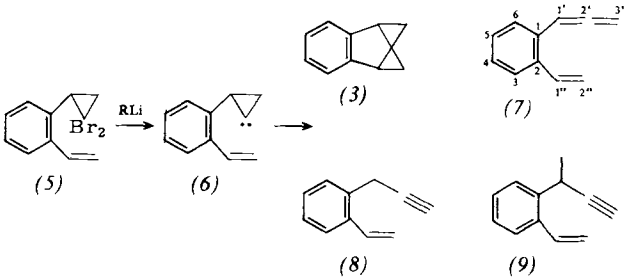
Intramolecular additions of carbenes to C=C double bonds are often the decisive reaction step in the synthesis of uncommon, highly strained hydrocarbons[1]. Strained polycyclics containing bicyclo[1.1.0]butane[2] and spiropentane units *(1)* ($n = 2, 3$)[3] can be prepared according to this principle. In tricyclo[4.1.0.0^{1,3}]heptane *(2)*[3a,b] there is high angular strain, which is reflected in its thermal behavior[4]. In the hitherto unknown unsaturated hydrocarbons *(3)* and *(4)*[5] for the first time the cyclopropane rings of the spiropentane moiety can interact with the aromatic or olefinic π-electron system.



(1) *(2)* *(3)* *(4)*

We report here on a facile synthesis and some properties of 4,5-benzotricyclo[4.1.0.0^{1,3}]hept-4-ene *(3)*, the first representative of this class of hydrocarbons.

Addition of dibromocarbene to *o*-divinylbenzene affords *o*-(2,2-dibromocyclopropyl)styrene *(5)*[6]. Reaction of *(5)* with methyllithium (molar ratio 1:1, ether) at −50 °C leads only to a mixture of the hydrocarbons *(3)* and *(7)* (35:65) in 90–95% yield. The product ratio of *(3)* and *(7)* shows a similar temperature-dependence as that already observed by *Skattebøl* in the reaction of 1,1-dibromo-2-(3-butenyl)cyclopropane with methyllithium[3a,b]. Under otherwise identical conditions, the reaction is more selective with increasing temperature [*(3)* and *(7)* at 25 °C = 15:85]. Assuming that the competing reactions of *(6)*, *i.e.* intramolecular addition of the cyclopropylidene[7] to the vinyl group to give *(3)* and cyclopropylidene-allene rearrangement to give *(7)*, proceed from the same intermediate, this finding would indicate that the temperature-dependence of the ratio of *(3)* and *(7)* is determined by a low isoselective temperature[8]; T_{iso} is estimated at −80 °C.



(5) *(6)* *(3)* *(7)* *(8)* *(9)*

At room temperature the mixture of *(3)* and *(7)* is accompanied by traces of the alkyne *(8)*, which could have been formed by isomerization of the allene *(7)* under the basic conditions employed[9]. In the presence of an excess of methyllithium, *(9)*[10] is formed, probably by methylation of the benzyl anion of *(8)*[9]. Temperatures between −55 and −90 °C favor the formation of *o*-(2-bromocyclopropyl)- and *o*-(2-bromo-2-methylcyclopropyl)styrene(s). These products could be formed by protonation and methylation, respectively, of the intermediate resulting from halogen-metal exchange in *(5)*.

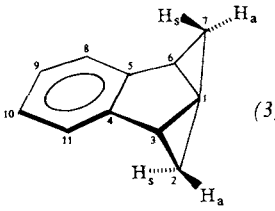
The separation of *(3)* and *(7)* by standard chromatographic methods (LC, TLC, GC, HPLC) is difficult. However, the pure substances can be obtained as follows: After reaction of the mixture of *(3)* and *(7)* with sodamide (3 equivalents) in liquid ammonia, *(3)* can be separated by distillation from any sodium acetylide that is probably formed. Reaction of the mixture with a saturated ethanolic silver nitrate solution enables isolation of *(7)* in pure form. Apparently, only *(3)* reacts to give high-boiling products, from which *(7)* can be separated by distillation (see Table 1)[10].

(3)[10] crystallizes as colorless needles, m.p. 13.5–15.5 °C (pentane), which are sensitive to atmospheric oxygen. Owing to the C_2 symmetry the ^{1}H-NMR spectrum is simple (Table

[*] Dr. U. H. Brinker, J. Streu
Abteilung für Chemie der Universität
Universitätsstr. 150, D-4630 Bochum 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We thank Degussa (Frankfurt) for supplying us with chemicals, Dr. *W. Dietrich* for the ^{13}C- and 250 MHz ^{1}H-NMR spectra of the title compound, Dipl.-Chem. *U. Günther* for the analysis of the ^{1}H-NMR spectrum, and Prof. *Klärner* for valuable discussions.

1). The aromatic protons form an AA'BB' system and the three-membered ring protons and ABX system. The detailed analysis of both systems permits exact determination only of the parameters of the aromatic protons. Protons and coupling constants of the ABX system can be assigned on the assumption that the benzylic hydrogen atoms H-3 and H-6 resonate further downfield than H-2_a and H-7_a. Table 1 lists the proton sequence for this assignment.



(3)

Table 1. Some spectral data for compounds *(3)* and *(7)*.

(3), ^{1}H-NMR (C_6D_6, 250 MHz): $\delta = 7.24$ (2H, H-9, 10), 7.03 (2H, H-8, 11), $J_{9,10} = 7.45$ Hz, $J_{8,9} = 7.38$ Hz, $J_{8,10} = 1.42$ Hz, $J_{8,11} = 0.58$ Hz, 1.74 (2H, H-3, 6), 1.66 (2H, H-2_a, 7_a), 1.28 (2H, H-2_s, 7_s), $J_{3,2a} = J_{6,7a} = 6.7$ Hz, $J_{3,2s} = J_{6,7s} = 3.3$ Hz, $J_{2s,2a} = J_{7s,7a} = -4.4$ Hz; ^{13}C-NMR ($CDCl_3$, 22.6 MHz): $\delta = 149.0$ (C-4, 5), 126.0 (C-8, 9, 10, 11), 25.1 (C-3, 6), 19.1 (C-1), 15.7 (C-2, 7); MS (70 eV): $m/e = 143$ (15%, $M^+ + 1$), 142 (100, M^+), 141 (73, $M^+ - 1$), 115 (11), 91 (6); UV (*n*-hexane): $\lambda_{max} = 209$ nm ($\varepsilon = 59\,500$), 230 (8400, sh), 275 (2900), 283 (3200)
(7), ^{1}H-NMR (CCl_4, 60 MHz): $\delta = 5.04$ (d, $J_{1',3'} = 7$ Hz, 2H, H-3'), 5.28 (dd, $J_{2'',E,1''} = 11$ Hz, $J_{2'',E,2'',Z} = 1.5$ Hz, 1H, H-2''*E*), 5.56 (dd, $J_{2'',Z,1''} = 17.5$ Hz, 1H, H-2''*Z*), 6.43 (t, $J_{1',3'} = 7$ Hz, 1H, H-1'), 6.76—7.56 (m, 5H, H-1'', 3, 4, 5, 6); IR (CCl_4): $\nu = 1940$ cm^{-1} (C=C=C); UV (*n*-hexane): $\lambda_{max} = 228$ ($\varepsilon = 38000$), 258 (32000)

The ^{13}C-NMR spectrum shows only five signals, which can be assigned by "off-resonance" decoupling (Table 1). The symmetry of *(3)* is reflected in its IR spectrum, which contains only few bands. The UV bands are shifted bathochromically by about 4—9 and 5—11 nm, respectively, compared to the corresponding bands of model compounds such as 2,3-benzobicyclo[4.1.0]hept-2-ene[11] and 2,3-benzobicyclo[3.1.0]hex-2-ene[11]. *(3)* is only moderately thermostable, its half-life in CCl_4 at 56 °C is *ca.* 40 min. The chemical and thermal properties of *(3)* are currently under intensive investigation.

Received: March 3, 1980 [Z 525 IE]
German version: Angew. Chem. *92*, 641 (1980)

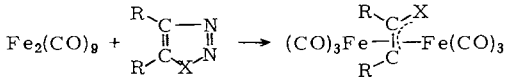
CAS Registry numbers:
(3), 74410-87-0; *(5)*, 74410-88-1; *(7)*, 74410-89-2; dibromocarbene, 4371-77-1; *o*-divinylbenzene, 91-14-5

[1] a) *W. Kirmse:* Carbene Chemistry. 2nd Edit. Academic Press, New York 1971; *A. P. Krapcho*, Synthesis *1978*, 77; b) *A. Greenberg, J. F. Liebman:* Strained Organic Molecules. Academic Press, New York 1978; *A. de Meijere*, Angew. Chem. *91*, 867 (1979); Angew. Chem. Int. Ed. Engl. *18*, 809 (1979).
[2] *D. M. Lemal, F. Menger, G. W. Clark*, J. Am. Chem. Soc. *85*, 2529 (1963).
[3] a) *L. Skattebøl*, Chem. Ind. (London) *1962*, 2146; b) J. Org. Chem. *31*, 2789 (1966); c) *M. S. Baird*, J. Chem. Soc. Chem. Commun. *1974*, 197; d) *G. Becher, L. Skattebøl*, Tetrahedron Lett. *1979*, 1261.
[4] *Z. Smith, B. Andersen, S. Bunce*, Acta Chem. Scand. *A 31*, 557 (1977); *(2)* isomerizes to 3-methylene-1,5-hexadiene with an activation energy about 20 to 22 kcal/mol lower ($E_A = 35.56 \pm 0.25$ kcal/mol, $\log A = 14.21 \pm 0.12$) than spiropentane: *H. M. Frey, R. G. Hopkins, L. Skattebøl*, J. Chem. Soc. *B 1971*, 539.
[5] *(4)* is formally the product of the intramolecular addition of *cis*-2-(1,3-butadienyl)cyclopropylidene: *U. H. Brinker, J. Fleischhauer*, Angew. Chem. *91*, 424 (1979); Angew. Chem. Int. Ed. Engl. *18*, 396 (1979).
[6] *L. Skattebøl*, J. Org. Chem. *29*, 2951 (1964).
[7] The intramolecular reactions of cyclopropylidene-bromolithium carbenoids generated *via* an organometallic route largely correspond with those of the free cyclopropylidenes: *W. M. Jones, U. H. Brinker* in *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions. Vol. 1. Academic Press, New York 1977.
[8] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).
[9] *E. V. Dehmlow, G. C. Ezimora*, Tetrahedron Lett. *1971*, 563, 1599.
[10] Correct elemental analyses were obtained for compounds *(3)*, *(7)*, and *(9)*.
[11] *A. L. Goodman, R. H. Eastman*, J. Am. Chem. Soc. *86*, 908 (1964); *R. C. Hahn, P. H. Howard, S.-M. Kong, G. A. Lorenzo, N. L. Miller*, J. Am. Chem. Soc. *91*, 3558 (1969).

Reactions of Cycloalkeno-1,2,3-selenadiazoles with Transition Metal Carbonyls[**]

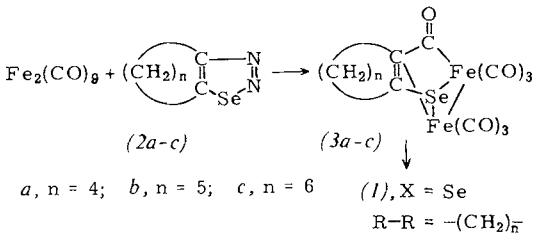
By *Keith H. Pannell, Armin J. Mayr, Rodney Hoggard,* and *Roger C. Pettersen*[*]

The stabilization of thioxo- and selenoxoketenes by iron carbonyls has been reported by *Rees et al.*[1] and *Schrauzer et al.*[2]. Using the reaction between the appropriate thia- or selena-diazole and $Fe_2(CO)_9$ they obtained complexes of the general structure *(1)*.



(1), X = S, Se

During a study of the properties of related cycloalkeno-1,2,3-selenadiazoles *(2a—c)*[3] we observed that the reactions of these ligands with $Fe_2(CO)_9$ in hexane at room temperature resulted in the formation of two complexes in good yield. These complexes may be readily separated using an alumina column, such that elution with hexane yields complexes *(1a—c)*, X = Se, while elution with CH_2Cl_2 yields complexes *(3a—c)*. Complexes *(3a—c)* are examples of a new class of complex.



(2a-c) *(3a-c)*

a, n = 4; *b*, n = 5; *c*, n = 6 *(1)*, X = Se
R–R = $-(CH_2)_n-$

An X-ray diffraction analysis of *(3a)* is illustrated in Figure 1. The molecule possesses a selenaferrole ring which is complexed to the second $Fe(CO)_3$ group *via* the selenium and iron atoms, and the double bond.

Upon heating to 60 °C, or upon irradiating with ultraviolet light, the complexes *(3a—c)* readily decarbonylate and rearrange to complexes *(1)*. This observation suggests that these latter complexes are not formed directly. Both *Rees* and *Schrauzer* performed their reactions in polar solvents at elevated temperatures, *i. e.* conditions under which the transformation *(3)*→*(1)* would be extremely rapid. This probably explains their failure to detect *(3)*.

Reactions of the selenadiazoles *(2)* with other metal complexes such as Group VI hexacarbonyls, norbornadienetetra-

[*] Prof. Dr. K. H. Pannell [+], Dr. A. J. Mayr, R. Hoggard
Department of Chemistry, University of Texas at El Paso
El Paso, Texas 79968 (USA)
Prof. Dr. R. C. Pettersen
Department of Chemistry, Texas A. & M. University
College Station, Texas 77483 (USA)
[+] To whom correspondence should be addressed.

[**] Organometallic Heterocyclic Reactions, Part 4. Support of this research by the Robert A. Welch Foundation, Houston, Texas, and the N.I.H. Institute of Arthritis, Metabolism, and Digestive Diseases (S06 RR-08012-09) is gratefully acknowledged.—Part 3: *K. H. Pannell, Ramon Iglesias*, Inorg. Chim. Acta *33*, L 161 (1979).

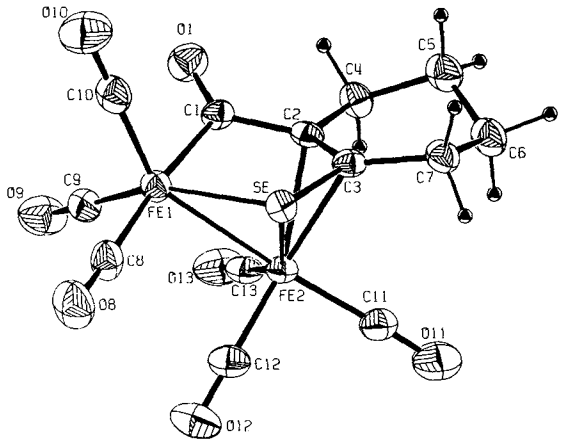


Fig. 1. Molecular structure of *(3a)*. Monoclinic, space group $P2_1/c$; $a = 7.399(2)$, $b = 12.509(4)$, $c = 18.429(6)$ Å, and $\beta = 114.83(2)$. Bond lengths: Fe—Fe = 2.631(1); Fe1—Se = 2.327(1); Fe2—Se = 2.353(1); Fe2—C2 = 2.214(8); Fe2—C3 = 2.132(7) Å.

carbonyls, and tris(acetonitrile)tricarbonyls yield only complexes in which the selenadiazole unit of *(2)* remains intact and acts as a monodentate ligand (bonding *via* a nitrogen lone pair), *e.g.* in (selenadiazole)$M(CO)_5$, or as a bridging ligand, *e.g.* in (selenadiazole)$_3(M(CO)_3)_2$.

Received: December 10, 1979 [Z 524 IE]
German version: Angew. Chem. *92*, 650 (1980)

CAS Registry numbers:
(1a) (X = Se), 74498-53-6; *(1b)* (X = Se), 74498-54-7; *(1c)* (X = Se), 74498-55-8; *(2a)*, 35676-30-3; *(2b)*, 35676-32-5; *(2c)*, 35676-31-4; *(3a)*, 74498-56-9; *(3b)*, 74498-57-0; *(3c)*, 74498-58-1; $Fe_2(CO)_9$, 15321-51-4

[1] *T. L. Gilchrist, P. G. Mente, C. W. Rees*, J. Chem. Soc. Perkin Trans. I, 2165 (1972).
[2] *G. N. Schrauzer, H. Kisch*, J. Am. Chem. Soc. *95*, 2501 (1973).
[3] *H. Meier, E. Voigt*, Tetrahedron *28*, 187 (1972).

Template Polymerization of Rhodium(I) with Rigid Bent Diisocyanide Ligands[**]

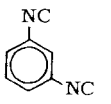
By *Avi Efraty, Irene Feinstein, Lorenz Wackerle*, and *Felix Frolow*[*]

Non-chelating bidentate ligands capable of forming stereochemically rigid bridges between metal nuclei are of special interest in the molecular design of rather unusual coordination polymers. This novel concept is exemplified in the current communication by the molecular design of two-dimensional coordination polymers of rhodium(I) having an unusual shape of a Greek cross with bent arms, and a stacked layers arrangement.

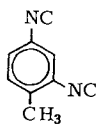
$[Rh(Bridge)_2^+\ Cl^- \cdot xH_2O]_n$, x = 0-8 *(1)*, *(2)*

Bridge in

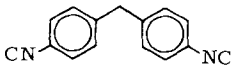
(1a):



(1b):



(2):



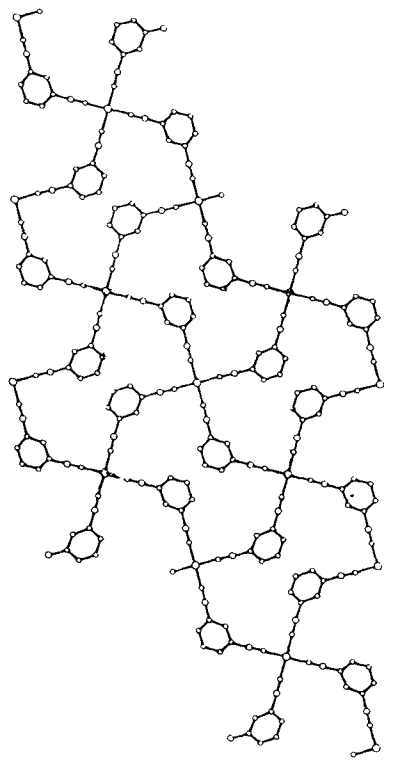
[*] Prof. Dr. A. Efraty, I. Feinstein, L. Wackerle
Department of Organic Chemistry
The Weizmann Institute of Science
Rehovot (Israel)
F. Frolow
Department of Structural Chemistry
The Weizmann Institute of Science, Rehovot (Israel)

[**] This work was supported by K. F. A. and N. R. C. D.

1,3-Diisocyanobenzene, 2,4-diisocyanotoluene and 4,4′-diisocyanodiphenylmethane[1] are rigid bent-bridging ligands capable of separating metal nuclei by approximately 10 and 14 Å, respectively. These ligands undergo a facile reaction with $[Rh(CO)_2Cl]_2$ to afford insoluble green polycrystalline polymers of the type *(1a)*, *(1b)*, and *(2)* in quantitative yields. The new air-stable polymers readily absorb water when exposed to air, and therefore, unless rigorously dried under vacuum these materials are best formulated as $[Rh(Bridge)_2^+Cl^- \cdot xH_2O]_n$ ($x = 0$—8). The IR spectra of these polymers exhibit one strong ν(NC) frequency (2142 ± 3 cm^{-1}) which is characteristic of terminally coordinated isocyanides in a symmetric environment.

The models in Figure 1 simulate the two-dimensional networks formed by template polymerization of tetragonal Rh^I with 1,3-diisocyanobenzene to give *(1a)* and with 4,4′-diisocyanodiphenylmethane to give *(1b)*. The models were con-

(1a)



(2)

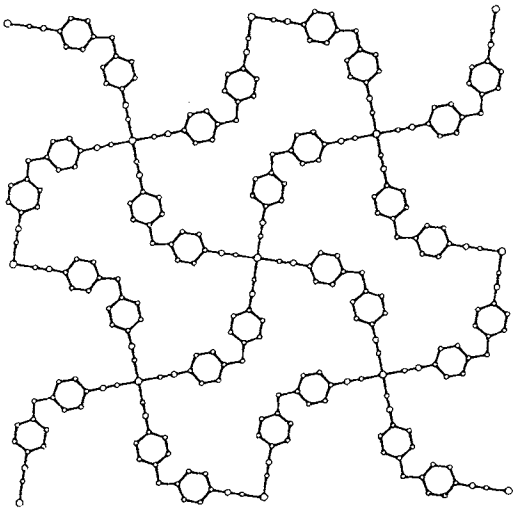


Fig. 1. Two-dimensional models of the polymer network in *(1a)* and *(2)*.

structed using idealized bond angles and distances similar to those reported for certain related complexes[2,3].

Model calculated cell dimensions are $a = 14.47$ Å *(1a)* [and *(1b)*] and $a = 20.26$ Å *(2)*. Inspection of these coplanar models reveals certain unrealistically short inter-bridging distances in *(1a)* (*e.g.* C5$\cdots$C5), as well as some constraint associated with the intra-bridging C2$\cdots$C2 distance in *(2)*. In the case of *(2)*, the constraint is either reduced or removed by the change in relative orientation of the phenylene rings. The established tendency of monomeric cations of type $Rh(CNR)_4^+$ to oligomerize *via* weak $Rh^1\cdots Rh^1$ bonding interaction[2] may suggest the stacking of the two-dimensional models *(1)* and *(2)* in an eclipsed fashion[3].

In the absence of suitable single crystals, powder X-ray diffractometric traces of the new polymers *(1a)*, *(1b)*, and *(2)* were measured. Especially informative results were obtained for *(1b)* and *(2)*. Both polymers have the space group P4; the cell constants are $a = 15.42(6)$, $c = 3.21$ Å and $a = 21.95(8)$, $c = 3.36$ Å, respectively. The powder diffraction data appear to be consistent with the presence of a tetragonal system[4] of rhodium atoms in these polymers. The most intense reflection found in these traces has been assigned to the 110 rhodium-containing planes, whose spacings correspond to the distance of separation of the metal nuclei by the bridging unit (10.91 and 15.49 Å, respectively). Besides other hk0 reflections[4], each trace also contained one reflection which was assigned to the 001 plane. The Rh—Rh distances [*d*(001)] in *(1b)* (3.21 Å) and *(2)* [3.36 Å] are similar to those found in dinuclear cationic complexes of the type $[Rh_2(CNAryl)_8]^{2+}$ (*e.g.*, 3.19[2], 3.21[3] and 3.25 Å[3]), as well as in a related rhodium polymer with colinear 1,4-diisocyanobenzene bridging units (3.31 Å)[5].

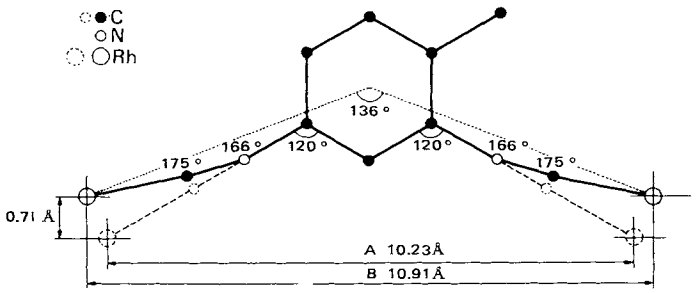


Fig. 2. *d*(110) in the polymer *(1b)*; A: calculated for the model; B: determined experimentally.

The shortcomings associated with the model are resolved in the real polymer *(1b)* by the small increase (≈ 0.68 Å) in the bridge span of 2,4-diisocyanotoluene (see Fig. 2); this corresponds to a ≈ 0.71 Å displacement of the methylphenylene unit towards the 110 plane. In a presumed situation involving the presence of proximity related eclipsed 2,4-diisocyanotoluene units, the inter-bridging distances in the real polymer *(1b)* (*e.g.*, C6$\cdots$C6 ≈ 3.64 Å; $CH_3\cdots CH_3 \approx 4.90$ Å) are estimated to be considerably longer compared with the respective (*e.g.*, ≈ 1.54 and ≈ 2.80 Å) model derived terms. The increase in the bridge span can be rationalized by the non-idealized C—N—C(Rh) and N—C—Rh bond angles (see Fig. 2).—The powder X-ray diffractometric trace of the polymer *(1a)* deviates from the expected pattern of a tetragonal system; interpretation of this trace has not yet been completed.

Experimental

1,3-Diisocyanobenzene (1.06 g, 8.28 mmol) dissolved in CH_2Cl_2 (100 ml) was added dropwise into a stirred solution (CH_2Cl_2, 50 ml) of $[Rh(CO)_2Cl]_2$ (0.4 g, 1.03 mmol) at room temperature. The dark green polycrystalline *(1a)* formed during this reaction in a quantitative yield (based on the Rh reactant), was filtered off, washed with CH_2Cl_2 (5 × 50 ml), and then vacuum dried (80 °C/0.1 torr). The polymers *(1b)* and *(2)* could be prepared utilizing essentially the same procedure. The complete elemental composition data of the new polymers are consistent with their formulation as $[Rh(Bridge)_2^+Cl^-\cdot x H_2O]_n$.

The powder X-ray diffractometric traces were obtained on a Phillips Diffractometer using filtered Cu radiation and a scan speed of 1° (2θ) min^{-1}.

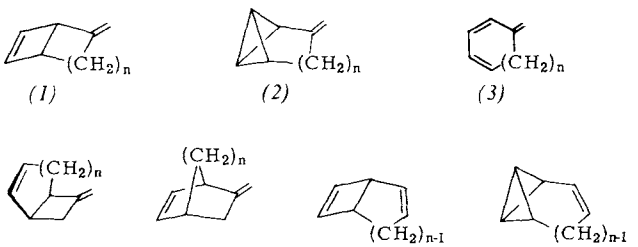
Received: April 9, 1980 [Z 526 IE]
German version: Angew. Chem. 92, 649 (1980)

[1] *I. Ugi*: Isonitrile Chemistry. Academic Press, New York 1971.
[2] *K. R. Mann, N. S. Lewis, R. M. Williams, H. B. Gray, J. G. Gordon II*, Inorg. Chem. *17*, 828 (1978).
[3] *H. Endres, N. Gottstein, H. J. Keller, R. Martin*, Z. Naturforsch. *B 34*, 827 (1979).
[4] *H. Lipson, H. Steeple*: Interpretation of X-ray Powder Diffraction Patterns. Macmillan, London 1970.
[5] *A. Efraty, I. Feinstein, F. Frolow, L. Wackerle*, unpublished.

New C_8H_{10} Isomers: 2-Methylenebicyclo[3.2.0]hept-6-ene and 3-Methylenetricyclo[4.1.0.0^{2,7}]heptane—Thermal and Metal-Catalyzed Rearrangements[**]

By *Dieter Hasselmann* and *Klaus Loosen*[*]

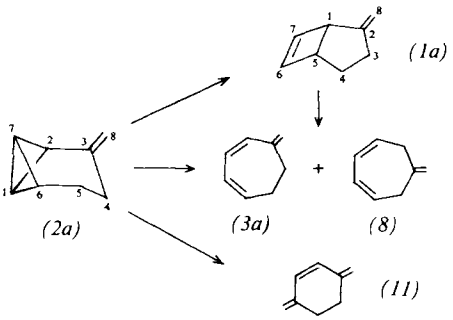
Strained small-ring hydrocarbons are of interest owing to their reactivity as well as their spectroscopic and structural properties[1]. The bicyclic isomer *(1b)*[2a] of toluene undergoes thermal isomerization exclusively *via* rupture of the central bond to give 5-methylene-1,3-cyclohexadiene *(3b)*, which should also be accessible from its isomer *(2b)* having a bicyclo[1.1.0]butane structural unit. In contrast, methylenebicycloalkenes *(4)* are observed to undergo both structural isomerization to methylenebicyclo[2.2.*n*]alkenes *(5)* and a degenerate methylenecyclobutane rearrangement[2b,c]. In comparison with this behavior and with the hydrocarbons *(6)* and *(7)* having an endocyclic double bond, the reactions of 2-methylenebicyclo[3.2.0]hept-6-ene *(1a)* and 3-methylenetricyclo[4.1.0.0^{2,7}]heptane *(2a)*, respectively, would appear particularly interesting[3]. We now report on thermal and metal-catalyzed rearrangements of the C_8H_{10} isomers *(1a)* and *(2a)*.



[*] Priv.-Doz. Dr. D. Hasselmann, Dr. K. Loosen
Abteilung für Chemie der Universität
Universitätsstrasse 150, D-4630 Bochum 1 (Germany)

[**] Reorganizations of Strained Methylenecycloalkanes, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Prof. *M. Christl*, Universität Würzburg, for communication of unpublished results.—Ref. [2b] is to be regarded as Part 5.

(1a) and *(2a)* were obtained by methylenation of the appropriate ketones[4] with methylenetriphenylphosphorane in dimethyl sulfoxide in 42 and 65% yield of the pure compounds after preparative gas chromatography[5]. Assignment of structure is based on spectroscopic data[5c], hydrogenation (Pd/C) [*(1a)* giving *endo*- and *exo*-2-methylbicyclo[3.2.0]heptane (90:10)[5a,b], and *(2a)* giving *cis*- (24%) and *trans*-1,4-dimethylcyclohexane (72%) and methylcycloheptane (4%)], and their rearrangements.



Thermolysis of *(1a)* in the stationary gas phase leads only to the methylenecycloheptadienes *(3a)* and *(8)*[6a], which are in equilibrium (*(3a)*:*(8)* = 98.8:1.2 at 198.6 °C) under the reaction conditions[6b]. The temperature dependence of the rate of the pressure-independent (0.1–7 mbar) monomolecular cycloreversion of *(1a)* can be described between 163 and 208 °C by the Arrhenius parameters listed in Table 1. In *(1a)* the exocyclic methylene substituent not only effects the expected lowering of activation energy ($\Delta E_a = 7.7$ kcal/mol) relative to the unsubstituted system *(9)*[7a], but also a lowering relative to the certainly more strained compound *(6a)* with endocyclic double bonds[7b] ($\Delta E_a = 1.7$ kcal/mol) (Table 1).

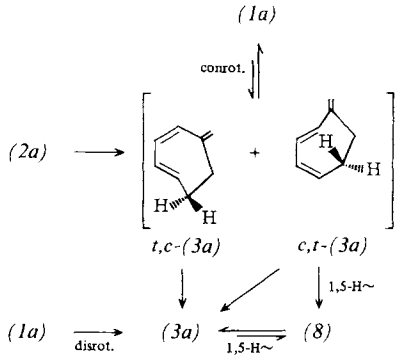
Table 1. Activation parameters.



Cpd.	Phase	E_a [kcal/mol] [a]	log$A$ [s^{-1}]	Ref.
(1a)	Gas	37.80 ± 0.16	13.61 ± 0.08	
(2a)	*n*-C_7H_{16}	33.41 ± 0.32	13.27 ± 0.17	
	Gas	32.54 ± 0.44	12.48 ± 0.23	
(6a)	Gas	39.5	14	[7b]
(7a)	Solution [b]	32.4 ± 0.6	13.6 ± 0.4	[9b]
(9)	Gas	45.51	14.31	[7a]
	Solution [c]	45.86	14.65	[7a]
(10)	Solution	37.8	12.8	[9b]

[a] 1 cal = 4.184 J. [b] [D_8]-Toluene/tetramethylethylenediamine. [c] Dimethyl phthalate.

Two reaction pathways must be considered for the rearrangements *(1a)*→*(3a)* + *(8)*: (a) a disrotatory route, forbidden by orbital symmetry, in which rupture of the bridgehead bond in the transition state profits more from formation of the conjugated system than the less flexible species *(6a)*; this leads directly to *(3a)*, which subsequently equilibrates with *(8)* *via* 1,5-hydrogen shift; (b) conrotatory, symmetry-allowed opening of *(1a)* to give *trans,cis*- and/or *cis,trans*-methylenecycloheptadienes [*t,c-(3a)* and *c,t-(3a)*, respectively], which relieve their considerable strain by direct *trans-cis* isomerization, initially giving *(3a)*, and/or by 1,5-hydrogen shift [conformationally preferred *c,t-(3a)*→*(8)*] initially giving *(8)*. Enhanced formation of *(8)* as compared with the equilibrium *(3a)*⇄*(8)* at small conversions of *(1a)* can be taken as experimental evidence for participation of *trans*-cycloheptadienes[8].



Thermolysis of the tricyclic compound *(2a)* in *n*-heptane (123—153 °C) primarily gives only the monocyclic species *(1a)*. Small amounts of *(3a)* and *(8)* are attributable to decomposition of *(1a)*. In the stationary gas phase (123—173 °C), the rate of consumption of *(2a)*, which is pressure independent between 0.1 and 5 mbar, is strictly of first order, but only half as high as in solution. This behavior is describable with Arrhenius parameters (Table 1) which lie in the expected range compared with those of tricycloheptane *(10)*[9b] and tricycloheptene *(7a)*[9b]. However, the product spectrum is more complicated than that obtained in solution. In addition to *(1a)*, more *(3a)* + *(8)* is formed than would be expected under the reaction conditions from the amount of *(1a)* formed; *(3a)* and *(8)* are apparently also formed directly from *(2a)*. For the same conversions of *(2a)*, the product ratio *(1a)*/[*(3a)* + *(8)*] decreases with falling pressure, *e.g.* $p = 5$ mbar→10^{-3} mbar: *(1a)*/[*(3a)* + *(8)*] = 10.0→0.8 (7 h, 154 °C). The rate of consumption of *(2a)* is concomitantly reduced by 15%. Surprisingly, *(11)*[10] appears as an additional product, accounting for up to 8% of the total[11].

In analogy to the thermolysis of other *endo,endo'*-bridged bicyclobutanes[9], the isomerization *(2a)*→*(1a)* can be regarded as a concerted [$_\pi 2_s + _\pi 2_a$]-reaction to give *c,t*- and/or *t,c-(3a)*, which subsequently recyclize to *(1a)*. However, diradical processes involving rupture of the C^2C^7 bond in *(2a)* as the initial step also appear to be energetically attainable (cf. [9b,c]). The pressure-dependent enhanced formation of *(3a)* in the gas phase could be due to reaction branching at the stage of vibrationally excited *c,t*- or *t,c-(3a)* or *(1a)*. Purely thermal formation of *(11)* is less readily understood. In doubly bridged bicyclo[1.1.0]butanes a similar thermal isomerization to transoid 1,3-butadienes has recently been interpreted in terms of a retro-carbene ring opening[12]. However, a reaction pathway *(2a)*→*(11)* with participation of a carbene [rupture of the C^2C^7 and the C^1C^7 bond in *(2a)*] and its insertion into the C^6—H bond should be relatively inaccessible from an energetic viewpoint.

An insight into the behavior of *(2a)* towards transition metals[1c] is provided by the following results: silver(I)-catalyzed rearrangement (benzene, 25 °C) leads *via* α-cleavage[1c] exclusively to *(3a)*. In contrast, on heating with copper(0) in benzene (1.5 h, 110 °C) primarily β-rearrangement[1c] is observed, giving *(11)* (81%) together with *(3a)* (17%) and *(1a)* (2%). This behavior resembles that of benzvalene *(7b)*: reaction with Ag^I gives only benzene, that with Cu^0 only fulvene[13].

Received: March 13, 1980 [Z 527 IE]
German version: Angew. Chem. 92, 651 (1980)

[1] a) *A. Greenberg, J. F. Liebman:* Strained Organic Molecules. Academic Press, New York 1978; b) *A. de Meijere*, Angew. Chem. *91*, 867 (1979); An-

gew. Chem. Int. Ed. Engl. *18*, 809 (1979); c) *K. C. Bishop*, Chem. Rev. *76*, 461 (1976).

[2] a) *D. Hasselmann, K. Loosen*, Angew. Chem. *90*, 641 (1978); Angew. Chem. Int. Ed. Engl. *17*, 606 (1978); b) *D. Hasselmann, P.-J. Rissing*, Tetrahedron Lett. *1979*, 1745; c) *D. Hasselmann*, Angew. Chem. *87*, 252 (1975); Angew. Chem. Int. Ed. Engl. *14*, 257 (1975); Tetrahedron Lett. *1972*, 3465; *1973*, 3739.

[3] Photoisomerization of a multiply alkylated derivative of *(1a)* to the correspondingly substituted *(2a)* has been described by *J. Ipaktschi*, Chem. Ber. *105*, 1996 (1972).

[4] a) Bicyclo[3.2.0]hept-6-en-2-one: *R. M. Coates, K. Yano*, J. Am. Chem. Soc. *95*, 2203 (1973); *T. Svensson*, Chem. Scr. *3*, 171 (1973); b) tricyclo[4.1.0.$0^{2,7}$]heptan-3-one: [3]; c) *M. Christl* and *E. Brunn* also obtained *(1a)* and *(2a)* from these ketones (*M. Christl*, personal communication, Feb. 1980).

[5] a) All new compounds gave correct elemental analyses and/or molecular weights; b) the structures given agree with the spectra. c) *(1a)*: ^{1}H-NMR (CCl_4): $\delta = 1.05$—1.80 (m, 2H-4), 1.85—3.00 (m, 2H-3), 3.27 (m, H-5), 3.38 (m, H-1), 4.71 (m, 2H-8), 5.86 (≈s, H-6, 7); ^{13}C-NMR ($CDCl_3$): $\delta = 25.7$ (t, C-4), 30.4 (t, C-3), 48.6 (d, C-5), 53.2 (d, C-1), 106.3 (t, C-8), 138.8 (d, C-6, 7), 151.5 (s, C-2); IR (CCl_4): *inter alia* 3120 (=CH), 3070 (—CH), 3040 (= CH), 1660 (C=CH_2), 1566 (C=C), 893, 703 cm^{-1}; MS (70 eV): *m/e* = 106 (4%, M^+), 91 (100), 78 (69); *(2a)*: ^{1}H-NMR ($CDCl_3$): $\delta = 1.35$—1.75 (m, 2H-5), 1.90—2.25 (m, H-1, 7, 4, 4), 2.45 (m, H-6), 2.82 (q, $J = 3$ Hz, H-2), 4.68 (m, 2H-8); ^{13}C-NMR ($CDCl_3$): $\delta = 8.0$ (d, $J_{CH} = 205$ Hz, C-1, 7), 21.4 (t, C-5), 28.9 (t, C-4), 37.9 (d, C-6), 45.3 (d, C-2), 106.8 (t, C-8), 146.1 (s, C-3); IR (film): *inter alia* 3070, 2995, 1643 (C=CH_2), 877, 705 cm^{-1}; MS (70 eV): *m/e* = 106 (11%, M^+), 91 (100), 78 (61).

[6] a) The structures of *(3a)* and *(8)* were confirmed by independent synthesis; *(3a)*: *L. A. Paquette, R. P. Hensel, R. F. Eizember*, J. Org. Chem. *38*, 3257 (1973); *(8)* was accessible in low yield from 3,5-cycloheptadienone only by treatment with CH_2I_2/Mg(Hg) [5b] (cf. *D. Hasselmann*, Chem. Ber. *107*, 3486 (1974)); b) the hydrogen shift *(8)*→*(3a)* [162.7 °C: $t_{1/2} = 10$ min] was faster than the rearrangement *(1a)*→*(3a)* + *(8)*; after >90% conversion of *(1a)* approx. 1% of the isomeric methylcycloheptatrienes are formed from *(3a)* and *(8)*.

[7] a) *G. R. Branton, H. M. Frey, D. C. Montague, I. D. R. Stevens*, Trans. Faraday Soc. *62*, 659 (1966); b) *M. R. Willcott, E. Goerland*, Tetrahedron Lett. *1966*, 6341.

^{13}C-NMR Spectroscopic Studies on [^{13}C]methylated Bituminous Coal

By *Matthias W. Haenel, Richard Mynott, Klaus Niemann, Udo-Burckhard Richter,* and *Lothar Schanne*[*]

A prerequisite for the spectroscopic characterization of coal by high-resolution NMR spectroscopy is the preparation of soluble coal derivatives largely retaining the original structure[1]. A mild chemical reaction meeting these requirements is reductive derivatization using the "blue solutions" of solvated electrons formed by potassium at low temperature in oligomeric polyethylene glycol dimethyl ethers[2]. Transfer of these electrons to bituminous coal and subsequent hydrolysis[2a] or reaction with electrophiles such as dimethyl sulfate or methyl iodide[2b] affords reduced or reductively methylated coal derivatives, respectively, having high pyridine solubilities in some cases.

In the coal skeleton, in which aromatic and hydroaromatic moieties are cross-linked by aliphatic chains[3], not only do methylations of acidic structures and Birch-Hückel reductions of arenes occur, but benzylic C—C bonds in diarylethane and diarylmethane structures are also cleaved, as demonstrated by quantitative IR spectroscopy on coal derivatives[2] and cleavage reactions on model compounds[4]. The associated degradation of the coal macromolecules is apparently responsible for the enormous increase in pyridine solubility—*e.g.* from 12 to 75% on reductive methylation of one bituminous coal[2b].

Reductive methylation of a medium volatile bituminous coal from the Ruhr coalfield (see Table 1) with [^{13}C]methyl iodide (90 mol-% ^{13}C) gave a methylated coal derivative whose [^{13}C]labeling and high pyridine solubility (74.4%) permitted an NMR study. As shown by the ^{13}C/^{12}C isotope ratio, determined by mass spectrometry after combustion of a sample to carbon dioxide, 4.4 methyl groups have been incorporated per 100 coal carbon atoms. The ^{13}C-NMR spectrum shows, apart from the [D_5]pyridine signals ($\delta = 149.9$, 135.5, 123.5), strong peaks in the range $\delta = 10$—65, which, in view of the high isotope enrichment, are essentially due only to the incorporated [^{13}C]methyl groups (Fig. 1a, expanded in Fig. 2); this follows from a comparison with the ^{13}C-NMR spectrum of a correspondingly prepared coal derivative having natural isotopic abundance (Fig. 1b).

The spectrum (Fig. 2) provides information about the nature of the methyl groups introduced. The ^{13}C-NMR spectra

Table 1. Composition and normalized empirical formulas of the starting coal and the methylated coal [Westerholt mine, seam "Robert": 23.6% volatile matter, 4.1% ash, 0.7% water, 12% soluble in pyridine].

	Composition [wt-%]					Empirical formula, normalized	Methyl/100 C [b]
	C	H	N	O [a]	S		
Starting coal	84.6	4.6	1.3	4.2	1.4 [c]	$C_{100}H_{64.1}N_{1.3}O_{3.7}S_{0.6}$	$C_{100}H_{64.1}$
[^{13}C]methylated coal	86.1	5.8	2.9	3.1		$C_{100}H_{80.6}N_{2.8}O_{2.6}$	$C_{100}H_{64.1}(CH_3)_{7.5}$ [d]
Methylated coal	85.8	5.5	1.0	4.0		$C_{100}H_{76.1}N_{1.0}O_{3.5}$	$C_{100}H_{64.1}(CH_3)_{5.4}$

[a] Determined directly. [b] From the H/C ratio, assuming that hydrogen is incorporated only by methylation. [c] Including pyrites. [d] By mass spectrometry after combustion to $^{13}CO_2/^{12}CO_2$: 4.4 CH_3 per 100 C atoms.

[8] The borderline case of both rotational nodes should have been reached with *(1a)*; bicyclo[4.2.0]oct-7-ene undergoes conrotatory opening: *J. J. Bloomfield, J. S. McConaghy, Jr.*, Tetrahedron Lett. *1969*, 3719, 3723.

[9] a) *K. B. Wiberg, G. Szeimies*, Tetrahedron Lett. *1967*, 1235; *L. A. Paquette, S. E. Wilson, R. P. Henzel, G. R. Allen, Jr.*, J. Am. Chem. Soc. *94*, 7761 (1972); b) *M. Christl, U. Heinemann, W. Kristof, ibid.* *97*, 2299 (1975); improved data for *(10)* (*M. Christl*, personal communication, Feb. 1980); c) according to *Dewar* and *Kirschner*, there is no contradiction between a diradical intermediate and stereoselective product formation in the rearrangement of bicyclo[1.1.0]butanes: *M. J. S. Dewar, S. Kirschner, ibid.* *97*, 2932 (1975).

[10] a) *R. E. Benson, R. V. Lindsey, Jr.*, J. Am. Chem. Soc. *81*, 4250 (1959); *W. J. Bailey, R. Barclay, Jr., ibid.* *81*, 5393 (1959); b) we synthesized *(11)* in simpler manner by cleavage of its cyclopentadiene adduct [5a, b].

[11] The results were obtained reproducibly without loss of material in two independent thermolysis apparatus; they were unaffected by a conditioning of the thermolysis vessel. *p*-Xylene, the acid-rearrangement product of *(11)*, was not formed. Treatment of *(2a)* with acids in solution at room temperature gave little *(3a)* in addition to considerable polymerization.

[12] *U. Szeimies-Seebach, G. Szeimies, M. Van Meerssche, G. Germain, J.-P. Declercq*, Nouv. J. Chim. *3*, 357 (1979); *U. Szeimies-Seebach, G. Szeimies*, J. Am. Chem. Soc. *100*, 3966 (1978); *U. Szeimies-Seebach, J. Harnisch, G. Szeimies, M. Van Meerssche, G. Germain, J.-P. Declercq*, Angew. Chem. *90*, 904 (1978); Angew. Chem. Int. Ed. Engl. *17*, 848 (1978).

[13] *U. Burger, F. Mazenod*, Tetrahedron Lett. *1976*, 2885; *1977*, 1757.

[*] Priv.-Doz. Dr. M. W. Haenel, Dr. R. Mynott, Dr. K. Niemann [**], Ing. grad. U.-B. Richter, and Dr. K. Schanne
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim a. d. Ruhr (Germany)

[**] Permanent address: Rheinische Braunkohlenwerke AG, D-5000 Köln (Germany).

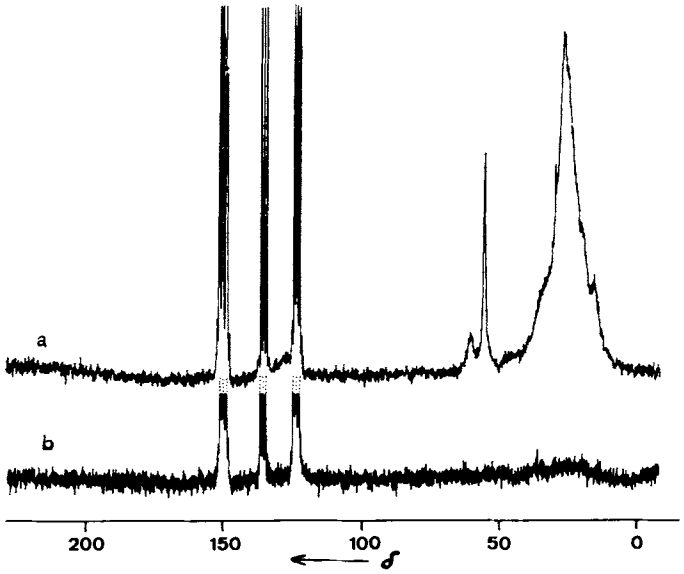


Fig. 1. $^{13}C\{^1H\}$-FT-NMR spectra (25.2 MHz, [D5]pyridine) of (a) [^{13}C]methylated coal and (b) methylated coal.

of reference compounds and ^{13}C-NMR data from our computer index were consulted during spectral analysis. (i) The signal around $\delta = 60.6$ [according to its integral it accounts for 0.12 (3%) of the 4.4 methyl groups/100 C atoms] is assigned to enolic methyl ethers apparently formed by Birch-Hückel reduction and methylation of phenolic structures[5].

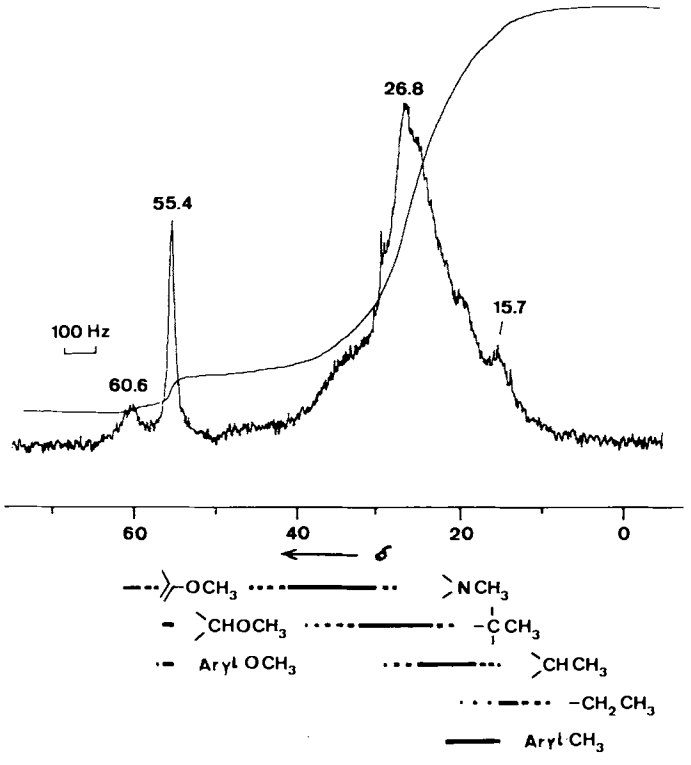


Fig. 2. $^{13}C\{^1H\}$-FT-NMR spectrum (25.2 MHz, [D5]pyridine) of [^{13}C]methylated coal, range between $\delta = 0$ and 60 expanded.

(ii) The signal at $\delta = 55.4$ [0.28 (6%)] corresponds to *sec*-alkyl methyl ethers and, above all, to aromatic methoxy groups. (iii) The shoulder at about $\delta = 35$ is assigned to *N*-methyl groups ($\delta = 29$—40)[6]. Nevertheless, owing to the low nitrogen content of the coal employed, the main absorption between $\delta \approx 10$ and 30 can essentially arise only from *C*-methyl groups, even assuming that all the nitrogen is methylated. (iv) Methyl groups bonded directly to aromatic rings, whose signals are found between $\delta \approx 21.3$ (without *ortho* substituents) aud $\delta \approx 15$ (with two *ortho* substituents), cannot represent the major component because of the low intensity in this region. (v) The center of the signal between $\delta \approx 22$ and 30 shows that most of the methyl groups are bonded to tertiary and quaternary carbon atoms. In particular, the results are consistent with methyl groups attached to tertiary and quaternary *benzylic* carbon atoms[7], such as arise on methylation of C—H acid structures, Birch-Hückel reductive methylation of polycyclic arenes, and on methylation of carbanions formed by cleavage of benzylic C—C bonds[8].

Chemical derivatization with isotopically labeled groups as a spectroscopic probe is an interesting method for investigating complicated substrates such as coal or polymers.

Procedure

Small pieces of potassium (2.7 g, 69 mmol) were added under argon to a stirred mixture of dimethoxyethane (150 ml; freshly distilled from sodium tetraethylaluminate) and polyethylene glycol dimethyl ether[9] (30 ml) at $-30\,^\circ$C. Once the solution had turned deep blue, finely ground coal[10] (2.7 g; see Table 1) was added. After 16 h, methyl iodide or [^{13}C]methyl iodide (90 mol-% ^{13}C, Merck Sharp & Dohme, Canada) (10 g, 70 mmol) was slowly added dropwise. Acidification with 2 N hydrochloric acid (0.5 l), filtration, washing with water, methanol extraction for 24 hours in a Soxhlet apparatus, and drying at 10^{-3} torr gave 2.6 g of coal product which was 74.4% soluble in pyridine (determined by Soxhlet extraction).

Received: March 25, 1980 [Z 528 IE]
German version: Angew. Chem. *92*, 653 (1980)

[1] For progress in NMR spectroscopy of solid coals see, *e.g.*, *V. J. Bartuska, G. E. Maciel, J. Schaefer, E. O. Steijskal,* Fuel *56*, 354 (1977); *H. L. Retcofsky, D. L. VanderHart, ibid. 75*, 421 (1978); *A. Pines, D. E. Wemmer,* Am. Chem. Soc. Div. Fuel Chem. Prepr. *23*, 15 (1978); *K. W. Zilm, R. J. Pugmire, D. M. Grant, R. E. Wood, W. H. Wiser,* Fuel *58*, 11 (1979).

[2] a) *K. Niemann,* Dissertation, Universität Bochum 1977; *H.-P. Hombach, K. Niemann,* Compendium 1977/78, Suppl. Vol. Erdöl, Kohle, Erdgas, Petrochem., 295; *K. Niemann, H.-P. Hombach,* Fuel *58*, 853 (1979); b) *K. Niemann, U.-B. Richter, ibid. 58*, 838 (1979).

[3] *D. W. van Krevelen:* Coal. Elsevier, Amsterdam 1961; *H. A. Lowry:* Chemistry of Coal Utilization, Suppl. Vol. Wiley, New York 1963; *J. W. Larsen,* Am. Chem. Soc. Symp. Ser. *71* (1978).

[4] *L. Schanne, M. W. Haenel,* Tetrahedron Lett. *1979*, 4245; cf. also *C. Collins, H.-P. Hombach, B. Maxwell, M. C. Woody, B. M. Benjamin,* J. Am. Chem. Soc. *102*, 851 (1980).

[5] *J. Fried, N. A. Abraham, T. S. Santhanakrishnan,* J. Am. Chem. Soc. *89*, 1044 (1967).

[6] Compare the ^{13}C-chemical shift of *N*-methyl in *N,N*-dimethylaniline ($\delta = 39.9$), *N*-methylpyrrole (35.2), -indole (32.4), -aniline (30.2), -carbazole (29.6): *M. Begtrup, R. M. Claramunt, J. Elguero,* J. Chem. Soc. Perkin Trans. *2*, 1978, 99.

[7] Compare some ^{13}C-chemical shifts (δ) of methyl groups attached to secondary, tertiary, and quaternary benzylic C atoms: ethylbenzene (15.7), 9-methylfluorene (18.2) [7b], 2,3-diphenylbutane (DL + *meso:* 21.0), 1,2-diphenylpropane (21.2), 1,1-diphenylethane (21.9), 1-methyl-1,2,3,4-tetrahydronaphthalene (22.9) [7c], 9,9-dimethylfluorene (27.1) [7b], 2,2-diphenylpropane (30.8), 1,1-dimethyl-1,2,3,4-tetrahydronaphthalene (31.9) [7d]; b) *H. Fritz, T. Winkler, A. M. Braun, C. Decker,* Helv. Chim. Acta *61*, 661 (1978); c) *R. Gretler, E. Askitoğlu, H. Kühne, M. Hesse, ibid. 61*, 1730 (1978); d) *K. S. Seshadri, R. G. Ruberto, D. M. Jewell, H. P. Melone,* Fuel *57*, 111 (1978).

[8] *S*-Methyl groups appear at $\delta = 14 \pm 2$. The absence of a signal in this region and the low sulfur content of the coal (0.6 S/100 C) rule out any significant contribution.

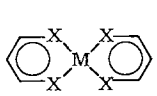
[9] Technical grade polyethylene glycol 400, containing mainly the octamer, was converted into the dimethyl ether. We wish to thank Dr. *W. Eisenbach* for this preparation.

[10] The previously crushed coal, mixed with Dry Ice to render it brittle and provide an inert atmosphere, was ground in a high speed impingement mill and a screening mill (average particle diameter 60 μm), dried at 10^{-3} torr for 3 d, and stored under argon.

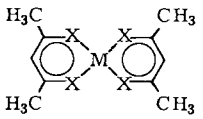
Transition-Metal Complexes of Malonaldehyde and Dithiomalonaldehyde

By *Ulrich T. Mueller-Westerhoff* and *Arnold Alscher*[*]

2,4-Pentanedionates *(3)* and 2,4-pentanedithionates *(4)* have been well documented[1]; complexes of the type *(1)* and *(2)*, however, which are derived from malonaldehyde and dithiomalonaldehyde, have so far not been described in the literature[2]. We report here on the complexes *(1)* and *(2)* of the d^8-metals Ni, Pd, and Pt.



(1), X = O, M(mal)$_2$
(2), X = S, M(ptt)$_2$



(3), X = O, M(acac)$_2$
(4), X = S, M(SacSac)$_2$

Of the three malonaldehyde complexes which we attempted to prepare, Pd(mal)$_2$[3] was by far the easiest to obtain. Hydrolysis of 1,1,3,3-tetraethoxypropane (malonaldehyde diacetal) in aqueous HCl, neutralization, and reaction with a suspension of $PdCl_2$ in ether affords the complex in more than 50% yield. Pd(mal)$_2$ was characterized by elemental analysis, mass spectrum ($m/e = 248$, $M_r = 248.5$), UV and NMR spectrum (see Table 1). Ni(mal)$_2$ and Pt(mal)$_2$ could not be prepared in an analogous way.

The Ni-, Pd-, and Pt-complexes of dithiomalonaldehyde are stable, yet reactive, deep-blue compounds. They are synthesized almost analogously[1b,4] to the SacSac complexes *(4)*. Reaction of tetraethoxypropane in anhydrous ethanol with dry HCl and H_2S in the presence of the corresponding metal chloride furnishes the M(ptt)$_2$ complexes *(2)* in varying yields (between 50% for M = Ni and over 80% for M = Pt, after column chromatographic purification on SiO_2 and recrystallization). In all three reactions $C_6H_6S_3$[3,5] is formed as side product, to which, on the basis of its ^{1}H-NMR spectrum, we assign the structure *(5)*; our data, however, are also consistent with the structure *(6)*.

(5) 

 *(6)*

Some physical properties of the complexes of type *(1)* and *(2)* are listed in Table 1. The strong interaction between the metal and the entire ligand in the complex Pt(ptt)$_2$ is manifested in the ^{195}Pt-^{1}H coupling constants: The signal of the α-proton at $\delta = 9.35$ has satellites at ± 52 Hz ($J = 104$ Hz) having one quarter of the intensity of the principal doublet (corresponding to the natural ^{195}Pt abundance of 33.8%); in the triplet at $\delta = 7.40$, the ^{195}Pt-$^1H_\beta$ coupling with $J = 8$ Hz is clearly recognizable. For the ^{13}C-^{195}Pt coupling the reverse order is found. The α-C atoms at $\delta = 155.56$ (rel. TMS) have $J_{C\text{-}Pt} = 40$ Hz, the β-C atoms at $\delta = 133.42$, $J_{C\text{-}Pt} = 137.2$. These data are indicative of strong electron delocalization. Whether or not the ppt-(and SacSac-)complexes are to be regarded as aromatic systems still has to be decided. In the case of the acac complexes there is clear evidence against aromatic character[6].

The dithiomalonaldehyde complexes M(ptt)$_2$ had been synthesized with the aim of obtaining planar, sterically undemanding transition-metal compounds, which can function as electron-donor components in charge-transfer complexes. Donor-acceptor complexes of the long known SacSac derivatives have so far not been described. Pd(ptt)$_2$ and Pt(ptt)$_2$ react with tetracyanobenzoquinodimethane (TCNQ) in acetonitrile to give the 1:1 charge-transfer complexes[3]. Our earlier predictions that such complexes show poor electrical conductivity, even if they form segregated donor and acceptor columns in the crystal, appeared to be borne out by the measurement of the electrical conductivity parallel to the principal axis of the crystal of Pt(ptt)$_2$-TCNQ ($\sigma_{\parallel} = 2 \times 10^{-8}$ Ω^{-1} cm^{-1}). However, the X-ray structure analysis[8] showed that mixed D-A-D-A columns are present in the molecular crystal, and moreover, as can be estimated from the bond lengths of TCNQ, that the charge-transfer must be small.

Equally insulating donor-acceptor complexes of TCNQ should likewise be prepared with the donors Pd(mal)$_2$, Pd(acac)$_2$, Pd(SacSac)$_2$, and Pt(SacSac)$_2$[3]. Reaction of the ptt-complexes with iodine as electron acceptor does not lead to any partially oxidized mixed-valence systems, but exclusively to oxidative addition: for example, reaction of Pt(ptt)$_2$ and iodine in chloroform affords *trans*-Pt(ptt)$_2$I$_2$ (dark red-brown crystals, m.p. 131 °C); Pt(SacSac)$_2$I$_2$ is formed analogously. The corresponding reaction of 2,4-pentanedionates such as Pt(acac)$_2$ is well known[9].

Table 1. Some physical properties of complexes of the type *(1)* and *(2)*.

	Pd(mal)$_2$	Ni(ptt)$_2$	Pd(ptt)$_2$	Pt(ptt)$_2$
Color (crystal)	yellow	black	black-red	black
Color (solution)	yellow	blue-green	purple-red	blue
UV/VIS [a]	342 (7500)	725 (225)	566 (2750)	725 (60)
(λ_{max} [nm] (ε))	278 sh	575 (2300)	527 (5800)	620 (4220)
	261 sh	410 sh (2690)	508 sh	595 (4020)
	255 sh	335 (21400)	450 sh	337 (10750)
	249 sh	284 sh (17400)	360 (4600)	280 (7300)
	243 sh	262 (51700)	295 (23050)	260 (12500)
	231 (27000)	237 (15250)	246 (106400)	235 (53600)
		206 (19600)	212 (18100)	
IR (in KBr [cm^{-1}], strong bands in italics)		2920, *1445*, *1325*, *1210*, 840, 710	2990, *1455*, *1325*, *1225*, 840, 710	2990, *1455*, *1330*, *1230*, 845, 710
M.p. [°C]	137	159	177	175
^{1}H-NMR (δ, J) in $CDCl_3$	H_β: t 5.56	t 7.40	t 7.48	t 7.40 [b]
	H_α: d 7.10 4 Hz	d 8.73 9 Hz	d 9.02 9 Hz	d 9.35 [c] 9 Hz

[a] In methanol; Pd(mal)$_2$ in cyclohexane. [b] Triplet with satellites at ± 4 Hz. [c] Doublet with satellites at ± 52 Hz.

Received: January 2, 1980 [Z 529 IE]
German version: Angew. Chem. 92, 654 (1980)

[*] Dr. U. T. Mueller-Westerhoff, Dr. A. Alscher
IBM Research Laboratory
5600 Cottle Road, San Jose, California 95193 (USA)

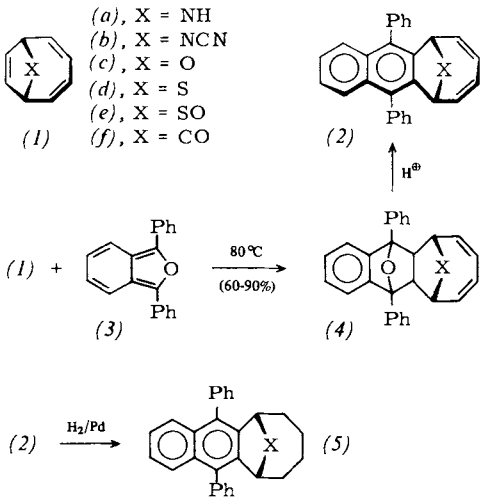
CAS Registry numbers:
(1a), 74498-74-1; *(2a)*, 74498-75-2

[1] a) *J. P. Fackler*, Prog. Inorg. Chem. *7*, 361 (1966); b) *S. W. Schneller*, Int. J. Sulfur Chem. *B 7*, 295 (1972).
[2] The chromium complex $Cr(C_3H_3O_2)_2$ with three malonaldehyde ligands is known: *J. P. Collman, E. T. Kittleman*, J. Am. Chem. Soc. *83*, 3529 (1961).
[3] Satisfactory elemental analyses were obtained for all the compounds listed. The only exception was in the case of $Pd(mal)_2$-TCNQ, which decomposes too rapidly.
[4] *R. L. Martin, I. M. Stewart*, Nature *219*, 522 (1966); *E. Fromm, P. Ziersch*, Chem. Ber. *39*, 3699 (1906).
[5] $C_6H_6S_3$, m.p. 98 °C; λ_{max}(methanol) = 255 nm (ϵ = 14600); *m/e* = 174, M_r = 174), ^{1}H-NMR ($CDCl_3$): δ = 4.85 (d, *J* = 7.5 Hz, 2H), 6.15 (dd, *J* = 7.5 and 11 Hz, 2H), 7.55 (d, *J* = 11 Hz, 2H), yields in the synthesis of $Ni(ptt)_2$, $Pd(ptt)_2$ and $Pt(ptt)_2$ *ca.* 10 to 15%.
[6] *M. Kuhr, B. Bock, H. Musso*, Chem. Ber. *109*, 1195 (1976).
[7] *U. T. Mueller-Westerhoff, F. Heinrich*, ACS Symp. Ser. *5*, 392 (1974); *U. T. Mueller-Westerhoff*, Adv. Chem. Ser. *150*, 31 (1976).
[8] *J. J. Mayerle*, Inorg. Chem. *16*, 916 (1977).
[9] *P. M. Cook, L. F. Dahl, D. Hopgood, R. A. Jenkins*, J. Chem. Soc. Dalton Trans. *1973*, 294.

The Question of Bicycloconjugation in Naphtho-Fused 9-Heterobicyclo[4.2.1]nona-2,4,7-trienes as Examined by ^{13}C-NMR Spectroscopy[***]

By *A. G. Anastassiou, H. S. Kasmai,* and *R. Badri*[*]

In previous work directed at assessing the electronic requirements for the development of heteroatom-induced bicycloconjugation it was first demonstrated[1] by use of PE spectroscopy and shortly thereafter confirmed[2] *via* ^{13}C-NMR analysis that of the three unrestricted π-excessive heteroatomic centers (NH, O, S) examined only the first, *i.e.*, NH, is capable of promoting bicycloconjugation in the 9-heterobicyclo[4.2.1]nonatriene molecular environment shown in *(1)*. Further, having prescribed to the notion that what might reasonably be considered a necessary first step for triggering three-center interaction in *(1)* is such symmetry-controlled coupling between the lone pair and the HFMO of the system's $(4n+2)\pi$ segment, *i.e.*, the ethylene bridge, as is required to raise the energy of the former (lone pair) and thus enhance its potential for nonbonded delocalization, we resolved to examine a derivative of *(1)* whose "ethylene"-bridge energetics are so modified as to provide for overall stabilization of nitrogen-bridge lone pair with attendant reduction of its ability to promote bicycloconjugation. Interestingly, replacement of the ethylene moiety in *(1)* with the naphthalene segment of *(2)* appears to satisfy this condition insofar as the highest filled symmetric[3] MO (ψ_4) of the latter is located at a significantly higher energy (ϵ_4 = 8.02 eV)[4] than the *isolated* NH lone pair of the fully saturated analog of *(1a)* [≡ *(6a)*] (ϵ_N = 8.50 eV)[1a].



Synthetically, the general skeleton depicted in *(2)* became available *via* thermally induced cycloaddition between *(1)* and isobenzofuran *(3)* followed by acid-induced dehydration of the resulting primary cycloadducts *(4)*[5], and, when called for, defunctionalization of X, *i.e.*, SO to S, NCN to NH, *etc.* The method of analysis employed in the present study relating to changes in "bridgehead" C—H coupling constants was entirely analogous to that employed earlier with the parent system *(1)*[2].

Examination of the tabulated information reveals the additively estimated magnitude of ΔJ for the key aza-bridged molecule *(2a)*, *i.e.*, $\Delta J(6\rightarrow 7) + \Delta J(6\rightarrow 5) = 7$ Hz to be essentially the same as that actually observed, *i.e.*, $\Delta J(6\rightarrow 2) = 8$ Hz. Within the validity of the ^{13}C-NMR criterion then, the obvious conclusion to be drawn from this observation is that the three-unit p-π system of naphtho-fused azabicycle *(2a)* is *not detectably bicycloconjugated.* While sharply contrasting with the well-documented[1a,2] ability of the parent molecule *(1a)* to partake in bicycloconjugation, the apparent failure of *(2a)* to do so is entirely in keeping with our prediction *(vide supra)* that the ability of the nitrogen lone pair to manifest a p-π effect suitable for the development of three-center delocalization is effectively impaired by the *stabilization* it experiences *via* interaction with the highest-filled *symmetric* MO of the system's $(4n+2)\pi$ segment.

Table 1. ^{13}C-H "bridgehead" coupling constants [Hz] of compounds having 9-heterobicyclo[4.2.1] skeletons and suitably chosen differences between ^1J values.

(6)   *(7)*

X	*(6)* [2]	*(7)* [2]	*(5)*	*(2)*	$\Delta(5\rightarrow 2)$	$\sum[\Delta(6\rightarrow 7), \Delta(6\rightarrow 5)]$	$\Delta(6\rightarrow 2)$	$\Delta[(6\rightarrow 2) - \sum]$
NH	138	141	142	146	+4	+7	+8	+1
NCN	145	148	148	153	+5	+6	+8	+2
O	148	148	150	155	+5	+2	+7	+5
S	140	142	140	140	0	+2	0	−2
SO			144	146	+2			
CO			139	141	+2			

[a] Spectra were uniformly recorded at 20 MHz on a Varian CFT-20 spectrometer equipped with a 5-mm probe. All determinations were made at *ca.* 30 °C employing Me_4Si as internal standard.

[*] Prof. Dr. A. G. Anastassiou, Dr. H. S. Kasmai [**], R. Badri
Department of Chemistry, Syracuse University
Syracuse, New York, 13210 (USA)
[**] On sabbatical leave from the Department of Chemistry, Shiraz University, Shiraz (Iran).

[***] This work was supported by the National Science Foundation.

Further emphasizing the basic differences between structural relatives *(1)* and *(2)* with regard to their ability to sustain bicycloconjugation is the fact that analysis of the ^{13}C-NMR information relating to the oxa counterpart of *(2a), i.e. (2c),* reveals the actual $\Delta J(6\rightarrow 2)=7$ Hz to be significantly greater (*ca.* 200%) than the additive value, $\Delta J(6\rightarrow 7)+\Delta J(6\rightarrow 5)=2$ Hz! (see Table 1). At this early stage, one can tentatively explain the apparent increase in three-center mobility of the oxygen lone pair of *(2c)* (originally located at 9.1 eV)[1c] chiefly on the basis of the destabilization it is expected to experience through interaction with the lower-energy (9.4 or 9.9 eV)[4,6] second highest occupied *symmetric*[3] MO of the naphthalene unit, *i.e.*, ψ_2 in free naphthalene. It is hoped that careful analysis of pertinent PE-spectroscopic information will allow us to further define the contrasting influences brought to play on the nitrogen and oxygen lone pairs by the molecular environment of *(1)* and *(2)*.

Received: November 28, 1979 [Z 531 IE]
German version: Angew. Chem. *92*, 657 (1980)

[1] a) *H. Schmidt, A. Schweig, A. G. Anastassiou, H. Yamamoto,* J. Chem. Soc. Chem. Commun. *1974*, 218; b) *C. Müller, A. Schweig, A. G. Anastassiou, J. C. Wetzel,* Tetrahedron *30*, 4089 (1974); c) *H. Schmidt, A. Schweig, A. G. Anastassiou, J. C. Wetzel, ibid. 32*, 2239 (1976).

[2] *A. G. Anastassiou, E. Reichmanis,* J. Am. Chem. Soc. *98*, 8267 (1976).

[3] The classification refers to the "long", nontrivial, plane of symmetry which is coincident with the single plane of molecular symmetry in *(2)*.

[4] Extracted from the PE spectrum of hydrocarbon model *(5)*, X = CH_2, kindly recorded for us by Prof. *A. Schweig* at Marburg.

[5] Entirely consistent spectroscopic (IR, ^{1}H-NMR, ^{13}C-NMR, UV, MS) and combustion (C, H, X) data were obtained for all new compounds prepared. The following "final product" melting points were recorded: 199—200 °C for *(2a)*, 241—242 °C for *(2b)*, 195—196 °C for *(2d)*, 238—239 °C for *(2d)*, 249—250 °C for *(2e)*, 239—240 °C for *(2f)*.

[6] While these two values are believed to correspond to ψ_3 and ψ_2 of the naphthalene segment of *(2)* it is not possible to offer a specific assignment without recourse to suitable calculation, insofar as it is not known whether the well-documented ordering in free naphthalene, *i.e.*, ψ_3(A) and ψ_2(S), is carried over unchanged to the naphthalene moiety of *(2)*. The possibility of a reversal in the ordering of unperturbed naphthalene MOs is certainly not to be dismissed since ψ_2(S), being associated with substantially larger (*ca.* × 2.5) HMO eigenvectors at key positions 2 and 3 than is ψ_3(A), ought to be proportionately more perturbed (destabilized) by the annulation process leading to *(5)*, X = CH_2.

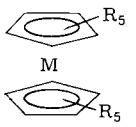


Permethylated Electron-Excess Metallocenes[**]

By *Ulrich Koelle* and *Fouad Khouzami*[*]

The exhaustive methylation of aromatic ligands can drastically change the properties of corresponding π-complexes[1]. An example from the metallocene series is provided by decamethylmanganocene *(1b)*, which unlike *(1a)* not only has a magnetically anomalous ground state in solution, but can also be reversibly oxidized and reduced[2]. We now report the first synthesis and reactions of the permethylated electron-excess metallocenes *(3b)* and *(4b)*.

Syntheses: The preparation of decamethylcobaltocene *(3b)* can be accomplished with $C_5(CH_3)_5$-Li in tetrahydrofuran (THF)/ether (12 h reflux) if an ether adduct, *e.g.* Co(DME)Br_2 (DME = dimethoxyethane) is employed instead of the usual hexaamminecobalt(II) chloride[3], and the neutral complex is oxidized *in situ* with $FeCl_3$ to $(3b)^+$,



R \ M	Mn	Fe	Co	Ni
H	*(1a)*	*(2a)*	*(3a)*	*(4a)*
CH_3	*(1b)*	*(2b)*	*(3b)*	*(4b)*

which can be precipitated from water as hexafluorophosphate [yield 85%, $\delta(^1H)=1.82$ (CD_3COCD_3)]. The paramagnetic neutral compound *(3b)* was obtained as black crystals by reaction of the salt with K/Hg in THF and sublimation [yield 82%, m.p. 300 °C, $\delta(^1H)=40$, $\Delta\nu=60$ Hz]. The green nickel complex *(4b)* could be isolated under the same conditions without intermediate oxidation and reduction[4] [yield 90%, m.p. 290 °C, $\delta(^1H)=237$, $\Delta\nu=615$ Hz].

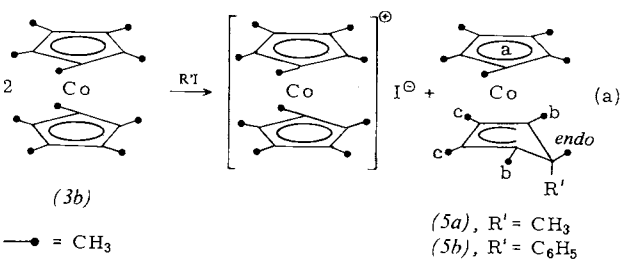
Redox potentials: Table 1 shows the redox potentials for the first oxidation of the metallocenes *(2)—(4)* and for the second oxidation of *(4b)* (cyclic voltammetry, dichloromethane, *vs.* SCE). The cathodic shift by the ten methyl groups increases from Fe to Ni, reflecting the greater ligand contribution to the e_{1g} orbital in *(3)* and *(4)*[5]. In contrast to *(4a)*[6], *(4b)* also undergoes an electrochemically reversible second oxidation [$(4b)^{+/2+}$]. Mild oxidizing agents such as C_2Cl_6 oxidize *(4b)* to $(4b)^+$, whereas stronger oxidants such as Br_2/CH_2Cl_2 or atmospheric oxygen in acid aqueous solution give the diamagnetic [$\delta(^1H)=2.20$ (CF_3COOH)] dication $(4b)^{2+}$ in the form of stable salts as the first π-complex of nickel(IV). *(4a)* does not form a dication.

Table 1. Redox potentials of metallocenes and permethylmetallocenes in dichloromethane (V rel. to SCE).

M		$M(C_5H_5)_2$		$M[C_5(CH_3)_5]_2$	Δ [a]
Fe	*(2a)*	+0.49	*(2b)*	−0.08	0.57
Co	*(3a)*	−0.86	*(3b)*	−1.48	0.62
Ni	*(4a)*	+0.07	*(4b)*	−0.73	0.80
$Ni^{+/2+}$		≃ +0.9		+0.37	≃0.53

[a] Difference between the potentials in columns 3 and 5.

Reaction of (3b) with electrophiles: Like *(3a)*, decamethylcobaltocene *(3b)* reacts with alkyl and aryl halides R′X *via* oxidative addition[7] [eq. (a)], thus demonstrating that this reaction can also take place at substituted positions of a π-ligand. Concomitant with the more strongly negative potential for the reduction of the cation, *(3b)* is considerably more reactive than *(3a)*. Thus weak electrophiles, which are inert towards *(3a)*, will also react. For example, CH_3I which reacts only slowly (2 h, 80 °C)[8] with cobaltocene *(3a)* gives *(5a)*



(3b)

—● = CH_3

(5a), R′ = CH_3
(5b), R′ = C_6H_5

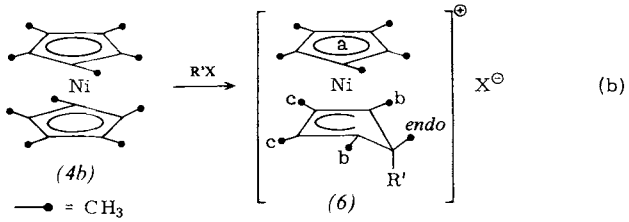
from *(3b)* within 1 h, and C_6H_5I which is totally inert towards *(3a)* yields *(5b)* from *(3b)* within 6 h at 20 °C. The

[*] Dr. U. Koelle, Dipl.-Chem. F. Khouzami
Institut für Anorganische Chemie der Technischen Hochschule
Professor-Pirlet-Strasse 1, D-5100 Aachen (Germany)

[**] This work was support by the Deutsche Forschungsgemeinschaft.

structures of the complexes *(5)* follow from their ^{1}H-NMR (Table 2) and mass spectra, and from elemental analysis. The yields of reaction (a) are *ca.* 90%.

Reaction of (4b) with electrophiles: Decamethylnickelocene *(4b)* is the first neutral 20-electron complex to which electrophiles can be added [eq. (b)]. The reaction yields the novel cyclopentadiene(cyclopentadienyl)nickel cations $(6)^+$ as green salts stable to air and water. For example, in contrast to *(4a)*[9], *(4b)* is protonated (CF_3COOH, pentane/water) to give the *exo*-addition product $(6a)^+$, which can be precipitated from water.



The variety of electrophilic substrates which can be reacted with *(4b)* demonstrate that, apart from the simple electrophilic addition (*e.g.* with CF_3COOH and $CF_3SO_3CH_3$), electron transfer to form $(4b)^+$ and radicals $R'^{\odot}$, with subsequent radical addition to $(4b)^+$, is a mechanistic possibility in the case of nonpolar electrophiles (*e.g.* CCl_4). Such radical additions are known in the case of the isoelectronic compound *(3a)*[10].

Structural evidence for the cations $(6)^+$ comes from the ^{1}H-NMR absorptions, which show a similar pattern for all the compounds (Table 2). In particular, the similar shifts of the *endo*-methyl signals of *(6a—c)* suggests *exo*-addition of R′ in all cases.

Table 2. ^{1}H-NMR data of the addition products *(5)* ($CDCl_3$) and $(6)^+$ (CD_3NO_2) (δ, int. TMS).

M	R′	R′X	Cpd.	CH_3-a	CH_3-b [a]	CH_3-c	CH_3-*endo*	R′-*exo*
Co	CH_3	CH_3I	*(5a)*	1.70	0.71	1.90	1.28	0.24
Co	C_6H_5	C_6H_5I	*(5b)*	1.72	0.77	1.95	1.25	
Ni	H	CF_3COOH	$(6a)^+$ [b]	1.75	1.28	2.25 (d)	1.35 (d)	
Ni	CH_3	$CF_3SO_3CH_3$	$(6b)^+$	1.76	1.33	2.24	1.42	0.75
Ni	$C_6H_5CH_2$	$C_6H_5CH_2Br$	$(6c)^+$	1.67	1.32	1.66	1.63	2.51 (CH_2)
Ni	CCl_3	CCl_4	$(6d)^+$	1.83	1.52	2.26	2.12	
Ni	C_6H_5CO	C_6H_5COCl	$(6e)^+$	1.75	1.33	2.02	1.84	

[a] The assignment of the absorptions to CH_3-c and CH_3-b in $(6a)^+X^-$ is established by the allylic coupling of CH_3-b with H_{exo}. Assignment in the other compounds was made analogously. [b] $^4J_{CH_3\text{-}b,H_{exo}} = 3$ Hz, $^3J_{CH_3\text{-}endo,H_{exo}} = 8$ Hz.

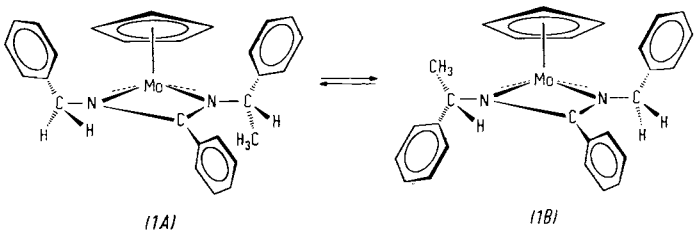
Received: January 18, 1980;
revised: April 22, 1980 [Z 532 IE]
German version: Angew. Chem. *92*, 658 (1980)

[1] Review: *W. E. Silverthorn*, Adv. Organomet. Chem. *13*, 48 (1975).
[2] *J. C. Smart, J. L. Robbins*, J. Am. Chem. Soc. *100*, 3936 (1978).
[3] *C. F. Cordes*, Chem. Ber. *95*, 3084 (1962).
[4] Compound *(4b)* was obtained simultaneously and independently by *H. Werner* and *Th. Dernberger*, Universität Würzburg. We thank Professor *Werner* for communicating his results.
[5] *D. R. Armstrong, R. Fortune, P. G. Perkins*, J. Organomet. Chem. *111*, 197 (1976).
[6] *R. J. Wilson, L. F. Warren, M. F. Hawthorne*, J. Am. Chem. Soc. *91*, 758 (1969).
[7] *G. E. Herberich, E. Bauer, J. Schwarzer*, J. Organomet. Chem. *17*, 445 (1969).
[8] *M. L. H. Green, L. Pratt, G. Wilkinson*, J. Chem. Soc. *1959*, 3753.
[9] *T. L. Court, H. Werner*, J. Organomet. Chem. *65*, 245 (1974).
[10] *G. E. Herberich, J. Schwarzer*, Angew. Chem. *82*, 883 (1970); Angew. Chem. Int. Ed. Engl. *9*, 897 (1970).

Conformational Analysis of 1-Phenylethyl Substituents in Metal Complexes and Their Importance for Asymmetric Catalysis[**]

By *Henri Brunner, Giuseppe Agrifoglio, Ivan Bernal*, and *Michael W. Creswick*[*]

The phenyl moieties of the $P(C_6H_5)_2$ groups in metal complexes of chelate phosphanes adopt axial/equatorial positions, in which they are almost perpendicular to each other[2]. In asymmetric catalysis, these phenyl orientations transmit the chiral information from the chelate backbone of the optically active phosphanes to the adjacent coordination positions of the metal atom at which the catalysis takes place[2]. In this study, we demonstrate the controlled influence of coordination positions in metal complexes by means of optically active 1-phenylethyl substituents at chelate rings.



In the reaction of $C_5H_5Mo(CO)_3Cl$ with optically active (*S*)-amidines HNR—CR′=NR*, $C_5H_5(CO)_2Mo$-amidinato complexes are formed which differ only in the configuration at the Mo atom. For $R = CH_2C_6H_5$, $R' = C_6H_5$, $R^* = CH(CH_3)(C_6H_5)$ the diastereoisomers *(1A)* and *(1B)* can be obtained optically pure by fractional crystallization. After equilibration with respect to the Mo configuration at 70 °C in acetone, a diastereoisomer ratio *(1A)*/*(1B)* = 70:30 is obtained. A single crystal X-ray structure analysis was carried out on the thermodynamically more stable isomer *(1A)* (Fig. 1).

The plane of the phenyl group R′ at the C atom of the chelate ring is approximately perpendicular to that of the chelate. The orientation of the substituents R and R* at the N

[*] Prof. Dr. H. Brunner, Dipl.-Chem. G. Agrifoglio
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)
Prof. Dr. I. Bernal, M. Creswick
Department of Chemistry, University of Houston
Houston, Texas 77004 (USA)

[**] Part 66 of the Series "Optically Active Transition Metal Complexes". This work was supported by Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie, and BASF AG, Ludwigshafen, as well as by the US National Science Foundation and the R. A. Welch Foundation.—Part 65: [1].

atoms is determined by the tendency of the C—H bonds of both substituents to lie in the ligand plane. Both phenyl rings point up towards the C_5H_5 ring while the methyl group of the (*S*)-1-phenylethyl substituent and a hydrogen atom of the benzyl substituent point down towards the CO ligands. Exactly the same conformation of (*S*)-1-phenylethyl was shown by X-ray structure analysis to occur in the thioacetamidato complex $C_5H_5(CO)_2MoSC(R')N(R^*)$[3] and in four other thioamidato complexes[4]. Like *(1A)*, these complexes are without exception the *A*-diastereomers favored at equilibrium. With the thioamidato complex $R' = 1\text{-}C_{10}H_7$, $R^* = CH(CH_3)(C_6H_5)$, for the first time, an X-ray structure analysis could be carried out of one of the *B*-diastereoisomers[4]. The following conformation of the (*S*)-1-phenylethyl moiety was found: C—H bond in the ligand plane, methyl group up towards the C_5H_5 ring, and phenyl ring down towards one of the two CO ligands, as indicated for *(1B)*.

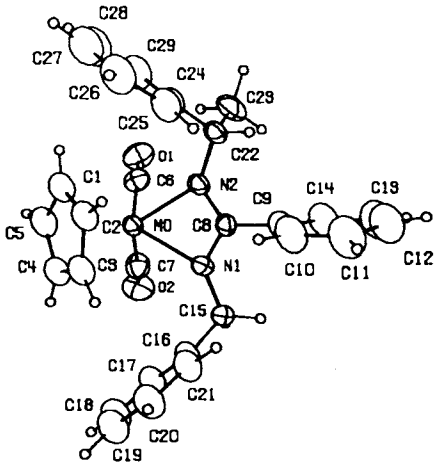


Fig. 1. ORTEP diagram of *(1A)*. Orange rhombs, space group P1, $Z=2$, $a=9.796(9)$, $b=11.875(4)$, $c=11.885(3)$ Å, $\alpha=88.27(2)$, $\beta=67.42(5)$, $\gamma=83.71(2)°$; $V=1268.21$ Å^3; $\rho_{calc}=1.400$, $\rho_{exp}=1.389$ g·cm^{-3}. From 3907 measured reflections ($Mo_{K\alpha}$ radiation, $\lambda=0.71073$ Å) 3575 with $I>2\sigma(I)$ were used for refinement of the structure; $R=3.77$, $R_w=3.82\%$, $w=1/\sigma^2(F)$]. The absolute configuration was determined by the Bijvoet method, using 12 strong reflections. The sequence $C_5H_5 > NCH(CH_3)(C_6H_5) > NCH_2C_6H_5$ defines the absolute configuration of Mo as (*R*) and the overall configuration of *(1A)* as (*R,S*). The unit cell contains two independent almost identical molecules I and II. Bond lengths, bond angles and dihedral angles for I: Mo—N1 2.175(7), Mo—N2 2.199(6), N1—C8 1.300(11), N2—C8 1.295(11), C15—N1 1.448(14), C22—N2 1.448(12) Å; N1—Mo—N2 59.2(2), N1—C8—N2 112.8(8), Mo—N1—C8 94.4(5), Mo—N2—C8 93.4(5), Mo—N1—C15 138.2(5), Mo—N2—C22 140.6(5)°; Cp—Ph(C16—C21) 58.8, Cp—Ph(C24—C29) 62.6, Cp—(ligand plane) 142.8, ligand plane—Ph(C16—C21) 89.3, ligand plane—Ph(C24—C29) 80.5°.

These results can be interpreted in the following way: the conformation-determining effect for the orientation of a (*S*)-1-phenylethyl substituent is the coplanar arrangement of the C—H bond of the asymmetric center with the C—R′ bond of the chelate ring. In addition, the weak attraction between the phenyl substituent of the asymmetric center R* and the MC_5H_5 group (the β-phenyl effect) as well as the weak repulsion between the alkyl group of the asymmetric center R* and the MC_5H_5 group are effective.

In [D_6]acetone, the C_5H_5 signals of diastereoisomers *(1A)* and *(1B)* lie at $\delta=4.73$ and 5.39, while those of the corresponding diastereoisomers *(2A)* and *(2B)*, with R = isopropyl instead of benzyl, appear at 5.11 and 5.77. These chemical shift differences are the result of a high field shift of the C_5H_5 signals in all the compounds, in which there is a MC_5H_5/phenyl interaction. This high field shift arises because the C_5H_5 protons lie within the inner anisotropy region of the phenyl ring. Such a shift or β-phenyl effect, observed twice for *(1A)*, once for *(1B)* and *(2A)*, and not at all for *(2B)*, characterizes the ^{1}H-NMR spectra of 46 $C_5H_5(CO)_2Mo$-amidinato and -thioamidato complexes[5,6]. It proves that the conformations determined by X-ray structure analyses are not only the result of crystal effects but also persist in solution as the favored conformations.

In the equilibrium $A \leftrightarrows B$ the isomers *A* are always present in higher concentrations than the isomers B. In the first place this is due to the attraction C_6H_5/MC_5H_5 which is possible for the (*R*)-configuration at the Mo atom in *(1A)* but not for the (*S*)-Mo configuration in *(1B)*. This β-phenyl effect, however, does not explain the trend in the equilibrium values $A:B = 70:30$, 87:13, 97:3 if in the amidinato complexes *(1)* the alkyl group at the asymmetric center R* varies in the series methyl, ethyl, *i*-propyl. For this it is necessary to assume an increasing repulsion alkyl/MC_5H_5 with increasing size of alkyl in R* according to a destabilization of *B*. If besides H, there are two different alkyl groups at the asymmetric center R*, the energy differences between the diastereomers *A* and *B* are only small. The diastereoisomer ratios $A:B$ lie between 50:50 and 60:40, with the bigger alkyl group probably pointing towards the C_5H_5 ligand in *A*.

The arrangement of a 1-phenylethyl substituent with respect to the ligand plane (shown as *A* or *B*) depends on the configuration at the Mo atom and is valid only for complexes carrying a large substituent at the neighboring C atom of the chelate ring. As the equilibrium ratios $A:B = 74:26$, 78:22, and 87:13 for the thioamidato complexes $C_5H_5(CO)_2MoSC(R')N(R^*)$ show, the effects increase along the series $R' = CH_3$, C_6H_5, $1\text{-}C_{10}H_7$[5,6]. In contrast, the conformations *A* and *B* are not the preferred conformations of the compounds in which a C—H bond in the chelate is adjacent to the 1-phenylethyl substituent, as in the $C_5H_5(CO)_2Mo$ thioformamidato and pyridinimine complexes[1,5]. This indicates that the conformation-determining effect (C—H of 1-phenylethyl in the ligand plane) can be ascribed to the steric hindrance of the phenyl and the methyl groups in R* with the big substituent R′ at the neighboring C atom. Also, the repulsion alkyl of R*/MC_5H_5 seems to be a steric effect. The attraction C_6H_5 of R*/MC_5H_5, obvious from the strongly negative λ-parameter for phenyl in the Ruch/Ugi model[6], is confirmed in present X-ray structure analysis especially by the orientation of the benzyl group.

The catalytic activity of amidinato complexes is documented[7]. Consequently, the conformational analysis presented above offers a way of controlling stereochemistry at coordination positions adjacent to the chelate ring in amidinato complexes, and similar compounds, by optically active 1-phenylalkyl substituents.

Received: February 15, 1980 [Z 533 IE]
German version: Angew. Chem. 92, 645 (1980)

[1] *H. Brunner, D. K. Rastogi,* Inorg. Chem. *19,* 891 (1980).
[2] *D. A. Slack, I. Greveling, M. C. Baird,* Inorg. Chem. *18,* 3125 (1979); *B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, D. J. Weinkauff,* J. Am. Chem. Soc. *99,* 5946 (1977); *M. D. Fryzuk, B. Bosnich, ibid. 99,* 6262 (1977); *100,* 5491 (1978); *R. G. Ball, N. C. Payne,* Inorg. Chem. *16,* 1187 (1977); *S. Brunie, J. Mazan, N. Langlois, H. B. Kagan,* J. Organomet. Chem. *114,* 225 (1976); *V. Gramlich, C. Saloman, ibid. 73,* C61 (1974).
[3] *M. G. Reisner, I. Bernal, H. Brunner, J. Wachter,* J. Organomet. Chem. *137,* 329 (1977).
[4] *I. Bernal,* unpublished.
[5] *H. Brunner, J. Wachter,* Chem. Ber. *100,* 721 (1977).
[6] *H. Brunner, R. Lukas,* Chem. Ber. *112,* 2528 (1979).
[7] *H. Brunner, G. Agrifoglio,* Monatsh. Chem. *111,* 275 (1980).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0642 $ 02.50/0

N-Fluoroiminosulfur Tetrafluoride, F—N=SF_4[**]

By *Darryl D. DesMarteau* and *Konrad Seppelt*[*]

Oriented double bonds on sulfur(VI) tetrafluoride systems open new theoretical and structural aspects[1,2]. Here we present the simplest fluorinated sulfur(VI) imide.

$$Cl_2N\text{–}SF_5 \xrightarrow[-\ ClF]{F_2} FClN\text{–}SF_5$$

$$FClN\text{–}SF_5 \xrightarrow{Hg/CF_3COOH} FHN\text{–}SF_5$$

$$FHN\text{–}SF_5 \xrightarrow[-\ HF]{KF} \overset{\cdot\cdot}{F}N{=}SF_4$$

Starting with Cl_2N—SF_5[3], chlorofluoroaminosulfur pentafluoride[4] (b.p. 25.3 °C (extr.)) is prepared first, which in turn is reduced by mercury in trifluoroacetic acid to fluoroaminosulfur pentafluoride[4] (b.p. 25.3 °C (extr.), m.p. −71 °C). From this, HF is eliminated by potassium fluoride, and the title compound F—N=SF_4 is obtained in 85% yield. It is a colorless gas, stable to at least 100 °C (b.p. −13.5 °C, m.p. −99 °C). The elemental composition has been secured by vapor density determination (M_r exp. 142.7, calc. 141.02), and by mass spectroscopy (70 eV, $m/e = 141$ (M_r^+) and fragments). Structural information was obtained by vibrational spectroscopy and ^{19}F-NMR. The IR spectrum (NaCl region) shows absorptions at 1128 (ν_{NS}), 930 (ν_{SF}), 870 (ν_{SF}), 757 (ν_{NF}), and 648 ($\delta_{S\ N}$) cm^{-1}. The spectrum is very similar to that of SOF_4[5] with an additional N—F stretching frequency. The N=S valence vibration occurs at about 100 cm^{-1} lower than expected, a surprising result in view of the rigidity of the molecule. The highly complicated ^{19}F-NMR spectrum could still be simulated as a A_2BCD spin system[6]. The spectrum shows the sulfur to have a trigonal bipyramidal environment, with one equivalent pair and one nonequivalent pair of fluorine atoms. The N—F group certainly occupies an equatorial position, and in analogy to CH_2=SF_4[1] the *N*-fluorine atom will be oriented in the axial plane.

This means that the molecule is rigid, with no change in position of the *N*-fluoro atom being observed. The rigidity of the F—N=SF_4 molecule is in sharp contrast to the nonrigidity of the molecules CH_3—N=SF_4, CF_3—N=SF_4, and O=SF_4[7], but is comparable to the behavior of CH_2=SF_4[1]. Only a Berry pseudorotation of the four *S*-fluorine atoms is possible; however, it cannot be observed because of the remaining nonequivalency of the participating atoms.

It is still not explainable why F—N=SF_4 does not form a dimer with a $(NS)_2$ four-membered ring unit, as is observed in $(Cl\text{—}NSF_4)_2$, which has not yet been observed as a monomer[8].

F—N=SF_4 is a weaker F^- donor than SOF_4[9]. AsF_5 forms an adduct at −78 °C that is completely dissociated at +20 °C. With SbF_5, an explosion occurs at −10 °C. Whether the adduct contains cationic species $N^{+}{\equiv}SF_4$ or $FN{=}\overset{+}{S}F_3$ remains to be seen.

Received: February 6, 1980 [Z 534 IE]
German version: Angew. Chem. *92*, 659 (1980)

[1] *G. Kleemann, K. Seppelt*, Angew. Chem. *90*, 547 (1978); Angew. Chem. Int. Ed. Engl. *17*, 516 (1978); *H. Bock, J. E. Boggs, G. Kleemann, D. Lentz, H. Oberhammer, E. U. Peters, K. Seppelt, A. Simon, B. Solouki, ibid. 91*, 1008 (1979) and *18*, 944 (1979), respectively.

[2] *R. Mews*, Angew. Chem. *90*, 561 (1978); Angew. Chem. Int. Ed. Engl. *17*, 530 (1978).

[3] *A. F. Clifford, G. A. Zeilenga*, Inorg. Chem. *8*, 979 (1969).

[4] *D. D. DesMarteau*, to be published.

[5] *K. O. Christe, C. J. Schack, E. C. Curtis*, Spectrochim. Acta *33A*, 323 (1977).

[6] Computer simulation with the LACOON 3 program. We wish to thank Professor *H. Friebolin* and his co-workers at Heidelberg for supplying the program.

[7] The temperature dependence of the ^{19}F-NMR spectrum of CH_3—N=SF_4 is drastic, but has not yet been analyzed [2]. An A_2BCX_3 spectrum is obtained for CF_3—N=SF_4 at −80 °C *E. L. Muetterties, W. Mahler, K. J. Packer, R. Schmutzler*, Inorg. Chem. *3*, 1298 (1964). Fluorine exchange in SOF_4 could not be frozen until −148 °C.

[8] *R. Mews, O. Glemser*, 9th International Fluorine Symposium, Avignon 1979.

[9] *F. Seel, O. Dettmer*, Z. Anorg. Allg. Chem. *301*, 113 (1959); *M. Brownstein, P. H. W. Dean, R. Gillespie*, J. Chem. Soc. Chem. Commun. *1976*, 9.

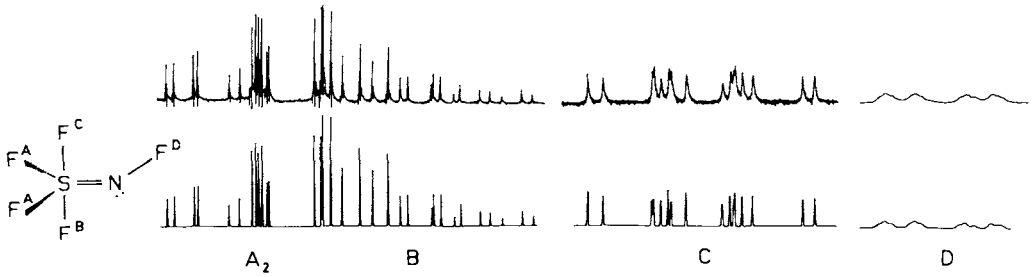


Fig. 1. ^{19}F-NMR spectrum of F—N=SF_4 (56.4 MHz, −80 °C): experimental (above) and simulated (below) as A_2BCD spin system with $\delta_A = -52.7$, $\delta_B = -45.0$, $\delta_C = -13.2$, $\delta_D = 43.9$, $J_{AB} = 213.9$ Hz, $J_{AC} = 194.0$ Hz, $J_{AD} = 19.6$ Hz, $J_{BC} = 10.7$ Hz, $J_{BD} = -92.7$, and $J_{CD} = 226.8$ Hz.

The spectrum retains its character from −80 to +100 °C. Only a broadening of the B, C, and mainly D signals is observed, probably due to quadrupole relaxation of the nitrogen atom.

[*] Prof. Dr. D. D. DesMarteau [+]
Department of Chemistry, Kansas State University
Manhattan, Kansas 66506 (USA)
Prof. Dr. K. Seppelt
Institut für Anorganische und Analytische Chemie der Freien Universität
Fabeckstrasse 34—36, D-1000 Berlin (Germany)

[+] To whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the U. S. Army Research Office, and by the Alexander von Humboldt Stiftung (fellowship for *D. D. D.*).

Structure of $[(CO)_5CrNEt_2]BF_4$, a Key Organometallic Compound; Reaction to Give the Carbene Complex $(CO)_5CrC(AsPh_2)NEt_2$[1]

By *Ulrich Schubert, Ernst Otto Fischer*, and *Dieter Wittmann*[*]

Our preparation of carbene complexes by reaction of hexacarbonylchromium, -molybdenum, or -tungsten with nucleophiles and alkylation of the resulting acylmetalates[2]

[*] Prof. Dr. E. O. Fischer, Dr. habil. U. Schubert, Dipl.-Chem. D. Wittmann
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

is not applicable to weak nucleophiles. In such cases, a route proceding *via* the sequence[3,4]

$$Cr(CO)_6 \xrightarrow[2)\ [Et_3O]BF_4]{1)\ LiNEt_2} (CO)_5Cr{=}C(NEt_2)(OEt) \xrightarrow{BF_3}$$

$$[(CO)_5Cr{\equiv}C{-}NEt_2]BF_4 \xrightarrow{Nu^{\ominus}} (CO)_5Cr{=}C(NEt_2)(Nu)$$

(1) *(2)*

i.e. indirect exchange of an alkoxy group for another nucleophilic substituent (Nu), gives the desired product.

The general applicability of step *(1)*→*(2)* has now been confirmed once again, *i.e.* by the successful synthesis of an arsenic-substituted carbene-complex by reaction of *(1)* with potassium diphenylarsenide (Nu = $AsPh_2$). The spectroscopic data of $(CO)_5CrC(AsPh_2)NEt_2$ are given in Table 1.

Table 1. Spectroscopic data of the diphenylarseniocarbene complex *(2)*, Nu = $AsPh_2$.

IR (ν_{CO} region, *n*-pentane NaCl optics): 2055 (m), 1942 (vs), 1936 (vs) cm^{-1}.
MS (CI source, 30 °C): m/e = 449 $[M-2CO]^+$, 421 $[M-3CO]^+$, 393 $[M-4CO]^+$, 313 [carbene]$^+$.
^{1}H-NMR ([D$_6$]-acetone, −30 °C, rel. to CD_3COCD_2H): δ = 7.39 (10H, S; C_6H_5), 4.62 and 3.97 (each 2H, Q; CH_2, *E,Z* isomers), 1.66 and 0.78 (each 3H, T; CH_3, *E,Z*).
^{13}C-NMR ([D$_6$]-acetone, −20 °C, rel. to CD_3COCD_2H): δ = 287.74 ($C_{carbene}$), 225.29 ($C_{CO,trans}$), 218.0 ($C_{CO,cis}$), 142.13, 133.85, 130.03 and 129.54 (C_{phenyl}), 59.69 and 56.69 (CH_2; *E,Z*), 15.11 and 14.21 (CH_3; *E,Z*).

Since the carbene complexes accessible by reaction of *(1)* with nucleophiles are themselves of preparative and theoretical interest (cf. [4,5]), the cationic carbyne complex *(1)* assumes a key role. Carbyne(pentacarbonyl)metal cations $[(CO)_5MCR]^{\oplus}$ (M = Cr, Mo, W) have also been discussed as intermediates in connection with the preparation of carbyne from carbene complexes[6] but so far only those with $R = NR_2'$ have been isolated. Thus, fundamental information about the nature of this class of compounds was expected from the X-ray structure analysis[7] of *(1)*.

The most striking features of the structure of *(1)* (cf. Fig. 1) are the long Cr—$C_{carbyne}$ bond relative to other aminocarbyne complexes of chromium[5a,8] and the large Cr—C_{CO} distance of the CO group *trans* to the carbyne ligand. The Cr—$C_{carbyne}$ bond in *(1)* is the longest observed so far, being 178 pm. Comparison with those of about 168—170 pm in *trans*-halo(tetracarbonyl)aryl or -alkylcarbyne complexes demonstrates the extensive participation of the resonance formula *(B)*.

$$(CO)_5\overset{\oplus}{C}r{\equiv}C{-}NEt_2 \longleftrightarrow (CO)_5Cr{=}C{=}\overset{\oplus}{N}Et_2 \longleftrightarrow (CO)_5Cr{=}\overset{\oplus}{C}{-}NEt_2$$

(A) *(B)* *(C)*

Consequently, the $C_{carbyne}$—N distance of 128 pm also lies in the double bond region. The influence of the resonance formula *(C)* is manifested not only in the reactions of *(1)* but also in the fact that, in spite of the greatest Cr—$C_{carbyne}$ distance in the series of aminocarbyne complexes, the C—N distance in *(1)* corresponds roughly to the value of 126 pm found for *trans*-$Ph_3Sn(CO)_4CrCNEt_2$ (Cr—$C_{carbyne}$ = 174 pm)[8b]. The extreme Cr—C_{CO} distance to the CO group located *trans* to the carbyne ligand finally indicates that the chromium atom also accepts some of the positive charge (resonance formula *(A)*).

The delocalization of the positive charge therefore extends over the entire Cr-C-N unit. Replacement of the amino group by an alkyl or aryl moiety increases the positive charge on the metal atom by eliminating *(B)*, thereby further weakening the Cr—C_{CO} *trans* bond. The corresponding cationic carbyne complexes are consequently destabilized to such an extent that they can no longer be observed or isolated under the usual conditions.

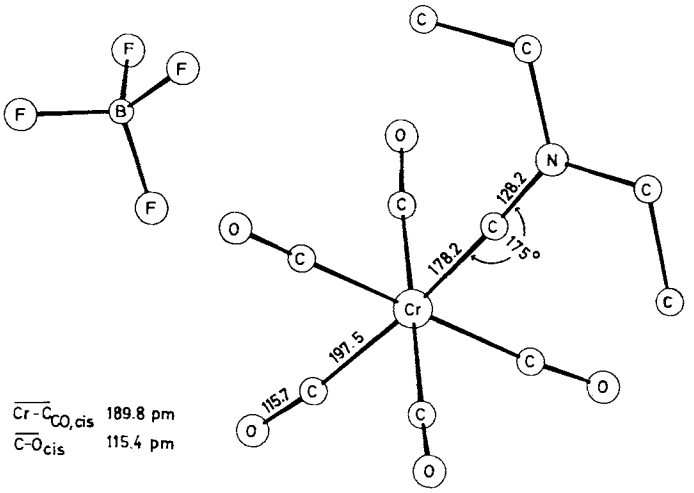


Fig. 1. Crystal structure of *(1)* with selected important distances (pm) and angles. The standard deviations of the distances are 1 pm for Cr—C and 2 pm for C—O and C—N.

Procedure

All operations are performed under N_2 with dried, O_2-free solvents.

A red solution of $KAsPh_2$ [prepared by adding $HAsPh_2$[9] (3 g, 13 mmol) in THF (20 ml) to a suspension of KH (0.53 g, 13 mmol) in THF (10 ml) at −30 °C and allowing the mixture to react at room temperature] is slowly added to a suspension of *(1)* (4.36 h, 12 mmol) in THF (50 ml) at −60 °C. The mixture turns dark brown and *(1)* dissolves on stirring for 30 min. The solvent is stripped off at −30 °C and the residue is extracted with CH_2Cl_2 prior to filtration. The filtrate is concentrated to 10 ml and purified by column chromatography on silica gel at −40 °C with pentane/CH_2Cl_2 (10:1) as eluent. After removal of solvent *(2)*, Nu = $AsPh_2$, is recrystallized from ether/pentane (5:1); yield 0.7 g (12%) of ocher crystals, m.p. 57 °C (dec.).

Received: March 3, 1980 [Z 537 IE]
German version: Angew. Chem. *92*, 662 (1980)

[1] Transition Metal-Carbyne Complexes, Part 58.—Part 57: *E. O. Fischer, W. Röll*, Angew. Chem. *92*, 206 (1980); Angew. Chem. Int. Ed. Engl. *19*, 205 (1980).
[2] *E. O. Fischer*, Pure Appl. Chem. *24*, 407 (1970); *30*, 353 (1972); Angew. Chem. *86*, 651 (1974).
[3] *E. O. Fischer, W. Kleine, F. R. Kreissl*, Angew. Chem. *88*, 646 (1976); Angew. Chem. Int. Ed. Engl. *15*, 616 (1976).
[4] *E. O. Fischer, R. B. A. Pardy, U. Schubert*, J. Organomet. Chem. *181*, 37 (1979); and references cited therein.
[5] a) *E. O. Fischer, H. Fischer, U. Schubert, R. B. A. Pardy*, Angew. Chem. *91*, 929 (1979); Angew. Chem. Int. Ed. Engl. *18*, 872 (1979); b) *H. Fischer*, J. Organomet. Chem., in press.
[6] *E. O. Fischer, U. Schubert*, J. Organomet. Chem. *100*, 59 (1975); *H. Fischer, A. Motsch, W. Kleine*, Angew. Chem. *90*, 914 (1978); Angew. Chem. Int. Ed. Engl. *17*, 842 (1978).
[7] $[C_{10}H_{10}CrNO_5]BF_4$; −30 °C, orthorhombic, $Pca2_1$ (Z = 4), a = 1361(2), b = 863(1), c = 1282(2) pm, $V = 1506 \times 10^6$ pm^3, ρ_{calc} = 1.60 g/cm^3. λ = 71.069 pm ($Mo_{K\alpha}$, graphite monochromator, Syntex $P2_1$), $2° \leqq 2\theta \leqq 45°$. 808 structure factors ($F_0 \geqq 3.0\sigma(F)$), R_1 = 0.075, R_2 = 0.081.
[8] a) *E. O. Fischer, G. Huttner, W. Kleine, A. Frank*, Angew. Chem. *87*, 781 (1975); Angew. Chem. Int. Ed. Engl. *14*, 760 (1975); b) *U. Schubert*, Cryst. Struct. Commun. 9, 383 (1980); c) *U. Schubert, D. Neugebauer, P. Hofmann, H. Fischer, A. Motsch, W. Kleine*, Chem. Ber., in press.
[9] *F. G. Mann, M. J. Prangell*, J. Chem. Soc. *1965*, 4123.

Molecular and Crystal Structure of β-SeBr[**]

By *Detlef Katryniok* and *Rüdiger Kniep*[*]

Contributions to the structural chemistry of compounds belonging to the class A_2B_2 (A = S, Se; B = F, Cl, Br) have so far come mainly from spectroscopic studies[1]. Most of these electron-rich chalcogen halides are readily accessible and have been known for several decades. We now report the first crystal structure analysis of a representative of this class, *i.e.* β-SeBr; both the structure of the individual molecule and the three-dimensional structure of the crystalline state are considered. A resemblance to a tellurium subiodide[2] is clearly seen.

DTA and powder photographs show the Se-Br system to contain the thermodynamically stable phases α-SeBr and α-$SeBr_4$[3]; both compounds are dimorphous, each with another β-phase which is metastable with regard to the phase diagram. A single crystal of β-SeBr was grown from the melt (SeBr) in a glass capillary (i.d. 0.2 mm) on a diffractometer assembly as described by *Simon et al.*[4] in a temperature gradient of 25 °C → −13 °C; its structure was analyzed at −80 °C[5].

The crystals of β-SeBr contain BrSeSeBr molecules, whose geometry and bonding are shown in Figure 1. The Se-Se distance of 2.241 Å in the molecule is significantly smaller than in the elemental structure (Se_{hex}, 2.373; Se_{mcl}, 2.318 Å[6]), and comparable with the corresponding distance determined by IR spectroscopy in FSeSeF (2.25 Å[1]); the Se—Br bond lengths in β-SeBr correspond to the terminal bond lengths in the cubane-type molecules $(SeBr_4)_4$ of α-$SeBr_4$ (average values 2.368(1) and 2.36(3) Å[3]).

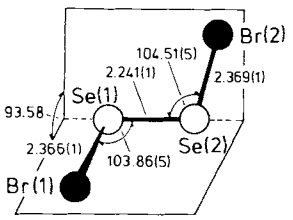


Fig. 1. Se_2Br_2 molecular geometry in β-SeBr (bond lengths [Å], bond angles (dihedral angles) [°]; standard deviations in brackets).

The β-SeBr structure also exhibits some intermolecular Se...Br contacts which are significantly closer than the sum of the van der Waals radii of 3.95 Å[7] (cf. Fig. 2). The shortest interaction of this kind (3.373(1) Å) exists between the Se(2) and Br(1) atoms of two adjacent BrSeSeBr molecules (generated *via* symmetry centers of the structure). Along the short crystallographic *c*-axis, translationally equivalent adjacent molecules exhibit Se(1)...Br(2) contacts of 3.514(1) Å. Each Se(1) atom also has a relatively short distance of 3.773(1) Å to Br(1) atoms of molecules that are adjacent along the *b*-axis.

A certain degree of similarity between the X-ray powder diagrams of β-SeBr and macromolecular β-TeI has already been reported[3]. If the $\left(\begin{smallmatrix}1\\ \infty\end{smallmatrix}\right)$-structural unit[2] extending along the direction of the shortest repeat distance (b = 4.182(2) Å)—a Te chain with alternatingly bridging and terminal I atoms—is regarded as being made up of n covalently bonded ITeTeI units, then a similar sequence of

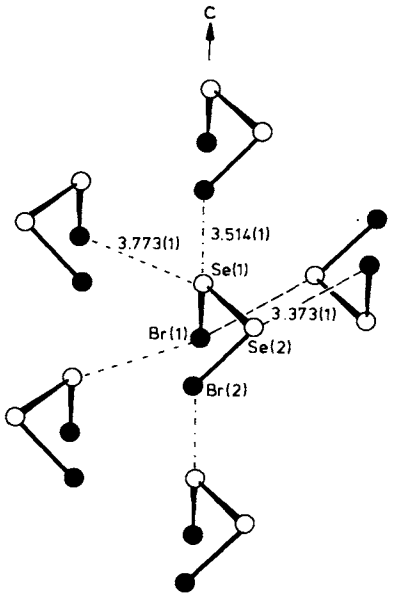


Fig. 2. Intermolecular Se...Br distances <3.95 Å (sum of the van der Waals radii [7]); standard deviations in brackets.

BrSeSeBr molecules[8] is found for β-SeBr along the shortest repeat distance (c = 4.974(2) Å; see also Fig. 2).

Received: April 10, 1980 [Z 538 IE]
German version: Angew. Chem. 92, 646 (1980)

CAS Registry number:
β-SeBr, 7789-52-8

[1] Review: *K. Seppelt*, Angew. Chem. *91*, 199 (1979); Angew. Chem. Int. Ed. Engl. *18*, 186 (1979); selenium fluorides: *A. Haas, H. Willner*, Z. Anorg. Allg. Chem. *454*, 17 (1979); chlorides and bromides: *e.g. P. J. Henda, P. J. D. Park*, J. Chem. Soc. *A 1968*, 908.

[2] *R. Kniep, D. Mootz, A. Rabenau*, Z. Anorg. Allg. Chem. *422*, 17 (1976).

[3] *P. Born, R. Kniep, D. Mootz*, Z. Anorg. Allg. Chem. *451*, 12 (1979).

[4] *A. Simon, H. J. Deiseroth, E. Westerbeck, B. Hillenkötter*, Z. Anorg. Allg. Chem. *423*, 203 (1976).

[5] 1503 symmetry-independent reflections ($Mo_{K\alpha}$, $P2_1$ four-circle diffractometer, ω scan), 1168 being significant ($F_0 > 3\sigma_F$). Structure analysis with E-XTL program system: monoclinic, $P2_1/c$, a = 7.345(2), b = 14.282(5), c = 4.974(2) Å, β = 97.11(3)°, Z = 4 Se_2Br_2, ρ_{calc} = 4.01 g cm^{-3}; R = 4.8%. Identification of the phase as β-SeBr from the X-ray powder diagram calculated from the structural model. Crystal growth and structure analysis of α-SeBr (m.p. 5 °C; growth conditions according to [3]) are under study.

[6] *P. Cherin, P. Unger*, Acta Crystallogr. *21*, A 46 (1966).

[7] *L. Pauling*: The Nature of the Chemical Bond, 3rd Ed. Cornell University Press, Ithaca, N. Y. 1960.

[8] Further structural resemblances between β-SeBr and β-TeI will be discussed in greater detail in connection with the crystal structure of α-SeBr [5].

Photolysis of Water Catalyzed by Transition Metal Dithiolenes

By *Rainer Henning, Wilhelm Schlamann*, and *Horst Kisch*[*]

The photochemical cleavage of water permits the conversion of solar energy into the environmentally unobjectional energy source hydrogen[1]. One of the principal prerequisites for this conversion is the availability of a suitable photocatalyst ($\lambda_{max} \approx 400$—800 nm). Since many transition metal complexes absorb in this wavelength region, their photochemical behavior—especially their photoredox reactions—lie at the center of current interest. All the systems so far described as

[*] Priv.-Doz. Dr. R. Kniep, Dr. D. Katryniok
Institut für Anorganische Chemie und Strukturchemie der Universität Universitätsstrasse 1, D-4000 Düsseldorf (Germany)

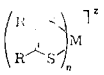
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[*] Priv.-Doz. Dr. H. Kisch, Dr. R. Henning, W. Schlamann
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung Stiftstrasse 34—36, D-4330 Mülheim/Ruhr (Germany)

active for photochemical water cleavage in homogeneous solution require either strongly acid conditions[2a] or stoichiometric amounts of a mild reducing agent such as triethanolamine[2b]. We now report the photoreduction of water proceeding in neutral solution in the presence of transition metal dithiolene complexes ($\lambda_{max} \approx 800$ nm)[3].

We irradiated ($\lambda \geq 290$ nm) one of the complexes of Table 1[4] in tetrahydrofuran (THF)/H_2O (11.5:1 v/v), and detected H_2 by gas chromatography of the gas phase; no H_2 is detected on exclusion of light. The first quantitative H_2 determinations[5] were performed with the nickel complex *(1)*: irradiation in THF/H_2O at $\lambda \geq 290$ nm for 185, 350, and 483 h, respectively, generates 46, 100, and 225% of H_2[6], after irradiation for the same time in anhydrous THF, 9, 16, and 77% of H_2 were detected; a simultaneously irradiated blank (THF/H_2O) containing no compound *(1)* yielded traces of hydrogen (*ca.* 0.5%) after 165 h. On irradiation ($\lambda \geq 254$ nm) in a quartz apparatus, H_2 formation is much faster: 141 mg (0.26 mmol) of *(1)* in 200 ml of THF/H_2O (9:1) gives 209 Nml (9.4 mmol) of hydrogen in 22 h.

Table 1. "Transition metal dithiolenes".

	n	M	R	*Z*	
	2	Ni	Ph	0	*(1)*
	2	Pd	Ph	0	*(2)*
	2	Pt	Ph	0	*(3)*
	2	Fe	Ph	0	*(4)*
	2	Co	Ph	0	*(5)*
	3	W	Ph	0	*(6)*
	3	Mo	Ph	0	*(7)*
Cation:	2	Ni	Me	0	*(8)*
Me_4N^+	2	Ni	Ph	−1	*(9)*
Bu_4N^+	2	Ni	Ph	−2	*(10)*
Bu_4N^+	2	Ni	CN	−2	*(11)*
Ph_4P^+	3	W	CN	−2	*(12)*

The fact that even the reaction in anhydrous THF[7] gives some H_2 suggests that part of the H_2 could come from *(1)* and/or the solvent. The former appears highly unlikely since irradiation of *(1)* in CCl_4 fails to produce H_2. In order to elucidate the second possibility, several irradiation runs were performed ($\lambda \geq 290$ nm) in the presence of D_2O and the composition of the gas phase was determined by mass spectrometry[8]. At the same solvent/D_2O ratio (12:1), the following values were found for the HD/D_2 ratio: THF, 13 and CH_3CN, 2.1; the D/H ratio is accordingly about 1 and 2. These results confirm the cleavage of D_2O and H abstraction from the solvent. The formation of hydrogen, though in small amounts, on irradiation of *(1)* in heterogeneous aqueous solution demonstrates that the organic solvent is not an essential component of the system.

The mechanism of this novel photochemical cleavage of water is still unknown. It is uncertain whether electronically excited *(1)* and/or its mono- or dianion, *(9)* and *(10)*, respectively, promote the reaction; since formation of *(10)* was observed in all reactions of *(1)*[9], the last two possibilities cannot be ruled out[10].

Procedure

Depending upon their solubility, up to 0.1 mmol of the "metal dithiolene" is dissolved in 25 ml of a THF/H_2O mixture (11.5:1, v/v). The solution is flushed with argon for *ca.* 30 min in a screw-cap vials with a magnetic stirrer and gas-tight rubber seal; the vials are then closed and irradiated in a merry-go-round apparatus at room temperature in a water bath for 5—7 d with an Hg high pressure lamp (Philips HPK 125 W). GC analysis of the gaseous products was performed on a molecular sieve column (5 Å)[12].

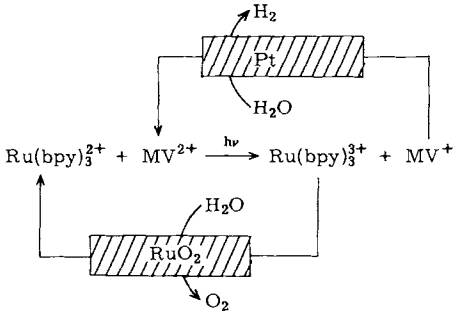
Received: October 30, 1978;
supplemented: June 24, 1980 [Z 540 IE]
German version: Angew. Chem. 92, 664 (1980)

[1] Cf. *N. Getoff*: Wasserstoff als Energieträger. Springer-Verlag, Berlin 1977, p. 173; *E. Schumacher*, Chimia *32*, 193 (1978).
[2] Cf., *e.g.*, *K. R. Mann, N. S. Lewis, V. M. Miskowski, D. K. Erwin, G. S. Hammond, H. B. Gray*, J. Am. Chem. Soc. *99*, 5525 (1977); *W. C. Trogler, D. K. Erwin, G. L. Geoffroy, H. B. Gray, ibid. 100*, 1160 (1978); b) *J.-M. Lehn, J.-P. Sauvage*, Nouveau J. Chim. *1*, 449 (1977).
[3] In this contribution, λ_{max} always refers to the lowest energy absorption maximum.
[4] Review: *G. N. Schrauzer*, Adv. Chem. Ser. *110*, 73 (1972); *E. Hoyer, W. Dietzsch, W. Schroth*, Z. Chem. *11*, 41 (1971); *J. A. McCleverty*, Prog. Inorg. Chem. *10*, 49 (1968).
[5] Compound *(1)* (0.024 mmol) in 8 ml of solution was irradiated (Philips HPK 125 W) in a Solidex reaction vessel ($\lambda \geq 290$ nm) at room temperature in a water bath. The total amount of H_2 was then determined by gas chromatography [0.8 m molecular sieve 5 Å; *F. Weeke, E. Bastian, G. Schomburg*, Chromatographia *7*, 163 (1974)].
[6] Assuming that 1 mol of *(1)* leads to the formation of 1 mol of H_2.
[7] Distilled over $LiAlH_4$.
[8] No H_2 was found; we thank Dr. *P. Potzinger*, Mülheim, for these analyses.
[9] Detected by isolation of *(10)* after addition of Bu_4NI to the irradiated reaction solution.
[10] *Note added in proof* (June 19, 1980): Catalysts of type *(1)* (M = Zn, R = CN, R—R = trithiocarbonate [11]) meanwhile produce more than two liters of hydrogen in 24 h [in 120 ml of 2,5-dihydrofuran/D_2O (1:1), immersion well apparatus, Philips HPK 125 W lamp, $\lambda \geq 254$ nm, turnover number 1600 mmol hydrogen/mmol catalyst, gas composition: 76% D_2, 21% HD, 3% H_2].
[11] *G. Steinmecke, H.-J. Sieler, R. Kirmse, E. Hoyer*, Phosphorus Sulfur *7*, 49 (1979).
[12] Cf. *P. G. Jeffery, P. J. Kipping*: Gas Analysis by Gas-Chromatography. Pergamon Press, London 1964.

Cyclic Water Cleavage by Visible Light: Drastic Improvement of Yield of H_2 and O_2 with Bifunctional Redox Catalysts[**]

By *John Kiwi, Enrico Borgarello, Ezio Pelizzetti, Mario Visca*, and *Michael Grätzel*[*]

The photoinduced reduction of methylviologen (*N,N'*-dimethylbipyridine dication, MV^{2+}) by a suitable sensitizer, such as $Ru(bpy)_3^{2+}$, can be exploited to achieve cleavage of water into hydrogen and oxygen[1]. The photoredox process is performed in the presence of two redox catalysts, one of which, *i.e.* colloidal platinum, effects reduction of water[2], and the other, *e.g.* RuO_2, oxidation of water[3]:



Scheme 1

[*] Prof. Dr. M. Grätzel, Dr. J. Kiwi, E. Borgarello
Institut de Chimie Physique
Ecole Polytechnique Fédérale
CH-1015 Lausanne (Switzerland)
Prof. Dr. Pelizzetti
Istituto di Chimica Analitica, Università di Torino
Torino (Italy)
Dr. M. Visca
Centro Richerche SIBIT (Montedison)
Spinetta Marengo (Italy)

[**] This work was supported by the Swiss National Foundation for Scientific Research as well as Ciba-Geigy and Engelhard Industries Corporation.

In order to render the water decomposition by light effective, one has to employ an extremely active platinum catalyst. At moderately high Pt concentrations ($\approx 2 \times 10^{-4}$ M) this has to react with the reduced electron relay (MV^+) in the microsecond time domain. Use of a catalyst system comprising an ultra fine Pt sol protected by a copolymer of styrene and maleic anhydride, and colloidal or macrodispersed RuO_2 gave quantum yields of *ca.* 1.5×10^{-3}. This is 100 times smaller than the H_2-yield obtained with a sacrificial system[4] were EDTA instead of water served as the reductant of $Ru(bpy)_3^{3+}$. Undoubtedly, the decreased quantum yield arises from undesirable cross reactions, in particular the reaction of oxygen with the reducing MV^+. This report describes the performance of a new cofunctional redox catalyst which achieves astonishingly high quantum yields in the water splitting process.

The catalytic material consists again of a combination of Pt and RuO_2. However, in contrast to the previous experiments[1] where individual particles of the two catalysts were suspended in solution, the new preparation contains Pt and RuO_2 codeposited on a common carrier, *i.e.* colloidal TiO_2. A mixed oxide of RuO_2 and TiO_2 was first prepared from a solution of the respective chlorides. The TiO_2 powder produced has a grain size of 1000 to 2000 Å and contains *ca.* 0.1% RuO_2. The TiO_2 is made n-type conducting through doping with Nb. The powder is subsequently charged with finely divided Pt by stirring it in a solution containing a Pt-sol (mean particle diameter 30 Å). Thereby colloidal particles are produced which can act simultaneously as *oxidation and reduction catalysts* (cofunctionality). Results obtained from the photolysis of aqueous solutions containing this catalyst are shown in Table 1. Irradiation of a solution containing $Ru(bpy)_3^{2+}$ (10^{-4} M), MV^{2+} (5×10^{-3} M), and EDTA (5×10^{-2} M) with visible light illustrates the high efficiency of this catalyst with respect to hydrogen generation. In this system no oxygen is produced. Instead of water, EDTA is irreversibly oxidized[2d,4]. One notes that for a given Pt concentration (40 mg/l) the H_2-evolution rate is influenced by the TiO_2 content of the solution. Optimal yields are obtained with a TiO_2 concentration of 50 mg/100 ml. Interestingly, with such a system one obtains a hydrogen generation rate which exceeds that obtained with colloidal platinum alone (particle diameter 30 Å, protected by Carbowax-20 M) by a factor of 4.

Table 1. Evolution of hydrogen from aqueous solutions with various redox catalytic systems under the action of visible light.

Catalyst [a]	Amount (mg/100 ml)	System	pH	ml H_2/l/h
$Pt/TiO_2/RuO_2$	100	$Ru(bpy)_3^{2+}$/	4.7	50
	50	MV^{2+}/EDTA		300
	25			260
	10			250
	5			200
Carbowax/Pt	80			80
$Pt/TiO_2/RuO_2$	50	$Ru(bpy)_3^{2+}$/	4.7	45
		MV^{2+}	3.0	3
			1.0	2
$Pt/TiO_2/RuO_2$	50	H_2O	4.7	0
		$Ru(bpy)_3^{2+}$ [b]		0
		MV^{2+}/EDTA		0

[a] Concentration of platinum 40 mg/l. [b] No illumination.

In the second part of Table 1 are listed results obtained with a cyclic system, *i.e.* in the absence of EDTA. The quantum yield for hydrogen generation is astonishingly high. If one accounts for the fact that EDTA doubles the quantum yield for MV^{2+} reduction, the efficiency of the cyclic system is only a factor of three lower than that of the sacrificial one. This may be further improved by optimization. It is noted from Table 1 that the rate of hydrogen evolution decreases with the solution pH. This is attributed to the decrease in the driving force for water oxidation by $Ru(bpy)_3^{3+}$.

A further important feature of the cyclic system is that the H_2 evolution can be sustained over long irradiation times. Thus after two days of irradiation there was no noticeable decrease in the hydrogen generation rate.

Oxygen production occurs simultaneously with the formation of hydrogen under illumination. Thus in the experiment where 45 ml of H_2 was generated during one hour of photolysis the quantity of O_2 produced was 16 ml. This value is distinctly below the stoichiometric proportion. Presumably part of the O_2 generated in the photolysis is absorbed on the surface of TiO_2 which under our conditions may be more than 100 m^2/l solution.

A series of blank experiments was performed to confirm the above results: There is no H_2 formation in the absence of light. Both the electron relay and sensitizer have to be present to obtain light-induced water decomposition: If the RuO_2,Pt-doped TiO_2 particles are illuminated alone in aqueous suspensions there is neither hydrogen nor oxygen formation. Presumably visible light is inefficient in directly exciting the TiO_2 semiconducting particles which have a band gap of 3 eV. When excited by UV-light TiO_2 can mediate a number of photosynthetic processes[5] and has been claimed to cleave water[6].

The surprisingly high activity of our cofunctional redox catalyst may be rationalized in terms of adsorption of the redox species in solution on the TiO_2 surface. This favors the catalytic processes and eliminates rate limits imposed by three-dimensional diffusion of the reactants. It is feasible that the whole process of water cleavage occurs on a single TiO_2 particle *via* adsorbed species. Whether electronic levels of the TiO_2 participate in this reaction remains to be investigated.

Experimental

For the preparation of the Pt-doped TiO_2/RuO_2 particles a platinum sol with a mean particle diameter of 30 Å was first produced[7]. (100 mg H_2PtCl_6 was dissolved in 250 ml H_2O and subsequently reduced with 35 ml of a 1% solution of citrate. The mixture was heated during *ca.* 4 h at 90 °C and the excess of citrate was removed with an Amberlite ion exchange resin.) To disperse the Pt on TiO_2 it suffices to stir the mixture containing the required amount of TiO_2 for approximately 1 h.

Figure 1 shows results obtained from applying the quasi-elastic light-scattering technique to the particle dispersions. Correlation functions were measured with a Chromatix[8] instrument. The Pt-doped RuO_2/TiO_2 particles show a mean hydrodynamic radius of 470 Å which lies distinctly below the grain size of the powder. Apparently a higher degree of dispersion is achieved in solution.

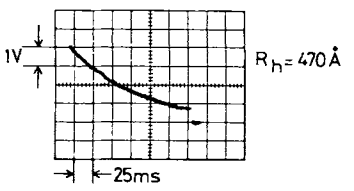


Fig. 1. Correlation function obtained from aqueous solutions of the $Pt/TiO_2/RuO_2$ particles (10 mg/l). Scattering angle $\theta = 4.5°$.

Illuminations were carried out with a XBO 450-W Xe lamp. The IR and UV content of the light was removed by a 16 cm water jacket and a 450 nm cut-off filter. Hydrogen and oxygen were analyzed by gas chromatography. Alternatively O_2 detection was carried out with an END-O-MESS instrument[9].

Received: May 29, 1980;
revised: June 18, 1980 [Z 539 IE]
German version: Angew. Chem. 92, 663 (1980)

CAS Registry numbers:
Pt, 7440-06-4; TiO_2, 13463-67-7; RuO_2, 12036-10-1; $Ru(bpy)_3^{2+}$, 15158-62-0; H_2, 1333-74-0; carbowax, 25322-68-3; MV^{2+}, 4685-14-7; H_2O, 7732-18-5

[1] *K. Kalyanasundaram, M. Grätzel,* Angew. Chem. *91*, 759 (1979); Angew. Chem. Int. Ed. Engl. *18*, 701 (1979).

[2] a) *B. V. Koryakin, T. S. Dzhabiev, A. E. Shilov,* Dokl. Akad. Nauk SSSR *238*, 620 (1977); *K. Kalyanasundaram, J. Kiwi, M. Grätzel,* Helv. Chim. Acta *61*, 2720 (1978); *A. Moradpour, E. Amouyal, P. Keller, H. Kagan,* Nouveau J. Chim. *2*, 547 (1978); b) *B. O. Durham, W. J. Dressick, T. J. Meyer,* J. Chem. Soc. Chem. Commun. *1979*, 381; c) *P. J. Delaive, B. P. Sullivan, T. J. Meyer, D. G. Whitten,* J. Am. Chem. Soc. *101*, 4007 (1979); *T. Kawai, K. Tanimura, T. Sakada,* Chem. Lett. *1979*, 137; *M. Kirsch, J. M. Lehn, J. P. Sauvage,* Helv. Chim. Acta *62*, 1345 (1979); *K. Kalyanasundaram, M. Grätzel,* J. Chem. Soc. Chem. Commun. *1979*, 1138; *A. I. Krasna,* Photochem. Photobiol. *29*, 267 (1979); *31*, 75 (1980).

[3] a) *J. Kiwi, M. Grätzel,* Angew. Chem. *90*, 900 (1978); *91*, 659 (1979); Angew. Chem. Int. Ed. Engl. *17*, 860 (1978); *18*, 624 (1979); Chimia *33*, 289 (1979); *M. Grätzel* in *H. Gerischer, J. J. Katz:* Dahlem Conferences 1978 on Light-Induced Charge Separation. Verlag Chemie, Weinheim 1979, p. 299; b) *J. M. Lehn, J. P. Sauvage, R. Ziessel,* Nouveau J. Chim. *3*, 423 (1979); c) *K. Kalyanasundaram, O. Micic, E. Pramauro, M. Grätzel,* Helv. Chim. Acta *62*, 2432 (1979).

[4] *J. Kiwi, M. Grätzel,* Nature (London) 657 (1979); J. Am. Chem. Soc. *101*, 7214 (1979).

[5] *A. J. Bard,* J. Photochem. *10*, 59 (1979); *T. Inone, A. Fujishima, J. Konishi, K. Honda,* Nature (London) *277*, 637 (1979).

[6] *A. V. Bulatov, M. L. Khidekel,* Izv. Akad. Nauk SSSR Ser. Khim. *1976*, 1902; *H. van Damme, W. K. Hall,* J. Am. Chem. Soc. *101*, 4373 (1979).

[7] *J. Turkevich* in "Electrocatalysis of Fuel Cell Reactions", Proc. Brookhaven Symp. p. 123.

[8] Chromatix Application Note LS-8 (1978), 560 Oakmead Parkway, Sunnyvale, Calif. 94086 (USA).

[9] Details are given in [3c].

Photochemistry of Sulfonamides and Sulfonylureas: A Contribution to the Problem of Light-Induced Dermatoses

By *Bernd Weiss, Heinz Dürr,* and *Hermann Josef Haas*[*]

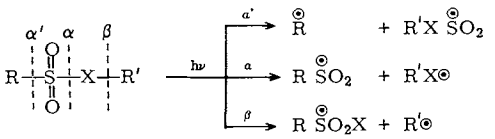
Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Sulfonamides and sulfonylureas have acquired great importance as pharmaceuticals, but they can elicit light-induced dermatoses or photosensitization of the human organism as side effect[1]. Surprisingly, the photochemistry of the sulfonamides and sulfonylureas has previously not been studied in very great detail. The compounds are relatively photostable, but give complex product mixtures on prolonged irradiation.

We report here on (i) model studies on the simple sulfonamides *(1a—d)*, (ii) the photochemistry of the chemotherapeutic sulfathiazole *(1e)* and (iii) the photochemistry of the antidiabetics tolbutamide (Rastinon) *(7a)* and carbutamide (Invenol) *(7b)*.

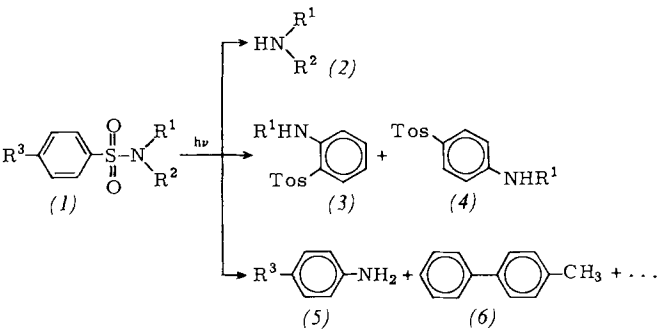
[*] Prof. Dr. H. Dürr, Dr. B. Weiss
Fachbereich 14 der Universität
D-6600 Saarbrücken (Germany)
Prof. Dr. H. J. Haas
Fachbereich 3 der Universität Saarbrücken
D-6650 Homburg (Germany)

In principle, the bonds marked in Scheme 1 can be cleaved (α'-, α-, and β-cleavage) on photolysis of sulfonamides and sulfonylureas. The radicals $R'X\overset{\ominus}{S}O_2$, $R\overset{\ominus}{S}O_2$, and $R\overset{\ominus}{S}O_2X$ should eliminate SO_2 and form simple alkyl or aryl radicals, which then stabilize by recombination or by abstraction of hydrogen from the solvent[2].

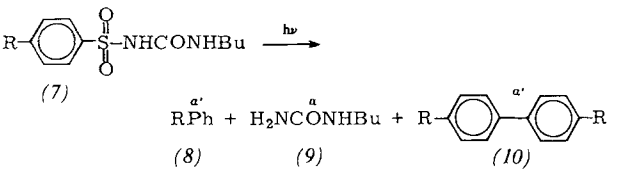


Scheme 1

The sulfonamides *(1a—e)* were irradiated in a Gräntzel apparatus (Hg low-pressure lamp, 70 W) at room temperature in ether, methanol, or ethanol. Low-boiling components were identified by GC analysis (comparison with authentic samples), solids were separated by column or thin-layer chromatography and identified by comparison with authentic material or spectra (Table 1).



The sulfonylureas tolbutamide (Rastinon) *(7a)* and carbutamide (Invenol) *(7b)* were photolyzed under conditions similar to those in the case of *(1)* (see Table 2). In the photolysis of *(7a)*, both in ether as well as in methanol, toluene *(8a)*, *n*-butylurea *(9)*, and 4,4'-dimethylbiphenyl *(10a)* were formed. In $MeOH/O_2$, however, no toluene or dimethylbiphenyl was obtained thus indicating chemical rather than physical quenching by O_2. Prolonged photolysis (100 h) of *(7b)* in methanol yielded aniline *(8b)*, *n*-butylurea *(9)*, and three products of unknown structure. Thus, a *p*-amino group drastically increases the photochemical stability of the sulfonamides *(1)* as well as the sulfonylureas *(7)*.



In mechanistic studies on *(7a)* we obtained the following results: 1) The excited state is likely to have $n\pi^*$ or $\pi\pi^*$ character. 2) The effectiveness of the photofragmentation of *(7a)* is moderate, *i.e.* the quantum yield is only 0.04 (disappearance of the educt). 3) Sensitization experiments with xanthone ($E_T = 73$ kcal/mol) proceeded negatively, while the findings with $MeOH/O_2$ indicate chemical rather than physical quenching of the excited state. No luminescence is observed with *(7a)* [however, in the case of *(7b)* and *(1e)* fluorescence was observed]. 4) A cage-effect participates in product formation.—All these findings indicate that the photo-

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0648 $ 02.50/0

Table 1. Photolysis of the sulfonamides *(1a—e)*.

(1)	R^1	R^2	R^3	Solvent	Products [%] *(2)*	*(3)*	*(4)*	*(5)*	*(6)*	Other products
a	H	Ph	Me	Et_2O	21 [a]	6	13	—	—	
b	Ph	Ph	Me	Et_2O	24	20	30	—	—	
				MeOH	7	17	35	—	—	
c	H	PhCO	Me	Et_2O	4			1	20	$H_2N—CO_2Et$ 7% + PhCO—NH—C_6H_4Ph 2%
				EtOH	32	—	—	—	31	$H_2N—CO_2Et$ 7% + PhCO—NH—C_6H_4Ph 1%
d	PhCO	Ph	Me	Et_2O	31	35	20			PhCO—NPh—C_6H_4—NH—COPh 5%
e	H	2-Thiazolyl	NH_2	Et_2O	traces	—	—		—	$PhNH_2$ 23% + 2-Aminothiazole <1%

[a] Isolated as $PhNH_3^{\oplus}Tos^{\ominus}$.

Table 2. Photolysis of the sulfonyl ureas *(7a)* in ether (2 h, 50% conversion), methanol (2 h, 50% conversion) or CH_3OH/O_2 and *(7b)* in methanol (100 h).

(7)	R	Solvent	Products [%] *(8)*	*(9)*	*(10)*
a	Me	Et_2O	34	80	10
		MeOH	30	26	1
		$MeOH/O_2$	—	40	—
b	NH_2	MeOH	24	27	— [a]

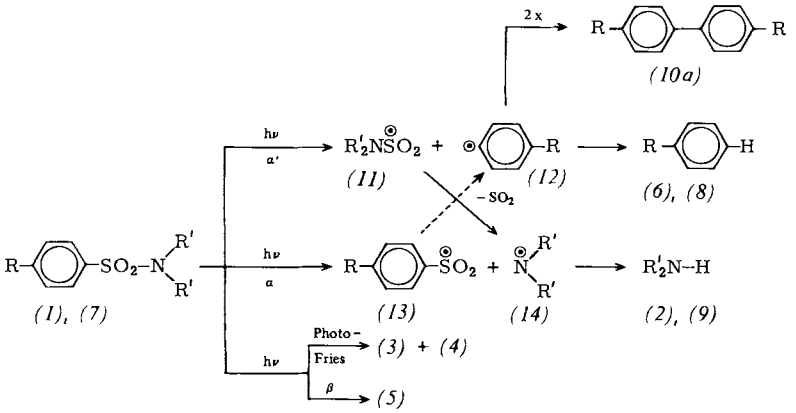
[a] Also three unidentified products.

fragmentation of *(7a, b)* originates from an excited singlet-state. 5) No long-lived intermediates can be detected by the ED- and EDQ technique of *Mauser*[2]. 6) Radical intermediates can be established by ESR spectroscopy (direct methods and spin-trap technique).

cleavage. The products toluene *(8a)* and aniline *(8b)* point to additional α′-cleavage. A direct cleavage of the arylsulfonyl radicals with formation of hydrocarbons is endothermic and therefore fairly unlikely[4].

In spite of the "non-physiological" conditions in the photolysis of *(7)* the following conclusions drawn from the mechanistic findings might be of importance for the problem of photosensitization: The results of the sulfonamide photolysis depend upon the solvent. Since *(7a)* ($\lambda = 222$ nm) absorbs far below 280 nm it should not be directly excited by sunlight. A secondary reaction of the products *(8)—(10)* formed in the photofragmentation could hardly be plausible in the photosensitization caused by *(7a)* [the same applies for *(7b)* and *(1e)*]. The following hypothesis would appear more attractive:

(7a) could absorb UV light directly; the radicals formed would then react with the cell components and give rise to



Scheme 2

The reaction mechanism of the photofragmentation of sulfonamides *(1)* and sulfonylureas *(7)* is outlined in Scheme 2. The key-fragment in the α-cleavage is the radical pair *(13)* + *(14)*, in the α′-cleavage *(11)* + *(12)*.

Summary: 1) The *N*-arylsulfonamides *(1a)* and *(1b)* undergo α-cleavage to *(2a)* and *(2b)*, while the *N*-aroylsulfonamides *(1c)* and *(1d)* preferably undergo α-cleavage to *(2c)* and *(2d)*; in *(1c)* some β-cleavage to ethyl carbamate and *(5c)* is observed as side reaction. The decisive spin state for the photoreaction might have S_1-character. 2) If the nitrogen atom of the sulfonamides *(1a, b, d)* bears a phenyl group, Photo-Fries rearrangement to *(3a, b, d)* + *(4a, b, d)* occurs as main competing reaction. 3) The α-cleavage of the alkylsulfonamides of type *(1)*[3] and of the sulfothiazole *(1e)* proceeds *via* T_1-states; *(1e)* gives aniline by α′-cleavage *via* a S_1-state. 4) The sulfonylureas *(7a, b)* fragment essentially in the sense of a α-

the observed damage. Any SO_2 formed could bring about additional complications. This would amount to a *phototoxic reaction*. Furthermore, *(7a)* could attack at the cell protein directly as hapten. This system would now be light sensitive through a bathochromic shift and could be cleaved to products having a long-term effect, which could be regarded as a *photoallergic process*.

Received: April 20, 1980 [Z 515 IE]
German version: Angew. Chem. 92, 647 (1980)

CAS Registry numbers:
(1a), 68-34-8; *(1b)*, 4703-19-9; *(1c)*, 6971-74-0; *(1d)*, 74542-54-4; *(1e)*, 72-14-0; *(2a)* tosylate, 14034-57-2; *(2b)*, 122-39-4; *(2c)*, 55-21-0; *(2d)*, 93-98-1; *(2e)*, 96-50-4; *(3a)*, 1213-33-8; *(3b)*, 52914-18-8; *(3d)*, 74542-55-5; *(4a)*, 4094-38-6; *(4b)*, 61654-49-7; *(4d)*, 74542-56-6; *(5c)*, 106-49-0; *(6)*, 644-08-6; *(7a)*, 64-77-7; *(7b)*, 339-43-5; *(8a)*, 108-88-3; *(8b)*, 62-53-3; *(9)*, 592-31-4; *(10a)*, 613-33-2; ethyl carbamate, 51-79-6; 4-benzamidiobiphenyl, 20743-57-1; *N*-phenyl-*N*,*N*′-[phenylene]-4,4′-diylbisbenzamide, 74542-57-7

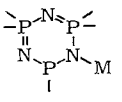
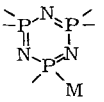
[1] *M. A. Pathak, T. B. Fitzpatrick*, Ration. Drug Ther. *6*, 1 (1977).
[2] *H. Mauser*, Z. Naturforsch. *B 23*, 1025 (1968).
[3] a) *H. Dürr* in Houben-Weyl: Methoden der Organischen Chemie, 4th Edit. Thieme, Stuttgart 1975, Vol. IV/2; b) *J. P. Pete et al.*, Tetrahedron Lett. *1971*, 4555; *J. P. Pete, C. Portella*, J. Chem. Res. *(S) 1979*, 20; *J. Reisch, J. H. Niemeyer*, Arch. Pharm. (Weinheim) *305*, 135 (1972); *J. Haas*, private communication; *P. C. Rowbotham et al.*, Pharm. Acta Helv. *51*, 364 (1976); *L. D. Souza, R. A. Day*, Science *160*, 882 (1968); *F. A. Davies, U. K. Nader*, Tetrahedron Lett. *1977*, 1721; *H. Nozaki et al.*, Tetrahedron *22*, 2177 (1966).
[4] *J. L. Kice* in *J. K. Kochi*: Free Radicals. Wiley, New York 1973, Vol. II, p. 527.

Cyclotri(phosphazene) Complexes with *P*-Coordinated PdX_2 and PtX_2[**]

By *Alfred Schmidpeter, Klaus Blanck, Heinz Hess,* and *Heinz Riffel*[*]

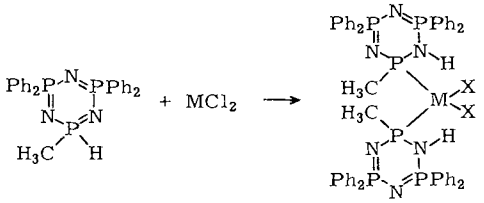
Dedicated to Helmut Behrens on the occasion of his 65th birthday

The chemistry of electropositively substituted cyclotri(phosphazenes) is still in its infancy[1]. Metalated cyclotri(phosphazenes) *(1)*, M = Li[2] and Cu[1][3], have proven to be preparatively useful species despite their being sensitive or even unisolable intermediates. They are tentatively formulated ionically or as *(1a)* with *N*-coordinated metal M.

(1a)   *(1b)*

We report here on derivatives of coordination type *(1b)*, M = Pd and Pt.

The cyclotri(λ^5-phosphazene) *(2)*[4] reacts with the nitrile complexes of $PdCl_2$ and $PtCl_2$ or also directly with $PdCl_2$ and K_2PtCl_4, respectively, to give the crystalline 2:1 complexes *(3)*. The metal displaces the hydrogen at P-2 towards N-1. Thus, in the complex, the otherwise unobservable[4] NH-form prototropic to *(2)* is fixed. In the complexes, chloride can readily be replaced by bromide to give *(3)*, X = Br.



(2) M = Pd, Pt *(3)*, X = Cl

Structure *(3)* is supported by the NMR spectra (Table 1), particularly by the strong and metal-dependent downfield shift of the P-2 signal [in *(2)*: $\delta(^{31}P) = 6.9$] and by the disappearance of the $^1J_{PH}$- and appearance of a $^1J_{PPt}$-coupling. As expected this coupling lies between the regions characteristic for phosphane- and phosphite-complexes, *i.e.* between 3500 and 6200 Hz, respectively. By protonation of N-1, which is more strongly basic than N-5[5], P-4 and P-6 become anisochronic; in pyridine or nitrobenzene as solvent or, partly also in dichloromethane at high concentrations of *(3)*, the exchange of the proton between N-1 and N-3 is rapid enough for them to appear equivalent again (at averaged ^{31}P-shift).

Table 1. NMR and IR spectroscopic data of the complexes *(3)*. *J* in Hz.

M	Pd	Pd	Pt	Pt
X	Cl	Br	Cl	Br
Solvent	CH_2Cl_2	$CHCl_3$	CH_2Cl_2	$C_6H_5NO_2$
$\delta(^{31}P)$ P-6	17.9	18.4	16.8 }	15.1
P-4	13.3	15.2	13.5 }	
P-2	69.8	70.5	36.3	37.5
J_{PtP}			4590	4590
$\delta(^1H)$ CH_3 [a]	1.77	1.76	1.88	2.15
$J_{PCH} + J_{PMPCH}$	9.8	9.8	11.2	6.4 [b]
J_{PNPCH} [c]	0.8	1.0	0.9	1.0
J_{PtPCH}			22.8	
νM—Cl [d]	260		260	
	289		288	

[a] X-part of a $[ABCX_3]_2$ system. [b] L = 14.6: $J_{PCH} = \pm 10.5$, $J_{PPtPCH} = \pm 4.1$ Hz. [c] Estimated from the linewidth of the N-doublet. [d] KBr disk, ν in cm^{-1}.

Since two M—Cl vibration bands are observed for *(3)*, they ought to be *cis*-complexes; however, the ^1H-multiplets of the 2-methyl groups are consistent with this assumption only when M = Pt, whereas in the case of M = Pd they indicate a $^2J_{PPdP}$ coupling, which is too large for a *cis*-arrangement and therefore would suggest an equilibrium with the *trans*-form in solution.

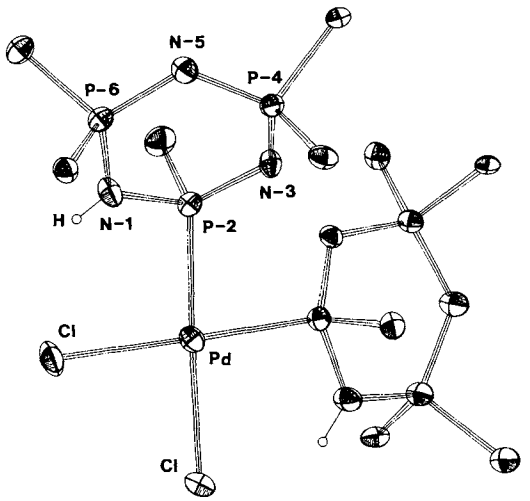


Fig. 1. Molecular structure of the $PdCl_2$ complex *(3)* in the crystal; most important bond lengths [pm], angles at Pd, and internal ring angles (mean values):

Pd—Cl	239.8(1)	Cl—Pd—Cl		89.5(5)°	
Pd—P-2	224.2(1)	P-2—Pd—P-2′		87.4(5)°	
P-2—N-1	170.4(4)	P-2	106.7(2)°	N-1	126.2(3)°
P-6—N-1	165.2(4)	P-4	115.4(2)°	N-3	124.2(2)°
P-6—N-5	157.9(4)	P-6	111.3(2)°	N-5	124.7(2)°

For simplicity only the C atom 1 of the phenyl substituents on P-4 and P-6 is shown.

An X-ray structure analysis[6] of *(3)*, M = Pd, X = Cl, confirms the bonding of the metal to the phosphorus and supports the *cis*-arrangement in the crystal (Fig. 1). The cyclo-

[*] Prof. Dr. A. Schmidpeter, Dr. K. Blanck
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Prof. Dr. H. Hess, Dr. H. Riffel
Institut für Anorganische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Phosphazenes, Part 72. This work was supported by the Fonds der Chemischen Industrie.—Part 71: *J. Högel, A. Schmidpeter*, Z. Naturforsch. *B 34*, 915 (1979).

phosphazene rings have a distinct boat-conformation and project outwards in opposite directions from the P_2PdCl_2 plane. The endocyclic angle at the Pd-substituted P-2 is unusually small, evidencing its partial P^{III} character. The angle at the neighboring protonated N-1, on the other hand, is slightly wider; the bonds from N-1 to the phosphorus are lengthened considerably[7]. The rest of the PN-bonds, however, are in good agreement with the comparative value of 160 pm for $(Ph_2PN)_3$.

Procedure

(2) (920 mg, 2 mmol) is added to a hot solution of $PdCl_2$ (178 mg, 1 mmol) in CH_3CN (20 ml). *(3)*, M = Pd, X = Cl, separates out as pale-yellow crystals of m.p. 267—268 °C (dec.); yield 1000 mg (92%).

A solution of K_2PtCl_4 (415 mg, 1 mmol) in water (10 ml) is added to a boiling solution of *(2)* (920 mg, 2 mmol) in ethanol (45 ml). The red color immediately disappears, and on evaporation *(3)*, M = Pt, X = Cl, precipitates out; colorless crystals, m.p. 279—281 °C (from anisole); yield 1130 mg (95%).

For Cl/Br exchange a solution of *(3)*, X = Cl in dichloromethane (M = Pd) or hot anisole (M = Pt) is stirred for 10 h with an excess of finely powdered KBr. From the filtered (if necessary concentrated) solution, *(3)*, X = Br, is precipitated by addition of ether; bright yellow (M = Pd) or yellow crystals (M = Pt).

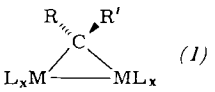
Received: January 29, 1980 [Z 530 IE]
German version: Angew. Chem. *92*, 655 (1980)

[1] *A. Schmidpeter, J. Högel, K. Blanck*, 2nd Symposium on Inorganic Phosphorus Compounds, Prague 1974, Abstract 3.6.
[2] *J. Högel, A. Schmidpeter*, Z. Anorg. Allg. Chem. *458*, 168 (1979).
[3] *P. J. Harris, H. R. Allcock*, J. Chem. Soc. Chem. Commun. *1979*, 714; *H. R. Allcock, P. J. Harris*, J. Am. chem. Soc. *101*, 6221 (1979).
[4] *A. Schmidpeter, J. Ebeling, H. Stary, C. Weingand*, Z. Anorg. Allg. Chem. *394*, 171 (1972).
[5] *A. Schmidpeter, H. Eiletz*, Chem. Ber. *109*, 2340 (1976).
[6] Space group $P\bar{1}$; $a = 1090.5(2)$, $b = 1327.2(1)$, $c = 1954.9(2)$ pm, $\alpha = 80.34(1)$, $\beta = 79.88(1)$, $\gamma = 54.34(1)°$, $V = 2517.1(5) \times 10^6$ pm^3, $Z = 2$, $\rho_{X\text{-ray}} = 1.446$ g/cm^3. $\mu Mo_{K\alpha} = 7.0$ cm^{-1}. Low temperature measurements, Syntex-P2$_1$ diffractometer, $2\theta \leq 45°$; 6578 reflections, 5146 with $I > 2\sigma$, structure solution with MULTAN program, structure refinement with anisotropic temperature factors, H atoms from the difference-Fourier-synthesis, $R_1 = 0.049$, $R_2 = 0.033$.
[7] A corresponding distortion of the phosphazene ring is observed in the protonated half of a spirobi(cyclophosphazene): *A. Schmidpeter, H. Eiletz, J. von Seyerl, G. Huttner*, Z. Naturforsch. *B 34*, 911 (1979).

Synthesis of the First Methylidyne-Rhodium Cluster by Proton-Induced H_2/CH_4-Elimination from a μ-Methylene Complex[**]

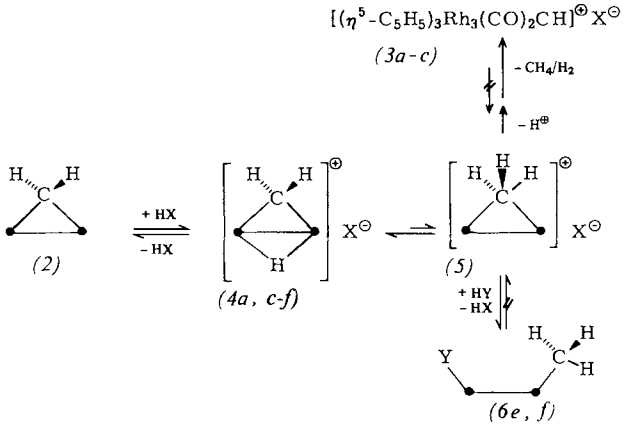
By *Wolfgang A. Herrmann, Johann Plank, Ernst Guggolz,* and *Manfred L. Ziegler*[*]

While carbene complexes $L_xM{=}CRR'$ represent a well-documented class of compounds, both from the preparative point of view and regarding their reactivity[1], the chemistry of μ-methylene complexes *(1)* has rarely been reported on in the literature apart from occasionally observed intramolecular isomerism phenomena[2]. Stimulated by theoretical considerations[3a] and NMR spectroscopic findings[3b], according to which the complexes *(1)* can be formulated as dimetallacyclopropanes and appear to display a high electron density at the bridgehead carbon, we have investigated the nucleophilic activity of the latter. Here, we report for the very first time on acid-induced reactions of the readily accessible prototypal rhodium compound *(2)* containing an unsubstituted methylene bridge[4].



(1)

Surprisingly enough, HBF_4 reacts with *(2)* in tetrahydrofuran (THF) essentially quantitatively to give the trinuclear, ionic cluster compound *(3a)*, which crystallizes straight away as black, lustrous, air-stable and exceedingly thermally stable needles. The same is true for the completely analogous trifluoroacetate *(3b)* and trifluoromethanesulfate *(3c)*[5].



● = $(\eta^5\text{-}C_5H_5)Rh(CO)$; *(a)*, X = BF_4; *(b)*, X = CF_3COO; *(c)*, X = CF_3SO_3; *(d)*, X = FSO_3; *(e)*, Y = Cl; *(f)*, Y = Br

Although NMR spectra strongly indicated the presence of μ_3-methylidyne functions in the cations of *(3a—c)*, a conclusive assignment of structure proved possible only by means of a single crystal analysis (Fig. 1, Table 1). The cluster ion which electronically meets the EAN rule essentially consists

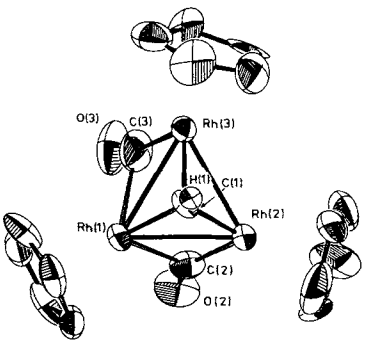


Fig. 1. ORTEP diagram of the cation di-μ_2-carbonyl-μ_3-methylidynecyclotris[(η^5-cyclopentadienyl)rhodium] (3*Rh—Rh*) of *(3b)* in the crystal. The thermal vibration ellipsoids correspond to 50% probability. *(3b)* crystallizes from acetonitrile (−18 °C) in the monoclinic system, space group C_{2h}^5-C2/c, $a = 1772.54(56)$, $b = 1060.67(34)$, $c = 2270.90(74)$ pm, $\beta = 103.895(25)°$; $Z = 8$. 2045 independent non-zero reflections were recorded on a computer-controlled single crystal diffractometer (AED Siemens) (Mo-Kα; $65° \leq 2\theta \leq 4°$) and corrected in the usual way. $R_F = 0.042$.

[*] Prof. Dr. W. A. Herrmann, Dipl.-Chem. J. Plank
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)
Prof. Dr. M. L. Ziegler, Dipl.-Chem. E. Guggolz
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] Transition Metal Methylene Complexes, Part 11. This work is being supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, Hoechst AG, and Degussa Hanau.—Part 10: *W. A. Herrmann, J. Plank, I. Bernal, M. Creswick*, Z. Naturforsch. *B 35*, 680 (1980).

Table 1. Selected bond parameters of *(3b)*.

Bond lengths [pm]		Angles [°]	
Rh(1)Rh(2)	267.8(1)	Rh(1)Rh(2)Rh(3)	60.8(0)
Rh(1)Rh(3)	271.4(1)	Rh(3)Rh(1)Rh(2)	59.7(0)
Rh(2)Rh(3)	268.4(2)	Rh(1)Rh(3)Rh(2)	59.5(1)
Rh(1)C(1)	193.0(9)	C(1)Rh(1)Rh(2)	47.3(4)
Rh(2)C(1)	197.0(14)	Rh(1)C(1)Rh(2)	86.7(5)
Rh(3)C(1)	198.6(14)	Rh(3)C(1)Rh(1)	87.7(5)
Rh(1)C(2)	221.2(15)	Rh(3)C(1)Rh(2)	85.5(5)
Rh(2)C(2)	192.1(12)	Rh(1)C(2)Rh(2)	80.4(5)
Rh(1)C(3)	246.3(20)	Rh(1)C(2)O(2)	128.3(1.3)
Rh(3)C(3)	188.1(16)	Rh(2)C(2)O(2)	151.1(1.5)
C(1)H(1)	99.8(120)	Rh(1)C(3)Rh(3)	76.0(6)
C(2)O(2)	115.9(20)	Rh(1)C(3)O(3)	122.9(1.5)
C(3)O(3)	115.4(24)	Rh(3)C(3)O(3)	161.0(1.8)
		H(1)C(1)Rh(1)	135.0(8.5)
Rh—C_5H_5(centroid)	219—227	H(1)C(1)Rh(2)	129.0(8.3)
C—$C(C_5H_5)$	137—145	H(1)C(1)Rh(3)	117.5(8.3)

of an equilateral triangular Rh_3-skeleton symmetrically bridged by the CH group, while the two carbonyl ligands resemble unsymmetrical edge-bridging functionalities. The methylidyne building block of *(3a)* can be recognized in the ^{1}H-NMR spectrum through its extremely deshielded proton (symmetric quartet at $\delta = 16.23$, $^2J_{Rh,H} = 2.6$ Hz) and is confirmed ^{13}C-NMR spectroscopically by a downfield resonance at $\delta = 303.6$[5].

Strikingly, the acid-induced synthesis of the first CH-rhodium compounds *(3a—c)* from the μ-methylene complex *(2)* proceeds *via* H_2- and CH_4-elimination[6], in a curious twist with the formation of stable μ-methyl derivatives which arise from protonation of *Wilkinson*'s $(\mu\text{-}CH_2)_3Ru_2[P(CH_3)_3]_6$[7]. The initial steps of protonation were characterized by the following experiments:

1. The methylene species *(2)* is converted by HBF_4 (CF_3SO_3H or FSO_3H) in prompt and quantitative precipitation reactions in diethyl ether, without evolution of gas, into yellow, rather heat- and moisture-sensitive derivatives, which on the basis of their conductivity, composition (complete elemental analysis) and IR and ^{1}H-NMR spectra[8] were shown to represent the novel ionic carbonyl-bridged protonation products *(4a)*[8], *(4c)* and *(4d)* in the solid state. Methyl groups are not detectable ^{1}H-NMR spectroscopically in solutions of *(4)*: While signals of terminal and bridging CH_3-ligands are absent in the range $\delta = 3 \ldots -7$[3b,7], the symmetric triplets centered around $\delta = -12.91$ or -12.97 in the case of *(4a)*[8] are, on the basis of the chemical shift, the intensity, the multiplicity, and the coupling constants ($^1J_{Rh,H} = 23.0$ Hz) unambiguously diagnosable as signals of Rh—*H*—Rh functions; the signals in the range $\delta = 10 \ldots 6$ can be exclusively assigned to methylene protons[3b,7]. The observed signal-doublings highly likely originate from the equilibria of the diastereomeric forms *cis*-Cp/*trans*-Cp ($K(20\,°C) = 45:55$).

2. Even weakly basic solvents such as THF, dimethyl sulfoxide, or hexamethylphosphoric triamide effect the deprotonation *(4)*→*(2)*. A rapid CH_2/Rh*H* exchange has been proven to occur by labeling experiments; *e.g.*, the complex [D]-*(4d)* precipitated with FSO_3D reacts with CD_3OD/$NaOCH_3$ or else CH_3OD/$NaOCH_3$ yielding the labeled precursor *(2)* (36% D_0, 38% D_1, 26% D_2; MS). Accordingly, reaction of excess [D]-trifluoroacetic acid with *(2)* in THF under otherwise equal conditions leads to the D-labeled methylidyne species [D]-*(3b)* (80 ± 5% D; ^{1}H-NMR). It is thus demonstrated that mechanistically decisive methyl intermediates participate in the synthesis of *(3)*. Besides, this is the only reasonable interpretation which fully accounts for the formation of deuterated methylidyne products *(3)* in the course of subsequent H_2/CH_4(!)-elimination.

3. The kinetics of the reaction [D]-*(4d)*→[D]-*(3d)* shows (NMR investigation) that the synthesis of the trinuclear methylidyne complex proceeds *via* partial deprotonation of the hydrido(methylene) precursor *(4)* and includes unsymmetrically substituted dinuclear complexes of previously unknown constitution.

4. The protonation of *(2)* which starts at the electron-rich metal-metal bond rather than at the bridgehead carbon is consistent with the likewise surprising observation that the μ-carbonyl complex $(\mu\text{-CO})[(\eta^5\text{-}C_5H_5)Rh(CO)]_2$ which is isostructurally[4] and electronically[3a] completely analogous to *(2)*, can be smoothly converted with HBF_4/ether into the readily isolable cation $[(\mu\text{-CO})(\mu\text{-H})\{(\eta^5\text{-}C_5H_5)Rh(CO)\}_2]^+$, which is again reversibly deprotonatable with bases[9].

5. The irreversible shift to the methyl tautomers *(5)*[10] of the equilibrium *(4)* ⇄ *(5)* circumstantially evidenced by labeling experiments and shown by NMR findings to lie practically completely on the side of the hydrido(methylene) compound *(4)*[10], was accomplished with nucleophiles capable of coordination: thus HCl or HBr reacts rapidly with *(4a)* under anhydrous conditions to give the new dinuclear, neutral halogeno(methyl) complexes *(6e)*, Y = Cl, and *(6f)*, Y = Br[11].

These results demonstrate the acid-induced synthesis of the methylidyne cluster *(3)* to be initiated by protonation of the electron-rich metal-metal bond of the μ-methylene complex *(2)* and to proceed *via* tautomeric organometallic hydrido(methylene)/methyl cations. This most simple synthetic approach is also applicable to μ-carbonyl complexes[12].

Received: May 13, 1980 [Z 535 IE]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 660 (1980)

CAS Registry numbers:
(2), 62154-28-3; *(3a)*, 74542-98-6; *(3b)*, 74542-99-7; [D]-*(3b)*, 74543-01-4; *(3c)*, 74543-02-5; *(4a)*, 74543-04-7; *(4c)*, 74543-05-8; *(4d)*, 74543-06-9; [D]-*(4d)*, 74543-08-1; *(6e)*, 74543-09-2; *(6f)*, 74543-10-5

[1] Synopsis: *E. O. Fischer*, Adv. Organomet. Chem. *14*, 1 (1976); see also *R. R. Schrock, P. R. Sharp*, J. Am. Chem. Soc. *100*, 2389 (1978); *R. R. Schrock*, Acc. Chem. Res. *12*, 98 (1979).

[2] a) *E. O. Fischer, V. Kiener, R. D. Fischer*, J. Organomet. Chem. *16*, P 60 (1969); *W. A. Herrmann, I. Schweizer*, Z. Naturforsch. *B 33*, 1128 (1978); b) *R. B. Calvert, J. R. Shapley*, J. Am. Chem. Soc. 99, 5225 (1977).

[3] a) *P. Hofmann*, Angew. Chem. *91*, 591 (1979); Angew. Chem. Int. Ed. Engl. *18*, 554 (1979); b) *M. Creswick, I. Bernal, W. A. Herrmann*, J. Organomet. Chem. *172*, C 39 (1979).

[4] *W. A. Herrmann, C. Krüger, R. Goddard, I. Bernal*, J. Organomet. Chem. *140*, 73 (1977).

[5] Procedure for *(3a)*: A solution of *(2)* (2.0 mmol) in THF (30 ml) is treated with 0.8 ml of 48% aqueous HBF_4. The mixture is briefly stirred, and then allowed to stand without any agitation at 10—20 °C for 3—4 d. After *ca.* 15 min, the first needle-shaped crystals begin to separate, with concomitant deepening in color of the solution from red to dark brown. The final product is washed with THF (4 × 5 ml) and ether (3 × 10 ml) and dried on a vacuum line; yield 832 mg (95%). No m.p. up to 280 °C. Soluble in acetonitrile, acetone, dimethylformamide (DMF), methanol, insoluble in ether and CH_2Cl_2.—IR (νCO): 1929, 1884 cm^{-1} (KBr); 1925, 1882 cm^{-1} (CH_3CN); ^{1}H-NMR (90 MHz, [D$_7$]-DMF, int. TMS, 25 °C): $\delta C_5H_5 = 6.00$ ("s", 15 H; $^2J_{Rh,C_5H_5} < 0.4$ Hz), $\delta CH = 16.23$ (q, 1 H); ^{13}C-NMR (22.63 MHz, [D$_7$]-DMF, int. TMS, 33 °C): $\delta C_5H_5 = 98.4$, $\delta CH = 303.6$, $\delta CO = 209.1$ (assignment by off-resonance decoupling).—Equivalent conductivity: $\Lambda = 96$ $cm^2 \cdot \Omega^{-1} \cdot mol^{-1}$ (CH_3NO_2, 21.6 °C, 2×10^{-4} mol/l).—*(3b)* and *(3c)* are similarly accessible and have analogous properties and spectra. The composition of *(3a)* is confirmed by C, H, Rh, B, F analyses; C, H, Rh analyses have been carried out on *(3b, c)*.—The CO ligands in *(3)* are fluxional; *W. A. Herrmann et al.*, unpublished results.

[6] Gas chromatograph, Varian 1860-42; Porapak Q (5 m × *ca.* 0.32 mm), carrier gas N_2 (35 ml/min, *ca.* 1.2 bar), Program −43 °C isothermal. The gas liberated in the formation of *(3a)* contains *ca.* 60% H_2 and *ca.* 37% CH_4, but only traces of CO, C_2H_4, C_2H_6, H_2CO, CH_3OH, CH_3CHO, and C_2H_5OH were not detected.—We thank Dr. *E. Eibler* for performing the GC analyses.

[7] *M. B. Hursthouse, R. A. Jones, K. M. Abdul Malik, G. Wilkinson*, J. Am. Chem. Soc. *101*, 4128 (1979).

[8] Procedure for *(4a)*: A stirred solution of *(2)* (203 mg, 0.5 mmol) in ether (10 ml) is treated with 10 drops of HBF_4/ether (54%). The yellow precipitate immediately formed is quickly filtered off, washed with ether, and dried *in vacuo*. Yield 235 mg (100%).—IR (νCO): 1881, 1843 cm^{-1} (KBr). ^{1}H-NMR (90 MHz, CD_3NO_2, 20 °C): $\delta C_5H_5 = 5.99$ ("t", 10H, $^2J_{Rh,C_5H_5} = 0.5$ Hz), $\delta CH_2 = 7.95$ ("s"), 8.80 (m), 9.19 (2 × t; $^2J_{Rh,H} = 2.6$ Hz), total int. 2H, $\delta RhHRh = -12.91$, -12.97 (2 × t, $^1J_{Rh,H} = 23.0$ Hz, total int. 1H. $\Lambda = 95$ $cm^2 \cdot \Omega^{-1} \cdot mol^{-1}$ (CH_3NO_2, −20 °C, 5.5×10^{-4} mol/l).—Reaction of *(4a)* with aqueous HBF_4/THF gives *(3a)* in quantitative yield.

[9] IR (νCO; CH_3NO_2; −25 °C): 2082, 2058, 1869 cm^{-1}. ^{1}H-NMR (90 MHz, CD_3NO_2, int. TMS, −20 °C): $\delta C_5H_5 = 6.07$ ("s", 10H), $\delta RhHRh = -10.67$ (t, 1H, $^1J_{Rh,H} = 18.3$ Hz). $\Lambda = 85$ $cm^2 \cdot \Omega^{-1} \cdot mol^{-1}$ (CH_3NO_2, −9.0 °C, 2.7×10^{-4} mol/l).

[10] The precise geometry of *(5)* is not known for the present system. The observed H/D exchange very probably proceeds *via* unsymmetric Rh—CH_2H···Rh bridges; cf. *R. B. Calvert, J. R. Shapley*, J. Am. Chem. Soc. *100*, 7726 (1978).

[11] Black, rhombic, slightly air-sensitive crystals (from CH_2Cl_2); m.p. 152—154 °C *(6e)*, and dec. >138 °C *(6f)*, resp. *(6f)*: IR (νCO): 1879, 1844 cm^{-1} (KBr); 1892, 1849 cm^{-1} (CH_2Cl_2); ^{1}H-NMR (90 MHz, [D_6]-DMSO, int. TMS, 25 °C): $\delta C_5H_5 = 5.53$ (d, 5H; $^2J_{Rh,H} = 0.65$ Hz), 5.64 (d, 5H; $^2J_{Rh,H} = 0.45$ Hz), $\delta CH_3 = 1.33$ (d, 3H; $^2J_{Rh,CH_3} = 2.4$ Hz). We thank Dr. *Th. Burgemeister* for recording the NMR spectra.—The composition of *(6e, f)* is also confirmed by C, H, Rh, Cl(Br) analyses. A single-crystal X-ray structure analysis proved the presence of symmetrical CO bridges and the *cis*-configuration of the ligands CH_3, Br, and C_5H_5, C_5H_5, respectively. *W. A. Herrmann, J. Plank, M. L. Ziegler, B. Balbach*, J. Am. Chem. Soc. *102* (1980), in press.

[12] *W. A. Herrmann, J. Plank, D. Riedel*, J. Organomet. Chem. *190*, C47 (1980).—Meanwhile the synthesis of $(\eta^5\text{-}C_5Me_5)_2Rh_2(CO)_3$ from $(\eta^5\text{-}C_5Me_5)Rh(CO)_2/HBF_4$ has also been accomplished by this method; the intermediate product $[(\eta^5\text{-}C_5Me_5)_2Rh_2(CO)_3H]^+BF_4^-$ can be isolated in pure form.

similar S_4N_3 skeleton is found in 1,7-bis(*p*-tolyl)tetrasulfur trinitrogen chloride[7c].

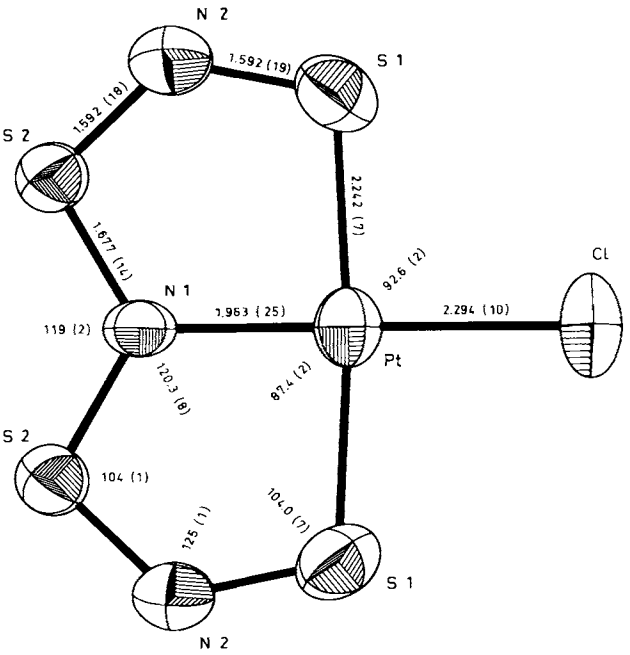


Fig. 1. Molecular structure of $PtCl(S_4N_3)$ in the crystal, with bond lengths [Å] and angles [°].

A Novel SN-Ligand: Structure of $PtCl(S_4N_3)$

By *Helmut Endres* and *Elisabeth Galantai*[*]

As starting compounds for reactions connected with our current studies we require complexes of Ni, Pd, Pt which keep the S_4N_4 molecule as intact as possible. When halides of these metals are allowed to react with S_4N_4, cleavage of the molecule occurs and complexes containing bidentate S_2N_2H- and S_3N-ligands are formed[1,2]. The formation of $(Ph_3P)_2Pt(S_4N_4)$, besides other products, in the reaction of $(Ph_3P)_4Pt^0$ with S_4N_4 has been reported[3]; however, an X-ray structure analysis of this compound has so far not been described. The complex $CuCl(S_4N_4)$ contains Cu—Cl—Cu chains, the Cu atoms of neighboring chains each being bridged by two S_4N_4 molecules[4]. Numerous Lewis acid/Lewis base adducts of S_4N_4 with stronger Lewis acids have been isolated[1].

We investigated the reaction of S_4N_4 with *cis*-$PtCl_2(NCPh)_2$[5], for we assumed that S_4N_4 would readily replace the benzonitrile moiety, known as a good leaving group. If a solution of equimolar amounts of the reactants in toluene is heated under reflux for 5 h, a black powder interspersed with rectangular, deep-violet crystals precipitates on cooling. As the X-ray structure analysis of such a crystal shows (Fig. 1)[6], a novel type of complex is formed, in which a formally singly negatively charged S_4N_3 group is coordinated as planar tridentate ligand to the Pt^{II}. The molecule displays mirror symmetry with N1, Pt, and Cl in the plane of symmetry. All S—N bond lengths have values between those for a single bond and a double bond, the shorter distances of 1.59 Å (N2—S1, N2—S2) corresponding to those in S_4N_4, 1.60—1.63 Å[7a], the longer distances of 1.68 Å (N1—S2) to those in $S_4N_4H_4$, 1.663—1.669 Å[7b]. A geometrically very

The planar complex molecules form stacks along the *a*-axis with the normals of the planes tilted at 48.8° relative to the stacking direction. The projection of two neighboring molecules of a stack onto each other does not reveal any marked intermolecular interactions.

Formally the anionic ligand S_4N_3 is formed by cleavage of a positively charged N-atom from S_4N_4. The Pt^{II} starting complex loses the two benzonitrile ligands and a Cl^-. An indication of the reaction mechanism might be given by the observation that NH_4Cl precipitates in the reflux condenser during the reaction.

The new compound can be obtained in the form of black dendritic crystal aggregates after extraction of the powdery precipitate with toluene; recrystallization, even on slow cooling (2—3 d), does not afford crystals suitable for single crystal studies. The identity of the substance thus isolated with the crystals employed for the structure analysis is proven by elemental analysis and Debye-Scherrer diagrams. The compound dissolves in toluene, acetone *etc.* to give a red solution. It is stable towards air, and does not melt below 250 °C.

Procedure

A mixture of *cis*-$PtCl_2(NCC_6H_5)_2$ (4 mmol) and S_4N_4 (4 mmol) in toluene (*ca.* 100 ml) is heated under reflux for 5 h, whereupon the color of the solution changes from yellow to wine-red. The flask is left in the heating mantle and the solution is allowed to cool down slowly overnight. A powdery black precipitate mixed with deep-violet crystals settles out; this is filtered off and extracted with toluene in a Soxhlet extractor. On cooling the extract, $PtCl(S_4N_3)$ crystallizes out. Evaporation of the reaction solution furnishes a further crop of the compound. Yield *ca.* 10%, m.p. >250 °C. IR (nujol): 1005, 834, 820, 730, 717, 696, 663, 502, 334 cm^{-1}, all bands

[*] Dr. H. Endres, Dipl.-Chem. E. Galantai
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

strong. UV (in dioxane, values in brackets in acetone): 576 (534), 413 (408), 378 (373) nm[8].

Received: November 15, 1979 [Z 536 IE]
German version: Angew. Chem. 92, 644 (1980)

CAS Registry numbers:
$PtCl(S_4N_3)$, 74525-20-5; *cis*-$PtCl_2(NCPh)_2$, 15617-19-3; S_4N_4, 28950-34-7

[1] *J. Weiss*, Fortschr. Chem. Forsch. *5*, 635 (1966); *G. G. Alange, A. J. Banister*, J. Inorg. Nucl. Chem. *40*, 203 (1978).
[2] *D. T. Haworth, G. Y. Lin*, J. Inorg. Nucl. Chem. *39*, 1839 (1977).
[3] *A. A. Bhattacharyya, J. A. McLean, Jr., A. G. Turner*, Inorg. Chim. Acta *34*, L199 (1979).
[4] *U. Thewalt*, Angew. Chem. *88*, 807 (1976); Angew. Chem. Int. Ed. Engl. *15*, 765 (1976).
[5] *F. R. Hartley*: The Chemistry of Platinum and Palladium. Applied Science Publ., London 1973, p. 462.
[6] Rhombic, D_{2h}^{16}-Pbnm, $a=5.165(4)$, $b=10.750(3)$, $c=13.173(4)$ Å, $Z=4$, $\rho_{calc}=3.64$ g/cm³. $R=0.066$ for 683 absorption-corrected independent reflections with $I>3.0\sigma(I)$ (Siemens-AED, $Mo_{K\alpha}$ radiation, 5-value method, $2\theta_{max}=60°$).
[7] a) *B. D. Sharma, J. Donohue*, Acta Crystallogr. *16*, 891 (1963); b) *S. N. Nabi, M. B. Hursthouse, K. M. A. Malik, ibid. B33*, 2309 (1977); c) *J. J. Mayerle, J. Kuyper, G. B. Street*, Inorg. Chem. *17*, 2610 (1978).
[8] We thank Dipl.-Chem. *A. Kratz* for measuring the spectra.

MoS_4^{2-} and $MoOS_3^{2-}$ as Structurally Versatile and Biochemically Interesting Ligands in Crystalline Multinuclear Cu- and Fe-Complexes

By *Achim Müller, Hartmut Bögge, Heinz-Gerhard Tölle, Rainer Jostes, Uwe Schimanski*, and *Mechtild Dartmann*[*]

The importance of thiomolybdates and especially of MoS_4^{2-} ions in various biological processes has recently been recognized[1,2]. Thiomolybdates were detected (on the basis of the electronic absorption spectra of the species which we previously investigated in aqueous solution) in the hydrolysis product of nitrogenase (FeMo-protein of *Clostridium pasteurianium*)[1]. Thiomolybdates are most probably formed in the rumen of grazing animals[2] and also appear to be involved in human medicine in disorders of Cu metabolism. MoS_4^{2-} is generally the strongest antagonist of Cu metabolism[2b], and the Cu deficiency caused by high contents of Mo in pasture soils (the interaction in grazing animals takes place both in the rumen and in cell tissues) constitutes a very serious problem for ruminants in some parts of the world[2]. We have now been able to show that thiomolybdates, which together with thiotungstates were introduced by us as ligands in coordination chemistry[3], have a strong tendency to form various types of multinuclear Cu-complexes (reaction already detectable with *ca.* 10^2 ppm of the reactants referred to the amount of solvent!), and that there is also a high tendency for the complex $[Cl_2FeS_2MoS_2]^{2-}$ *(1)* to be formed. *(1)* is interesting, since the complex can serve as precursor for the synthesis of the low-molecular weight FeMo cofactor (FeMo-co)[4]. Because of the Mo/W antagonism[2a], the W-derivatives would also appear to be of interest from the biochemical point of view.

We have now been able to isolate the compounds *(2)*, *(3)*, and *(4)* listed in Table 1 and to characterize them by elemental analysis, ^{57}Fe-Mössbauer, IR and electronic absorption spectra, magnetic measurements, and complete crystal structure analyses (Syntex $P2_1$, $Mo_{K\alpha}$) (cf. Fig. 1, 2 and Table 1).

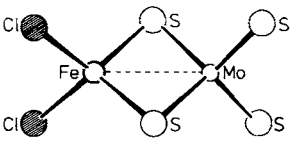


Fig. 1. Molecular structure of $[Cl_2FeMoS_4]^{2-}$ in crystals of *(4)*; Fe...Mo = 2.775 Å (structure of thiometalato complexes: Type I with tetrahedrally coordinated Fe central atom).

In the Cu/Mo multinuclear complexes[5] *((3):* trinuclear complex with trigonal-planar and tetrahedral coordination of Cu; *(2):* with central cubic skeleton; Type IV: with cage structure of two six-membered metal-sulfur rings) the MoS_4^{2-} (and $MoOS_3^{2-}$) ion functions as twofold (in *(3)*) and threefold bridging ligand (in *(2)* and Type IV). Noteworthy is that in *(2)* and Type IV three S atoms of the $MoOS_3^{2-}$ ion are each linked with two different Cu atoms, so that *one thiometalate ion* participates in a total of *six Cu—S bonds.*

Table 1. Multinuclear Mo-complexes and their properties.

Compound and Color	X-Ray Crystallographic Data	Physical Data
$\{Cu_3MoS_3Cl\}(PPh_3)_3O$ *(2):* red	orthorhombic, $P2_12_12_1$; $a=12.839(2)$, $b=17.553(3)$, $c=22.761(3)$ Å; $Z=4$; 3016 reflections, $R_w=0.059$; Mo—S_{av}: 2.259, Mo—O: 1.769(10), Cu—S: 2.277(5)—2.322(5) Å	IR [a]: ν(Mo—S) = 444/451, ν(Mo—O) = 908
$(PPh_3)_3Cu_2MoS_4 \cdot 0.8\,CH_2Cl_2$ *(3):* red	monoclinic, $P2_1/c$; $a=18.394(4)$, $b=16.653(3)$, $c=17.714(3)$ Å, $\beta=95.53(1)°$; $Z=4$; 3699 reflections, $R_w=0.070$; Mo—S_{av}: 2.208, Cu—S: 2.212(5)—2.315(6) Å	IR [a]: ν(Mo—S) = 465
$[Ph_4P][(C_6H_5CH_2)(CH_3)_3N]$ $[Cl_2FeMoS_4]$ *(4):* dark red	triclinic, P1; $a=13.224(5)$, $b=14.978(2)$, $c=10.042(2)$ Å, $\alpha=82.07(2)$, $\beta=81.72(3)$, $\gamma=74.41(2)°$; $Z=2$; 5740 reflections, $R_w=0.078$; Fe—Mo: 2.775 Å [d]	IR [a]: ν(Mo—S)$_t$ = 488/504, ν(Mo—S)$_{br}$ = 448, ν(Fe—Cl) = 322/332; VIS [b]: 588, 512, 464, 427; NIR: 1050; ^{57}Fe-Mössbauer [c]: QS = 2.100 ± 0.005, IS (α-Fe) = 0.480 ± 0.006 (293 K); $\mu_{eff}^{corr}=5.0\ \mu_B$ (293 K)

[a] Solid state (KBr), cm^{-1}. [b] Dimethylformamide, nm. [c] mm/s (Prof. Dr. *A. Trautwein*, Saarbrücken). [d] The Fe—Mo distance can be determined in spite of the disorder.

The great affinity of Cu cations (strong soft acids) for thiomolybdate ions (strong soft bases) is also clear from the strong tendency to form various (and structurally interesting) types of multinuclear complexes, since their formation depends only on the relative concentrations of the reaction partners (Cu: thiomolybdate: ligand). These facts, and *in vivo* experiments with molybdates, MoS_4^{2-}, sulfur-containing compounds, and Cu salts (also with radioactive Cu and Mo isotopes) on ruminants and rats[2b] indicate a participation of multinuclear thiomolybdato complexes in Cu metabolism.

[*] Prof. Dr. A. Müller, Dr. H. Bögge, Dipl.-Chem. H. G. Tölle, Dipl.-Chem. R. Jostes, U. Schimanski, M. Dartmann
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0654 $ 02.50/0

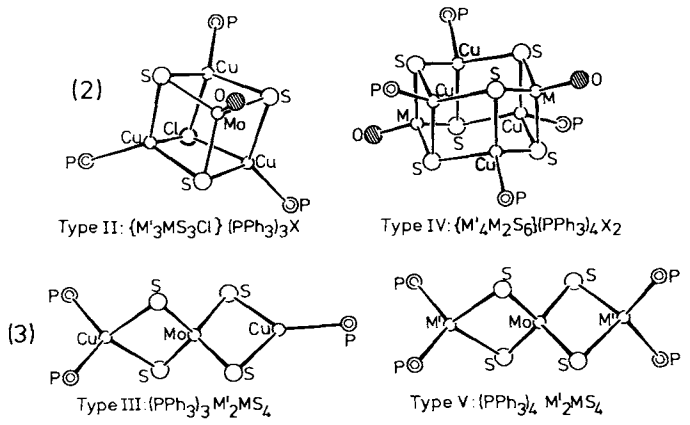


Fig. 2. Molecular structure of the multinuclear Mo complexes (Type II-IV: M' = Cu, Ag; M = Mo, W; X = O, S [5]).

Complexes containing a FeS_2Mo unit as in *(1)* are interesting because the Fe···Mo distance is comparable with that in nitrogenase (2.72 ± 0.03 Å) where the molybdenum is surrounded by three to four sulfur atoms[6]. M···M' distances of this order of magnitude (M' = 3d-metal, M = Mo, W) are found in *(1)* as well as other multinuclear thiometalato complexes containing bidentate thiometalate ligands[7]. These short distances in the four-membered ring systems $M'^{II}S_2M^{VI}$, with a large difference in the *formal* valencies of M and M', are responsible for the particular electronic properties of these systems, which have been studied in detail by us by SCCC extended Hückel calculations on *(1)* and complexes of the type $[M'(MS_4)_2]^{n-}$. These investigations gave the following qualitative results for *(1)*:

Since the Fe-3d level lies at practically the same energy as the nonbonding S-3p level, MoS_4^{2-} acts as a strong σ-donor and because of low-lying unoccupied orbitals, at the same time also as strong π-acceptor. On complex formation the electron density at the Fe center is reduced, at the Mo center it is increased in comparison to the free MoS_4^{2-} (electron delocalization Fe→Mo), and at the terminal S atoms it remains practically unchanged. Fe-Mössbauer data for *(1)* likewise prove the strong Fe→Mo electron delocalization, the tetrahedral coordination of the Fe and, in accord with the μ_{eff} values, the presence of a high-spin complex. The Fe_mS_nMo group of FeMo-co (proof of its presence: analytical composition Mo:Fe:S ≈ 1:8:6 (?)[4] and Mo-EXAFS data[6]) should, on account of the catalytic properties of the cofactor (or of the enzyme), likewise show a strong electron delocalization and easy displaceability of electron density (complexes of the type $[M'(MS_4)_2]^{n-}$ with differing electron population also exist![8]).

From the MO calculation it follows that addition reactions should be possible at the terminal S atoms owing to the high electron density. Hence, in Fe complexes the MoS_4^{2-} ligand should show multidentate and multibridging behavior resembling that in Cu complexes[9a]. It should be possible to use *(1)* as starting substance for the synthesis of a multinuclear Fe—Mo complex, since on the basis of the first finding substitution reactions can also be carried out at the chloro-ligand, and since the metal atoms are not coordinatively saturated (cf. first reports on other multinuclear Fe—Mo—S compounds[9]).

Present investigations would indicate that direct interactions between the three bio-metals Fe, Cu, and Mo (MoS_4^{2-}) are likely in biological processes (besides the well-known antagonistic Fe/Cu and Cu/Mo relationships[2b]).

Procedure

(2) [and *(3)*]: An aqueous solution (100 ml) of 0.23 g Cs_2MoOS_3 [0.21 g $(NH_4)_2MoS_4$] is extracted with a solution of 0.17 g $CuCl_2 \cdot 2H_2O$ and 0.4 g PPh_3 [0.6 g] in 25 ml CH_2Cl_2. The organic phase is separated, filtered, and covered with a mixture of 40 ml *n*-pentane [50 ml] and 20 ml acetone [10 ml]. After 2—3 d, red crystals of *(2)* separate out. Yield *ca.* 0.1 g [0.15 g red platelets of *(3)*].

(4): A filtered solution of 0.2 g $FeCl_2 \cdot 4H_2O$ and 0.4 g $[(C_6H_5CH_2)=(CH_3)_3N]Cl$ in 50 ml CH_3CN is added with stirring to a solution of 1 g $[(C_6H_5)_4P]_2MoS_4$ in 100 ml CH_3CN. The reaction mixture is filtered and treated with 80 ml diethyl ether (analytically pure). *(4)* precipitates as dark-red crystals. Yield: 0.55 g.

Received: April 25, 1980 [Z 541 IE]
German version: Angew. Chem. *92*, 665 (1980)

CAS Registry numbers:
(2), 74542-93-1; *(3)*, 74542-94-2; *(4)*, 74561-80-1; $(NH_4)_2MoS_4$, 15060-55-6; Cs_2MoOS_3, 14348-14-2; $[C_6H_5)_4P]_2MoS_4$, 14348-10-8

[1] *W. G. Zumft*, Eur. J. Biochem. *91*, 345 (1978).
[2] a) *E. J. Underwood:* Trace Elements in Human and Animal Nutrition, 4th Ed. Academic Press, New York 1977; b) *C. F. Mills*, Chem. Br. *15*, 512 (1979); Philos. Trans. R. Soc. London *B 288*, 51 (1979) and references cited therein; private communication 1980; c) *N. J. Clark, S. H. Laurie*, J. Inorg. Biochem. *12*, 37 (1980).
[3] *F. A. Cotton, G. F. Wilkinson:* Advanced Inorganic Chemistry, 4th Ed. Wiley, New York 1980; *A. Müller, E. Diemann*, Chem. Commun. *1971*, 65; *E. Diemann, A. Müller*, Coord. Chem. Rev. *10*, 79 (1973).
[4] *W. E. Newton, B. K. Burgess, E. I. Stiefel* in *W. E. Newton, S. Otsuka:* Molybdenum Chemistry of Biological Significance. Plenum, New York 1980; *V. K. Shah, W. J. Brill*, Proc. Nat. Acad. Sci. USA *74*, 3249 (1977).
[5] Compounds of Type III and V are formed with tetrathio- but not with trithiomolybdate (because of the thiophilic character of, *e.g.* Cu). It is therefore remarkable and also serves as proof for the strong tendency of cage structures II and IV to be formed, that compounds of this type can be isolated with trithio- and also tetrathiometalates [*A. Müller, H. Bögge, U. Schimanski*, J. Chem. Soc. Chem. Commun. *1980*, 91; *A. Müller, H. Bögge, E. Königer-Ahlborn, ibid. 1978*, 739]. However, a compound with a composition corresponding of Type III (with $Cu^+/MoOS_3^{2-}$), but according to preliminary X-ray structure data another structure (Type VI), could be obtained. So far the Cu/Mo compounds of Type IV and V could not be isolated in pure form; however, the corresponding Cu^+/WOS_3^{2-} (Type IV) and Ag^+/MoS_4^{2-} (Type V) species could be isolated.
[6] *S. P. Cramer, W. O. Gillum, K. O. Hodgson, L. E. Mortenson, E. I. Stiefel, J. R. Chisnell, W. J. Brill, V. K. Shah*, J. Am. Chem. Soc. *100*, 3814 (1978); *T. E. Wolff, J. M. Berg, C. Warrick, K. O. Hodgson, R. H. Holm, R. B. Frankel, ibid. 100*, 4630 (1978).
[7] *A. Müller, N. Mohan, H. Bögge*, Z. Naturforsch. *B 33*, 978 (1978).
[8] *A. Müller, R. Jostes, V. Flemming, R. Potthast*, Inorg. Chim. Acta *44*, L33 (1980).
[9] a) *A. Müller, S. Sarkar*, Angew. Chem. *89*, 748 (1977); Angew. Chem. Int. Ed. Engl. *16*, 705 (1977): as mentioned therein the compound $[Ph_4P]_2\{Fe(MoS_4)_2\}$ with polymeric anion is X-ray amorphous and not pure; from IR data, however, it follows that all S atoms of the ligand are coordinated to Fe centers. b) Cf. references cited in ref. [6]; c) *D. Coucouvanis, E. D. Simhon, D. Svenson, N. C. Baenzinger*, J. Chem. Soc. Chem. Commun. *1979*, 361.

Handbook of Liquid Crystals. By *H. Kelker* and *R. Hatz.* Verlag Chemie, Weinheim 1980. xviii, 917 pages, bound, DM 420.00.

In recent years the field of liquid crystals has undergone a tempestuous growth, which is still by no means over. The reasons for this particular interest in the research and technology of liquid crystals lie above all in their unique electro-optical properties. Now that liquid-crystal materials with a large meso-phase region and suitable electro-optical parameters have been developed, liquid crystals have found a wide field of application in electronic displays for clocks, calculators, and measuring instruments and will shortly be used in motor vehicle instrumentation as well.

This development has been accompanied by an immense flood of publications, too many even for the expert to take in. In the light of this situation the present book emerges as a valuable aid at exactly the right time. It differs from the monographs that have appeared to date in that it deliberately does not aim at a textbook-like introduction but attempts to cover the field as completely as possible. The emphasis is thus more on the general picture than on details.

One of the authors' special concerns was to cover the literature. With its more than 8000 citations, the book is of great informative value, particularly because the titles of the publications are also included. This part is 266 pages long and constitutes by far the largest section of the book. The literature is practically complete up to and including 1976, and even covers the bulk of the papers that appeared in 1977.

The following aspects have also received closer attention: "Chemical Constitution" (Chapter 2) with a detailed (44-page) Table of Mesogens, "Behavior in Magnetic and Electric Fields" (Chapter 4), "Optical Properties" (divided into optically inactive and optically active meso-phases, Chapters 6 and 7), and finally "Nuclear Magnetic Resonance and Electron Spin Resonance Studies" (Chapter 10, by *C. Schumann*). In contrast to this, Chapter 14 on "Technical Applications" is rather short (24 pages).

Even though in a rapidly advancing field it is fundamentally impossible to give a definitive picture, the two authors have succeeded after years of research in creating a work worthy of regard. The vast wealth of collected material arranged by subject matter in this book never fails to impress. The clear layout greatly facilitates the use of the handbook: at the start of each chapter its list of contents is given once more (even the general index is preceded by a summary!). Increasingly specific subdivision leads the reader step by step to the required specialist field, so that the book is easy to use in spite of its extensive scope. All in all, an extremely valuable work that can be recommended without hesitation.

Gerhard Meier [NB 515 IE]

Metal Complexes in Organic Chemistry. By *R. P. Houghton.* Cambridge University Press, Cambridge 1979; 308 pages, bound, £ 7.50.

The present book gives a survey of metal complexes in organic chemistry. In Chapters 1 (general principles), 2 (effects and applications of complex formation), 3 (metal complexes in addition reactions), and 5 (oxidative addition and insertion) many fields of application are summarized in a synoptic arrangement. Metal-catalyzed polymerization processes have been deliberately excluded. Aside from the comments below it must be borne in mind that the book was written in 1978 and accordingly does not reflect the rapid development of the field. In addition to this, the examples seem to have been selected only from the point of view of the inorganic chemist and the materials chemist.

In Chapter 1 there is no mention of the significance of metals as couplers of π-systems. The wide range of ring closure reactions and H displacements by metalation is not dealt with. In the discussion of the difficulties of separating several effects of complex formation no mention is made of regression analysis. Furthermore, reference should surely have been made in the "General principles" to the different thermodynamic conditions within and outside the complex. In the discussion of the reaction mechanisms one would like to see a good example of the attack on complex-bound π-systems from the metal and from outside the complex.

In the discussion of the effects and applications of complex formation in Chapter 2 it should have been mentioned that the stability of complexes does not always change monotonically as the properties are changed, but can also exhibit minima or maxima. To demonstrate the wide application of metal complexes for purposes of synthesis, reference should have been made *e.g.* to the diethylzinc/Cu variants for the Simmons-Smith reduction and the metathesis reaction.

These critical remarks may serve as an illustration of the difficulties facing an author engaged in writing a book on a rapidly developing field.

Paul Heimbach [NB 514 IE]

Metal and Metalloid Amides. By *M. F. Lappert, P. P. Power, A. R. Sanger,* and *R. C. Srivastava.* John Wiley & Sons, Chichester 1980. 847 pages, bound, £ 50.00.

This compact but highly informative book is the first to present a comprehensive inventory of the field. Up to now the number and the significance of compounds with the ligands NR^1R^2 (and also their oligomers and polymers) have only been the subject of summaries in extract or synoptic form, and complete documentation of the above amides, which have grown tremendously in number of the last 25 years, has been long overdue.

To restrict the scope of the work to reasonable limits, compounds with macrocyclic ligands and amides of the nonmetals have been excluded from the discussion of the element amides, whereas the data on the amides of phosphorus, silicon, and boron and on ionic amides such as $M^+NH_2^-$ have been kept very concise. Three-quarters of the contents (eight chapters) are dedicated to the synthesis, the structure, and the physical properties of the metal amides; in the last quarter typical reactions are discussed over nine chapters. Because of its systematization, it is precisely this section that exhibits the advantages of a comprehensive discussion of all metal and metalloid amides, and will prove particularly useful and stimulating for those engaged in active research. Thus, in addition to inclusion, protolysis, reactions with hydrides, exchange, and dehydrochlorination reactions as well as Lewis base and Lewis acid reactions, there is a discussion of applications such as polymerization catalysis.

The larger, reference-type first part, set out mainly in the form of tables, is divided into chapters on amides of elements in the 1st, 2nd, 3rd, and 4th main groups (except carbon), amides of phosphorus, arsenic, antimony, and bismuth and amides of the transition elements. The sections on amides of elements in the 3rd and 4th main groups and on phosphorus

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0808-0656 $ 02.50/0

amides occupy, corresponding to the importance of these, more than half of the book; a more far-reaching selection would have made it possible to shorten the work by 100—200 pages. Similarly, the structures have not always been reproduced in the most economical manner, as in Fig. 16, page 495, in comparison with Fig. 4, page 248.

However, criticism of the book is unjustified. Rather, the authors deserve thanks and an acknowledgement of their competent description of an important field of molecular chemistry. Points worthy of emphasis are the well-balanced arrangement and the painstaking care that can be perceived even in minor details such as of umlauts. The book finishes with a brief subject index and a 60-page author index covering some 2500 literature citations up to and including 1978. It can be recommended not only to chemists working on amides and to libraries, but also—in spite of its price—to all inorganic and organic chemists and to polymer and structure chemists who want reliable information on a relatively uniform "inter-disciplinary" class of substances.

Hans Bürger [NB 517 IE]

Macromolecules. An Introduction to Polymer Science. Edited by *F. A. Bovey* and *F. H. Winslow.* Academic Press, New York 1979. xiii, 549 pages, bound, $ 39.50.

This is a new textbook compiled from an introductory course for polymer scientists at the Bell Laboratories, Murray Hill, N. J. offering a short but understandable review of the current state of the field.

Following a brief introduction (in which reference is already made to such problems as tacticity and mechanical properties), which also contains a very interesting excursion into the history of polymers, Chapter 2 "Formation of Macromolecules" deals with the most important reactions giving rise to macromolecules. Some important aspects of the reaction kinetics are discussed in each case. The section on copolymerization kinetics deserves special emphasis. Chapter 3 is concerned with the clarification of the structure of polymers by means of physical methods, but here it is assumed that the reader is familiar with the basic principles of IR and NMR spectroscopy. The influence of geometric isomerism on the spectra is explained for some well-chosen examples. At this point the authors also discuss in comprehensible language the problems of chain statistics. Chapter 4 considers the thermodynamics of polymer solutions and methods of molecular-weight determination. The mathematics are restricted to essentials and there are no confusing calculations. Morphological aspects of macromolecules, their physical characteristics such as viscoelasticity, amorphous and crystalline polymers, and transport in polymers are the subjects of Chapters 5 and 6. On the subject of polymer reactions the editors regrettably restrict themselves to degradation and cross-linking. The introduction of functional groups into polymers is not dealt with, but it would be desirable to include a section on this topic in a new edition. The work is rounded off with a chapter on biological macromolecules and their significance. Every chapter contains a collection of well-chosen literature references which provide the reader with rapid entry into the original literature. In a second edition it would be desirable to give the data in SI units.

The book can be recommended to any reader interested in polymer science. It represents a valuable and reasonably priced addition to the reference library of any polymer scientist.

Josef Skura [NB 516 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

The Biosynthesis of aromatic compounds. By *U. Weiss* and *J. M. Edwards.* John Wiley & Sons, New York 1980. xiii, 728 pp., bound, £ 18.50.—ISBN 0-471-92690-6

Chemical Experimentation under Extreme Conditions. Vol. 9. Edited by *B. W. Rossiter.* John Wiley & Sons, New York 1980. x, 369 pp., bound, £ 25.30.—ISBN 0-471-93269-8

Die Funktion von Sequestriermitteln im Waschprozeß unter besonderer Berücksichtigung des Natriumtriphosphats. By *H. Krüssmann, R. Bercovici, A. Barbu,* and *P. Vogel.* Westdeutscher Verlag, Opladen 1980. vi, 221 pp., sewed, DM 35.00.—ISBN 3-531-02918-5

Studien über fossile und rezente Verwitterungsvorgänge im Vulkangestein der Insel Fuerteventura (Islas Canarias). By *L. Hempel.* Westdeutscher Verlag, Opladen 1980. 32 pp., sewed, DM 8.00.—ISBN 3-531-02927-4

Handbuch: Festkörperanalyse mit Elektronen, Ionen und Röntgenstrahlen. Edited by *O. Brümmer, J. Heydenreich, K.-H. Krebs,* and *H. G. Schneider.* Friedr. Vieweg & Sohn, Braunschweig 1980. 432 pp., bound, DM 86.00.—ISBN 3-528-08398-0

Coherence and Correlation in Atomic Collisions. Edited by *H. Kleinpoppen* and *J. F. Williams.* Plenum Publishing Corporation, New York 1980. xiv, 706 pp., bound, $ 59.50.—ISBN 0-306-40250-5

Gas Solubilities. Widespread Applications. By *W. Gerrard.* Pergamon Press, Oxford 1980. xxi, 497 pp., bound, $ 67.50.—ISBN 0-08-025248-6

Crystals. Growth, Properties, and Applications. Edited by *H. C. Freyhardt.* Springer-Verlag, Berlin 1980. vi, 199 pp., bound, DM 88.00.—ISBN 3-540-09697-3

Structure and Bonding. Vol. 40. Edited by *J. D. Dunitz, J. B. Goodenough, P. Hemmerich, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Springer-Verlag, Berlin 1980. vii, 146 pp., bound, DM 88.00.—ISBN 3-540-09816-X

Topics in Current Chemistry. Vol. 88. Organic Chemistry. Syntheses and Reactivity. Edited by *F. L. Boschke.* Springer-Verlag, Berlin 1980. iv, 170 pp., bound, DM 98.00.—ISBN 3-540-09817-8

Free Radicals in Biology. Vol. 4. Edited by *W. A. Pryor.* Academic Press, New York 1980. xxi, 348 pp., bound, $ 46.00.—ISBN 0-12-566504-0

The Lewis Acid-Base Concepts. By *W. B. Jensen.* John Wiley & Sons, New York 1980. xi, 364 pp., bound, £ 20.60.—ISBN 0-471-03902-0

Frontiers of Bioorganic Chemistry and Molecular Biology. Edited by *S. N. Ananchenko.* Pergamon Press, Oxford 1980. ix, 473 pp., bound, $ 80.00.—ISBN 0-08-023967-6

Treatise on Analytical Chemistry. Part II. Vol. 16: Functional Groups. Edited by *I. M. Kolthoff* and *P. J. Elving.* John Wiley & Sons, New York 1980. xix, 560 pp., bound, £ 26.95.—ISBN 0-471-05857-2

Holography and Coherent Optics. By *L. M. Soroko.* Plenum Publishing Corporation, New York 1980. xvi, 818 pp., bound, $ 59.50.—ISBN 0-306-40101-0

Nichtnumerische Informationsverarbeitung. Linguistische Datenverarbeitung, künstliche Intelligenz, Computerschach, Computerkunst, automatische Dokumentation, Bibliotheksautomatisierung, Rechtsinformatik. By *H. E. Bruderer.* Verlag Linguistik, Rorschach 1979. xii, 190 pp., sewed, SFr. 39.00.—ISBN 3-85784-001-3

How to Succeed in Organic Chemistry. By *J. E. Gordon.* John Wiley & Sons, New York 1979. xiv, 594 pp., sewed, $ 8.95.—ISBN 0-471-03010-4

Modern Physics in Chemistry. Vol. 2. Edited by *E. Fluck* and *V. I. Goldanskii.* Academic Press, London 1980. 640 pp., $ 85.50.

Growth and Properties of Metal Clusters. By *J. Bourdon.* Elsevier Scientific Publishing Company, Amsterdam 1980. xviii, 550 pp., $ 97.50.—ISBN 0-444-41877-6

Lehrbuch Höhere Festigkeitslehre. Band 1. Edited by *H. Göldner.* Physik Verlag, Weinheim 1979, 236 pp., bound, DM 22.00.—ISBN 3-87664-042-3

Spectres d'absorption ultraviolets de composés organiques azotés et corrélations spectrochimiques. By *P. Grammaticakis.* Technique et Documentation, Paris 1980. 106 pp., sewed, F 150.00.—ISBN 2-85206-061-2

Extraction with Supercritical Gases. Edited by *G. M. Schneider, E. Stahl,* and *G. Wilke.* Verlag Chemie, Weinheim 1980. IX, 190 S., geb. DM 78.00.—ISBN 3-527-25854-X

Basic Chemical Kinetics. By *H. Eyring, S. H. Lin,* and *S. M. Lin.* John Wiley & Sons, New York 1980. vii, 493 pp., bound, 20.00.—ISBN 0-471-05496-8

Unit Process Series. Organic Chemical Industries. Vol. 1: Unit Process Guide to Organic Chemical Industries. Edited by *E. C. Herrick, J. A. King, R. P. Quellette,* and *P. N. Cheremisinoff.* Ann Arbor Science Publishers, Ann Arbor, Mich. 1980. x, 146 pp., bound, £ 11.00.—ISBN 0-250-40328-5

Unit Process Series. Organic Chemical Industries. Vol. 2: Amination Process Pollutant Discharges Identification. Edited by *J. A. King, E. C. Herrick, R. P. Ouellette,* and *P. N. Cheremisinoff.* Ann Arbor Science Publishers, Ann Arbor, Mich. 1980. xiii, 111 pp., bound, £ 11.00.—ISBN 0-250-40329-3

Abriss der Bierbrauerei. By *L. Narziss.* Ferdinand Enke Verlag, Stuttgart 1980. viii, 384 pp., sewed, DM 54.00.—ISBN 3-432-84134-5

Advances in Chemical Physics. Vol. 41. Edited by *I. Prigogine* and *S. A. Rice.* John Wiley & Sons, New York 1980. xi, 539 pp., bound, £ 27.10.—ISBN 0-471-05742-8

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar.* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

Advertising insert: In this issue is a leaflet from Springer-Verlag, Berlin.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 9
September 1980
Pages 659—748

Structure and Function of the Energy-Converting System of Mitochondria

By Gebhard von Jagow and Wolf Dieter Engel[*]

Dedicated to Professor Otto H. Wieland on the occasion of his 60th birthday

The main energy source for all endergonic processes occurring in living organisms is the phosphate bond energy of nucleoside triphosphates, especially adenosine triphosphate (ATP). In aerobic organisms, as for instance in mammals, more than 90% of ATP is formed during the process called oxidative phosphorylation. In this process, similar to that of muscle contraction and nerve excitation, nature works with vectorial processes taking place at a membrane separating distinct spaces from each other. The present article deals with the operation of a set of water-insoluble membrane proteins and enzymes vectorially transporting electrons, protons and other ions, which finally leads to the formation of ATP. This machinery transforming substrate oxidation energy into chemical energy in the form of the phosphoric anhydride bond of ATP operates with a very high efficiency.

The structure and function of the machinery of mitochondrial oxidative phosphorylation are described. It consists of the electron transfer chain, the ATP-synthetase, the adenine nucleotide translocase and the phosphate carrier. The electron transfer chain can be resolved into multiprotein complexes—at three of them energy conversion takes place—and into the electron carriers ubiquinone and cytochrome c. The substrate oxidation energy is converted into the chemical energy of ATP with an electrochemical proton gradient as intermediary form. The energetic aspects of the processes are analyzed by linear irreversible thermodynamics. Great success has been gained during the past few years on the structural characterization of the participating proteins. The function of the various systems is partially elucidated on the molecular level; this concerns especially the mechanism of proton and adenine nucleotide translocation, as well as ATP formation.

1. Introduction

The interaction of the enzymes involved in oxidative phosphorylation is treated on the basis of the chemiosmotic theory[1,2], which may be applied to interpret not only the energy-converting processes in the mitochondrion, but also in bacteria, algae and green plants[3–6]. The theory postulates a proton gradient at the inner mitochondrial membrane as an intermediary form of energy[7]. It should be mentioned, however, that there exists some reservation with respect to the free release of protons. There may exist microspaces at the inner mitochondrial membrane which may prevent such a free proton release[8]. The article will show that the main part of the protons is transported across the membrane by proton pumps.

[*] Prof. Dr. G. von Jagow and Dipl.-Biochem. W. D. Engel
Institut für Physiologische Chemie, Physikalische Biochemie und Zellbiologie der Universität München
Goethestrasse 33, D-8000 München 2 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0909-0659 $ 02.50/0

Recent and former results have gained new meaning by their interpretation with the aid of irreversible thermodynamics[9,10].

The proton/electron stoichiometries that have been under discussion since the development of the chemiosmotic hypothesis 20 years ago[1] are now thoroughly analyzed and agree with the thermodynamic requirements. The number of protons transported across the inner mitochondrial membrane per electron transferred from substrate to oxygen, as well as that of protons consumed per ATP synthesized, are twice as high as reported previously[11,12]. Previous data proved false, since the proton consumption of the phosphate:proton co-transporter was not taken into account.

In the present description of the mitochondrial machinery of energy conversion, particular attention has been paid to the multitude of new results concerning the structure of the participating enzymes, most of which are multiprotein complexes.

2. The Mitochondrion

The machinery for the conversion of substrate oxidation energy into chemical energy in the form of adenosine triphosphate (ATP) is located in the mitochondrion, an organelle of most eukaryotic cells. The mitochondrion possesses two membranes, the outer membrane and the inner membrane (Fig. 1). The outer membrane, which is freely permeable to molecules with molecular weights of up to several thousands[13], encloses the organelle. This membrane is of minor importance for the mechanism of energy conversion; it is therefore not further discussed in this article. The inner mitochondrial membrane, impermeable to most metabolites, is folded into cristae mitochondriales in order to enlarge its surface. This membrane contains the enzymes of oxidative phosphorylation. Furthermore, the inner membrane contains a multitude of proteins which are embedded in the phospholipid bilayer, so-called integral membrane proteins, for instance the acyl-CoA dehydrogenase[14], the α-glycerophosphate dehydrogenase[15], the β-hydroxybutyrate dehydrogenase[16], and the energy-dependent pyridine nucleotide transhydrogenase[17,18,19]. In addition, as it is impermeable to mono- or multivalent ions, the inner membrane contains numerous transport systems[20]. Furnished with all these systems, the inner membrane has an exceptionally high content of proteins (>70%). The lipids of the inner membrane consist almost entirely of phosphatidylcholine, phosphatidylethanolamine and diphosphatidylglycerol. In contrast to most eukaryotic membranes, the inner mitochondrial membrane contains no cholesterol.

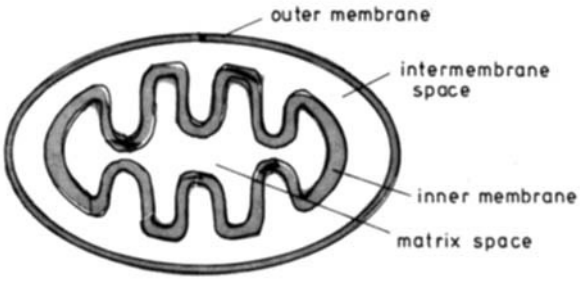


Fig. 1. Schematic diagram of the structure of the mitochondrion.

The two membranes delimit two spaces. The inner membrane surrounds the matrix space, between the two membranes lies the intermembrane space. The outer membrane separates the mitochondrion from the cytosol of the cell. For discussion of the process of energy conversion only the two terms 'matrix space' and 'cytosolic space' will be used here. The localization of the various enzymes, the metabolism, and the metabolic interactions of the mitochondrial compartments have been treated extensively in recent reviews[21,22].

3. The Electron Transfer Chain

In accordance with its structural and functional aspects, the mitochondrial electron transfer chain can be resolved into multiprotein complexes which are linked by the electron carriers ubiquinone and cytochrome c[23,24]. Each complex crosses the phospholipid bilayer[25]. The relatively small mobile ubiquinone molecule, situated in the phospholipid phase, presumably undergoes a transverse movement from one to the other face of the membrane[26]. Cytochrome c, finally, is a peripheral membrane protein located at the cytoplasmic face, where it is probably subject to lateral diffusion and rotational movement[27]. The four complexes of the respiratory chain are traditionally indicated by the roman numerals I—IV.

3.1. Complex I (NADH:Ubiquinone Oxidoreductase)

The NADH:ubiquinone oxidoreductase is the complex of the respiratory chain about which the least information has been gained so far. In contrast to the values of the other three complexes, an unusually high number of 16—18 polypeptides has been reported for complex I (Table 1)[28–30]. This, as well as enzymatically measurable contaminations, indicate that some foreign proteins, for instance the pyridine nucleotide-transhydrogenase[29,31], are present in the complexes isolated so far. As redox centers the complex carries a non-covalently bound flavin mononucleotide (FMN) and various non-heme iron centers (Fig. 2). By means of EPR studies seven different iron-sulfur centers have been identified[32], but the association of some of these centers with complex I is not generally accepted[33]. The exact arrangement of the FMN and the iron-sulfur centers is still unknown. From a content of 1.5 μmoles FMN/g protein for the purest preparation a minimum molecular weight of 670000 can be calculated. This represents a molecular weight about three times larger than that of the minimum units of the other complexes.

Complex I is the entry port for the redox equivalents of NADH, produced mainly in the course of the nutrient oxidation, as given in equation (1) (S = substrate):

$$SH_2 + NAD^{\oplus} \rightarrow S + NADH + H^{\oplus} \quad (1)$$

The electron transfer from NADH to ubiquinone is coupled to a proton translocation across the membrane, as has been shown for mitochondria[34] and submitochondrial particles[35], as well as for complex I incorporated into phospho-

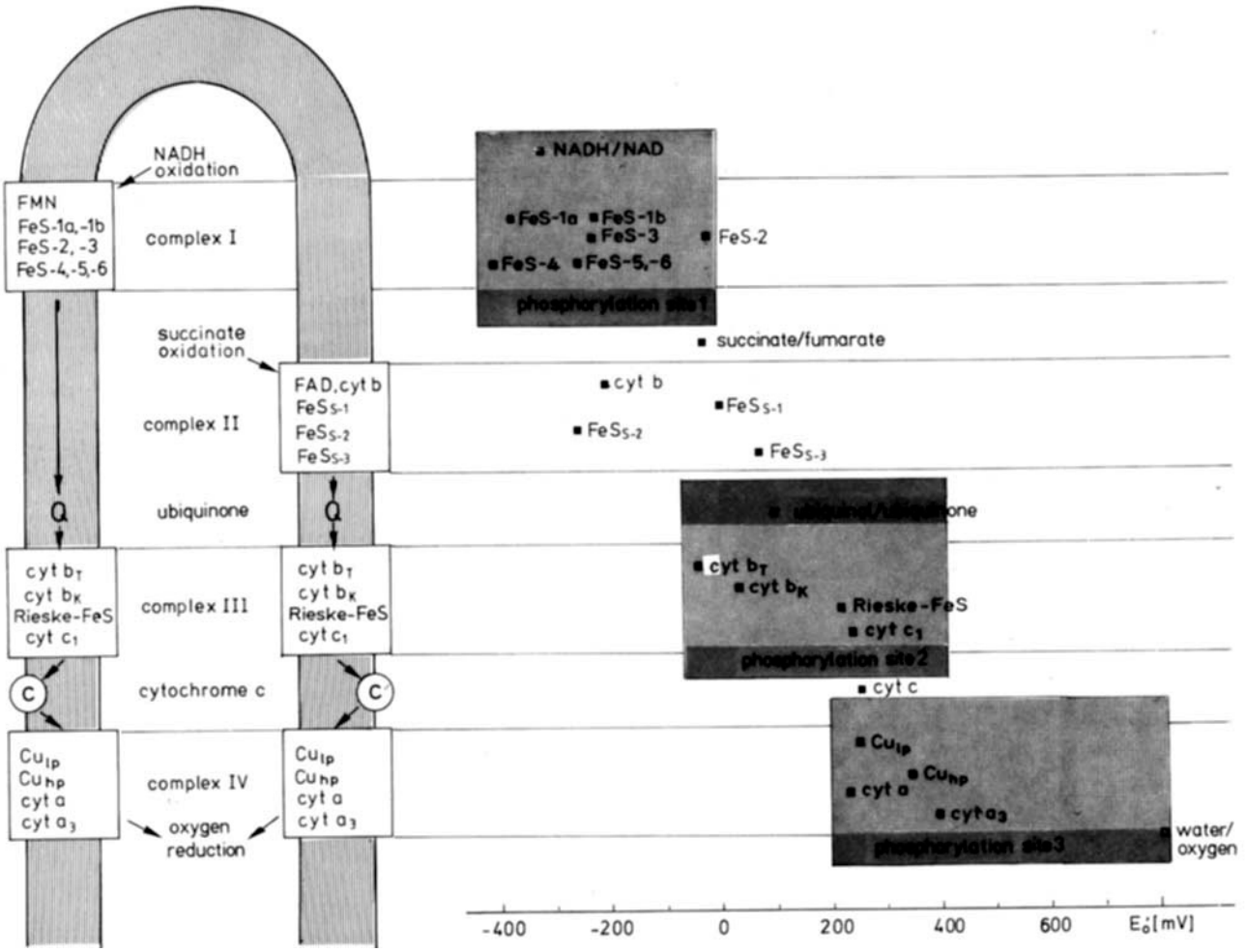


Fig. 2. Schematic representation of the arrangement and electrochemical connection of the four electron-transferring complexes within the inner mitochondrial membrane. On the left side of the membrane the connection between complex I and complexes III and IV is pointed out, on the right side of the membrane the connection between complex II and complexes III and IV. Complexes I and III, as well as complexes II and III are connected by ubiquinone (Q); complexes III and IV are connected by cytochrome c (C). The diagram on the right-hand side of the figure depicts the half-reduction potentials (E_0') of the redox components at pH 7.0. In order to calculate the free energy of the various redox steps the actual redox potentials had to be given, which, of course, depend on the respective energetic state. The deviations, however, generally do not amount to more than 50—100 mV. The subscripts lp and hp denote low and high potential, respectively.

lipid vesicles[36]. The protons are translocated from matrix to cytosolic space with a stoichiometry of $4H^{\oplus}/1$ NADH oxidized, corresponding to $4H^{\oplus}/2e^{\ominus}$ transferred to ubiquinone (Fig. 3)[7]. Hence the enzymatic activity of complex I can be defined by equation (2), where the transported protons are italicized. The function of the two hydrogen atoms taken up in the course of ubiquinone (Q) reduction is discussed in Section 3.4.

$$NADH + H^{\oplus} + Q + 4H^{\oplus}_{in} \rightarrow NAD^{\oplus} + QH_2 + 4H^{\oplus}_{out} \quad (2)$$

The mechanism of the proton translocation at site 1 of energy conservation is not yet elucidated. In the first version of the chemiosmotic theory a hydrogen transport *via* FMN was assumed[1]. This type of mechanism would represent a vectorial hydrogen movement through the membrane connected with a $2H^{\oplus}/2e^{\ominus}$ release upon oxidation of $FMNH_2$. Since now a $4H^{\oplus}/2e^{\ominus}$ stoichiometry seems to be established for site 1, however, another type of mechanism must be involved in proton translocation responsible for the missing two protons or perhaps for all four protons (if FMN is not involved in the process of translocation). Two mechanisms have been suggested so far: i) A ubiquinone radical mechanism, in which a protein-bound ubiquinone would connect iron-sulfur centers FeS-1 and FeS-2[3]; during the uptake of $1e^{\ominus}$ by this ubiquinone from FeS-1, $1H^{\oplus}$ would be taken up from the matrix side, yielding ubisemiquinone $QH^{\odot}$; on oxidation at FeS-2, this $H^{\oplus}$ would be released to the cytosolic side. ii) in contrast to a ubiquinone-mediated proton transfer, a pump mechanism[37] could translocate not only the missing two protons if FMN is involved in proton translocation, but also all four protons, without any further mechanism. Such a proton pump mechanism will be discussed in Section 3.4.

3.2. Complex II (Succinate:Ubiquinone Oxidoreductase)

The second multiprotein complex, transferring redox equivalents onto ubiquinone, is the succinate:ubiquinone oxidoreductase. The smallest possible unit consists of only four protein subunits[38] (Table 1). The redox centers are formed by one covalently bound flavin adenine dinucleotide (FAD), one heme b, and three non-heme iron centers (Fig. 2)[39]. The polypeptide of molecular weight 70000 carries the FAD which is bound to the N-3 of a histidyl residue by its C-8 methyl group[40,41]. The two iron-sulfur centers, FeS_{s-1} and

FeS_{s-2}, which are Fe_2S_2-type centers[42], are also on the largest subunit, whereas the third iron-sulfur center, FeS_{s-3}, which is a Fe_4S_4-type iron-sulfur protein[43], is present in the 27000 subunit[44]. The heme b center can presumably be ascribed to the polypeptide of molecular weight 15000. The minimum molecular weight of complex II amounts to 125000, assuming the presence of one specimen of each polypeptide subunit.

ferred to as succinate dehydrogenase, a term normally used for the whole enzyme as component of the citric acid cycle. The subcomplex cannot transfer electrons from succinate to ubiquinone, but only onto artificial electron acceptors, for instance *N*-methylphenazonium methyl sulfate. The lipophilic subcomplex consists of the two smaller polypeptides; it has been suggested that one of these smaller subunits carries a ubiquinone-binding site[48-51] (see also Section 3.3).

Table 1. Molecular weight, polypeptide and prosthetic group composition of complexes I—V from beef heart mitochondria.

Complex	Molecular weight per min. unit	Number of subunits	Molecular weight of subunits ($\times 10^3$)	Name or assignment of subunits	Content of prosthetic groups [μmol/g]
I					
NADH: ubiquinone reductase	670000	16—18	75, 52, 49, 45, 36, 33, 27, 24, 21, 19, 16, 13, 9, 8	no definite assignment	FMN 1.5 Fe; S 26; 26
II					
succinate: ubiquinone reductase	125000	4	70 27 15 13	FAD, $2 \times Fe_2S_2$ Fe_4S_4 cyt. b	FAD 5.0 Fe; S 38; 38 heme b 4.8
III					
ubiquinol cytochrome c reductase	250000	9	49, 47 30, 30 29 25 12, 11, 8	core proteins $2 \times$ cyt. b cyt. c_1 Fe_2S_2	heme b 8.0 heme c 4.0 Fe; S 8; 8
IV					
cytochrome c oxidase	166000	12	36 26 22 17 12 14, 11, 11 10.5 5.5, 6, 6	I II III IV V VI a, b, c VII VIII, a, b, c	heme a 12.0 copper 12.0
V					
ATP synthetase					
F_1	295000	5	2×55 2×52 2×30 2×13 2×8	α, β, γ, δ, ε (tight binding sites)	FAD 1.0 Fe; S 4; 4
F_0	(?)	4	29 20 10 7	DCCD binding [a]	uncertain whether prosthetic groups are inherent components

[a] DCCD = dicyclohexylcarbodiimide.

The sequence of the redox centers in the path of electron flow is only partially understood so far. The function of the heme b center is not yet quite clear either. The measured half-reduction potential of -200 mV[45] is far too negative to indicate an involvement in the path of the electron flow from succinate to ubiquinone. Therefore it has been argued that cytochrome b may be involved in special metabolic pathways, or may possess regulatory functions on the rate of electron flow[46]. The same applies to the FeS_{s-2} center.

Complex II can be dissociated by means of chaotropic agents, for instance $ClO_4^{\ominus}$, into two subcomplexes[47]. The water-soluble part obtained consists of the two large polypeptides (70000 and 27000). Erroneously this part has been re-

The electron flow from succinate to ubiquinone is not connected with a vectorial proton transport, therefore this part of the respiratory chain does not contribute to the process of energy conversion, but it channels reducing equivalents from a reduced substrate (succinate) to Q (ubiquinone), as do other enzymes. The catalytic activity of complex II can therefore be summarized by the simple reaction equation (3):

$$\text{succinate} + Q \rightarrow \text{fumarate} + QH_2 \qquad (3)$$

Complex II is subject to a regulatory mechanism[52]. There exist at least two forms of the enzyme. The inactive form is stabilized by oxaloacetate, which is tightly bound to the com-

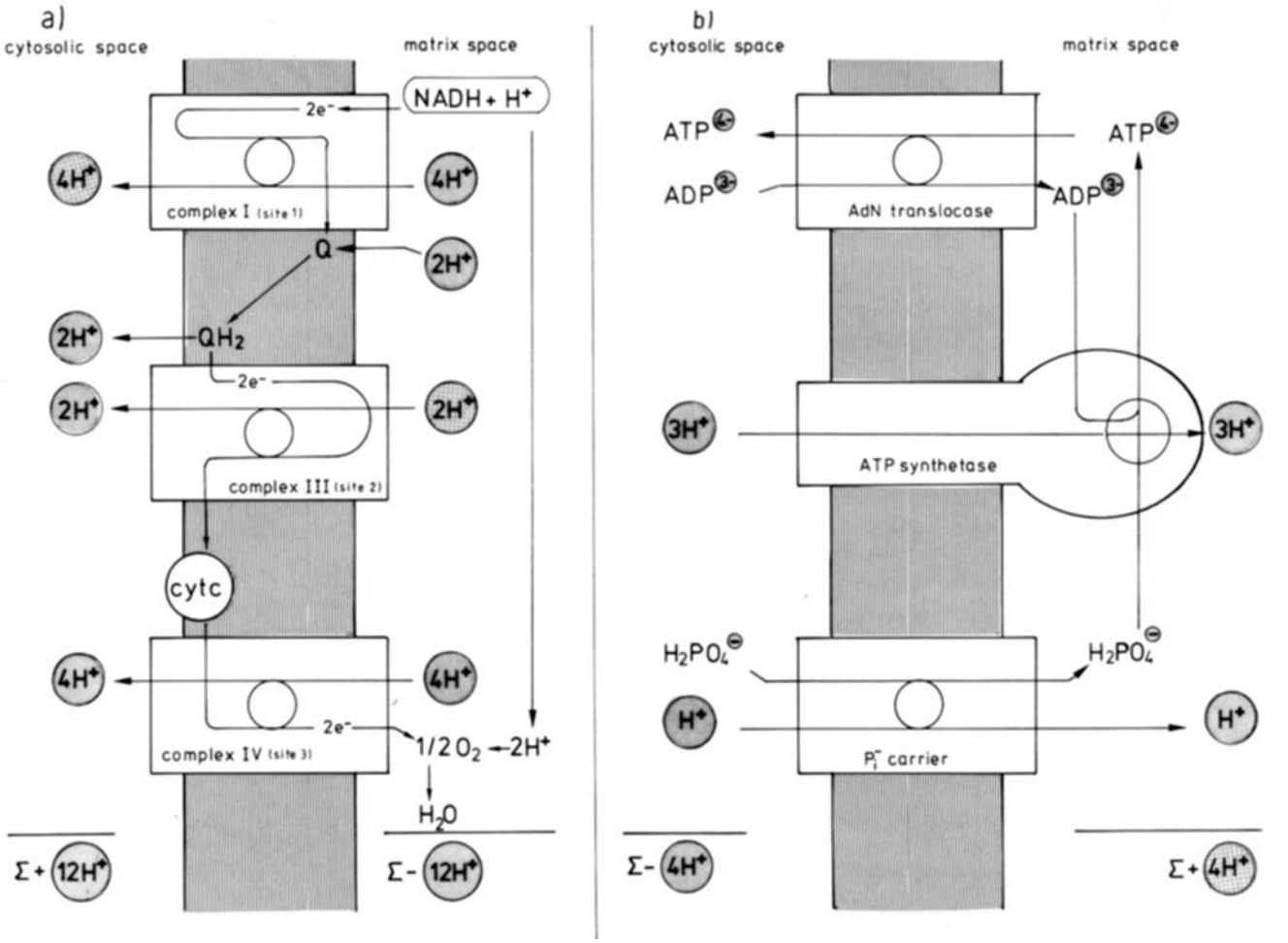


Fig. 3. Schematic representation of the creation and consumption of the proton gradient during oxidative phosphorylation. a) Electrogenic proton movement established by complexes I, III, IV and ubiquinone during transfer of $2e^{\ominus}$ from NADH to oxygen. The shaded area indicates the inner mitochondrial membrane. The complexes are depicted as horizontal rectangles 'plugged' through the membrane; b) Proton back-flow taking place during formation of one molecule of ATP. The charge imbalance of the adenine nucleotide transport is balanced by the positive charge remaining at the cytosolic face during neutral phosphate $H^{\oplus}$ cotransport.

plex in a 1:1 stoichiometry[53,54]. The enzyme can be converted into the active form by incubation with activating ligands, such as some dicarboxylic acids[55], some anions like perchlorate, nitrate, or bromide[56,57], as well as ATP[58], ubiquinol[59], or succinyl-CoA[60]. One striking difference between the active and the inactive form is seen in the half-reduction potential of FAD. It changes from about 0 mV to less than -190 mV when the enzyme is converted from the active into the inactive form. This diminution is explained in terms of a conformational change: the planar oxidized flavin assumes a bent configuration reminiscent of the reduced flavin[52]. No data are available so far for the cytochrome b subunit and the FeS_{s-2} iron-sulfur center, which may show a similar behavior. Complex II is very sensitive to SH-blocking agents; the reactive SH-groups can be protected by substrates and competitive inhibitors[61].

3.3. Ubiquinone

Ubiquinones are derivatives of 2,3-dimethoxy-5-methyl-1,4-benzoquinone, substituted at C-6 with isoprenoid side chains comprising 6—10 isoprene units (Fig. 4). The length of the side chain depends on the species; mammalian ubiquinone, for instance, possesses a side chain of 10 isoprene units[62], whereas that of baker's yeast possesses a side chain of only 6 isoprene units[63]. The highly lipophilic molecules are integral membrane components, occurring in about 10-fold molar excess over complex III[64,65]. In order to visualize the mechanism of ubiquinone action, which is still under discussion, some introductory remarks are necessary.

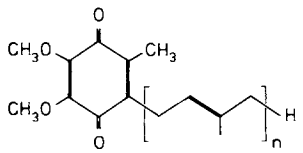


Fig. 4. Oxidized form of ubiquinone (Q); $n = 6$—10. Q-6 is present in some microorganisms, Q-10 in mitochondria of mammals.

Although ubiquinones are very small molecules compared with other redox components (proteins) of the respiratory chain, the length of about 5.5 nm for one fully extended ubiquinone-10 molecule suffices to span a phospholipid bilayer with a diameter of about 6.0 nm (cf. Fig. 5). Two possibilities of orientation seem to exist for ubiquinone in the membrane, *i.e.* either an arrangement perpendicular to the plane of the membrane, or one parallel to the plane of the membrane[66]. A perpendicular orientation would imply that the ubiquinone molecule spans the membrane, its quinone ring ex-

posed to one surface of the membrane. A lateral movement of the molecule would be possible in this case, but a flip-flop of the molecule, bringing the quinone ring from one to the other face of the membrane, would be hindered due to its high activation energy[67]. The second possibility, a planar arrangement in the middle of the membrane at the interface of the two phospholipid layers, would cause an inaccessibility of the ubiquinone molecule for hydrophilic compounds.

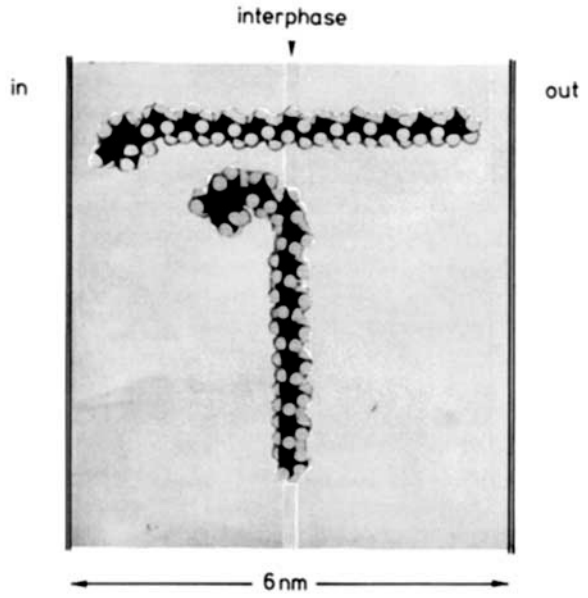


Fig. 5. Hypothetical arrangement of ubiquinone-10 (Q-10) in the inner mitochondrial membrane, demonstrated by the lower ubiquinone molecule. Q-10 is arranged with the main part of its isoprene side chain along the interphase of the phospholipid bilayer of the mitochondrial membrane, but with the head region and the first two isoprene units perpendicular to the plane of the membrane due to a kink of about 90° in the side chain. The respective reaction centers arranged at opposite faces of the membrane are reached by an 'anchor-facilitated flip-flop mechanism' as discussed in the text.

Both conceptions of arrangement are supported as well as questioned by experimental results. In one set of experiments the quinone ring, when placed in the mitochondrial membrane, was found to be inaccessible to hydrophilic compounds such as dithiothreitol, irrespective of the side of attack; in other experiments, ubiquinone was found to be accessible, as demonstrated by the reduction of ferricyanide, trapped in phospholipid vesicles, by external dithionite. In these experiments, the reduction was mediated by both short and long chain ubiquinones[68], but with remarkable kinetic differences depending on the length of the isoprenoid side chains. Thus, ubiquinone-9 catalyzed the reduction of ferricyanide considerably faster than ubiquinone-1, but the activation energy required was much higher for the long-chain than for the short-chain ubiquinone-mediated reaction. An involvement of the double bonds in the reaction was excluded by experiments with ubiquinone-9 analogs carrying a saturated side chain, which behaved similarly to ubiquinone-9[68].

The contradictory results concerning the accessibility of ubiquinone embedded in the membrane for polar reducing agents may be due to a different composition of the membranes under study (*i.e.* mitochondrial membranes having a high content of negatively charged cardiolipin and more than 70% protein content versus phospholipid vesicles consisting of neutral phosphatidylcholine). The different curvatures of the investigated membranes affecting packing of the molecules may also have influenced the results.

A more direct approach in studying the localization of ubiquinone in the membrane has been undertaken by tracing the quenching of a fluorescent probe (12-(9-anthroyl)-stearic acid) penetrating the membrane to a depth of 1.4 nm[69]. The quenching was ascribed to the presence of the ubiquinone ring at this region of the membrane.

The arrangement of the lower molecule in Figure 5 represents our own present view on the orientation of ubiquinone in the membrane. It combines the two types of orientation discussed above. Long-chain ubiquinones are arranged with the main part of the isoprene side chain along the interphase of the phospholipid bilayer, but with the head region plus the first two isoprene units perpendicular to the plane of the membrane. The penetration of the quinone head into the phospholipid layer is made possible by a kink of the side chain between the second and the third isoprene units, as demonstrated by the space-filling model shown in Figure 5. According to this arrangement, the transfer of redox equivalents from one to the other side of the membrane is made possible by a rotation of the head region around the axis of the tail region of ubiquinone situated in the interphase of the membrane. This movement may be defined as an 'anchor-facilitated flip-flop mechanism'.

Ubiquinones with less than three isoprene units probably simply diffuse through the membrane so that a transfer of redox equivalents is established, a process which obviously requires less activation energy than the proposed facilitated flip-flop mechanism. The higher rate of reduction of ferricyanide by long-chain ubiquinones than by short-chain ubiquinones may be due to a definite fixation of the ubiquinone tail in the interphase region, inducing a more successful collision of the ubiquinone head with the appropriate reaction center.

Several mechanisms have been proposed to explain the function of ubiquinone in the respiratory chain. Without any doubt ubiquinone acts as a coenzyme that transfers reducing equivalents from complexes I and II, as well as from several other dehydrogenases to complex III (Figs. 2 and 3).

Many experimental results have led to the postulate that the main part of ubiquinone forms a homogeneous redox pool connecting the individual dehydrogenases with complex III[70,71]. In contrast to this view there is a recent accumulation of experimental findings which indicate that, besides this class of ubiquinone, a second class of ubiquinone exists, namely a protein-bound ubiquinone. Recent results, for instance, suggest that complexes I and III can combine to a single unit transferring electrons from NADH to cytochrome c. Less than three ubiquinone molecules per unit have been shown to suffice for near-maximum activity[72]. Using excess of phospholipids and ubiquinone, a pool behavior of ubiquinone was restored[73], which was explained by frequent dissociation-reaggregation of the complex I-III-unit, rather than by the existence of a ubiquinone pool transporting the redox equivalents between the various complexes. From a kinetic point of view, a redox-connection by the ubiquinone pool seems more probable than the proposed aggregation process, which would need a proper arrangement of huge complexes.

An analogous unit (a kind of 'supercomplex'), consisting of complexes II and III, has been described recently[74].

From recent EPR studies it has been concluded that a ubisemiquinone pair exists with the oxygen-oxygen axis perpendicular to the plane of the membrane[51]. So far, this type of orientation as well as the functioning of semiquinones seem to be unlikely, unless a stabilization of the radical species by a protein moiety takes place. The 15000 subunit of complex II, supposed to be a ubiquinone binding protein, could perhaps play such a role[48].

The involvement of ubiquinone in proton translocation has not yet been fully clarified. As originally proposed[2], it may act as a hydrogen carrier across the membrane (Fig. 6).

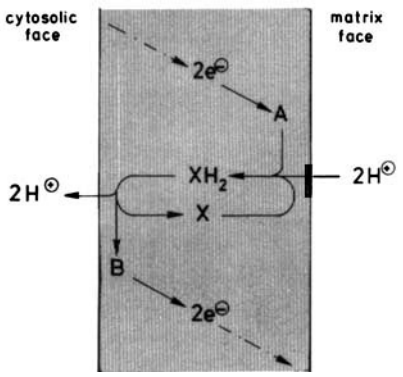


Fig. 6. Schematic diagram of a redox loop mechanism working with a $2H^{\oplus}/2e^{\ominus}$ stoichiometry. The mobile hydrogen-transferring component X accepts at a reaction center A (situated at the matrix side of the membrane) two electrons and two protons from the matrix space; XH_2 donates to the reaction center B (situated at the cytosolic side of the membrane) two electrons and releases two protons into the cytosolic space. In the case of the ubiquinone loop, X = ubiquinone.

During this process, defined as a redox loop mechanism, ubiquinone (X) is reduced at the active center of redox component A on the matrix face. The reduction is accompanied by an uptake of two protons. After ubiquinol (XH_2) migration across the membrane, it is oxidized at the redox center of component B on the cytosolic face, associated with a release of two protons; the two electrons are subsequently transferred onto the next electron acceptor. Judging from chloroplast studies, it seems likely that the proposed mechanism exists in nature[11].

3.4. Complex III (Ubiquinol:Cytochrome c Oxidoreductase

Complex III transfers the redox equivalents from ubiquinol onto cytochrome c. Its smallest possible unit is composed of 8—9 polypeptides (Table 1)[46,75,76]. The two largest polypeptides with molecular weights of 49000 and 47000 are traditionally called 'core proteins'[77]. Although they do not carry redox centers, they probably have a function besides a structural one, as discussed below. The four polypeptides of intermediate molecular weight all possess a redox center. They consist of two cytochromes b with a molecular weight of 30000 each[78,79], the Rieske iron-sulfur protein, a Fe_2S_2-type protein with a molecular weight of 25000[80,81] and, finally, cytochrome c_1 with a molecular weight of 29000[82] (Fig. 2). The remaining two to three polypeptides are small molecules with molecular weights of about 12000, 11000 and 8000, containing no redox centers[76]. The function of the four to five polypeptides without redox centers has not been elucidated so far, although they constitute half of the mass of the complex. The cytochrome b molecules of complex III are coded for on mitochondrial DNA[83], whereas the remaining polypeptides are coded for on nuclear genes[84]. In contrast, the gene of cytochrome b of complex II is found in the nuclear DNA[85].

Adding up the molecular weights of the individual polypeptides and assuming two heme b and one heme c per complex, an apparent molecular weight of 250000 is calculated for the smallest possible unit. However, when the complex is isolated in the presence of mild detergents and studied by gel chromatography and ultracentrifugation, it behaves as a molecule of molecular weight 500000[86]. It has therefore been speculated that this 2×250000 complex (involving four cytochromes b, two iron-sulfur proteins and two cytochromes c_1) represents the functional structure of the complex existing in the mitochondrial membrane[86]. The same quaternary structure also emerged in recent electron micrographic studies obtained from 'two-dimensional crystals' formed by the isolated complex inlayed in a phospholipid bilayer[87]. The molecules of molecular weight 500000 are arranged in an up-and-down manner in the crystal lattice. The gross architecture of the molecule has been derived from final reconstruction of the image-processed ultramicrographs (Fig. 7). A good third of the dimer protrudes above the inner surface and about one quarter above the outer surface of the phospholipid bilayer. The halves of the dimeric complex are in contact with each other within the interior of the phospholipid bilayer. The contact surfaces are probably formed by the four cytochrome b subunits. Thus the possibility arises that the four cytochromes b of the complex III dimer function cooperatively as a tetramer in the process of energy transformation *(vide infra)*.

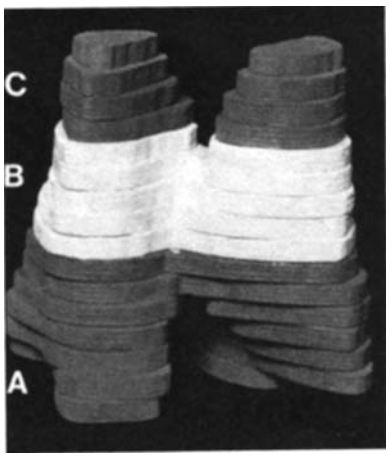


Fig. 7. Model of the gross structure of a single dimer of complex III, with the dimer axis running from top to bottom (by courtesy of *K. R. Leonard* and *H. Weiss*, unpublished). The white region (B) is the part of the complex embedded in the membrane. The upper dark region (C) extends into the cytosol, the lower dark region (A) into the matrix space.

The sequence of the redox components in the path of electron flow is not yet quite clear. The following arrangement is proposed: ubiquinone, two cytochrome b molecules, iron-sulfur protein, cytochrome c_1, cytochrome c[46].

One crucial point giving rise to many questions pertains to the complicated arrangement of the two or four cytochrome b molecules. These molecules show two different absorbance spectra and half-reduction potentials, as well as an intricate kinetic behavior[46,81,88]. From these findings the existence of two different molecular entities has been suggested[89]. However, genetic and DNA sequence studies revealed only one single structural gene coding for cytochrome b of complex III[90,91,92]. In addition, the partial amino acid sequence analysis, including the amino and carboxyl terminals of the peptide, offered no indication of the existence of heterogeneous monomers[79]. In a model published recently, a homodimer was assumed. The functional differences of the cytochrome b molecules have therefore been explained by a cooperative interaction[37].

Complex III accepts the redox equivalents from ubiquinol, which is reduced by complexes I or II and by some other dehydrogenases *(vide supra)*, and transfers them onto cytochrome c. A large difference in the half-reduction potentials occurs between cytochromes b and the iron-sulfur protein; accordingly, this part of the complex was attributed to energy conversion site 2 (Fig. 2).

The electron transfer through complex III is coupled with proton translocation resultung in a $4H^{\oplus}/2e^{\ominus}$ net yield, analogous to the situation existing in complex I (Fig. 3)[7,93]. Thus the overall reaction of complex III can be summarized as:

$$QH_2 + 2\,\text{cyt.}\,c^{3\oplus} + 2H_{in}^{\oplus} \rightarrow Q + 2\,\text{cyt.}\,c^{2\oplus} + 4H_{out}^{\oplus} \qquad (4)$$

The mechanism of the vectorial proton movement is still being studied. As described in Section 3.3, a proton-motive ubiquinone loop could only transport half of the protons. Alternatively, a ubiquinone cycle mechanism has been considered (Fig. 8)[94,95]. It is characterized by a back-flow of one electron (dashed line), thus doubling the $H^{\oplus}/e^{\ominus}$ stoichiometry. The cycle starts with a reduction of ubiquinone by one electron from cytochrome b of complex III, accompanied by an uptake of one $H^{\oplus}$ from the matrix side (Reaction 1). Subsequently the semiquinone radical $QH^{\ominus}$ is reduced by a further electron supplied from an iron-sulfur center of complex I or complex II, accompanied by an uptake of a second $H^{\oplus}$ from the matrix side (Reaction 2). After its migration across the membrane, ubiquinol is reoxidized by complex III, releasing two $H^{\oplus}$ to be cytosolic side. One electron flows to cytochrome b (Reaction 3), where it is required for the reduction of the next ubiquinone molecule. The second electron is fed into the Rieske iron-sulfur protein of complex III, finally reducing cytochrome c (Reaction 4). The mechanism involves two ubiquinone radicals as intermediary states. The occurrence of the radical acting between reactions 3 and 4 is feasible, since it may be stabilized at a common reaction center. However, the radical occurring as product of reaction 1 has to move from complex III to complexes I or II. Due to the low stability of this species, this radical migration is hardly imaginable, if one does not assume a structural association of the two complexes. Therefore, it is worthwhile to deliberate whether additionally, or alternatively, to the proton transfer *via* a ubiquinone loop, protons may be pumped across the membrane by means of a proton translocator. The cytochrome b molecules of complex III suitably act as proton translocator[37,96].

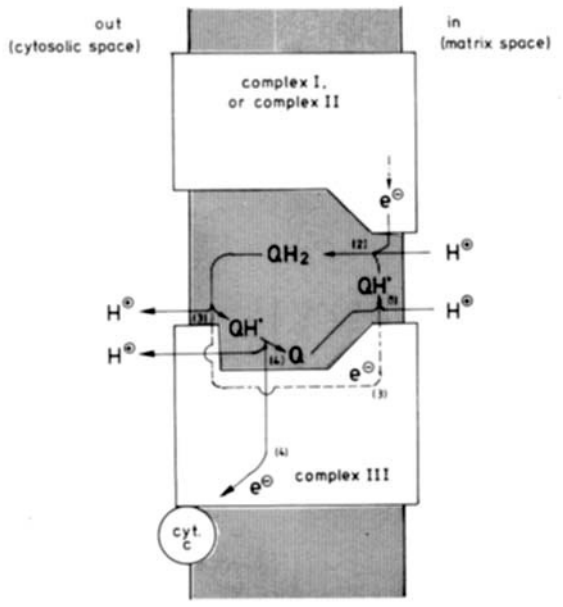


Fig. 8. Hypothetical scheme of the ubiquinone cycle working with a $4H^{\oplus}/2e^{\ominus}$ stoichiometry. The sequence of the reactions and sites of the reaction centers are described in the text.

Cytochrome b undergoes a protonation:deprotonation reaction in dependence of its state of reduction (Fig. 9). From an analysis of published redox titrations[97,98] it has been deduced that at physiological pH the protonation reaction 1 of group R precedes the reduction reaction 2 of the heme center. The cycle consists of a symmetrical sequence, since the oxidation reaction 4 precedes the deprotonation reaction 5. Reactions 3 and 6 represent changes in the conformation of cytochrome b. During reaction 3 the amino acid residue R is transferred from a matrix position, *i. e.* inner position, to a cytosolic, *i. e.* outer position. Reaction 6 represents the return of group R to its original position. It has been calculated that group R has a pK of 6.9 if the heme center is oxidized and a pK >8.5 if the heme center is reduced[37]. According to the symmetric reaction sequence, protonation and deprotonation occur on both sides of the membrane with a pK value of 6.9. At the inner position the change in pK (6.9 to >8.5 due to reduction) stabilizes the protonated state of R during translocation (Reaction 3); at the outer position the change in pK (>8.5 to 6.9 due to oxidation) facilitates the release of $H^{\oplus}$ to the cytosolic face. A reversal of the reaction sequence can be experimentally induced by a high phosphorylation potential ($[ATP]/([ADP]\cdot[P_i])$). The electrons flow in reverse direction in the electron transfer chain in this process, which is driven by a proton gradient built up by the reverse reaction of the ATP synthetase, *i. e.* the ATPase activity (cf. Section 4).

The model presented here of the cytochrome b proton pump implies that the main prerequisite for a redox component, enabling it to act as a proton translocator, is its intrinsic ability to undergo conformational changes in accordance with the redox changes of its metal center. In the case of cytochrome b, the heme center undergoes a change from the ferric to the ferrous state, which is supposed to cause a conformational change that involves a shift of an amino acid residue, R, (*e. g.* histidine). In dependence on the redox state of the heme center, the shifting residue undergoes a pK change

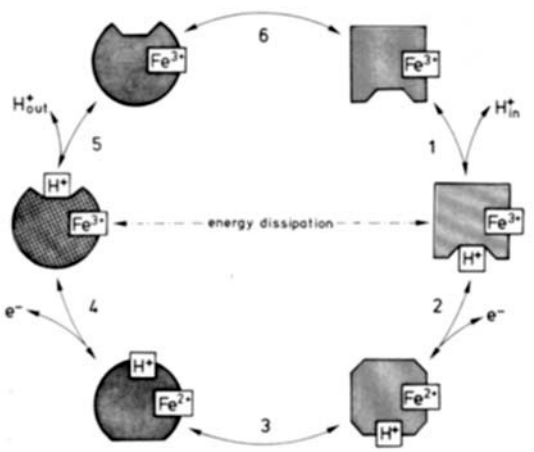


Fig. 9. Hypothetical scheme of the reaction sequence of cytochrome b acting as a proton translocator with a $2H^{\oplus}/2e^{\ominus}$ stoichiometry. The angular conformations indicate group R (which undergoes protonation) as situated on the matrix side; the circular conformations indicate group R (which undergoes deprotonation) as situated on the cytosolic side. Reduction of cytochrome b leads to a change in the pK of group R from 6.9 to about 8.5 as indicated by the closed conformation of the respective proton-binding sites. The dotted arrow indicates the possibility of a non-productive transition, which presumably occurs to only a small extent (see text).

which facilitates the process of proton translocation. An analogous model was proposed for cytochrome oxidase[99] acting as a proton pump.

The shift of the amino acid residue R across probably only a few tenths of a nm would suffice to cover a distance between two proton channels establishing the connection to the matrix and cytosolic faces of the membrane[100]. These proton channels may be formed by an α-helical structure[101] of the proton translocator (cytochrome b) arranged perpendicularly to the plane of the membrane, or, additionally by α-helical structures of adjacent polypeptide subunits, for instance the core proteins. In contrast to a conceivable shift of a group R due to a proton back-flow which may take place at the proton-driven ATP-synthetase[102], the movement of $RH^{\oplus}$ of the proton translocator occurs against a proton gradient and membrane potential, driven by the substrate oxidation energy.

The question arises whether the non-productive transition from $(Cyt\,b^{3}H^{\oplus})_{out}$ to $(Cyt\,b^{3\oplus}H^{\oplus})_{in}$ (indicated by the dotted line in Figure 9) takes place, diminishing the $2H^{\oplus}/2e^{\ominus}$ stoichiometry. It is tempting to speculate that—in analogy to other enzyme-catalyzed systems[103]—a certain unspecificity is always present in a proton translocator to ensure a sufficiently high velocity of the translocation. A decrease in the cytosolic pH under experimental conditions may further increase the amount of this energy dissipation due to an accumulation of $(Cyt\,b^{3\oplus}H^{\oplus})_{out}$. Under physiological conditions the proton translocator may act with an average yield slightly below $2H^{\oplus}/2e^{\ominus}$. In this case we would have to correct our former statement[37] that the $H^{\oplus}/e^{\ominus}$ stoichiometry of such a system is always an integer one. This small extent of energy dissipation inherent in a proton translocator has to be distinguished from the high extent of energy dissipation inherent in the $OH^{\ominus}$-ion translocator of brown adipose tissue, a machinery specifically designed for energy dissipation in the form of heat (see Section 8).

Summarizing, it should be stated that at complex III, *i.e.* at energy conversion site 2, if no ubiquinone-mediated proton transport occurs, two redox proton pumps would have to operate, since one cytochrome b pumps only with a $2H^{\oplus}/2e^{\ominus}$ stoichiometry. The work could be done by the two cytochrome b molecules if they were connected in series. This would be in contrast to our recent model[37].

3.5. Complex IV (Ferrocytochrome c:Oxygen Reductase)

Complex IV, the terminal segment of the respiratory chain, is also known as cytochrome oxidase. Compared to the other complexes, it has been the most intensively investigated regarding structure and function[99, 104, 105]. The multisubunit molecule accepts electrons from ferrocytochrome c and finally transfers them onto oxygen, reducing one molecule of oxygen to two molecules of water (Fig. 2). Details of the mechanism of oxygen activation will not be described here; they are the subject of recent comprehensive reviews[106, 107]. This section will concentrate on structural aspects and on the presumable mechanism of proton transfer in this region of the respiratory chain. The energy conversion site involved in complex IV is traditionally termed site 3.

The smallest possible unit of the complex consists of 12 polypeptides[108] (Table 1). It contains four electron-accepting centers, two copper centers, referred to as $Cu_{low\,potential}$ and $Cu_{high\,potential}$[109] (Fig. 2) and two types of hemes, termed cytochrome a and cytochrome a_3[110]. It has not yet been possible to assign the four redox centers to individual polypeptides, as has been done for complex III (see Section 3.4), owing to the fact that complex IV could not be dissociated into its functional polypeptides under mild conditions; the use of high concentrations of salt and detergent leads to a loss of the redox centers from the apoproteins.

The three largest and most hydrophobic polypeptides are coded for by mitochondrial DNA[111, 112] and translated on mitochondrial ribosomes; the remaining ones are products of cytosolic protein synthesis.

More analogies probably exist between complexes IV and III than has been realized to date. This concerns not only the different systems of protein synthesis for the individual subunits, the mechanisms of assembly of the whole complex, and the mechanism of proton translocation, but also the quaternary structure of the molecule and the possible cooperative function of the heme centers.

The molecular weight of the smallest possible unit of complex IV amounts to 166000, calculated from the heme content (12 μmol/g protein), assuming two heme a/minimum unit. From the sum of the molecular weights of the single subunits, it amounts to 178000. In ultracentrifugal studies the molecule behaves as a dimer.

Complex IV has been crystallized in two different forms. When the protein was isolated in Triton X-100 by negative extraction, it had a higher phospholipid content[113] than when it was prepared in deoxycholate[114]. The Triton preparation forms vesicles containing the complex in a dimeric aggregation state[115], the cholate preparation forms sheets containing the complex in a monomeric state[116]. In both kinds of 'two-dimensional crystals' the monomeric complex reveals the same rough shape of a lopsided 'Y', 11 nm in length (Fig. 10). The domains which form the arms of the Y are 5.5 nm in length. They are arranged on the matrix side of the membrane and are thought to be buried in the phospholipid bi-

layer. The stem of the Y, also 5.5 nm in length, is situated on the cytoplasmic face of the membrane and probably protrudes above the surface.



Fig. 10. Model of the gross structure of the monomeric complex IV. M1 and M2 are the matrix side domains and C is the cytoplasmic domain (by courtesy of *R. Henderson*).

These studies led to the speculation that the dimer (not shown), containing four cytochromes a and four copper centers, represents the functional state of complex IV in the inner mitochondrial membrane[115].

Apart from a knowledge of the gross structure and boundaries of the molecule, however, no precise data exist so far regarding the geometrical arrangement of the individual subunits in the complex. The sequence and function of the four metal centers in the path of electron flow are only partially understood. The half-reduction potentials of cytochrome a and a_3 differ by about 200 mV (Fig. 2)[117]; a much larger potential jump, however, occurs between cytochrome a_3 and oxygen, amounting to about 400 mV.

During the past three years it has been proven that the electron flow from ferrocytochrome c to oxygen is coupled with a vectorial proton transport (Fig. 3)[118]. The data emerged from numerous studies on complex IV incorporated into phospholipid vesicles and from studies on the complex residing in the mitochondrial membrane[119,120]. A $2H^{\oplus}$ $2e^{\ominus}$ stoichiometry was found in the isolated and reconstituted enzyme[99], but the stoichiometry of the process in the biological membrane amounts to $4H^{\oplus}/2e^{\ominus}$[121]. The lower, $2H^{\oplus}/2e^{\ominus}$, stoichiometry found in the vesicle preparation may stem from a merely partial restoration of the pumping device in the artificial system. The overall process catalyzed by cytochrome oxidase can be summarized as follows:

$$2\,\mathrm{cyt.c}^{2\oplus} + \tfrac{1}{2}\mathrm{O_2} + 4H^{\oplus}_{in} + 2\mathrm{H}^{\oplus}_{in} \rightarrow 2\,\mathrm{cyt.c}^{3\oplus} + \mathrm{H_2O} + 4H^{\oplus}_{out} \quad (5)$$

The italicized protons are the transported ones (cf. Fig. 3).

Complex IV is a segment of the electron transfer chain which does not dispose of quinone or other mobile hydrogen carriers. Therefore, in the authors' opinion, the results almost force the conclusion that the proton movement in complex IV is established by means of two proton pumps that may be connected in sequence. Cytochromes a and a_3 may be regarded as likely candidates, since they show a pH-dependence of their half-reduction potentials, like the cytochromes b of complex III[122].

3.6. Cytochrome c

In contrast to most of the other components of the respiratory chain, cytochrome c is a protein that has been structurally and functionally characterized on the molecular level. It differs from the other components in that it is a hydrophilic molecule. It is a peripheral membrane protein that can be extracted without the aid of detergents. Thus it is detached from its location on the outer side of the mitochondrial inner membrane by high ionic strength. It is easily purified by taking advantage of its high isoelectric point[123]. The molecular weight of cytochrome c is about 12000[124]. Characteristically for most c-type cytochromes, protoporphyrin IX is covalently bound to the apoprotein by two thioether bridges formed by the vinyl groups of protoporphyrin IX and two cysteine thiol groups of the protein[125]. The amino acid sequence of cytochrome c is known for more than 50 species[126]. From these data a phylogenetic tree of evolution has been constructed[127]. Moreover, the three-dimensional structure of tuna heart cytochrome c has been established at a 0.2 nm resolution[128]. The heme is held in a hydrophobic crevice by the two thioether bridges formed by Cys-14 and Cys-17 (Fig. 11). The fifth and sixth ligands of the iron, His-18 and Met-80, can be recognized on the right and on the left of the heme

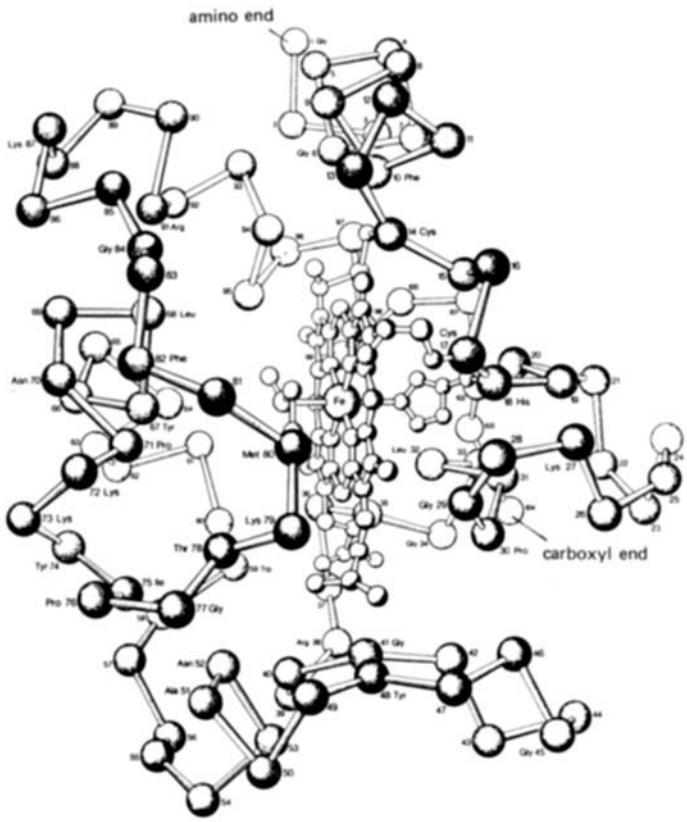


Fig. 11. Skeletal structure of the amino acid α-C atoms of horse cytochrome c (by courtesy of *R. E. Dickerson*).

system, that is exposed to the medium at one edge. The mass of basic amino acid residues (Lys-5, Lys-7, Lys-8, Lys-13, Lys-27, Lys-72, Lys-73, Lys-86, Lys-87) surround the opening of the crevice; this is a general feature in cytochrome c from different sources.

A half-reduction potential (pH-independent at physiological pH range) of about +250 mV has been determined for cytochrome c, indicative of its localization in the respiratory chain between the b-type and a-type cytochromes. Indeed, cytochrome c is reduced by the cytochrome b-containing complex III and oxidized by the cytochrome a-containing complex IV (Fig. 2).

From acetylation studies performed with free cytochrome c and in a state bound to cytochrome c_1 or to complex III, it has been concluded that cytochrome c binds to the cytochrome c_1 subunit of complex III[129, 130]. The binding domain lies in the region of the lysine residues 13, 72, 73, 83, 87 and 88 in the left upper part of cytochrome c (Fig. 11), shown by the fact that these residues were shielded and therefore less accessible to the acetylation reagent. The same binding domain was found for the binding to cytochrome oxidase[131, 132], indicating that cytochrome c does not form a fixed link between complexes III and IV, but moves or turns the opening of its heme crevice to the distinct reaction centers of complexes III and IV.

After establishment of the three-dimensional structure of cytochrome c, it has been suggested that the aromatic amino acid residues Tyr-74, Trp-59 and Tyr-67 are involved in the electron conduction to the iron atom *via* the fourth pyrrole ring[133]. The proposed free radical transfer mechanism had to be rejected, however, when the three-dimensional structure of cytochrome c_{550} from *P. denitrificans* became known[134]. This cytochrome c possesses a Leu-residue instead of Tyr-74, but it is still active with complex III[135]. A further argument against the free radical transfer mechanism—regarded as a kind of electron hopping—consists in the fact that a high energy barrier exists, demanding an activation energy of about 250 kJ/mol[136].

To date, two other mechanisms of electron transfer have drawn attention: i) an outer sphere process[137], and ii) an electron tunneling mechanism[138, 139]. The first mechanism presumes an overlap between the π-orbital system of the heme of cytochrome c at its exposed edge with a prosthetic group of the reductase or oxidase. The distance that can be spanned between the two systems by this mechanism can reach maximally 0.3 nm. The term 'electron tunneling' is used to describe the motion of particles across energy barriers which would be impossible according to classical mechanics, but which is predicted by the quantum theory regarding electrons in their particle wave function. According to a simple description of this process it is possible by electron tunneling to span a maximal distance of 3 nm[138, 139], which is in the same order of magnitude as the distance between the hemes of cytochrome oxidase and cytochrome c[140, 141]. An exclusive tunneling process would show no temperature dependence, which was found, however, above 100 K for the system that has been most investigated in this field, namely the photo-oxidation of cytochrome c in the purple membrane of the sulfur bacterium *Chromatium*.

A more elaborate description of the electron tunneling mechanism, termed 'thermally activated electron tunneling', does involve a temperature dependence[142]. The calculations predict the bridging of a distance of only about 1 nm. The shorter distance does not necessarily represent a disadvantage, since a tunneling distance of 3 nm might include the involvement of various redox centers, whilst the shorter distance of 1 nm may cause an even sharper discrimination between the reaction centers.

4. ATP-Synthetase (Complex V)

Proton-driven ATP-synthetases are found not only in the inner mitochondrial membrane, but also in the cytoplasmic membrane of bacteria and in the thylakoid membrane of chloroplasts. The ATP-synthetases from these different sources are very similar in structure and function[143, 145]. The mitochondrial enzyme is easily split into two multiprotein subunits and at least two additional polypeptide components (Fig. 12).

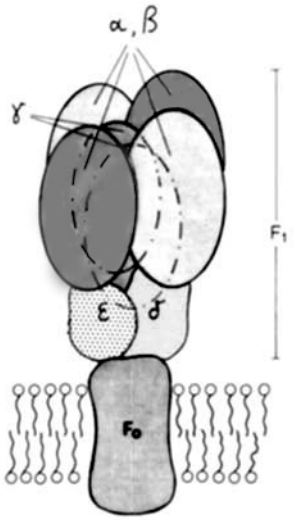


Fig. 12. Subunit composition of the ATP-synthetase. The subunits of F_0 as well as the oligomycin-sensitivity-conferring protein (OSCP) and the coupling factor F_6 are not represented in the drawing.

One of these multiprotein subunits, called coupling factor F_1, is a water-soluble component which has been crystallized recently[146, 147]. It consists of five different polypeptide subunits (α, β, γ, δ, ε). Possibly the stoichiometry is α_2, β_2, γ_2, δ_2, ε_2 (Table 1), but this is still controversial[148-150]. F_1 has the rare property of a cold-lability due to a dissociation occurring at low temperatures[151].

In contrast to F_1, the second multiprotein subunit—called F_0—is an integral membrane component. Presumably it consists of four polypeptide subunits (see Table 1)[152, 153].

In addition to the multiprotein subunits F_1 and F_0, the mitochondrial ATP-synthetase contains two other proteins: the oligomycin-sensitivity-conferring protein (OSCP) with a molecular weight of 19000[154, 155], binding directly to F_1 with a 1:1 stoichiometry[156]; and the coupling factor F_6 (molecular weight 8000)[157], believed to participate in the binding of OSCP—F_1 to F_0[158, 159].

A further protein, the F_1 inhibitor protein, was isolated from bovine heart mitochondria[160]. It can bind to the F_1 part at a low ATP/ADP ratio, apparently inhibiting the ATPase but not the ATP-synthetase reaction[161, 162].

In electron micrographs the ATP synthetase was seen in the form of spheres connected by stalks to the membrane. The spheres, which are oriented towards the matrix space, are attributed to the F_1 part. The stalks should consist of OSCP and F_6, whereas the membrane part is attributed to the F_0 unit[163, 164]. It should be mentioned, however, that the appearance of the electron micrographs has also been ascribed to fixation artefacts.

Certain catalytic activities can be attributed to the individual subunits of the ATP synthetase[144]. The isolated F_1 part, and even F_1 depleted of subunits γ and δ, reveals ATP hydrolytic activity, but has lost the ATP synthetase activity[165]. This finding is in agreement with the postulate, that energy transduction occurs *via* an electrochemical proton gradient across the inner mitochondrial membrane, which cannot be created by a soluble enzyme residing in a uniform phase. The F_0 part forms a proton channel[166]. If the mitochondrial membrane is depleted of F_1, it is no longer able to maintain a proton gradient, but preserves a proton conductivity which is sensitive to dicyclohexylcarbodiimide[167, 168]. This inhibition is due to the covalent binding of dicyclohexylcarbodiimide (DCCD) to a glutamate residue of the smallest subunit of F_0[169].

The coupling factor F_1 has several binding sites for adenine nucleotides[143] which may have different functions in ATP synthesis and regulation. The present description will be restricted to 'tight binding sites' for adenine nucleotides. The non-covalent linkages of ADP and ATP to these sites are stable during dialysis and gel filtration. As has been shown by photo-affinity labeling, the tight binding sites are located on the β-subunits[170–172].

It has been shown in artificial systems that either a pH gradient or an electrical field can drive the flow of protons which is coupled to ATP synthesis[173, 174]. The mechanism by which this proton flow drives ATP synthesis is unknown so far, but several proposals are under discussion[175–177]. One hypothetical reaction scheme for ATP synthesis is described here[178] (Fig. 13). It is based on the assumption that there are

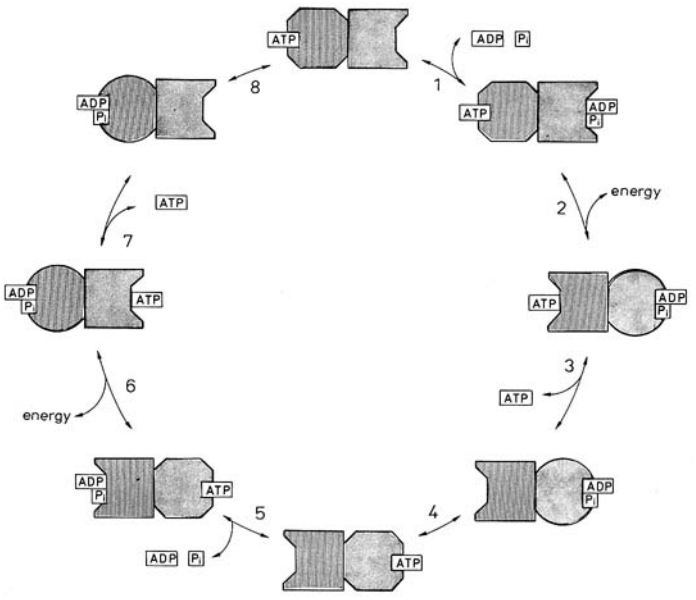


Fig. 13. Modified scheme of the reaction sequence taking place during ATP-synthesis at the two alternating binding sites of the ATP-synthetase (after *P. D. Boyer et al.* [177]). The two binding sites are indicated by different shading.

two identical binding sites for ATP or ADP + P_i on the two β-subunits of one F_1 molecule, with the two binding sites functioning alternatively. As one ATP is bound tightly to the first site, ADP and P_i are bound weakly to the second site (Reaction 1). Then, in an energy-dependent reaction, ADP and P_i are bound tightly, whereas the binding of ATP at the other site is weakened (Reaction 2). It is the weakening of the ATP binding that is thought to be the energy-consuming step, not the formation of the anhydride bond. In the next step, ATP is released (Reaction 3). Finally, the tightly bound ADP and P_i are transformed into ATP (Reaction 4). The second half of the cycle runs in the same sequence, but utilizing the same binding sites in an alternate fashion (Reactions 5 to 8). Contradictory results, indicating more than two binding sites involved in the process of ATP synthesis[143] may be due to the fact that a population of some of the intermediary states may have been 'frozen' and interpreted as different binding sites.

The view that the step with the high energy expenditure is the release of tightly bound ATP and not the formation of the anhydride bond of ATP is assumed also for the Na,K-ATPase[178], for the $Ca^{2\oplus}$-ATPase[179] and for the myosin-ATPase[180].

The action of the ATP synthetase is reversible in that it can also work as an electrogenic proton pump (ATP-driven proton pump)[181, 182, 183]. A $3H^{\oplus}$/ATP stoichiometry now seems to be established for the actual ATP synthetase reaction (Fig. 3) (see Section 9)[7].

5. Adenine Nucleotide Translocase

The adenine nucleotides ADP and ATP have to be transported across the inner mitochondrial membrane, since this membrane is impermeable to the highly charged and bulky molecules $ADP^{3\ominus}$ and $ATP^{4\ominus}$[184, 185, 186]. The transporting enzyme, adenine nucleotide translocase, has a minimum molecular weight of 30000, as shown in sodium dodecyl sulfate gel electrophoresis[187]. In mild detergents used for analytical ultracentrifugal studies, however, the carrier reveals a molecular weight of 60000[188]. Here it is present in a dimeric state of aggregation. Since only one binding site for adenine nucleotides and the specific inhibitors has been found per dimer, which is available for both ADP and ATP[185], it is tempting to speculate that the dimer represents the functional state of the protein in the inner mitochondrial membrane. Partial amino acid sequence analysis has not indicated any heterologies. It has therefore been assumed that the enzyme is a homodimer. The carrier is a highly hydrophobic integral membrane protein, comparable in this respect to the cytochrome b dimer of complex III. Due to its function, a transmembranous arrangement has been presumed[189, 190].

The adenine nucleotides ADP and ATP are translocated across the membrane in a strict 1:1 type of counter-exchange (Fig. 3)[185, 190]. The enzyme is highly specific for ATP and ADP when compared to other nucleotides. AMP is not transported by the enzyme. Specific inhibitors of the carrier exist, *e.g.* the plant toxin atractylate (a diterpenoid derivative)[191], and the bacterial toxin bongkrekate (a polyisoprenoid derivative)[192]. In a model, the mechanism of the transport has been described as a 'gated pore mechanism'[193]. The carrier represents a highly active membrane transport system, con-

stituting about 14% of the whole protein of the inner mitochondrial membrane. The rate of translocation can be compared to that of the phosphate translocase (see Section 6). The adenine nucleotide transport does not seem to limit the supply of the cytosol with the mitochondrially synthesized ATP, *i.e.* the adenine nucleotide carrier may work at a higher rate than the proton-driven ATP synthetase (cf. Fig. 3).

The adenine nucleotide transport is a secondary active transport, consuming energy that is provided in the form of the membrane potential[194]. The transport takes place against a phosphorylation potential ($[ATP]/([ADP]\cdot[P_i])$) that is higher in the cytosol (about 66 kJ) than in the matrix space (about 55 kJ)[195]. The exchange system works asymmetrically in the energized state, *i.e.* the ADP uptake is highly preferred over ATP uptake and vice versa the ATP release is preferred over ADP release[194]. When the membrane potential is collapsed by means of uncouplers, like dinitrophenol, the asymmetry of the transport is abolished, *i.e.* ATP is then taken up at the same rate as ADP, and ADP is released with the same activity as ATP; theoretically, then also a pure ADP:ADP or ATP:ATP counter-exchange can occur.

The influence of the membrane potential on the exchange activities and on the asymmetry due to the electrical nature of the transport process have recently been elucidated in more detail in a reconstituted system consisting of purified carrier protein incorporated into phospholipid vesicles[196, 197].

The interrelation between the electron transfer creating the electrochemical membrane potential, and the three processes consuming the potential (ATP synthesis, adenine nucleotide exchange and phosphate transport), are discussed in Section 7.

6. Phosphate Transport System

Mitochondria possess two carrier systems capable of transporting phosphate across the inner membrane: the dicarboxylate carrier and the phosphate carrier[20, 198, 199]. The dicarboxylate carrier exchanges $HPO_4^{2\ominus}$ against dicarboxylates, *e.g.* succinate or malate. This transport system differs from the phosphate carrier in that it can be inhibited by some non-physiological dicarboxylates like *n*-butyl malonate[198], whereas the phosphate carrier is highly sensitive to SH-blocking reagents[199, 200]. The dicarboxylate carrier does not seem to function as P_i-supplier for ATP synthesis taking place in the matrix space, but rather to be involved in a dicarboxylate uptake by a dicarboxylate : $HPO_4^{2\ominus}$ counter-exchange.

Phosphate is delivered mainly by a specific phosphate carrier, a protein that reveals a molecular weight of about 30000 in sodium dodecyl sulfate electrophoresis when it is labeled by *N*-Ethylmaleimide[201, 202, 203]. This transport system is probably the most active one in the inner mitochondrial membrane[199]. The phosphate uptake is electroneutral[204], following either an $H_2PO_4^{\ominus}/OH^{\ominus}$ counter-exchange or an $H_2PO_4^{\ominus}/H^{\oplus}$ cotransport. For the sake of simplicity, the latter type of exchange will be adhered to in the following. In any case the uptake is governed by the proton gradient existing at the membrane (Fig. 3).

Since the phosphate carrier transports only $H_2PO_4^{\ominus}$ from the cytosolic to the matrix space under physiological conditions, it may be speculated that the ΔpH across the mitochondrial membrane may be affected to a greater extent than expected from the cotransported proton, due to the removal of $H_2PO_4^{\ominus}$ from the dissociation equilibrium of phosphoric acid in the cytosolic phase and due to its enrichment in the matrix phase. This secondary influence on the pH gradient can be neglected, however, since phosphate is formally added as $H_2PO_4^{\ominus}$ to ADP in the matrix space during phosphorylation and released as $H_2PO_4^{\ominus}$ from ATP at the cytosolic space during ATP consumption. As shown in Figure 3, the balance is therefore re-established.

7. Proton and Charge Balance of the Whole Set of Systems Converting Oxidative Energy into Chemical Energy

The transfer of electrons from NADH to oxygen *via* complexes I, III and IV is coupled to an electrogenic translocation of 12 $H^{\oplus}$ across the inner mitochondrial membrane[11, 12, 93, 205–208] (Fig. 3a). For succinate oxidation 8 $H^{\oplus}$ were measured (not shown). Since it has been known for a long time that NADH oxidation approaches a maximum of 3 ATP and succinate oxidation one of 2 ATP, it seems evident that mitochondrial ATP formation needs 4 $H^{\oplus}$ per molecule of ATP synthesized (Fig. 3b).

Electrogenic proton translocation without cotransport of anions generates both a proton gradient (ΔpH) and a membrane potential ($\Delta\Psi$). As the phosphate uptake is electroneutral, only the ΔpH is affected, *i.e.* the corresponding positive charge of the proton transported electrogenically during electron flow remains at the outer face of the membrane. This positive charge is balanced by the electrogenic ADP, ATP counter-exchange (Fig. 3b). Therefore three electrogenic protons remain for the ATP synthesis reaction. This stoichiometry is in general agreement with thermodynamic considerations (see Section 9).

The ATP production of submitochondrial particles is most informative as regards the energy yield induced by a change of side of the individual processes. In submitochondrial particles obtained by ultrasonication of mitochondria, the inner membrane has been inverted (inside out) and a transport of adenine nucleotides and phosphate is no longer necessary for ATP synthesis. In agreement with this consideration, a stoichiometry of 3 $H^{\oplus}$/ATP formed was reported for submitochondrial particles[209, 210]. From these values a stoichiometry of 4 ATP/NADH oxidized is derived, which is calculated from the values of 12 $H^{\oplus}$ translocated per NADH oxidized, and 3 $H^{\oplus}$ consumed per 1 ATP formation.

8. Thermogenesis in Mitochondria of Brown Adipose Tissue

In mammals heat is usually produced by fine random contractions of skeletal muscle, called muscle shivering[211]. However, another possibility exists for heat production, a non-shivering thermogenesis occurring in the mitochondria of the brown adipose tissue[212–214]. The process is unique to new-born mammals (including man), hibernators and cold-adapted small mammals. Brown adipose tissue differs from white adipose tissue in that it contains multilocular triglycer-

ide droplets and possesses an extremely high content of mitochondria[215].

The brown adipose tissue mitochondria dispose of an energy dissipation pathway that is not present in other tissues. It is a reaction that competes with the ATP synthetase for the electrochemical membrane potential $\Delta\tilde{\mu}_{H^{\oplus}}$, built up by the proton-translocating electron flow[212]. The mitochondria respire free fatty acids at a high rate, but produce scarcely any ATP. They possess a 32000 protein which spans the membrane[216]. The protein forms a pore for $H^{\oplus}$ or $OH^{\ominus}$ ions, the permeability of which is regulated by a specific binding of purine nucleotides. Binding of GDP or GTP or, less effectively, that of ADP or ATP, inhibits the $OH^{\ominus}$ ion flow[213,217,218], driven by the membrane potential.

9. The Irreversible Thermodynamic Approach to Energy Coupling in Mitochondria

The analysis of the process of oxidative phosphorylation has received fresh impetus in the past few years by the application of irreversible thermodynamics[9,10,219]. Since an exact treatment within the framework of this theory is too complicated, a linear first order approximation to the nonlinear problem has been developed. The approximation, termed 'linear nonequilibrium thermodynamics', proved to be valuable for a description of the processes under study. Concepts such as 'P/O ratio' (the number of ATP molecules synthesized from ADP and P_i per oxygen atom reduced) or 'respiratory control' have gained a new meaning and interpretation. The respiratory control ratio r is defined as the quotient of the respiration rate which occurs at substrate saturation in the presence of ADP and the respiration rate under the same condition if ADP is lacking. Thus it has been shown that, even at a low respiratory control r, a high degree of coupling, q, can occur. The degree of coupling, which can reach values from 0 (no coupling) to 1, is related to the respiratory control r, in accordance with the following equation:

$$q = 1 - \sqrt{1 - 1/r} \qquad (6)$$

The degree of coupling q is a far better indicator for coupling of oxidation with phosphorylation than the respiratory control r, used previously to describe the quality of preparations of mitochondria.

Of further significance is the finding that the measured P/O values, although they are not equivalent to the mechanistic stoichiometries, can be good approximations of the stoichiometries if they are measured at a high degree of coupling. The application of linear nonequilibrium thermodynamics, however, permits a calculation of phenomenologic stoichiometries, not from the flow ratio (rate of ATP synthesized/rate of oxidation) at state 3, but from the force ratio (free energy of ATP hydrolysis/free energy of substrate oxidation) at state 4 and the degree of coupling. Thus, P/O stoichiometries of 3.0 for NADH oxidation and of 2.1 for succinate oxidation were calculated. Of special interest are the $H^{\oplus}/O$ and the $H^{\oplus}/ATP$ stoichiometries for mitochondria as well as for submitochondrial particles, calculated from the respective force ratios at state 4 and the degree of coupling. Stoichiometries of 11.8 $H^{\oplus}/O$ for NADH oxidation, 8.1 $H^{\oplus}/O$ for succinate oxidation and 3.9 $H^{\oplus}/ATP$ for proton-driven ATP synthesis have been obtained for mitochondria[6]. Due

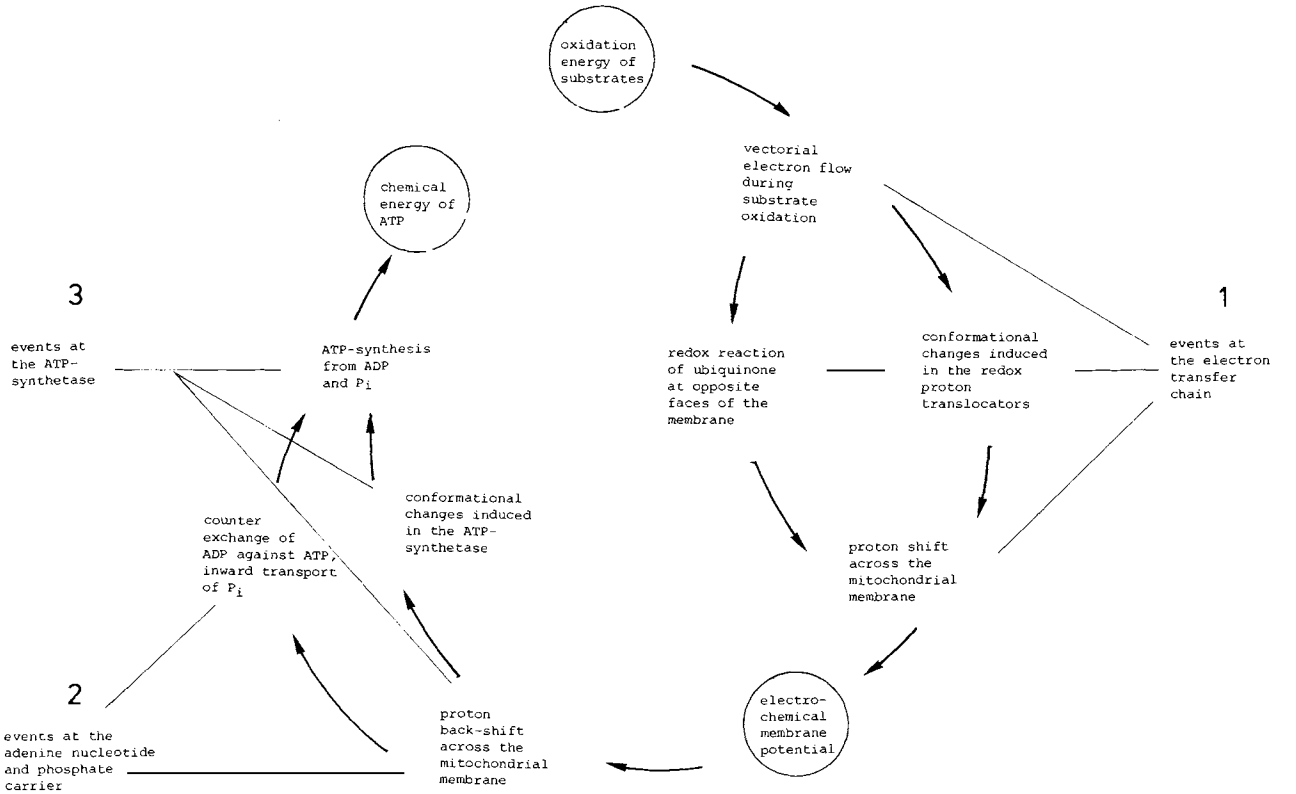


Fig. 14. Sequence of events taking place during mitochondrial oxidative phosphorylation. The three existing forms of energy are encircled. The spiral of events embraces the two probable mechanisms of proton transport: i) The proton pump mechanism. ii) The redox (carrier-mediated) loop mechanism. The latter may occur at energy conversion site 2.

to the fact that no proton motive force is discharged for adenine nucleotide exchange and phosphate transport in submitochondrial particles, P/O stoichiometries of 3.9 for NADH oxidation, 2.7 for succinate oxidation and 2.8 $H^{\oplus}$/ATP for ATP formation were obtained. All these data, calculated on the basis of state 4 force ratio values and the degree of coupling q, are in good agreement with the stoichiometries that were actually measured at state 3 conditions with mitochondria or submitochondrial particles that showed a high degree of coupling.

A very intriguing result reached by the use of irreversible thermodynamics is that a degree of coupling q close to unity is not realized in mitochondria operating *in vivo*, although the efficiency of oxidative phosphorylation, defined as:

$$\eta = \frac{\text{phosphorylation flow} \times \text{phosphorylation potential}}{\text{oxidation flow} \times \text{redox potential}}$$

increases with increasing degree of coupling q. At a degree of coupling close to unity, however, the phosphorylation flow vanishes, which leads to a small output (phosphorylation flow × phosphorylation potential). Maximization of the output with respect to the degree of coupling results in an ideal degree of coupling of about 0.9[9].

10. Summary and Outlook

To sum up the causal relationship of mitochondrial energy conversion, the whole process is depicted in a simple energy flow diagram drawn in the shape of a spiral of events (Fig. 14). The sequence of reactions shows that the proton translocation driven by the redox proton pumps (1) and, vice versa, the ATP formation catalyzed by the ATP synthetase (3), depend on conformational changes taking place at the enzymes. These conformational changes may occur within polypeptides and between individual polypeptides of the respective multiprotein complexes. The scheme, however, does not take into account a direct conformational interaction between the electron-transferring complexes and the ATP-synthetase complex, as proposed extensively in previous models[220]. A ubiquinone-mediated proton transport by aid of a loop mechanism is also considered in the scheme, since it probably takes place at energy conversion site 2 (cf. Section 3.4)[3]. The postulation of a sophisticated reaction mechanism such as the ubiquinone cycle is hardly necessary, however, since probably additionally to the ubiquinone loop a proton pump works at energy conversion site 2.

Two-dimensional crystals have been obtained so far from mitochondrial complexes III[87] and IV[115,116], as well as from bacteriorhodopsin[221,222]. The gross structure of these membrane proteins has been elucidated. Attempts are being made to achieve the high resolution required for analyzing the fine structure of the proteins. The isolation of the residual proteins of oxidative phosphorylation, as well as the determination of the primary structure of these proteins will continue and support the elucidation of the reaction mechanisms on a molecular level.

The authors thank Prof. Dr. M. Klingenberg, Dr. R. Krämer and Dr. W. Wintermeyer for valuable discussions. We are very grateful to Drs. R. E. Dickerson, R. Henderson and K. R. Leonard for permission to include Figs. 7, 10, and 11. The assistance of Dr. M. Stitt in correcting the manuscript is greatly appreciated. Some of the cited studies were aided by grants from the Deutsche Forschungsgesellschaft to G. v. J. and from the Studienstiftung des Deutschen Volkes to W. D. E.

Received: May 29, 1980 [A 333 IE]
German version: Angew. Chem. *92*, 684 (1980)

[1] *P. Mitchell*, Nature *191*, 144 (1961).
[2] *P. Mitchell*, Biol. Rev. *41*, 445 (1966).
[2a] *G. Schäfer, M. Klingenberg:* Energy Conservation in Biological Membranes. Springer, Berlin 1978.
[3] *A. Trebst* in [2a], p. 84.
[4] *W. A. Cramer, J. Whitmarsh*, Annu. Rev. Plant Physiol. *28*, 133 (1977).
[5] *H. T. Witt*, Biochim. Biophys. Acta *505*, 355 (1979).
[6] *R. E. Blankenship, W. W. Parson*, Annu. Rev. Biochem. *47*, 635 (1978).
[7] *P. Mitchell*, Angew. Chem. *91*, 718 (1979).
[8] *R. J. P. Williams*, FEBS Lett. *85*, 9 (1978).
[9] *J. W. Stucki* in [2a], p. 264.
[10] *H. Rottenberg*, Biochim. Biophys. Acta *549*, 225 (1979).
[11] *A. Alexandre, B. Reynafarje, A. L. Lehninger*, Proc. Natl. Acad. Sci. USA *75*, 5296 (1978).
[11a] *K. van Dam, B. F. van Gelder:* Structure and Function of Energy-Transducing Membranes. Elsevier/North-Holland Biomedical Press, Amsterdam 1977.
[12] *A. L. Lehninger, B. Reynafarje, A. Alexandre* in [11a], p. 95.
[13] *L. Ernster, B. Kuylensnerna* in *E. Racker:* Membranes of Mitochondria and Chloroplasts. Van Nostrand-Reinhold, New York 1970, p. 172.
[14] *F. J. Ruzicka, H. Beinert*, Biochem. Biophys. Res. Commun. *66*, 622 (1975).
[15] *M. Klingenberg, M. Buchholz*, Eur. J. Biochem. *13*, 247 (1970).
[16] *B. Fleischer, A. Casu, S. Fleischer*, Biochem. Biophys. Res. Commun. *24*, 189 (1966).
[16a] *P. D. Boyer:* The Enzymes. Vol. 13. Academic Press, New York 1976.
[17] *J. Rydström, J. B. Hoek, L. Ernster* in [16a], p. 51.
[18] *J. Rydström*, Biochim. Biophys. Acta *463*, 155 (1977).
[19] *R. S. Earle, R. R. Fischer*, Biochemistry *19*, 561 (1980).
[20] *K. F. La Noue, A. C. Schoolwarth*, Annu. Rev. Biochem. *48*, 871 (1979).
[21] *H. W. Heldt*, Angew. Chem. *84*, 792 (1972); Angew. Chem. Int. Ed. Engl. *11*, 792 (1972).
[22] *J. W. De Pierre, L. Ernster*, Annu. Rev. Biochem. *46*, 201 (1977).
[22a] *A. Martonosi:* The Enzymes of Biological Membranes. Wiley, London 1976.
[23] *Y. Hatefi* in [22a], Vol. 4, p. 3.
[24] *Y. Hatefi*, Methods Enzymol. *53*, 3 (1978).
[25] *Y. Hatefi, Y. M. Galante* in [2a], p. 19.
[26] *A. Kröger, M. Klingenberg*, Vitam. Horm. *28*, 533 (1970).
[27] *J. Vanderkooi, M. Erecinska* in [22a], Vol. 4, p. 43.
[28] *Y. Hatefi, D. L. Stiggall* in [16a], p. 175.
[29] *I. C. Ragan*, Biochim. Biophys. Acta *456*, 249 (1976).
[30] *I. C. Ragan*, Biochem. J. *154*, 295 (1976).
[31] *J. Rydström*, Biochim. Biophys. Acta *463*, 155 (1977).
[32] *T. Ohnishi*, Biochim. Biophys. Acta *387*, 475 (1975).
[33] *H. Beinert* in *W. Lovenberg:* Iron Sulfur Proteins. Academic Press, New York 1977, p. 61.
[34] *H. G. Lawford, P. B. Garland*, Biochem. J. *130*, 8029 (1972).
[25] *P. C. Hinkle, L. L. Horstman*, J. Biol. Chem. *246*, 6024 (1971).
[36] *C. I. Ragan, P. C. Hinkle*, J. Biol. Chem. *250*, 8472 (1975).
[37] *G. von Jagow, W. D. Engel*, FEBS Lett. *111*, 1 (1980).
[38] *R. A. Capaldi, J. Sweetland, A. Merli*, Biochemistry *16*, 5707 (1977).
[39] *Y. Hatefi, D. L. Stigall*, Methods Enzymol. *53*, 21 (1978).
[40] *P. Hemmerich, A. Ehrenberg, W. H. Walker, L. E. G. Erikson, P. Salach, P. Bader, T. P. Singer*, FEBS Lett. *3*, 37 (1969).
[41] *T. P. Singer, E. B. Kearney, W. C. Kenney*, Adv. Enzymol. *37*, 189 (1973).
[42] *T. Ohnishi, J. C. Salerno, D. B. Winter, J. Lim, C. A. Yu, L. Yu, T. E. King*, J. Biol. Chem. *251*, 2094 (1976).
[43] *T. Ohnishi, J. Lin, D. B. Winter, T. E. King*, J. Biol. Chem. *251*, 2105 (1976).
[44] *Y. Hatefi*, Methods Enzymol. *53*, 27 (1978).
[45] *G. von Jagow*, unpublished (1980).
[46] *G. von Jagow, W. Sebald*, Annu. Rev. Biochem. *49*, 284 (1980).
[47] *K. A. Davis, Y. Hatefi*, Biochemistry *10*, 2509 (1971).
[48] *C. A. Yu, L. Yu, T. A. King*, Biochem. Biophys. Res. Commun. *78*, 259 (1977).
[49] *C. A. Yu, L. Yu, T. E. King*, Biochem. Biophys. Res. Commun. *79*, 939 (1978).
[50] *C. A. Yu, L. Najaoka, L. Yu, T. E. King*, Biochem. Biophys. Res. Commun. *82*, 1070 (1978).

[51] *J. C. Salerno, H. J. Harmon, H. Blum, J. S. Leigh, T. Ohnishi,* FEBS Lett. *82*, 179 (1977).
[52] *M. Gutman,* Mol. Cell. Biochem. *20*, 41 (1978).
[53] *B. A. C. Ackrell, E. B. Kearney, M. Mayr,* J. Biol. Chem. *249*, 2021 (1974).
[54] *M. Gutman,* Biochemistry *15*, 1342 (1976).
[55] *L. Wojtczack, A. B. Wojtczak, L. Ernster,* Biochem. Biophys. Acta *191*, 10 (1969).
[56] *E. B. Kearney, B. A. C. Ackrell, M. Mayer, T. P. Singer,* J. Biol. Chem. *249*, 2016 (1974).
[57] *R. Gilles, P. Hogue, E. B. Kearney,* Life Sci. *10*, 1421 (1971).
[58] *M. Gutman, E. B. Kearney, T. P. Singer,* Biochemistry *10*, 4763 (1971).
[59] *M. Gutman, E. B. Kearney, T. P. Singer,* Biochem. Biophys. Res. Commun. *42*, 1016 (1971).
[60] *E. B. Kearney, M. Mayr, T. P. Singer,* Biochem. Biophys. Res. Commun. *46*, 531 (1972).
[61] *F. G. Hopkins, E. Morgan, C. Lutwak-Mann,* Biochem. J. *32*, 1829 (1938).
[62] *D. E. Wolf, C. H. Hoffman, N. R. Trenner, B. H. Arison, C. H. Shunk, B. O. Linn, J. F. McPherson, K. Folkers,* J. Am. Chem. Soc. *80*, 4752 (1958).
[63] *A. Castelli, G. Lenaz, K. Folkers,* Biochem. Biophys. Res. Commun. *34*, 200 (1969).
[64] *M. Klingenberg, A. Kröger* in *E. C. Slater et al.:* The Biochemistry of Mitochondria. Academic Press, London 1966, p. 11.
[65] *D. E. Green, D. C. Wharton,* Biochem. Z. *338*, 335 (1963).
[66] *F. L. Crane,* Annu. Rev. Biochem. *46*, 439 (1977).
[67] *J. W. Pierre, L. Ernster,* Annu. Rev. Biochem. *46*, 201 (1977).
[68] *A. Futami, E. Hurt, G. Hauska,* Biochim. Biophys. Acta *547*, 583 (1979).
[69] *B. Chance* in *G. F. Azzone et al.:* Biochemistry and Biophysics of Mitochondrial Membranes. Academic Press, New York 1972, p. 85.
[70] *A. Kröger, M. Klingenberg,* Eur. J. Biochem. *34*, 358 (1973).
[71] *A. Kröger, M. Klingenberg,* Eur. J. Biochem. *39*, 313 (1973).
[72] *C. I. Ragan, C. Heron,* Biochem. J. *174*, 783 (1978).
[73] *C. Heron, C. I. Ragan, B. L. Trumpower,* Biochem. J. *174*, 791 (1978).
[74] *T. E. King, C. A. Yu, L. Yu, Y. L. Chiang* in *E. Quagliariello et al.:* Electron Transfer Chains and Oxidative Phosphorylation. Elsevier-North Holland, Amsterdam 1975, p. 105.
[75] *B. D. Nelson, P. Gellerfors,* Methods Enzymol. *53*, 80 (1978).
[76] *W. D. Engel, H. Schägger, G. von Jagow,* Biochim. Biophys. Acta, in press.
[77] *P. Gellerfors, M. Lunden, B. D. Nelson,* Eur. J. Biochem. *67*, 463 (1976).
[78] *H. Weiss, B. Ziganke,* Methods Enzymol. *53*, 212 (1978).
[79] *G. von Jagow, H. Schägger, W. D. Engel, M. Machleidt, I. Machleidt,* FEBS Lett. *91*, 121 (1978).
[80] *J. S. Rieske, D. H. Mac Lennan, R. Coleman,* Biochem. Biophys. Res. Commun. *15*, 338 (1964).
[81] *J. S. Rieske,* Biochim. Biophys. Acta *456*, 195 (1976).
[82] *G. von Jagow, H. Schägger, W. D. Engel, P. Riccio, H. J. Kolb, M. Klingenberg,* Methods Enzymol. *53*, 92 (1978).
[83] *H. Weiss, B. Ziganke,* Eur. J. Biochem. *41*, 63 (1974).
[84] *H. Weiss,* Biochim. Biophys. Acta *456*, 291 (1976).
[85] *H. Weiss, H. J. Kolb,* Eur. J. Biochem. *99*, 139 (1979).
[86] *G. von Jagow, H. Schägger, P. Riccio, M. Klingenberg, H. J. Kolb,* Biochim. Biophys. Acta *462*, 549 (1977).
[87] *P. Wingfield, T. Arud, K. Leonard, H. Weiss,* Nature *280*, 696 (1979).
[88] *B. Chance, D. F. Wilson, P. L. Dutton, M. Erecinska,* Proc. Natl. Acad. Sci. USA *66*, 1175 (1970).
[89] *B. Chance,* FEBS Lett. *23*, 3 (1972).
[90] *A. Tzagaloff, G. Macino, W. Sebald,* Annu. Rev. Biochem. *48*, 419 (1979).
[90a] *Th. Bücher et al.:* Biological Chemistry of Organelle Formation. Springer, Berlin, in press.
[91] *A. Tzagaloff* in [90a].
[92] *B. G. Barrell,* private communication.
[93] *T. Pozzan, F. Di Virgilio, M. Bragadin, V. Miconi, G. F. Azzone,* Proc. Natl. Acad. Sci. USA *76*, 2123 (1979).
[94] *P. Mitchell,* FEBS Lett. *56*, 1 (1975).
[95] *P. Mitchell,* FEBS Lett. *59*, 137 (1975).
[96] *G. von Jagow, H. Schägger, W. D. Engel, H. Hackenberg, H. J. Kolb* in [2a], p. 43.
[97] *P. F. Urban, M. Klingenberg,* Eur. J. Biochem. *9*, 519 (1969).
[98] *D. F. Wilson, M. Erecinska, J. S. Leigh, M. Koppelmann,* Arch. Biochem. Biophys. *151*, 112 (1972).
[99] *M. Wikström, K. Krab,* Biochim. Biophys. Acta *549*, 177 (1979).
[100] *W. Stoeckenius, R. H. Lozier, R. A. Bogomolni,* Biochim. Biophys. Acta *505*, 215 (1979).
[101] *J. F. Nagle, H. J. Morowith,* Proc. Natl. Acad. Sci. USA *75*, 298 (1978).
[102] *P. D. Boyer,* FEBS Lett. *58*, 1 (1975).
[103] *A. Fersht:* Enzyme Structure and Mechanism. Freeman, Reading 1977, p. 274.
[104] *B. Chance, A. Waring, C. Saronio* in [2a], p. 56.
[105] *B. G. Malmström,* Biochim. Biophys. Acta *549*, 177 (1979).
[106] *P. Nicholss, B. Chance* in *O. Hayaishi:* Mechanisms of Oxygen Activation. Academic Press, New York 1974, p. 479.
[107] *W. S. Caughey, W. I. Wallace, I. A. Volpe, S. Yoshikawa* in [16a], p. 299.
[108] *G. Buse* in [90a].
[109] *L. S. Powers, W. Blumberg, B. Chance, C. Barlow, J. S. Leigh, J. Smith, T. Yonetani, S. Vik, J. Peisach,* Biochim. Biophys. Acta *546*, 520 (1979).
[110] *M. Wikström, H. J. Harmon, W. J. Ingiedew, B. Chance,* FEBS Lett. *65*, 259 (1976).
[111] *W. Sebald, W. Machleidt, J. Otto,* (1973) Eur. J. Biochem. *38*, 311 (1973).
[112] *G. D. Eytan, G. Schatz,* J. Biol. Chem. *250*, 767 (1975).
[113] *S. Seki, H. Hayashi, T. Oda,* Arch. Biochem. Biophys. *138*, 110 (1970).
[114] *G. Vanderkooi, A. E. Senior, R. A. Capaldi, H. Hayashi,* Biochim. Biophys. Acta *274*, 38 (1972).
[115] *R. Henderson, R. A. Capaldi, J. S. Leigh,* J. Mol. Biol. *112*, 631 (1977).
[116] *S. D. Fuller, R. A. Capaldi, R. Henderson,* J. Mol. Biol. *134*, 305 (1979).
[117] *D. F. Wilson, J. G. Lindsay, E. S. Brocklehurst,* Biochim. Biophys. Acta *256*, 277 (1972).
[118] *M. Wikström,* Nature *266*, 271 (1977).
[119] *M. Wikström,* Biochim. Biophys. Acta *462*, 347 (1977).
[120] *M. Wikström* in *G. F. Azzone et al.:* The Proton and Calcium Pumps. Elsevier/North Holland, Amsterdam 1978, p. 215.
[121] *R. P. Casey, J. B. Chappell, A. Azzi,* Biochem. J. *182*, 149 (1979).
[122] *B. F. van Gelder, J. Rign, G. Schilder, J. Wilms* in [11a], p. 61.
[123] *D. L. Bräutigam, S. Ferguson-Miller, E. Margoliash,* Methods Enzymol. *53*, 128 (1978).
[124] *F. R. Salemne,* Annu. Rev. Biochem. *46*, 299 (1977).
[125] *E. Margoliash, A. Schefter,* Adv. Protein Chem. *21*, 113 (1966).
[126] *M. D. Dayhoff* in: Atlas of Protein Sequence and Structure. Vol. 5 (1972). Suppl. 1 (1973), 2 (1976) and 3 (1978). National Biomedical Research Foundation. Washington, D. C.
[127] *W. M. Fitch, E. Markowitz,* Biochem. Genet. *4*, 579 (1970).
[128] *R. Swanson, B. L. Trus, N. Mandel, G. Mandel, O. B. Kallai, R. E. Dickerson,* J. Biol. Chem. *252*, 759 (1977).
[129] *H. R. Bosshard, M. Zurrer, H. Schägger, G. von Jagow,* Biochem. Biophys. Res. Commun. *89*, 250 (1979).
[130] *S. H. Speck, S. Ferguson-Miller, N. Osterhoff, E. Margoliash,* Proc. Natl. Acad. Sci. USA *76*, 155 (1979).
[131] *R. Riedler, H. R. Bosshard,* J. Biol. Chem. *253*, 6045 (1978).
[132] *R. Rieder, H. R. Bosshard,* FEBS Lett. *92*, 223 (1978).
[133] *T. Takeno, O. B. Kallai, R. Swanson, R. E. Dickerson,* J. Biol. Chem. *248*, 5234 (1973).
[134] *R. Timkovich, R. E. Dickerson, E. Margoliash,* J. Biol. Chem. *251*, 2197 (1975).
[135] *R. Timkovich, R. E. Dickerson,* J. Biol. Chem. *251*, 4033 (1976).
[136] *F. R. Salemne, J. Kraut, M. D. Kamen,* J. Biol. Chem. *248*, 7701 (1973).
[137] *H. L. Hodges, R. A. Holwerda, H. B. Gray,* J. Am. Chem. Soc. *96*, 3132 (1974).
[138] *D. De Vault, B. Chance,* Biophys. J. *6*, 825 (1966).
[139] *J. D. McElroy, D. C. Mauzerall, G. Fehder,* Biochim. Biophys. Acta *333*, 261 (1974).
[140] *M. E. Dockter, A. Steinemann, G. Schatz* in [11a], p. 169.
[141] *J. M. Vanderkooi, R. Landesberg, G. W. Hayden, C. S. Owen,* Eur. J. Biochem. *81*, 339 (1977).
[142] *J. I. Hopfield,* Proc. Natl. Acad. Sci. USA *71*, 3640 (1974).
[143] *D. A. Harris,* Biochim. Biophys. Acta *463*, 245 (1978).
[144] *Y. Kagawa,* Biochim. Biophys. Acta *505*, 45 (1978).
[145] *B. A. Baird, G. G. Hammes,* Biochim. Biophys. Acta *549*, 31 (1979).
[146] *L. M. Amzel, P. L. Pedersen,* J. Biol. Chem. *253*, 2067 (1978).
[147] *J. M. Amzel, P. L. Pedersen,* Methods Enzymol. *55*, 333 (1979).
[148] *A. E. Senior,* Biochemistry *14*, 660 (1975).
[149] *B. A. Baird, G. G. Hammes, J. Biol. Chem. 252*, 4743 (1977).
[150] *H. S. Penefsky,* Methods Enzymol. *55*, 297 (1979).
[151] *M. E. Pullman, H. S. Penefsky, A. Datta, E. Racker,* J. Biol. Chem. *232*, 3322 (1960).
[152] *W. Sebald,* Biochim. Biophys. Acta *463*, 1 (1977).
[153] *R. Serrano, B. I. Kanner, E. Racker,* J. Biol. Chem. *251*, 2453 (1976).
[154] *D. H. Mac Lennon, A. Tzagaloff,* Biochemistry *7*, 1603 (1968).
[155] *A. E. Senior,* Methods Enzymol. *55*, 391 (1979).
[156] *R. J. Van de Stadt, R. J. Kraipoel, K. van Dam,* Biochim. Biophys. Acta *267*, 25 (1972).
[157] *B. I. Kanner, R. Serrano, M. A. Kandrach, E. Racker,* Biochem. Biophys. Res. Commun. *69*, 1050 (1976).
[158] *A. F. Knowles, R. J. Guillory, E. Racker,* J. Biol. Chem. *246*, 2672 (1971).
[159] *A. Vadineann, J. A. Berden, E. C. Slater,* Biochim. Biophys. Acta *449*, 468 (1976).
[160] *M. E. Pullman, G. C. Monroy,* J. Biol. Chem. *238*, 3762 (1963).
[161] *L. L. Horstmann, E. Racker,* J. Biol. Chem. *245*, 1336 (1970).
[162] *E. I. Mileykovskaja, G. V. Tikhanova, A. A. Kondraskin, I. A. Kozlov,* Eur. J. Biochem. *62*, 613 (1976).
[163] *D. H. Mac Lennon, J. Asai,* Biochem. Biophys. Res. Commun. *33*, 441 (1968).
[164] *A. E. Senior,* Biochim. Biophys. Acta *301*, 249 (1973).
[165] *I. A. Kozlov, H. N. Mikelsaar,* FEBS Lett. *43*, 212 (1974).
[166] *E. Racker,* J. Membr. Biol. *10*, 221 (1972).
[167] *E. Racker, L. L. Horstman,* J. Biol. Chem. *242*, 2547 (1967).

[168] *K. J. Catell, C. R. Lindop, I. G. Knight, R. B. Beechey*, Biochem. J. *125*, 169 (1971).
[169] *W. Sebald, W. Machleidt, E. Wachter*, Proc. Natl. Acad. Sci. USA *77*, 785 (1980).
[170] *R. J. Wagenvoord, I. van Der Kraan, A. Kemp*, Biochim. Biophys. Acta *460*, 17 (1977).
[171] *I. Lunardi, G. L. M. Lauquin, P. V. Vignais*, FEBS Lett. *80*, 317 (1977).
[172] *F. S. Esch, W. S. Allison*, J. Biol. Chem. *253*, 6100 (1978).
[173] *A. T. Jagendord, E. Uribe*, Proc. Natl. Acad. Sci. USA *55*, 170 (1966).
[174] *H. T. Witt, E. Schlodder, P. Gräber*, FEBS Lett. *69*, 272 (1976).
[175] *I. A. Kozlow, V. P. Skulachev*, Biochim. Biophys. Acta *463*, 29 (1977).
[176] *P. D. Boyer, B. Chance, L. Ernster, P. Mitchell, E. Racker, E. C. Slater*, Annu. Rev. Biochem. *46*, 955 (1977).
[177] *D. A. Hackney, P. D. Boyer*, J. Biol. Chem. *253*, 3164 (1978).
[178] *Y. Fukushima, Y. Tonomura*, J. Biochem. *77*, 533 (1975).
[179] *A. F. Knowles, E. Racker*, J. Biol. Chem. *250*, 1949 (1975).
[180] *D. R. Trenthan, J. F. Eccleson, C. R. Bagshaw*, Quart. Rev. Biophys. *9*, 217 (1976).
[181] *P. Mitchell, J. Moyle*, Nature *208*, 1205 (1965).
[182] *J. Moyle, P. Mitchell*, FEBS Lett. *30*, 317 (1973).
[183] *W. S. Thayer, P. C. Hinkle*, J. Biol. Chem. *248*, 5395 (1973).
[184] *M. Klingenberg* in *P. N. Campbell, F. Dickens:* Essay in Biochemistry, Vol. 6. Academic Press, New York 1970, p. 119.
[185] *M. Klingenberg* in [22a], Vol. 3, p. 383.
[186] *P. V. Vignais*, Biochim. Biophys. Acta *456*, 1 (1976).
[187] *P. Riccio, H. Aquila, M. Klingenberg*, FEBS Lett. *56*, 129 (1975).
[188] *H. Hackenberg, M. Klingenberg*, Biochemistry *19*, 548 (1980).
[189] *M. Klingenberg, M. Buchholz*, Eur. J. Biochem. *38*, 346 (1973).
[190] *E. Pfaff, M. Klingenberg, H. W. Heldt*, Biochim. Biophys. Acta *104*, 312 (1965).
[191] *M. J. Weidemann, H. Erdelt, M. Klingenberg*, Eur. J. Biochem. *16*, 313 (1970).
[192] *M. Klingenberg, M. Buchholz*, Eur. J. Biochem. *38*, 346 (1973).
[193] *M. Klingenberg* in *L. Ernster et al.:* Dynamics of Energy Transducing Membranes. Elsevier, Amsterdam 1974, p. 511.
[194] *E. Pfaff, M. Klingenberg*, Eur. J. Biochem. *6*, 66 (1968).
[195] *M. Klingenberg*, Trends in Biochem. Sci., Nov. 1979, p. 1.
[196] *R. Krämer, M. Klingenberg*, FEBS Lett. *82*, 363 (1977).
[197] *R. Krämer, M. Klingenberg*, Biochemistry *19*, 556 (1980).
[198] *R. N. Johnson, J. B. Chappell*, Biochem. J. *134*, 769 (1973).
[199] *W. A. Coty, P. L. Pedersen*, J. Biol. Chem. *249*, 2593 (1974).
[200] *A. Fonyo, E. Ligeti, F. Palmieri, E. Quagliariello* in: Biomembranes. Structure and Function. Elsevier - North-Holland, Amsterdam 1975, p. 287.
[201] *W. A. Cory, P. L. Pedersen*, J. Biol. Chem. *250*, 3515 (1975).
[202] *P. Hadvary, B. Kadenbach*, Eur. J. Biochem. *67*, 573 (1976).
[203] *S. Touraille, Y. Briand, R. Durand*, FEBS Lett. *84*, 119 (1977).
[204] *J. D. McGivan, M. Klingenberg*, Eur. J. Biochem. *20*, 392 (1971).
[205] *A. Alexandre, A. L. Lehninger*, J. Biol. Chem. *254*, 11555 (1979).
[206] *T. Pozzan, V. Miconi, F. Di Virgilio, G. F. Azzone*, J. Biol. Chem. *254*, 10200 (1979).
[207] *G. F. Azzone, T. Pozzan, F. Di Virgilio*, J. Biol. Chem. *254*, 10206 (1979).
[208] *G. A. Azzone, T. Pozzan, M. Bragadin, V. Miconi*, J. Biol. Chem. *254*, 10213 (1979).
[209] *H. Rottenberg, M. Gutman*, Biochemistry *16*, 3220 (1977).
[210] *C. M. Sorgato, S. L. Ferguson, D. B. Kell, P. John*, Biochem. J. *174*, 237 (1978).
[211] *J. Himms-Hagen*, Annu. Rev. Physiol. *38*, 315 (1976).
[212] *D. G. Nicholls*, Biochim. Biophys. Acta *549*, 1 (1979).
[213] *D. G. Nicholls*, Eur. J. Biochem. *50*, 305 (1974).
[214] *J. Rafael* in *L. Girardier, J. Seydoux:* Effectors of Thermogenesis. Birkhäuser, Basel 1978, p. 25.
[215] *B. A. Afzelius* in *O. Lindberg:* Brown Adipose Tissue. Elsevier, Amsterdam 1970, p. 1.
[216] *C. S. Lin, M. Klingenberg*, FEBS Lett. *113*, 299 (1980); *C. S. Lin, H. Hakkenberg, M. Klingenberg*, FEBS Lett. *113*, 304 (1980).
[217] *H. J. Hohorst, J. Rafael*, Hoppe-Seylers Z. Physiol. Chem. *349*, 268 (1968).
[218] *J. Rafael, H. J. Ludolph, H. J. Hohorst*, Hoppe-Seylers Z. Physiol. Chem. *350*, 1121 (1969).
[219] *G. M. Heaton, D. G. Nicholls*, Biochem. Soc. Trans. *5*, 210 (1977).
[220] *L. Ernster*, Annu. Rev. Biochem. *46*, 955 (1977); *P. P. Slonimski* in [90a].
[221] *P. N. T. Unwin, R. Henderson*, J. Mol. Biol. *94*, 425 (1975).
[222] *R. Henderson, J. S. Judds, S. Whytock*, J. Mol. Biol. *123*, 259 (1978).

Photophysical and Photochemical Processes in Micellar Systems

By Nicholas J. Turro, Michael Grätzel, and André M. Braun[*]

A fascinating feature inherent to aqueous surfactant solutions is the phenomenon of self-organization: above a certain critical concentration (the critical micelle concentration, CMC) detergent molecules associate spontaneously to build up structural entities of colloidal dimensions called micelles. The architecture of these agglomerates is such that the interior contains the hydrophobic alkyl chain of the amphiphile while the hydrophilic head groups are located at the surface and are in contact with bulk water. In the case of ionic micelles the interface is charged giving rise to an electrical double layer and a potential difference of up to several hundred millivolts between the micellar pseudophase and water. Thus micellar systems are microheterogeneous in character: the electrostatic potential and polarity prevailing in the interior of the aggregate differ from those of the bulk aqueous phase. A particularly attractive aspect of photochemical studies in micellar systems is the possibility of organizing the reactants at a molecular level: by comparison of the data in micelles with similar data in homogeneous solution one can learn about the molecular details of a given reaction and establish which conditions favor one pathway or another. In simple surfactant systems differences in rate and efficiency of a reaction will often be controlled by local electrostatic potentials and the compartmentalization of the reagents within the surfactant aggregates. Through the latter effect the statistics of probe distribution over the micelles becomes important in controlling fast photochemical events. Functional micelles are distinguished by the fact that the surfactant molecule contains a group which itself participates in the photoprocess. These units are unique in that self-assembly often introduces striking cooperative effects.

[*] Prof. Dr. N. J. Turro
Department of Chemistry, Columbia University
New York, N. Y. 10027 (USA)
Prof. Dr. M. Grätzel, Priv.-Doz. Dr. A. M. Braun
Institut de Chimie Physique, Ecole Polytechnique Fédérale Ecublens,
CH-1015 Lausanne (Switzerland)

1. Introduction

The objectives of this article are to review the conventional model of micelles formed by ionic detergents in aqueous solution and to show how photoluminescence methods provide

information on the compositional, structural and dynamic characteristics of such micelles. We demonstrate how photoluminescence and photochemical probes may serve both as valuable sensors of micellar structure and microenvironments and as reporters of solute partitioning. Furthermore, we will show that photophysical and photochemical reactions in micellar systems may differ significantly from analogous reactions in homogeneous solution[1].

2. Luminescence Probes

A *chromophore* is an atom or group of atoms that may be conveniently considered as a unit which *absorbs* visible or ultraviolet light. A *lumophore* is an atom or group of atoms that may be conveniently viewed as a unit which *emits* visible or ultraviolet light. For example, aromatic hydrocarbons behave as lumophores, as do ketone groups. There are two commonly encountered luminescences: *fluorescence* and *phosphorescence*. Fluorescence is generally associated with the emission of light accompanying the transition of excited singlet states to the ground state and phosphorescence is generally associated with the emission of light from the lowest triplet state to the ground state (Fig. 1).

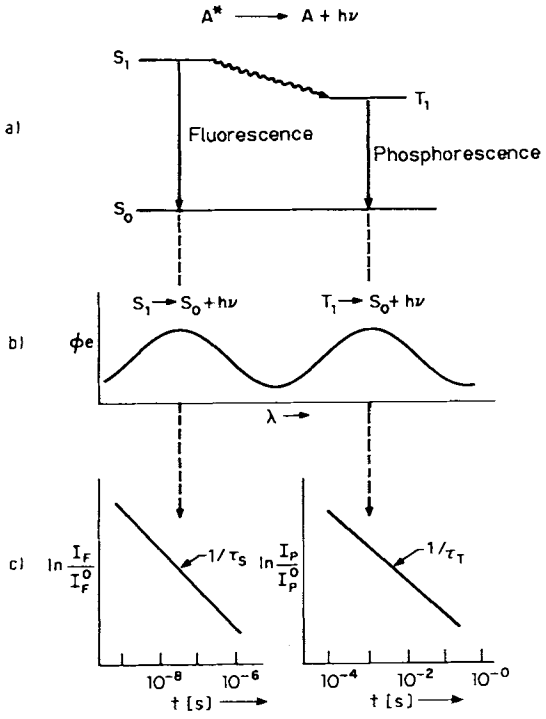


Fig. 1. a) The conventional "three level energy diagram" depicting the luminescent states of an organic molecule. Emission from the excited singlet state (S_1) is termed *fluorescence* whereas emission from the triplet state (T_1) is termed *phosphorescence*. b) Fluorescence bands generally occur at higher energies (shorter λ) than phosphorescence bands. c) Fluorescence decay is usually much shorter lived (τ_S) than phosphorescence decay (τ_T).

A *luminescent probe* is any molecule or group of atoms whose luminescent properties may serve to explore and examine the structural and dynamic features of systems of interest. Thus there exist *fluorescence probes* and *phosphorescence probes*. In order to be effective, a property of a luminescent probe must change and be measurable when the probe is added to the test system. The general idea behind a luminescence probe is that luminescence parameters are sensitive to changes in the microenvironment of the probe and that a luminescence probe in different microenvironments will display experimentally distinct luminescence properties which will characterize uniquely each environment.

2.1. Measurable Properties of Luminescent Probes

The readily measured quantities derived from the emission of lumophores are: (1) Emission spectrum (intensity of emission as a function of wavelength for a fixed absorbed intensity and fixed excitation wavelength). (2) Excitation spectrum (intensity of emission at fixed wavelength as function of absorbed intensity and variable excitation wavelength). (3) Luminescence decay (fall-off of the intensity of the emission spectrum as a function of time after an excitation pulse). (4) Quantum yield of luminescence (the number of photons emitted relative to the number of photons absorbed). (5) Polarization of luminescence (the orientation of the emitted light vector relative to the orientation of the absorbed light vector). (6) Quenching (a decrease in luminescence intensity or increase in decay rate as a function of added solute or changing environment). (7) Sensitization (an increase in luminescence intensity or decrease in decay rate as a function of added solute or changing environment). (8) Energy transfer (electronic excitation transferred from an initially excited lumophore to a second lumophore).

Each of the above quantities has been employed to measure properties of micellar aggregates.

3. Luminescence Probes as Sensors and Reporters of Microenvironments

Luminescence probes may be thought of a "sensors" of microenvironments. The photons emitted by such probes are "reporters" of the local structure in the vicinity of the probe at the time of emission. The emitted photons may be employed to "read back" a *map* of the microenvironment of the probe. In this mode, the probe serves as a *clock* of molecular dynamics of its environment (Fig. 2).

Luminescent probes provide the greatest degree of information for characterization of microenvironments when the probe exhibits a strong and selective affinity for a given environmental site or if, when it is distributed among distinct sites (*e.g.*, micellar environment and bulk aqueous solution), the measurable luminescence properties are distinctly different. For example, if the emission spectrum, the excitation spectrum, the decay time, the quantum yield of emission, the polarization of luminescence, or the quenching (or sensitization) of emission is environment dependent, the luminescence probe can be employed to characterize the environment. The effective use of luminescence probes requires a detailed knowledge of the nature of radiative and radiationless transitions and of the mechanisms of excited state interactions with different environments.

The "structure" examined by a luminescent probe may be of a "local" nature (*i.e.*, the immediate microenvironment of the probe) or of a more "expanded" nature (*i.e.*, the secondary or tertiary environmental characteristics).

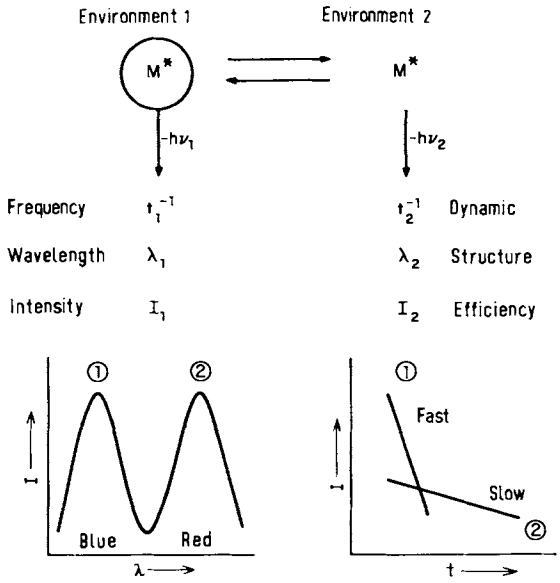


Fig. 2. Schematic representation of a luminescent probe (M*) in two environments. If the luminescence of M* (either fluorescence or phosphorescence) is different in decay time, wavelength, or intensity, a means of gaining information on the structure and dynamics of the probe and/or its environment is available. For example, suppose the emission of M* is "blue" and "fast" in a hydrophobic (say a micellar) environment and is "red" and "slow" in an aqueous environment, then a means of examining the two environments is available.

The measured changes in a luminescent probe have been related to molecular properties of the environment of the probe such as: (1) Polarity; (2) viscosity; (3) diffusion; (4) partitioning between phases; (5) concentration of quenchers; and (6) distance between groups.

The "dynamic range" of luminescence probes spans 13 orders of magnitude! Decay rates of fluorescence commonly range from $10^5\ s^{-1}$ to $10^9\ s^{-1}$ and those of phosphorescence range from $10^{-1}\ s^{-1}$ to $10^3\ s^{-1}$. Since quantum yields of emission of 10^{-3} are readily measured, the effective experimental dynamic range of fluorescence is $10^6\ s^{-1}$ to $10^{12}\ s^{-1}$ and that of phosphorescence is 10^{-1} to $10^6\ s^{-1}$. Thus there is a continuum for a potential dynamic measurement for the range $10^{-1}\ s^{-1}$ to $10^{12}\ s^{-1}$ (Fig. 3).

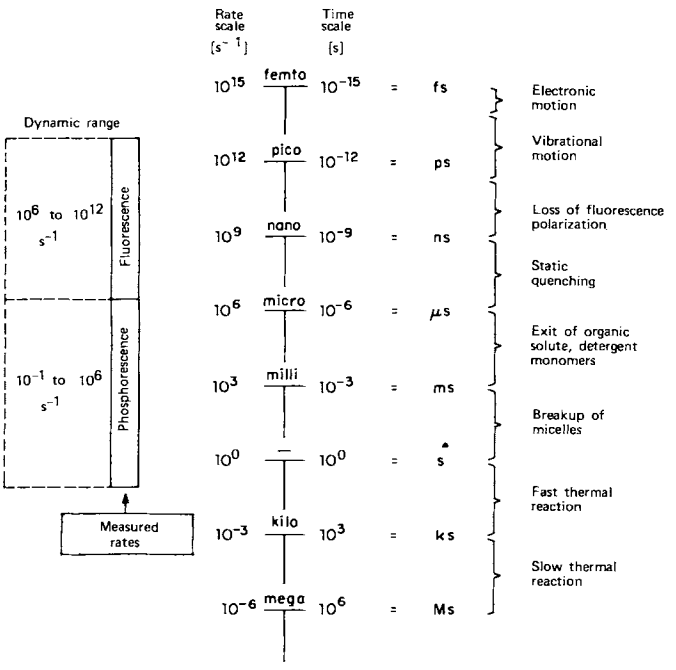


Fig. 3. The "dynamic range" of luminescence probes.

It should be stated that one difficulty must always be considered when interpreting results derived from the use of luminescence probes: the probe of necessity is a "foreign body" in the environment that is being probed. It is therefore crucial to provide independent evidence that the probe does not change the inherent quality of the measured property. For example, in the case of micellar systems, it must be established whether the association of the probe in the system causes a fundamental change in the nature of the "native" micelle. With the recognition that it is usually more desirable to use a direct spectroscopic measurement of some intrinsic property of a system, it is commonly not feasible to do so. If we view the utilization of probes as an exercise in information acquisition and in the strategy of experimental design, luminescence probes and methods may be profitably employed.

3.1. Fluorescence/Phosphorescence Probes

Fluorescence probes are probably the best known of all luminescent probes, and have been employed widely in the study of structure and dynamics of many systems. Fluorescence methods are often outstanding in terms of sensitivity and selectivity for the investigation of chemical and physical dynamic processes that occur on the time scale of 0.1–1000 ns. Processes such as rotational and diffusional motion, solvent reorganization, and energy transfer often occur in this time domain and have been investigated by means of fluorescence probes.

In contrast to the extensive use of fluorescence probes, just a few scattered cases have been reported in which phosphorescence probes were employed to investigate structure or dynamics in fluid solution (see Section 6). This is indeed unfortunate since a wealth of molecular information is potentially available from phosphorescence spectroscopy. The absence of literature on phosphorescence probes does not result from the lack of potential usefulness of such molecules, but more likely resides in the "conventional wisdom" that organic molecules do not phosphoresce in fluid solution or that the observation of phosphorescence in fluid solution requires very special (or exotic) solvents, elaborate purification procedures, and sophisticated, specially designed and ultrasensitive detection equipment. Since nearly all measurements of phosphorescence have been performed in rigid glasses at low temperatures, the general belief has arisen that such conditions are required for the observation of phosphorescence in solution.

"Conventional wisdom" is quite inappropriate for micellar systems. For instance, we shall see that the phosphorescences of simple organic molecules are readily observed in micellar solutions.

Indeed, both fluorescence and phosphorescence may be observed for the same molecule. Since the dynamic range of fluorescence is in the 10^{-11} to 10^{-6} s range and that of phosphorescence is in the 10^{-6} to 10 s range, the combination of fluorescence and phosphorescence probes allows (potentially) scanning of a dynamic range of 10^{13}!

4. Aqueous Solutions of Detergents and Micelles

A surfactant (surface active material) or detergent is a molecule that possesses both polar (or ionic) and nonpolar moieties, *i.e.*, they are "amphiphilic" or "amphiphatic" species[1b]. This property imbues detergents with a sort of molecular schizophrenia and causes aqueous solutions of detergents to exhibit a number of important and unusual properties. A typical detergent structure is RX where R is a straight chain hydrocarbon of 8—18 carbon atoms or some other hydrophobic residue, and X is a hydrophilic group. Depending on the nature of X, detergents may be classified as (a) nonionic, (b) cationic, R^+X^-, or (c) anionic, R^-X^+. Typical examples of ionic detergents are listed in Figure 4. In aqueous

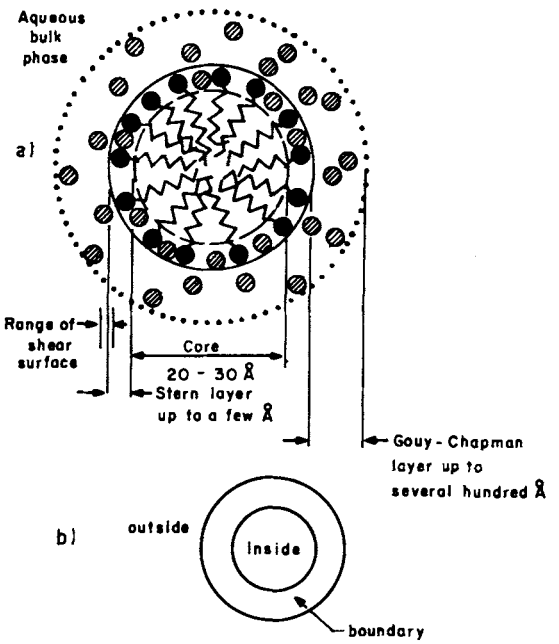


Fig. 4. a) Conventional representation of the micelles formed by an ionic detergent. Although represented as spherical, the instantaneous or even the average shape may be ellipsoid or irregular. The "topological" shape (b) is preserved, however. The "inside" or "core" of the micelle consists of the hydrocarbon "tails" of the detergent molecules. The "boundary" or Stern layer consists of the detergent "head" groups and bound gegenions. The immediate "outside" or Gouy-Chapman region is a diffuse double layer containing unbound gegenions. Typical ionic detergents are n-$C_{12}H_{25}OSO_3^{\ominus}Na^{\oplus}$ (SLS) and n-$C_{16}H_{33}N^{\oplus}(CH_3)_3Br^{\ominus}$ (CTAB) and the corresponding chloride (CTAC).

solutions the polar portion of the detergent is hydrophilic and the nonpolar portion is hydrophobic. The result of these conflicting chemical features is a tendency for cooperative self-association of detergent monomers to form aggregates. For example, the addition of detergent to water often results in formation of solutions that contain association colloids. The term *micelle* refers to such aggregates of colloidal dimensions, and implies a situation in which these aggregates are in a mobile equilibrium with the molecules or ions from which they are formed. It is commonly observed that there is a relatively small range of concentrations below which micelles are absent or present in very low concentrations and above which virtually all the detergent molecules exist as micelles. The "relatively small range of concentrations" defines a *"critical micelle concentration"* or CMC, which may be extracted from an experimental plot of some observable property *versus* detergent concentration.

In aqueous solution detergent molecules (Fig. 4) such as sodium dodecyl sulfate (SLS) or hexadecyl(trimethyl)ammonium bromide (CTAB) form micelles above a certain concentration (strictly speaking over a small range of concentrations), *i.e.* their *critical micelle concentration.* Depending on the temperature, concentration, and other experimental variables, the micelles may be roughly spherical, ellipsoidal, disk-like, or rod shaped (Fig. 5). The charged sulfate or ammonium head groups are directed toward the aqueous phase and the hydrocarbon chains are directed away from the water and the micellar "boundary", which separates the hydrophobic inferior from the bulk aqueous phase. This region is a diffuse double layer (Gouy-Chapman) containing unbound counterions.

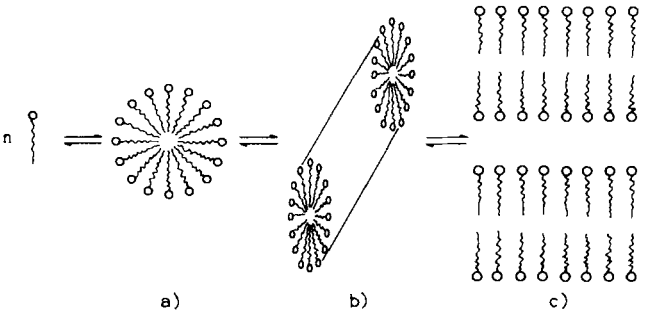


Fig. 5. A schematic representation of the conversion of detergents into (a) "spherical" micelles (recall Fig. 4), (b) "rod-shaped" micelles, and (c) bilayers.

Given this (oversimplified) model, a number of questions, both qualitative and quantitative, arise concerning the structure and dynamics of micellar aggregates. For example, how hydrocarbon-like is the interior, *i.e.*, how viscous, how nonpolar?

Micelles are responsible for many of the practical applications of detergents, such as enhancement of solubility of organic compounds in water and catalysis of organic reactions. Furthermore, in recent years micelles have been proposed as simple model systems for a variety of important "two phase" systems such as monolayers, colloids, proteins, enzymes, and membranes[1f]. Among the primary reasons for the usefulness of micelles as models are: (a) the thermodynamic stability and reproducibility of many micellar systems; (b) the simplicity of the structure of the micelle; (c) the two-phase nature of the micelle; (d) the ionic composition of many micelle surfaces.

For instance, the micelle aqueous interface incorporates features of electrical double layers, and may be typical of other interfacial systems such as membranes. The importance of micelles and mixed micelles in the transport and absorption of lipids as solubilizers in physiological systems has been pointed out[1f]. For example, the mobile monomer-micelle equilibrium may serve as a general model for hydrophobic interactions, a problem of central interest in biology. The most fundamental or topological features of a chemical system are those which are qualitatively preserved over a variety of specific conditions. These topological features are generally definable in terms of structural and dynamic characteristics. It is important to understand and to elucidate the

topological features of a system because it is precisely these features which are generally transferred from a model system to a system of interest.

For instance, the topological features of micelles (cf. Fig. 4 and 5) that are of major interest for *structural* comparison with biomolecules (*e.g.*, membranes) include: (a) the fact that a micelle has an inside, an outside, and a boundary; (b) the fact that the inside is hydrophobic, the outside is hydrophilic; (c) the fact that the micellar boundary is fluid (in the sense that it is undulating with time and not rigid) and possesses a finite (although not necessarily fixed) thickness; (d) the fact that the composition of the micelle (aggregation number) is fairly well defined; (e) the fact that molecules may be sequestered and organized in the micelle interior or on (or in) the micellar boundary.

Micelle formation may be viewed as a thermodynamic analogue of a phase separation with the CMC corresponding to a saturation concentration. Of course, the micelles differ from a macrophase separation in that they do not coalesce into a continuous phase at the CMC, but instead they are uniformly distributed in the bulk aqueous phase and form a "pseudophase".

The topological features of micelles that are of major importance for *dynamic* comparisons with biomolecules include: (a) the detailed mechanism of monomer-micelle equilibrium; (b) the influence of experimental variables (temperature, detergent concentration, presence of solutes, *etc.*) on this equilibrium; (c) the detailed mechanism of entrance and exit of solute molecules into and out of a micelle, *i.e.*, the mechanism by which a solute penetrates the barrier.

The actual quantitative rates of steps involved in the monomer equilibrium and of solute movement in and out of a micelle are important for calibration and for the experimental establishment of plausible limits for dynamic processes involving micelles.

5. Location and Orientation of Organic Molecules Solubilized in Micelles

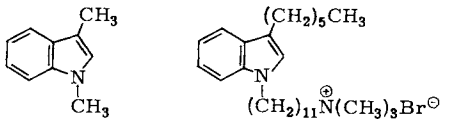
An organic molecule, solubilized in water by addition of detergent, evidently interacts with a micelle in some fashion. The question arises as to the nature of the interaction, as to the location and/or orientation of the solute with respect to the micelle.

For example, a completely non-polar solute (a) may be located, on the average, completely "inside" the hydrophobic core of the micelle, (b) may be absorbed on the surface of the micelle, or (c) may penetrate to a particular depth into the surface layer. An amphiphilic solute may be oriented with its polar portion in the surface layer and its non-polar portion in the hydrophobic core. Each situation possesses possible features with respect to "local" dynamics of the solute (*e.g.*, rotational motion) and "transport" dynamics of the solution (*e.g.*, diffusional motion within the micelle or on the surface, translational motion "inside and outside" of the micelle, *etc.*).

5.1. Functionalized Micelles as Luminescence Probes

Instead of incorporating a "guest" luminescence probe into a "host" micelle, it is possible to synthesize detergents that possess a luminescence probe as an integral part of their structure.

The indole lumophore shows significant solvent sensitivity. For example, 1,3-dimethylindole *(1a)* shows fluorescent maxima at 305 nm and 370 nm in cyclohexane and water, respectively[2]. Its fluorescence lifetime is also strongly solvent dependent (4×10^{-9} s and 16×10^{-9} s in cyclohexane and water, respectively).



(1a) *(1b)*

A survey of 1,3-dialkylindoles indicated that these compounds are associated with micelles from CTAB and CTAC (Fig. 6) but that they tend to remain close to the ionic interface. However, the indole detergent *(1b)* was found to be incorporated in micelles of CTAB and also form its own micelles (Fig. 7). Furthermore, *(1b)* shows a dramatic shift in its fluorescence maximum as it passes through the fluorescence lifetime of *(1b)* in both a micellar environment and in bulk aqueous solution. It is found that: (a) the fluorescence maximum of *(1b)* occurs at ≈ 370 nm in an aqueous environment and at ≈ 350 nm in a micellar environment. (b) The fluorescence lifetime of *(1b)* is $\approx 6 \times 10^{-9}$ s and $\approx 18 \times 10^{-9}$ s in a micellar and in an aqueous environment, respectively.

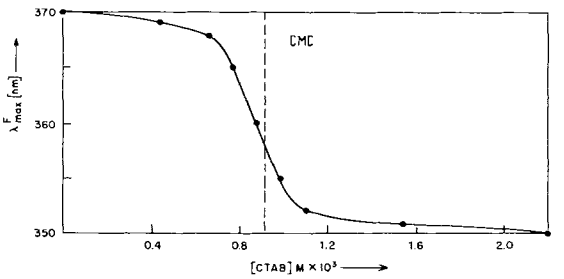


Fig. 6. Fluorescence maximum of *(1b)* as a function of the concentration of detergent *(1b)*. The concentration of *(1b)* is kept constant and the concentration of CTAB is varied. CMC = critical micelle concentration.

Wavelength-correlated single photon counting has been employed to resolve the two emissions of *(1b)* under conditions such that the molecule is partially in a micellar and partially in an aqueous environment (Fig. 8). The relative inten-

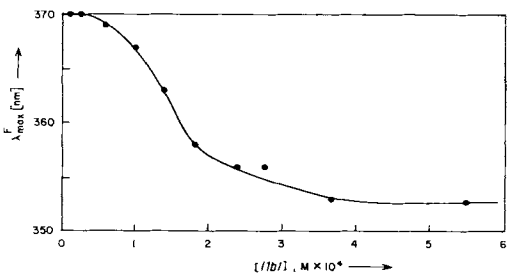


Fig. 7. See Fig. 6; the concentration of *(1b)* alone is varied.

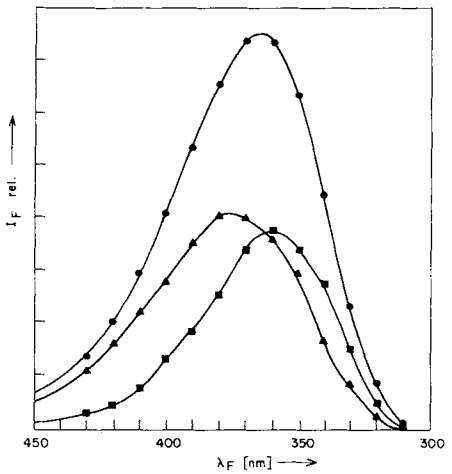


Fig. 8. Time-resolved fluorescence spectra (see Fig. 2) of aqueous *(1b)* at its CMC. ●, total spectrum; ▲, aqueous phase, $\tau_F = 18.0$ ns; ■, micellar, τ_F (micelle) = 6.6 ns.

sities of these emissions correlate qualitatively with the expected proportion of micellized surfactant as the surfactant concentration is increased beyond the CMC.

6. Phosphorescence in Micellar Solutions

An outstanding example of "micellar protection" of an excited molecule is available in the ready observation of phosphorescence from micellar solutions. The main deactivation pathways of organic triplets in homogeneous solutions usually involve quenching by impurities, by "self-quenching", or by triplet-triplet annihilation. At low occupancy numbers, *i.e.*, $\langle S \rangle < 0.1$ (for a definition and discussion of occupancy number, $\langle S \rangle$, see eq. (1), below), triplets may become virtually immune to deactivation, self-quenching, and triplet-triplet annihilation. Furthermore, oxygen molecules, well-known, ubiquitous and powerful triplet quenchers, are solubilized selectively into the micellar environment. For a micelle concentration of 10^{-3} M and an oxygen concentration of $\approx 10^{-4}$ M, $\langle O_2 \rangle = 0.1$, 90% of the micelles will be free of oxygen; thus, triplets which are formed in such micelles will be "protected" from oxygen quenching and display an enhanced phosphorescence. For example, the phosphorescence of 1-bromonaphthalene *(2)* in micelle solution is shown in Fig. 9[3].

"Functionalization" of SDS micelles by "heavy atom" gegenions (Ag^+, Tl^+) allows the observation of phosphorescence of aromatic hydrocarbons such as naphthalene and pyrene[4]. The "heavy atom" serves to enhance the radiative rate of triplets without a comparable enhancement of triplet quenching. The result is an enhanced quantum yield of phosphorescence. Figure 10 shows the emission spectrum of

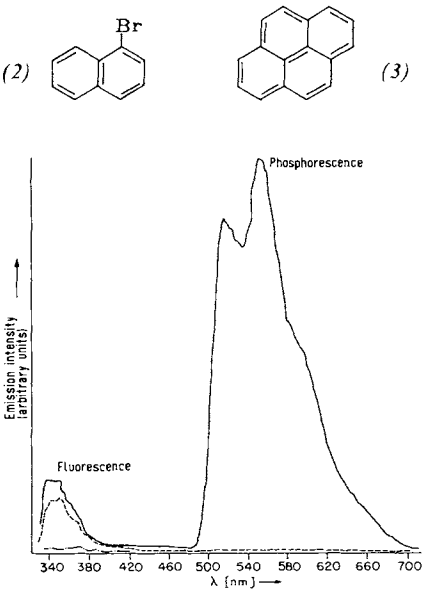


Fig. 9. Phosphorescence spectrum in micellar solution. Total emission of a 10^{-3} M solution of 1-bromonaphthalene *(2)* in aqueous solutions of 0.05 M CTAB. Below the CMC the phosphorescence of *(2)* in aqueous solution is not detectable. —, N_2-bubbled; – – –, aerated; – · – aerated (without CTAB).

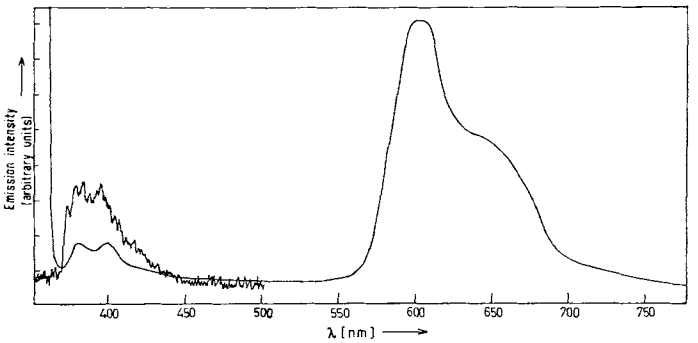


Fig. 10. Emission spectrum of pyrene *(3)*, 5×10^{-5} M in aqueous 5×10^{-2} M AgDS solution; insert: optimal sensitivity for fluorescence (AgDS = silver decyl sulfate).

pyrene *(3)* in 5×10^{-2} M AgDS solution. The fluorescence, though normally strong, is here barely visible, the spectrum being dominated by the strong phosphorescence peak with a maximum at 600 nm[4b].

7. Luminescence Probes of Microviscosity

The fluidity of the environment of a probe molecule that is associated with a micelle may differ substantially from that of the bulk aqueous phase. Thus, the "microviscosity" experienced by the probe molecule may be considerably different from the macroscopic viscosity of the micellar solution. Luminescence probes may serve to measure microviscosity since numerous quantities such as the loss of luminescence polarization, the efficiency of excimer formation, and the efficiency of quenching should depend on the magnitude of the microviscosity experienced by the probe.

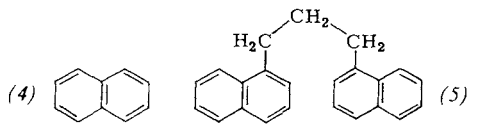
The depolarization of fluorescence from solubilized probes provides information concerning the probe mobility[5]. In homogeneous solutions the extent of loss of depolarization may be quantitatively related to the macroscopic viscosity of the solvent. Likewise, one can associate the extent of loss of polarization of a micellized probe with the microviscosity experienced by the probe. For the typical micelles formed from SLS and CTAB, the measured microviscosities near room temperature are about 15—30 cP[5]. These values can be compared to the 1—2 cP values of viscosities of typical hydrocarbons and pure water.

Although microviscosities may also be determined by intermolecular excimer formation[6], the analysis for micellar systems requires the use of Poisson statistics[7]. This complication may be circumvented by employing intramolecular excimer formation as a probe of microviscosity. Experimentally, the ratio of intensities of monomer to excimer emission (I_m/I_x) for several diarylalkanes are known to be viscosity dependent in homogeneous solution[8]. Comparison of the value I_m/I_x found in micellar solution with that found in homogeneous solution leads to an evaluation of microscopic viscosity. The values obtained are in good agreement with each other and with the values obtained from fluorescence depolarization. An exception is found in the case of 1,3-diphenylpropane as a probe[8c]. This result is interpreted to result from a different location of the smaller probe relative to the larger probes.

8. Naphthalene Fluorescence as a Luminescence Probe for Solute Partitioning

Depending on the time constant associated with luminescence decay and the exit and entrance rates associated with solute partitioning between micellar and aqueous environment, the luminescence quantities measured may represent an "instantaneous snapshot" or a "time-averaged snapshot" of the solute-micelle system. From the time scales listed in Figure 3 hydrophobic fluorescence probes of micelles will generally fall into the "instantaneous snapshot" category. This means that on the time scale for fluorescence (≈ 1—100 ns), micelles form physically discrete cells among which the solute molecules can distribute themselves. In this limit, excited probe molecules report, *via* their fluorescence, the micellar/aqueous partitioning of ground state probe molecules, *i.e.*, since probe fluorescence is faster than probe exit or entrance rates, emission reflects the initial, ground state distribution.

As discussed above, in order to be of practical use the fluorescence probe must show some measurable difference in micellar and aqueous environment. The absorption characteristics and the spectral distribution of naphthalene fluorescence are not significantly modified upon proceeding from an



aqueous to a micellar environment. However, for dilute ($<10^{-4}$ M) solutions of naphthalene *(4)* the fluorescence lifetime shows clear evidence of a two-component decay for solutions near the CMC of CTAB (Fig. 11)[8a]. The long-lived decay ($\tau_F \approx 35$ ns) is assigned to naphthalene molecules dissolved in the bulk aqueous phase and the short-lived decay ($\tau_F \approx 18$ ns) is assigned to naphthalene molecules associated with micelles. The shortening of the fluorescence lifetime in the latter environment is due to enhanced quenching of naphthalene singlets by $Br^{\ominus}$ gegenions in the Stern layer of CTAB micelles[9].

At higher concentrations of naphthalene ($>10^{-3}$ M) the fluorescence decay characteristics become more complex and the spectral distribution of fluorescence reveals evidence of naphthalene excimer emission (Fig. 12a). The dynamics of excimer formation are related to the viscosity of the medium in which excimer formation occurs. However, for the situation in which excimer formation is fast relative to entrance and exit times, the statistical distribution of solutes among the micelles must be considered in any quantitative treatment[10]. It has been found that Poisson statistics are appropriate for this distribution. Poisson statistics assume that the probability of a solute molecule going into a micelle does not depend on whether the micelle already contains a solute or not.

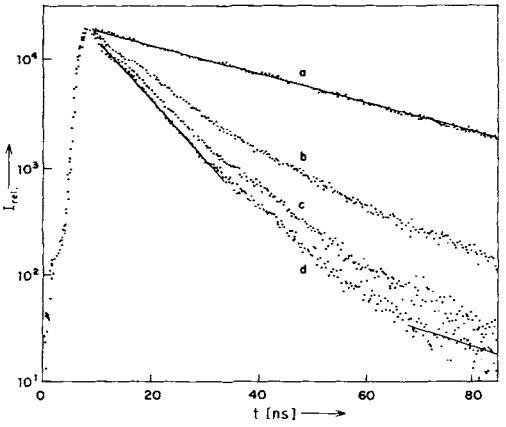


Fig. 11. Time-correlated emission of naphthalene *(4)* (3.9×10^{-3} M) in CTAB; $\lambda = 325$ nm; 20 °C. a) Water (saturated solution), b) 0.02 M CTAB, c) 0.05 M CTAB, d) 0.20 M CTAB.

Poisson statistics lead to a distribution of solutes that is given by

$$P(n) = \frac{\langle S \rangle^n}{n!} \exp(-\langle S \rangle) \qquad (1)$$

where $P(n)$ is the probability of finding a micelle containing n solute molecules and $\langle S \rangle$ is the "mean occupancy number" or the ratio of the bulk concentration of solute molecules to the bulk concentration of micelles. For easy visualization, Poisson statistics for partitioning of solutes in micelles is analogous to the completely random partitioning of "marbles in boxes", under conditions such that the probability that entry of a marble into a given box is independent of the number of marbles already in the box. Realistically, in analyzing micellar dynamics, Poisson statistics will not hold for very large values of $\langle S \rangle$, *i.e.*, the size of the micelle is finite and the inclusion of too many solute molecules will eventually cause gross disturbances of the micellar characteristics.

Table 1. Poisson distribution of solute molecules at various values of $\langle S \rangle$.

$\langle S \rangle$ ⟶	0.1	0.5	1.0	2.0
$P(0)$	0.90	0.61	0.37	0.13
$P(1)$	0.09	0.30	0.37	0.27
$P(2)$	0.00	0.06	0.18	0.27
$P(3)$	0.00	0.01	0.05	0.18
$P(4)$	0.00	0.00	0.00	0.04

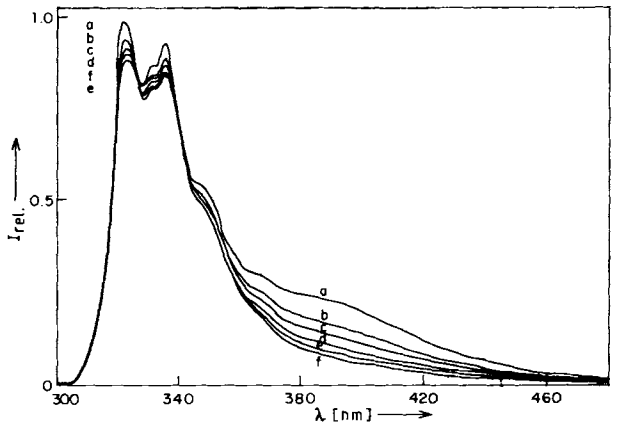


Fig. 12a. Dependence of the luminescence spectrum of naphthalene *(4)* in CTAC (2.7×10^{-3} M) on temperature. a) 2 °C, b) 10 °C, c) 22 °C, d) 30 °C, e) 40 °C, f) 55 °C.

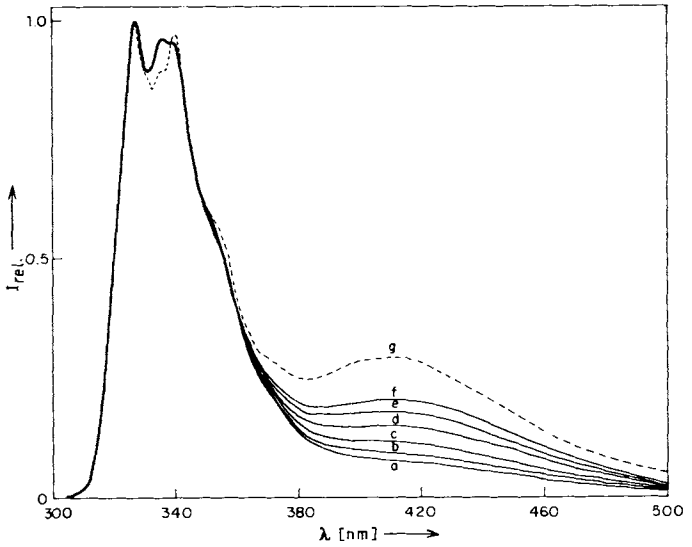


Fig. 12b. Dependence of the luminescence spectrum of 1,3-di-α-naphthylpropane *(5)* in CTAB (1.6×10^{-4} M) on temperature. a) 2 °C, b) 10 °C, c) 22 °C, d) 30 °C, e) 40 °C, f) 55 °C, g) *(5)* in hexane at 22 °C.

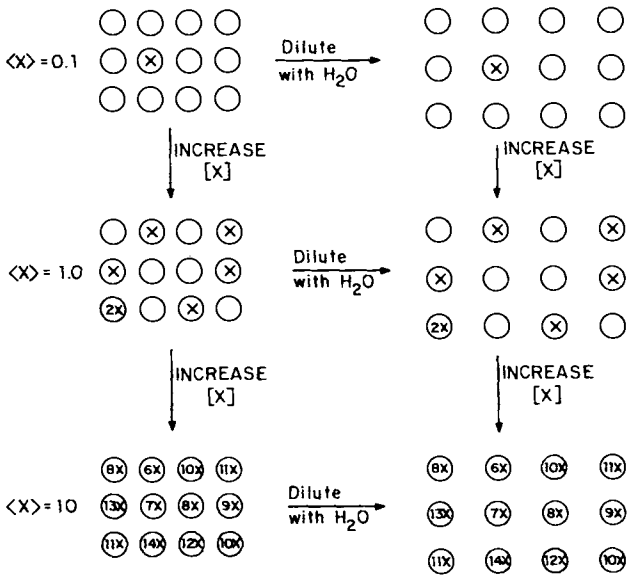


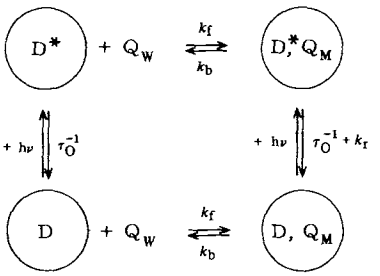
Fig. 13. Schematic representation of dilution (above the CMC) and increasing occupancy number (above the CMC) on solutes in micelles.

Table 1 lists some values of $P(n)$ for various values of $\langle S \rangle$. Notice that when $\langle S \rangle = 0.1$, most of the micelles are "empty" at any given instant, *i.e.*, less than 10% of the micelles contain one or more solute molecules. Even when $\langle S \rangle = 1.0$ (*i.e.*, equal concentration of solute and micelle) 37% of the micelles are empty and 63% will contain two or more solutes.

In Figure 13, an interesting feature of the dilution of micelles is shown. As long as the system is above the CMC, dilution preserves the number of micelles and serves only to separate them in space. This slows down the rate of "collisions" between micelles and the rate of exchange of solutes between micelles. The dilution procedure offers a simple method of distinguishing intramicellar events from intermicellar events.

9. Photoluminescence Quenching. Evaluation of Partition Coefficients, Aggregation Numbers, Entrance and Exit Rates

The use of Poisson statistics to describe the distribution of solute molecules among micellar aggregates allows derivation of relations which allow luminescence quenching to serve as a means for evaluating important micellar parameters[10]. For the commonly encountered case of a hydrophobic luminescence probe (donor D) which is completely micellized (Scheme 1), so that quenching occurs exclusively in the micellar environment, the following general expression for luminescence decay is obtained[10a]:



Scheme 1. Q_W = quencher in bulk aqueous phase; Q_M = quencher in micellar phase, D = probe (donor).

$$I(t)/I(0) = \exp - \{t/\tau + \langle Q \rangle \alpha_r^2 (1 - e^{-(k_r + k_b)t})\} \quad (2)$$

where

$$\tau^{-1} = \tau_0^{-1} + k_Q[Q_W] \quad (3)$$

$$k_Q = \alpha_r k_f; \quad \alpha_r = k_r/(k_r + k_b) \quad (4)$$

$[Q_W]$ = concentration of quencher in the aqueous phase

For the case of a completely micellized donor, four limiting situations are (1) the quencher of the luminescent probe is totally micellized (complete "static" quenching only); (2) the quencher is partially micellized (static quenching only); (3) the quencher is totally micellized ("non-static" and "static" quenching); (4) the quencher is partially micellized ("non-static" and "static" quenching). From the derived expressions we find that Case (1) yields information on the mean aggregation number of the micellar aggregates; Case

(2) yields information on the mean aggregation numbers of the micellar aggregates, the quencher binding constant and the entrance rate of the quencher into the aggregate; Case (3) yields information on the rate constant for quenching in micellar aggregates; Case (4) yields, in principle, all the information available from Cases (1—3), although in practice a complex fitting of experimental data may be required.

The mean aggregation number, $\bar{n}$, of micelles may be derived from luminescence quenching measurements when "static" quenching of a completely micellized donor occurs exclusively and when Q is selected to exclusively reside in the micellar phase. From eq. (2) the measured ratio of luminescence from D* in the presence of Q to that in the absence of Q is given by

$$I/I^0 = \exp\{-[Q]/[M]\} \tag{5}$$

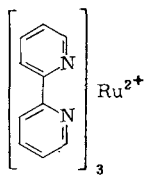
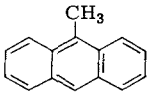
where [M] is the micelle concentration and is given by

$$[M] = \frac{[Det] - [free\ monomer]}{\bar{n}} \tag{6}$$

The combination of eqs. (5) and (6) yields

$$(\ln I^0/I) = \frac{[Q]\bar{n}}{[Det] - [free\ monomer]} \tag{7}$$

This expression allows evaluation of the aggregation number and the concentration of free monomer in equilibrium with micelles.

(6)  (7) 

An experimental example[11] which follows eq. (5) is the tris(α,α'-bipyridine)ruthenium(II) *(6)* and Q = 9-methylanthracene *(7)* system with Det = SLS. A plot of $\ln I^0/I$ *versus* [SLS] at fixed concentration of Q yields a straight line as shown in Figure 14. The slope is identified as $\{\bar{n}[Q]\}^{-1}$ and the intercept as $\{[Det] - [free\ monomer]\}$. Since [Q] and [Det] are known, $\bar{n}$ and [free monomer] may be evaluated. The experimental values of $\bar{n} = 60$ and [free monomer] $= 7.5 \times 10^{-3}$ M agree very well with values measured by other methods.

Situations other than those for which the donor is completely micellized have been encountered in the literature. The following general equation for the time evolution of the excited state has been developed[12]:

$$[D^*]_t = [D^*]_0 \exp\left[-\left(k + \frac{k_Q k_f [Q_w]}{k_b + k_Q}\right) t - \frac{K_M k_Q^2 [Q_w]}{(k_b + k_Q)^2}\left(1 - e^{-(k_b + k_Q)t}\right)\right] \tag{8}$$

where k is the specific rate constant of the decay of D* in the absence of quencher.

This equation may be used to evaluate kinetic parameters such as specific rate for entry and exit of the quencher and intramicellar diffusion rates.

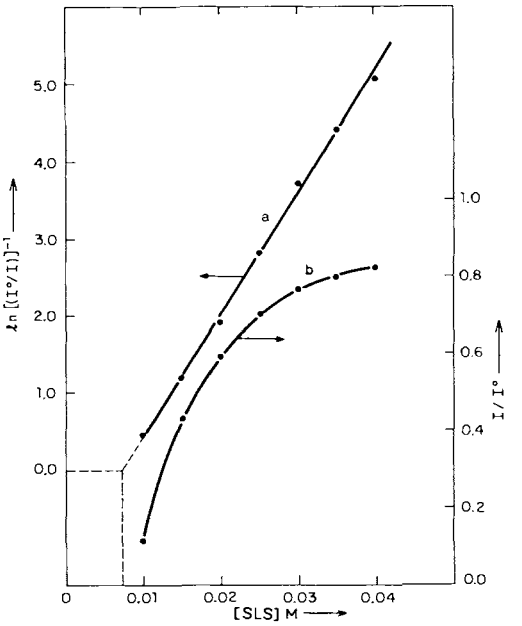


Fig. 14. Dependence on detergent concentration of $Ru(bpy)^{2+}$ *(6)* luminescence, with concentration of 9-methylanthracene quencher (Q) *(7)* fixed at 1.05×10^{-4} M. a) Intensity normalized relative to that in the absence of Q; b) analysis according to eq. (5). Slope $= 157\ M^{-1}$; $\bar{n} = [Q]^{-1} \times \text{slope}^{-1} \simeq 60 \pm 2$; intercept $= 7.5 \times 10^{-3}$ M; CMC $= 8.2 \times 10^{-3}$ M.

An important limiting case is the one for which all the quenching of a strongly micellized probe occurs in the aqueous phase. In this situation the exit of the probe from the micelle may become the rate limiting process for donor decay, *i.e.*, quenching occurs with unit efficiency at sufficiently high (aqueous) quencher concentration. The quenching of triplet 1-bromonaphthalene by NO_2^- ions in SLS solution was found to conform to this case[13]. The kinetics for this situation cannot be deduced from the formulation discussed above, but may be readily derived from standard steady state considerations. The resulting expression allows evaluation of k_b. If k_f can be evaluated, then the equilibrium constant, $K_M = k_f[Q]/k_b$, for partitioning of the quencher between the micelle and the aqueous phase may be evaluated.

Some values of K_M, k_f, and k_b obtained from luminescence quenching are gathered in Table 2.

From eq. (4), the rate constant k_Q, evaluated from experimental data is seen to be a composite of k_r, k_f, and k_b. The rate constant k_r has the characteristics of a pseudo-unimolecular rate constant, *i.e.*, $k_r = k_r'[Q]_M$. In cases for which the quencher carries the same charge as the surface of the micelle, $[Q]_M$ is substantially decreased relative to the bulk concentration of Q; correspondingly, if Q possesses the opposite charge as the surface of the micelle, $[Q]_M$ may be substantially increased relative to the bulk concentration of Q. These two situations lead to micellar "inhibition" of quenching and micellar "catalysis" of quenching.

For example, the quenching efficiency of the fluorescence by $Br^\ominus$ or Eu^{3+} of micellized aromatic hydrocarbons is very dependent on the charge of the micelle[9a]. Thus, $Br^\ominus$ is an effective quencher of the fluorescence of naphthalene *(4)* when the arene is dissolved in cationic (*e.g.*, hexadecyl(trimethyl)ammonium (CTA)) micelles, but $Br^\ominus$ is an ineffective quencher of naphthalene fluorescence when the hydrocarbon is dissolved in anionic micelles (*e.g.*, dodecyl sulfate

Table 2. Partitioning constants K_M, entrance and exit rate constants, k_f and k_b, respectively, for selected molecules in micellar aggregates of CTAB and SLS.

Molecule	CTAB			SLS			Ref.
	K_M [M^{-1}]	k_f [$M^{-1} s^{-1}$]	k_b [s^{-1}]	K_M [M^{-1}]	k_f [$M^{-1} s^{-1}$]	k_b [s^{-1}]	
Oxygen	3×10^2	1×10^{10}	5×10^7	3×10^2	1×10^{10}	5×10^7	[28]
Benzene	9×10^3	—	7×10^5	2×10^3	—	4×10^6	[13]
Naphthalene	9×10^4	—	—	2×10^4	—	2×10^5	[13]
Anthracene	2×10^6	—	3×10^3	4×10^5	—	2×10^4	[13]
Pyrene	1×10^7	—	2×10^3	2×10^6	—	4×10^3	[13]
1-Bromonaphthalene	2×10^6	—	4×10^3	2×10^5	—	3×10^4	[13]

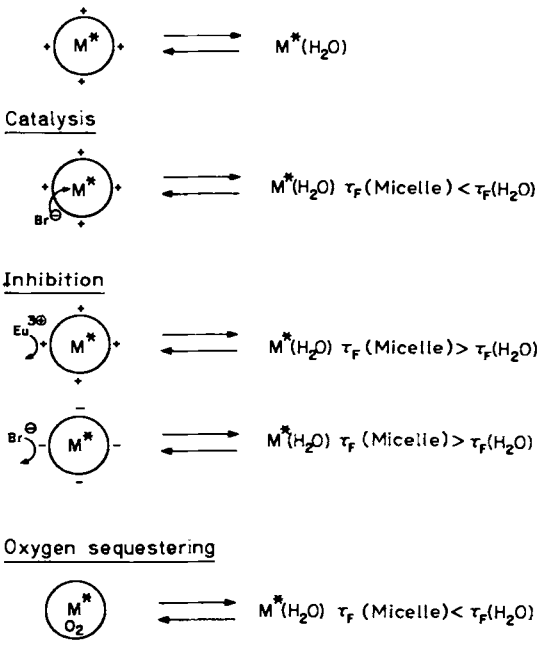


Fig. 15. Schematic representation of the "catalysis" of quenching of naphthalene *(4)* (M*) fluorescence in CTAB and the "inhibition" of naphthalene fluorescence in SLS.

(LS)). Just the opposite is true for quenching of the fluorescence of pyrene *(3)* by Eu^{3+}, even though $k_q > 10^9$ M^{-1} s^{-1} in water. These situations are summarized schematically in Figure 15.

10. Dynamics of Intramicellar Probe Diffusion

10.1. Excimer Formation, Pyrene

Pyrene *(3)* shows a number of photophysical features that make it an attractive fluorophore to probe the microenvironment present in micellar aggregates. The unusually long fluorescence lifetime[14] ($\bar{\tau}_F = 400$ ns) enables one to study the dynamics of its interaction with quenchers partitioning between the aqueous and micellar phase[7, 15]. From these studies, factors influencing the permeability of the lipid/water interface may be deduced[16]. The relative intensity of the vibrational fine structure peaks in the emission spectrum is sensitive to the probe environment (Ham effect[17]), allowing for the determination of the local polarity at the solubilization site[18, 19]. Finally, from the dynamics of excimer formation information may be derived about the microviscosity and dynamics of pyrene motion within the micelle. Only the latter point will be elaborated in more detail now, since the other subjects have been treated exhaustively in two recent reviews[1b, c].

Förster and *Selinger*[20] were the first to compare the relative intensities of monomer and excimer emission in homogeneous solvents and micellar solutions. The fact was recognized that in the latter system the pyrene molecules are compartmentalized through the surfactant aggregates—an effect which favors excimer formation. A simple kinetic model was introduced later by *Pownall* and *Smith*[6] to interpret these phenomena. Failure to take random distribution effects into account resulted in abnormal high viscosity values. Subsequently more advanced theories were developed[10d, 21-23] which take into account the statistics of probe distribution over the micellar aggregates. As the exchange of pyrene molecules between different micelles is much slower than the excimer formation itself, only multiply occupied micelles can contribute to the excimer emission. Their fraction can be calculated from the Poisson distribution function [cf. eq. (1)]. For example, in Figure 16 is shown a fluorescence spectrum of a solution containing 2×10^{-4} M pyrene *(3)* in aqueous so-

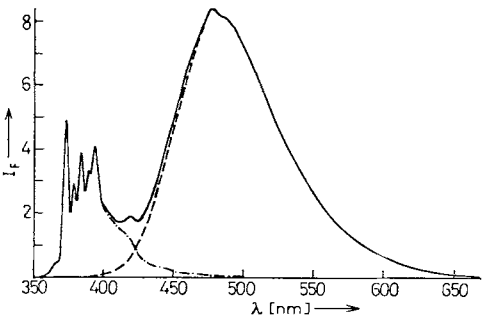


Fig. 16. Fluorescence spectrum of pyrene *(3)* (2×10^{-4} M) in aqueous 5×10^{-3} M CTOES solution. ——, total emission; – – – –, pure excimer emission; – · – · –, pure monomer emission. CTOES = n-$C_{16}H_{33}O(CH_2CH_2O)_3SO_3^{\ominus}Na^{\oplus}$.

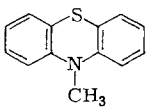
dium 3,6,9-trioxapentacosyl sulfate 5×10^{-3} M (sodium hexadecyltrioxyethylene sulfate, CTOES). Clearly the excimer emission dominates the spectrum, although it would be practically absent in a homogeneous solution at a comparable pyrene concentration.

A quantitative understanding of these phenomena is provided by a recent theoretical treatment[23] that takes into account the statistics of probe distribution and the intramicellar kinetics of the excimer formation. Apart from the CMC, a number of other important parameters were derived from this study, such as the micellar aggregation number ($n = 96$ for CTOES). Even more important is the fact that these studies provide information on the rate of intramicellar probe

diffusion. (The mean encounter time of two pyrene molecules in a CTOES aggregate is $\bar{c} = 110$ ns.)

10.2. Functional Micelles with Reactive Boundaries

Unusual effects are also observed when triplets are incorporated into functional micelles. Consider, for example, the quenching of *N*-methylphenothiazine (MPTH) *(8)* triplets by Ni^{2+} or Co^{2+} ions:


(8)

$$MPTH^T + Ni^{2+}(Co^{2+}) \rightarrow Ni^{2+}(Co^{2+}) + MPTH \quad (9)$$

In homogeneous solution, *i.e.* ethanol/water (1/2, v/v), this reaction occurs at a comparatively slow rate, the rate constants being $k_2(Ni^{2+}) = 7.7 \times 10^6$ and $k_2(Co^{2+}) = 1.4 \times 10^7$ $M^{-1} s^{-1}$, respectively. A drastic increase in the quenching efficiency is observed when *(8)* is solubilized in dodecyl sulfate micelles containing a Ni^{2+} or Co^{2+} counterion atmosphere. The lifetime of $MPTH^T$ is only 100 ns for Ni^{2+} and 50 ns for Co^{2+} counterions, irrespective of the micellar concentration[24]. Thus, through molecular organization one achieves high local quencher concentrations in the interface (3—6 M) even in very dilute solutions. This increases the quenching activity by several orders of magnitude with respect to a homogeneous solvent.

By selecting a different kind of counterion, *i.e.* Ag^+ instead of Co^{2+} or Ni^{2+}, the same effect may be exploited to obtain a drastic increase in the triplet yield and even room temperature phosphorescence. Micelles of silver decyl sulfate (AgDS) form readily above a surfactant concentration of 3×10^{-2} M and incorporate arene molecules such as pyrene *(3)* or naphthalene *(4)* (see Section 6 and Fig. 10).

10.3. Intramicellar Triplet Energy Transfer

The transfer of excitation energy from a triplet donor to a ground state acceptor

$$D^T + A \rightarrow A^T + D \quad (10)$$

proceeds *via* an exchange mechanism which requires close approach of the reactants. Consider the situation where both donor and acceptor are hydrophobic and hence solubilized in the interior of the micelle. Since on the time scale of reaction no intermicellar exchange of A or D molecules can take place, the energy transfer will occur within groups of only a few molecules that are compartmentalized within their host aggregates. As a result, statistical and proximity effects will influence the efficiency and rate of reaction. These have been illustrated for the reversible and irreversible transfer of energy from triplet *N*-methylphenothiazine ($MPTH^T$) to *trans-stilbene* and naphthalene respectively[25]. Both experiments were performed in CTAB micelles. In the $MPTH^T$-stilbene system the transfer is irreversible and occurs at a rate constant $k_q = 1.5 \times 10^7 s^{-1}$ for micelles containing one donor-acceptor pair. Conversely, the reaction between $MPTH^T$ and naphthalene is reversible, the respective rate constants for the forward and backward transfer being $k_q = 2.8 \times 10^6 s^{-1}$ and $k_{-q} = 3.3 \times 10^6 s^{-1}$. Confinement of the reaction space to micellar size induces both a drastic enhancement of the observed transfer rate as well as a reduction of the reaction order from two to one. Interestingly, these effects are predicted from applying diffusion reaction theory to the interaction of a small number of reactants in a small and confined reaction space. In fact, quantitative predictions of the rate constant of deactivation are possible for the three cases where: (1) the excited state quencher is identical with the counterion atmosphere (this case was discussed in Section 10.2); (2) the energy transfer occurs between a pair of reactants within the micelle (present case); and (3) the acceptor and donor are located on the surface of the micelle. These predictions are in excellent agreement with the experimental results[26].

11. Dynamics of Molecular Oxygen in Micellar Solutions

Molecular oxygen is a general and effective quencher of the fluorescence of hydrocarbons. The quenching process is commonly diffusion controlled in homogeneous solution, requiring that quenching within the "solvent cage" occurs with an efficiency close to unity. In two (or multiphase) pseudo-homogeneous aqueous solutions (micelle-containing detergent solutions, solutions containing protein membranes and other macrobiomolecules) the observed efficiency and reactivity of oxygen quenching will depend on the partitioning of molecular oxygen in the various phases, the lifetimes of the excited substrate and the dynamics of entrance, exit, and quenching interaction of the oxygen molecule in an "effective quenching volume" about the substrate. Thus, in extreme situations quenching (1) can be very effective if oxygen molecule and substrate are "pre-complexed" and confined to a small volume in a given phase or (2) can become very inefficient if the substrate and the molecular oxygen are in separate phases and volumes of space and the rate of penetration of oxygen into an "effective quenching volume" is slow compared to the decay rate of the excited substrate.

It has been shown that molecular oxygen readily penetrates the micelle aqueous boundaries[27]. The mechanism of penetration of molecular oxygen across such boundaries is potentially of great significance for important biological processes such as respiration and photodynamic effects.

The "observed" rate constant for quenching of fluorescent probes by molecular oxygen in micellar solutions is generally smaller than that obxerved for the same probes in homogeneous solution[15]. These results have been interpreted in terms of a smaller "effective" concentration of oxygen in the phase or aggregates containing the probe, in terms of a smaller rate constant for quenching interaction or some combination of both factors. The ability of association to "protect" excited probes from oxygen quenching is strikingly demonstrated by the ready observation of phosphorescence from organic molecules in micelle-containing detergent solutions[3,4].

Information on the solubilization, entry and exit of molecular oxygen into and out of micelles produced in detergent solution is potentially available from an investigation of the time-resolved measurement of fluorescence lifetime of a mi-

cellized probe as a function of oxygen pressure and application of eq. (2). A study of the oxygen quenching of 1,5-dimethylnaphthalene *(9)* fluorescence in micelle containing detergent solutions of hexadecyltrimethylammonium bromide (CTAB) and sodium dodecyl sulfate (SLS) allowed an estimation of dynamic and solubility parameter of molecular oxygen in this "two phase" system[28]. The results are summarized in Table 3.

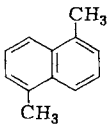

(9)

Table 3. Summary of parameters derived from fluorescence quenching of 1,5-dimethylnaphthalene *(9)* by oxygen in micellar solutions [28].

Parameter	Micelles	
	CTAB	SLS
k_i, entrance rate constant [$M^{-1}\,s^{-1}$]	$1.3 \pm 0.2 \times 10^{10}$	$1.4 \pm 0.2 \times 10^{10}$
k_b, exit rate constant [s^{-1}]	$< 4.6 \pm 0.5 \times 10^{7}$	$< 5.3 \pm 0.7 \times 10^{7}$
τ_m, residence time [s]	$< 2.2 \times 10^{-8}$	$< 1.9 \times 10^{-8}$
k_r, static quenching constant [s^{-1}]	$< 4.6 \pm 0.5 \times 10^{7}$	$< 5.3 \pm 0.7 \times 10^{7}$
α, quenching efficiency	0.89 ± 0.15	0.80 ± 0.17
$K_{eq} \equiv k_i/k_b$, equilibrium constant [M^{-1}]	$2.8 \pm 0.3 \times 10^{2}$	$2.6 \pm 0.4 \times 10^{2}$

The values of the entrance rate constants 1.3×10^{10} M^{-1} s^{-1} (CTAB) and 1.4×10^{10} M^{-1} s^{-1} (SLS) are comparable with those derived from fluorescence quenching by oxygen in homogeneous fluid solution of low viscosity. Values of 8.3×10^{9} M^{-1} s^{-1} (CTAB) and 9.2×10^{9} M^{-1} s^{-1} (SLS) were reported for the total "bulk" oxygen quenching of pyrene *(3)* monomer fluorescence. The long inherent lifetime of pyrene fluorescence ($\approx$200 ns in CTAB and $\approx$450 ns in SLS, respectively) probably allows oxygen escape from the micelle to be competitive with oxygen quenching; therefore, the observed quenching constant is somewhat lower than that for diffusion of oxygen into the micelle[27].

The value of the rate constant for interaction (quenching) of excited 1,5-dimethylnaphthalene *(9)* is expected to be of the order of that for intramicellar encounter of an oxygen molecule and an excited naphthalene molecule. From the values of the reported microviscosities of CTAB and SLS micelles (39 and 9 cp, respectively), a micelle radius of $\approx$20 Å and an effective radius of the probe of $\approx$3.0 Å, a value of $\approx 1 \times 10^{7}$ to $\approx 5 \times 10^{7}$ s^{-1} is calculated from diffusion theory for the encounter rate[26]. An experimental value of $\approx 10^{7}$ s^{-1} has been evaluated for the intramicellar encounter of two pyrene molecules in an anionic micelle. Finally, a value of $\approx 6 \times 10^{7}$ s^{-1} has been evaluated for the rate of intramolecular excimer formation of 1,3-di-α-naphthylpropane *(5)* in CTAB micelles (see Fig. 12b). All these data suggest micellar interaction rate constants of the order of 10^{7}—10^{8} s^{-1} for the systems studied. Our derived value of $\lesssim 4.6 \times 10^{7}$ s^{-1} or $\lesssim 5.3 \times 10^{7}$ s^{-1} is comparable with literature estimates.

The fact that the efficiency of quenching is close to unity is consistent with results from homogeneous solution where O_2 is found to quench the fluorescence of aromatic hydrocarbons at close to the diffusional limit.

Finally, the limit of K_{eq} of $\approx 3 \times 10^{2}$ M^{-1} implies a higher solubity of O_2 in the micellar phase relative to the aqueous phase (on a molar basis). This result is consistent with the observation that O_2 is generally an order of magnitude more soluble in organic solvents than it is in water. The comparable value of K_{eq} for CTAB and SLS is consistent with a recent investigation of the oxygen quenching of naphthalene fluorescence in aqueous solutions of these two detergents.

12. Photochemical Reactions in Micellar Systems

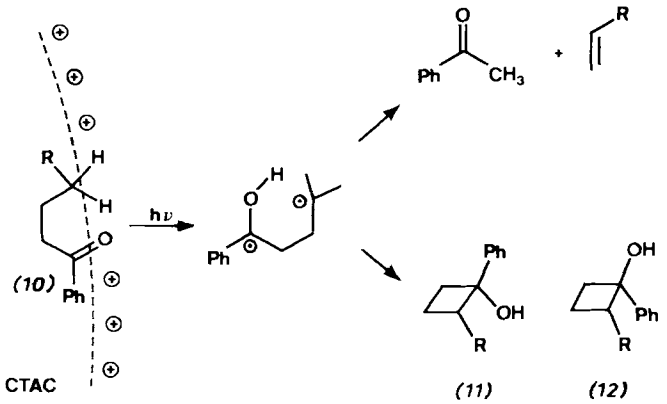
12.1. Photoinduced Hydrogen Abstraction Reactions

The triplet n,π* states of carbonyl compounds abstract hydrogen atoms from a variety of substrates including the relatively unactivated hydrogens of a saturated hydrocarbon[1g]. Employing the triplet n,π* state of an aryl ketone as "typical", the rate constant for hydrogen abstraction from a saturated methylene chain is expected to be $\approx 10^{4}$—10^{5} M^{-1} s^{-1}. Upon proceeding from nonpolar to polar solvents the rate constant for hydrogen abstraction occasionally decreases in cases where state "switching" or state "mixing" of n,π* and π,π* states occur. The efficiency of intramolecular hydrogen abstraction (Type II reaction) is enhanced upon proceeding from nonpolar to polar solvents. Thus, it should be possible to employ either hydrogen abstraction reactivity or efficiency measurements to serve as probes of the environment in which hydrogen abstraction occurs. Furthermore, "cage effects" on the type of products produced from intermolecular hydrogen abstraction are expected. Finally, there is a possibility that selective hydrogen abstraction might occur when flexible substrates are incorporated in micelles.

12.2. Intramolecular Hydrogen Abstraction Reactions

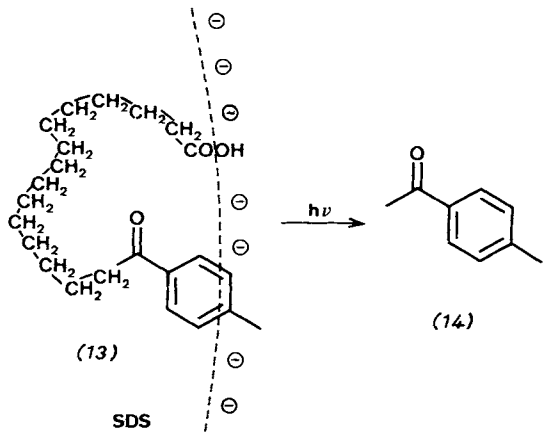
The "Type II" reaction of phenyl alkyl ketones is one of the best studied and understood of all organic photoreactions[29]. Both cleavage products (acetophenone and alkene) and cyclization products (cyclobutanols) are observed to occur *via* a primary product diradical. The quantum yield of overall reaction and the ratio of stereoisomeric cyclobutanols are solvent sensitive. Thus, measurement of the quantum yield and of the cyclobutanol ratio serve as monitors of local solvent properties of micelles. Experimentally[30], the quantum yield of Type II reactions of phenyl heptyl ketone (octanophenone) *(10)*, R = *n*-C_4H_9, is $\approx$0.7 in CTAC and the ratio of cyclobutanols *(11)/(12)* is 1.2 (Scheme 2). These values are much closer to those for Type II reaction in *t*-BuOH [$\Phi = 1.0$, *(11)/(12)* = 1.5:1] than those in benzene ($\Phi = 0.33$, *(11)/(12)* = 4.7:1).

These results are consistent with the ketones (or the intermediate diradicals) not being solubilized exclusively in the hydrocarbon core of the micelle. They suggest that the ketone (or the diradical intermediate) must spend at least some time in the polar Stern layer of the micelle. Quenching experiments with Eu^{3+} (a good quencher of the Type II reaction in water) show that no significant amount of probe reacts in the aqueous phase; *i.e.*, Eu^{3+} does not quench the Type II reaction of octanophenone *(10)* in CTAC solutions[30].



Scheme 2.

In another study, a surfactant ketone 16-oxo-16-(*p*-tolyl)hexadecanoic acid *(13)* was incorporated in SLS micelles[31]. The quantum yield of reaction was found to be 0.8 (as against 0.2 in benzene solution). 4-Methylacetophenone *(14)* was the only volatile product detected (Scheme 3).



Scheme 3.

These results can be interpreted to imply that hydrogen abstraction occurs when the fourteen carbon polymethylene chain is mostly bent such that both ends lie near the micellar surface. These results contrast sharply with those found for photolysis of *(13)* in monolayer assemblies made from arachidic acid, in which case the quantum yield for Type II reaction is $\approx 10^{-4}$, *i.e.*, Type II reaction is severely inhibited in the highly organized monolayer environment.

12.3. Intermolecular Hydrogen Abstraction Reactions

Aryl ketones should be capable of abstracting hydrogen atoms from the polymethylene chains of SLS and CTAC. In fact, the phosphorescence of benzophenone is quenched by such detergent molecules[32]. Interestingly, in a fluorinated micelle such as sodium perfluoro-octanoate ($CF_3(CF_2)_6COO^{\ominus}Na^{\oplus}$, SPFO) benzophenone phosphorescence is readily observed[32].

Product studies reveal that hydrogen abstraction occurs in the case of substituted benzophenones[33,34]. Several investigations have explored the selectivity of intermolecular hydrogen abstraction in micelles. For example, surfactant ketones have been photolyzed as "guests" in "host" micelles such as SLS and CTAB. The selectivity of hydrogen abstraction by triplet benzophenone along a detergent chain has been investigated[33], for both anionic and cationic C_{16} detergents. Benzophenone and several of its 4-carboxylate esters were employed as hydrogen abstractors. The general result was that attack occurs relatively non-selectively from positions ≈ 5 through 14, but in some cases a substantial selectivity for attack at 15 is observed (Fig. 17).

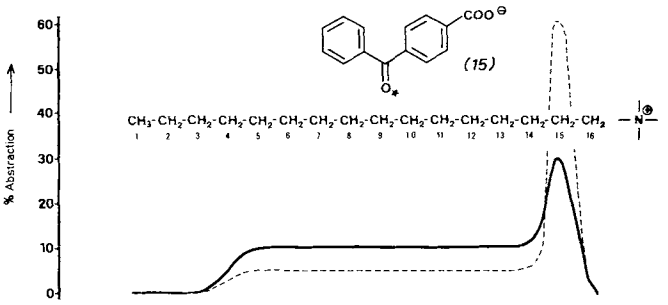


Fig. 17. Positions of hydrogen abstraction from the cationic detergent by the triplet of the 4-benzoylbenzoate anion *(15)*. (—) above CMC; (---) below CMC.

In the case of photolysis of mixed micelles of SLS and the 4-benzoylbenzoate anion *(15)* hydrogen abstraction from the detergent backbone methylene groups occurs and is followed by attachment of the benzophenone moiety to the detergent. Abstraction occurs from over positions 5 to 11 of the chain. The observed non-selectivity of the hydrogen abstraction suggests extensive coiling and folding of the detergent chains[33].

Interestingly, photolysis of 4-(4-benzoylphenyl)butyrate anion in CTAB solutions below the CMC leads to highly selective hydrogen abstraction at C-15 of CTAB. Above the CMC, attack becomes random. The reactions of benzophenones possessing different length chains in the 4-position with CTAB become less selective at C-15 as the chain is lengthened. This result is interpreted in terms of folding of the detergent chain[33].

Photolysis of the benzophenone derivative *(16)* in sodium tetradecanoate micelles results in a different selectivity: hydrogen is abstrated only from positions 5 through 8, with position 7 showing the highest reactivity (Fig. 18). In the case of *(15)*, abstraction from positions 3 through 8 is observed, with position 6 showing the highest reactivity[34].

These studies indicate that a certain selectivity is possible for reactions involving hydrogen abstraction from polyme-

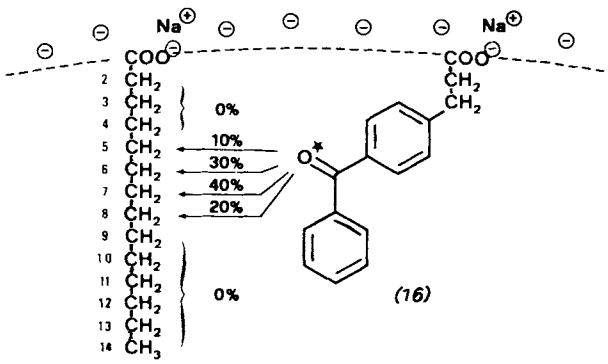


Fig. 18. Positions of hydrogen abstraction from sodium tetradecanoate by the triplet of sodium 2-(4-benzoylphenyl)propionate *(16)*.

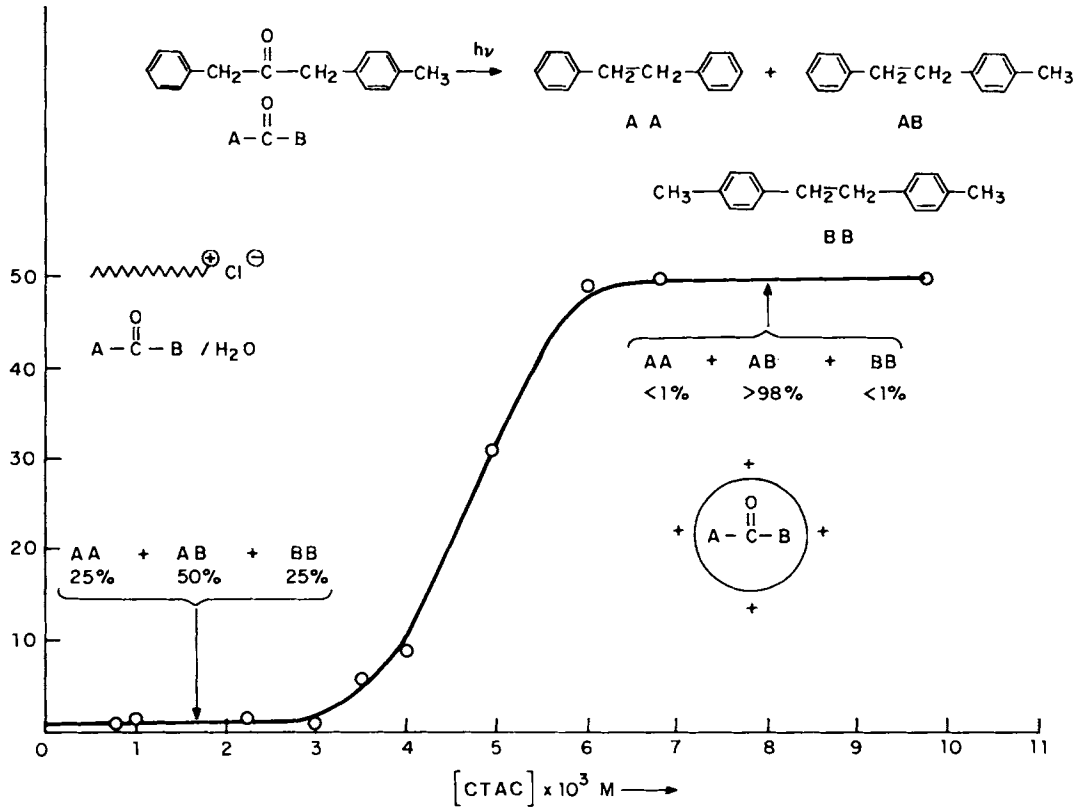


Fig. 20. The yield of recombination products on photodecarbonylation of benzyl *p*-methylbenzyl ketone (type A—CO—B) depends on the concentration of the detergent CTAC and shows a typical CMC profile.

thylene chains of detergents. The results are consistent with considerable folding of the detergent chain and a certain amount of preferential ordering of ketone probes in micelles.

12.4. Photochemical Fragmentation Reactions

A rather obvious application of micellar environments is the enhancement of radical cage reactions of hydrophobic radical pairs relative to homogenous solution. The idea is that if a hydrophobic radical pair is generated in a micelle, the probability of cage reaction between spin correlated radical pairs increases relative to reaction of free radicals without spin correlation.

For example, the photodecarbonylation of unsymmetrical dibenzyl ketones A—CO—B in homogeneous solution occurs *via* a free radical mechanism to produce 1,2-diarylethanes in quantitative yield[35]. The latter products (AA, AB, and BB) are formed in yields of 25, 50, and 25%, precisely the ratio expected for statistical, nonselective coupling of spin-noncorrelated radicals A and B produced by decarbonylation of A—CO—B.

In contrast[36], photolysis of A—CO—B in micelle-containing solutions of CTAC results in selective formation of AB (Fig. 19). The yield of AB relative to (AA + BB) is dra-

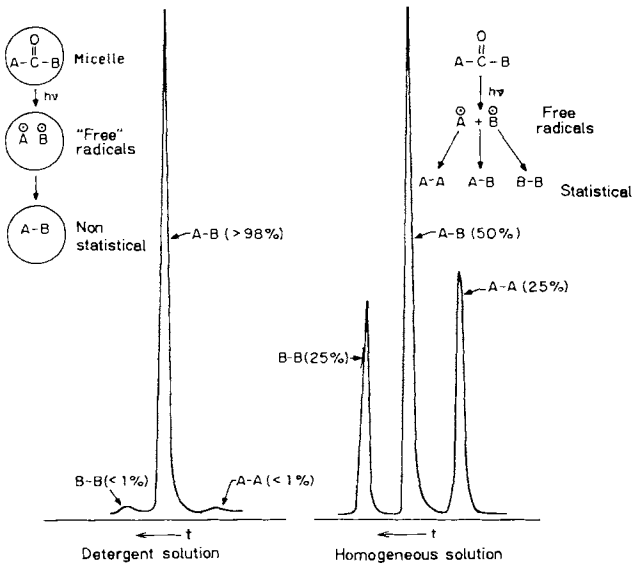
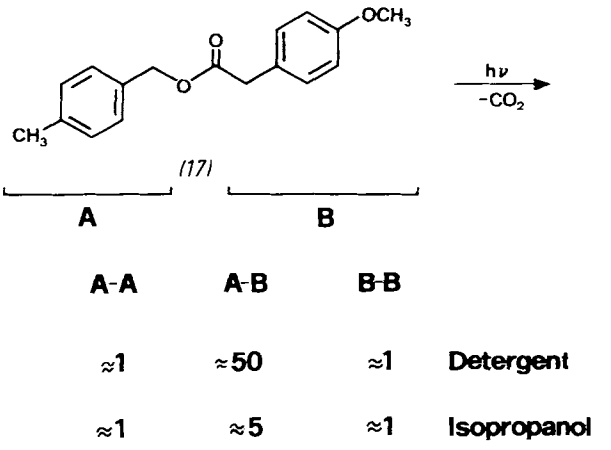


Fig. 19. Schematic representation of GC results of the photodecarbonylation of unsymmetrical dibenzyl ketones A—CO—B in detergent and homogeneous solution.



Scheme 4.

matically dependent upon the CTAC concentration and shows a typical CMC profile (Fig. 20).

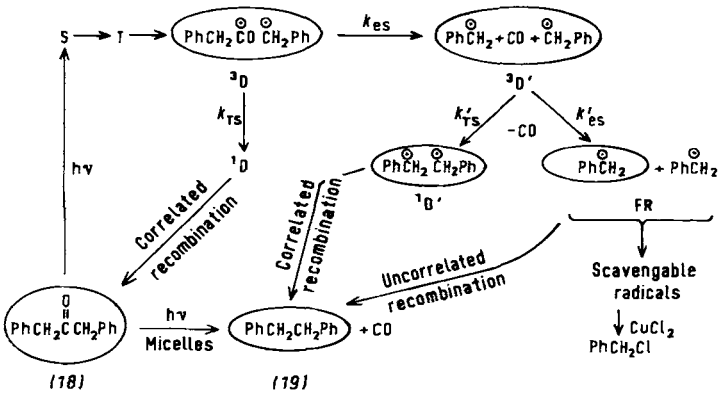
In analogy to the results with photolysis of dibenzyl ketones, benzyl phenylacetates, *e.g. (17)*, undergo a more regioselective decarboxylation in potassium dodecanoate solutions than that observed in homogeneous solution (*e.g.*, isopropanol, Scheme 4)[37].

12.5. Application of Photofragmentation in Micelles to ^{13}C-Enrichment

The photolysis of dibenzyl ketone *(18)* (Scheme 5; see also Section 12.4) proceeds *via* an initial triplet radical pair (^3D). These radical pairs may be classified in terms of the occurrence of a ^{13}C or a ^{12}C nucleus in the carbonyl group of the radical pair. This classification is informative because CIDNP studies suggest that intersystem crossing of a radical pair such as $PhCH_2\overset{\odot}{C}O\overset{\odot}{C}H_2Ph$ occurs *via* a nuclear hyperfine induced mechanism. Since ^{12}C does not possess a nuclear moment while ^{13}C does, it is expected, from the observation that hyperfine coupling is most effective at the carbonyl center, that radical pairs with a ^{13}CO group will undergo more rapid $^3D' \rightarrow {}^1D'$ intersystem crossing than radical pairs with ^{12}CO. Since $^1D'$ radical pairs can undergo cage reactions (*e.g.*, recombination) but $^3D'$ radical pairs cannot and since $^1D'$ radical pairs are formed enriched in ^{13}C, the cage products will also be enriched in ^{13}C.

In the case of dibenzyl ketone *(18)*, the relevant cage product is dibenzyl ketone *(18)*. Thus, as the photoreaction proceeds the recovered starting material is found[38] to be enriched in ^{13}C! The magnitude of the enrichment is relatively small for homogeneous solutions but increases by over an order of magnitude in micelles (measured by the single stage separation factor). In micelle solution, the quantum yield for photolysis of *(18)* (90% ^{13}CO) is $\approx 30\%$ less than for natural abundance of ^{13}C at the CO carbon. In homogeneous solution, the quantum yield for photolysis is the same for both ^{13}C-enriched and natural abundance materials.

The striking difference in the photochemistry of *(18)* in micellar and homogeneous solutions has been attributed to the reduced dimensionality available to a substrate in a micellar aggregate. This feature provides a "super cage" environment that allows a spin-correlated radical pair to diffuse sufficiently far apart to allow hyperfine interactions to develop effectively, but not so far apart that spin-uncorrelated free radicals result.



Scheme 5.

These results are consistent with the observation of CIDNP when micellar solutions of *(18)* are irradiated in an NMR spectrometer[38b]. It is interesting to note that the "super solvent cage" of a micelle serves to confer the maximum separation of radical centers of the $PhCH_2\overset{\odot}{C}O$ and $\overset{\odot}{C}H_2Ph$ fragments to a restricted region of space in a manner similar to the way that a chain of atoms separates the radical centers of a diradical.

12.6. Cage Effects and Magnetic Field Effects on Cage Reactions

Photolysis of dibenzyl ketone *(18)* in CTAC (Scheme 5) results in substantial cage decarbonylation to produce a triplet (spin-correlated) geminate radical pair ($Ph\overset{\odot}{C}H_2 + Ph\overset{\odot}{C}H_2$). Some of these radical pairs undergo intersystem crossing and geminate cage recombination to form diphenylethane *(19)*, and some pairs exit the micelle, enter the aqueous phase and eventually return to a micelle to undergo secondary cage recombination. The latter radical pairs are scavengable by Cu^{2+} which resides exclusively in the aqueous phase. Experimentally, it is found that in the presence of Cu^{2+} the yield of *(19)* is reduced by 25% of its value in the absence of Cu^{2+}. This means that a "cage effect" of 25% operates. The absolute quantum yield for this cage effect was found to be 0.06.

If the "cage effect" experiment is repeated in the presence of a laboratory magnetic field ($\gtrsim 200$ gauss) the quantum yield for geminate cage reaction drops to 0.02! This dramatic decrease in geminate recombination is ascribed to a splitting of two of the three triplet levels of the radical pair by the laboratory field. When this happens, only one of the three triplet levels is capable of intersystem crossing to a singlet diradical which can form cage products. The two radical pairs which do not form cage products leave the micelle and are scavenged by Cu^{2+}.

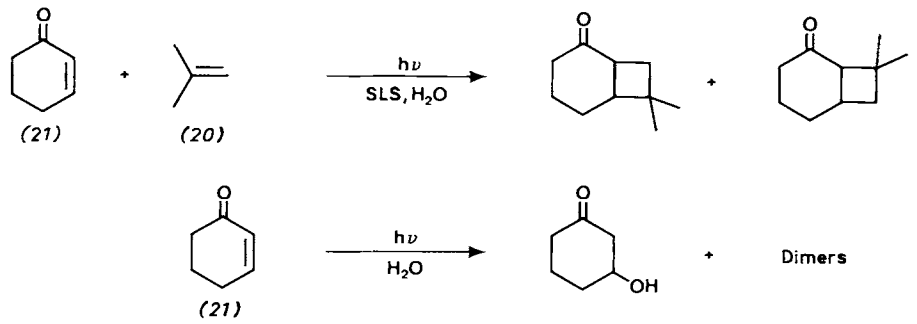
12.7. Photocycloaddition Reactions in Micelles

It is expected that, at comparable substrate concentrations, the quantum efficiency of intermolecular cycloaddition reactions of organic compounds might be higher for micellar solution than for homogeneous solution. This expectation is based on the high local concentrations of a substrate that are achieved by solubilization of the substrate into micellar aggregates. For example, if a solute is completely micellized at a macroscopic concentration of 10^{-4} M, the substrate concentration in the micelle aggregate is $\approx 10^{-1}$ to 10^{-2} M. Thus, rate enhancements of $\approx 10^2$—10^3 over those in homogeneous solution are expected and a cycloaddition reaction which is inefficient in homogeneous solution may be quite efficient in micellar solution.

In addition to simply serving as a means of achieving high local concentrations, photocycloadditions in micelles may also introduce unique features if the micelle is capable of speciate orienting effects.

Micellar solutions of SLS saturated with isobutylene *(20)* contain high local concentrations of the alkene within the micellar hydrophobic area. Cycloaddition to cyclohexenone *(21)* (Scheme 6), which is soluble in water and therefore only partially solubilized, becomes more efficient under these

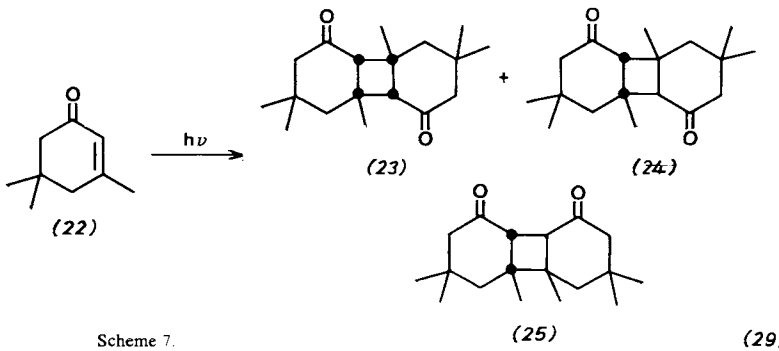
conditions than dimerization of *(21)*, which is a major side reaction in homogeneous solution[39].



(21) (20) (21)

Scheme 6.

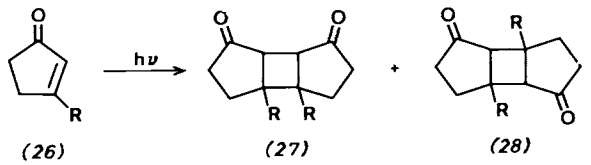
The enone *(21)* dissolved in the aqueous phase reacts mainly with the solvent yielding the expected γ-keto alcohol (Scheme 6). The dimerization of isophorone *(22)* (Scheme 7) has been found to be enhanced in micellar systems and microemulsions. In addition, the formation of isomers *(22)*—*(25)* depends strongly on the polarity of the solvent and the dominant phase, respectively[40].



(22) (23) (24) (25)

Scheme 7.

Photoexcitation of 3-alkylcyclopentenones *(26)* in solutions of potassium dodecanoate (KDC, above CMC) results in a greatly increased efficiency of dimerization compared to that which occurs in homogeneous solution such as benzene[41]. Furthermore, the photodimerization in detergent solutions occurs in a highly regiospecific manner; moreover, the relative yield of head-to-head *(27)* to head-to-tail dimer *(28)* is opposite to that observed in homogeneous solutions (Scheme 8).

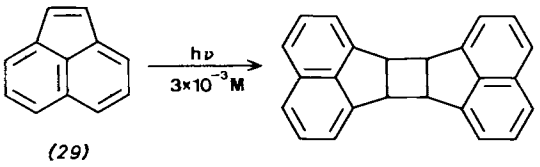


(26) (27) (28)

R = *n*-C_4H_9	KDC	98	:	2	100%
n-$C_{10}H_{21}$	C_6H_6	9	:	91	1–6%

Scheme 8.

Photodimerization of acenaphthylene *(29)* in micelle-containing solutions occurs readily under concentration conditions such that no dimeric products are produced in benzene solutions (Scheme 9)[42].

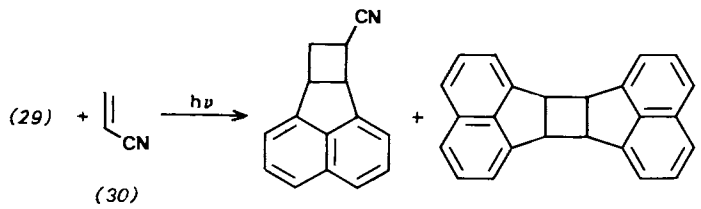


(29)

SLS	96%
C_6H_6	0%

Scheme 9.

In the photocrossed cycloaddition of acenaphthylene *(29)* to acrylonitrile *(30)* reaction occurs in much higher yields in non-ionic detergent solutions (*e.g.* in polyglycol ethers) (Scheme 10)[43].



(30)

Nippol PBC-34	30%	70%
C_6H_6	0%	30%

Scheme 10.

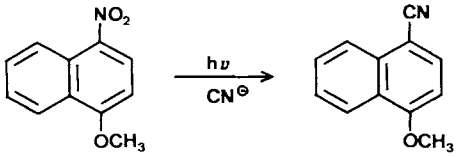
12.8. Photoinduced Substitution of Aromatic Compounds

Ionic detergents are known to alter the rate of thermal reactions of nucleophiles with organic substrates[40a]. Both retardation and acceleration of reaction rates in micelles may be achieved depending on whether the charge of the detergent causes repulsion of attacking nucleophile or causes organization of the attacking nucleophile and substrate.

Such effects have been observed in photoinduced substitution reactions of aromatic compounds[44]. Photoexcitation of aqueous solutions of 4-methoxy-1-nitronaphthalene *(31)* containing CN^- ions results in formation of 4-methoxy-1-naphthalenecarbonitrile *(32)* (Scheme 11). The efficiency of reaction is low even at $[CN^-] = 0.8$ M, *i.e.*, $\Phi \approx 0.002$. When the photoreaction was conducted in the presence of CTAC micelles, a large enhancement in the quantum yield of the

reaction was observed, even at relatively low [CN^-]. The enhancements in quantum yields (at comparable concentrations of CN^-) approached values of 10^3—10^4. In the case of SLS micelles quantum yields of reaction are exceedingly low.

The enhancement factor for reaction in CTAC is much larger than the characteristic rate enhancements commonly observed for micellar effects on ground state substitution reactions, suggesting that some factor other than substrate-nucleophile organization might be important. It was proposed that the polar local environment of excited 1-methoxy-4-nitronaphthalene *(31)* influences the rate constant for substitution. This postulate is supported by the observation of strong solvent dependence of quantum yields for photoinduced aromatic substitution reactions in homogeneous solution.

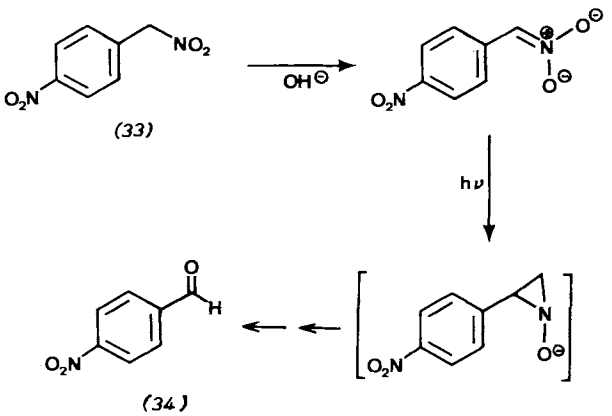


(31) *(32)*

Scheme 11. $\Phi(H_2O)=0.0$, $\Phi(SLS)=0.0$, $\Phi(CTAC)=0.2$.

12.9. Miscellaneous Photoreactions in Micelles

The photorearrangement of 4-nitrophenyl-nitromethane *(33)* into 4-nitrobenzaldehyde *(34)* was found to be much more efficient in a cationic detergent (CTAB) than in basic ethanol/water solution (Scheme 12)[45].

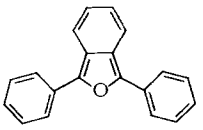


(33) *(34)*

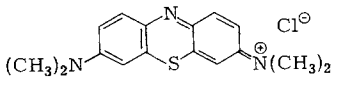
Scheme 12.

The anion of *(33)* is postulated as the key intermediate in this rearrangement. The effects of cationic detergent may be two-fold: (1) an organization effect and (2) a polarity effect. Both of these effects would be expected to enhance the equilibrium concentration of anion and thereby enhance the quantum yield of reaction.

Photosensitized oxidations have been performed in micellar solution[46,47]. Generally, singlet oxygen is the key reactive intermediate in such reactions. In one case, oxidation of 2,5-diphenylisobenzofuran *(35)* in SLS micelles in aqueous



(35)



(36)

solutions of methylene blue *(36)* was investigated. Because methylene blue is a cationic sensitizer and since *(35)* is expected to be totally micellized, it was proposed that singlet oxygen was produced in the aqueous phase and that diffusion to the micelle and penetration of the micelle barrier followed. Once in a micelle containing substrate, attack on the latter by singlet oxygen then led to products of oxidation. Assignment of $^1O_2$ as the reactive species should be made with care when oxidations are performed in aqueous solution because other oxidizing species may also participate.

These results and a later study comparing kinetic studies in H_2O and D_2O are consistent with an "averaging" of the lifetime of singlet oxygen as a result of rapid exit and entrance into the micelle during its lifetime (1×10^{-6} s in H_2O). In turn this conclusion is consistent with a number of investigations of the mobility of ground state oxygen in and out of micelles[48].

13. Synthetic Applications of Photochemistry in Micellar Systems; Practical Considerations

The selective capacity of solubilization of micellar aggregates based on their specific molecular organization opens, in principle, a wide variety of applications in preparative photochemistry. The present technological standard is, however, characterized by the limited capacity of solubilization of the applied surfactant, hence requiring vast volumes of solution to be photolyzed. Other limiting factors are: (1) the reactivity of the surfactant; (2) the restrictive temperature range in which micelles are stable; and (3) the low number of surfactants suitable for an eventually continuous separation of product and surfactant. Consequently, relatively few experiments with micellar solutions used in synthetic or preparative photochemistry have been reported.

Amphiphilic sensitizers[49] and quenchers may be separated from the aqueous phase like ordinary surfactants. For their crystallization upon addition of electrolytes and simultaneous extraction of the photoproducts by organic solvents, alkylsulfonic acid salts have been found to be convenient and practical.

Due to the temperature dependence of the solubility of these surfactants, the geometry of the photochemical reactors to be used should provide a clean separation of the micellar solution from the well. Experiments with immersion-type reactors have shown that the temperature difference between the photolyzed solution and the water-cooled jacket wall may cause the precipitation of the surfactant. In cases where immersion-type reactors have to be used, wells with evacuated outer jackets are recommended.

The use of substrate compounds on a preparative scale does not alter the technique of solubilization. While liquid substances are introduced with minute fluxes into well-agitated solutions of a chosen surfactant (concentration >CMC), solids are first dissolved in a suitable solvent of

high vapor pressure at a concentration as high as possible. A thin film of the substrate will coat the walls of a given flask after evaporating the stirred solution by a stream of inert gas. A solution of the surfactant placed into the flask and kept at high turbulence will solubilize the dispersed compound within hours.

Since aggregation of micellar systems varies with temperature changes, the use of thermostated vessels is highly recommended. Particularly, micelles containing substance solubilized in their hydrophobic core and surfactants with low solubilities tend to deposit insoluble films or to crystallize at the surface of cold spots. Consequently, film reactors providing a separation between the well and the liquid to be photolyzed are highly recommended[50]. For immersion type reactors, a well provided with an evacuated or thermostated outer compartment may prove helpful.

Work-up procedures consist basically of an extraction of the solubilized material by hydrocarbons, chlorinated hydrocarbons, or ethers of low boiling points. The use of special surfactants, such as amphiphilic redox chromophores[51] and sensitizers[49] may require a recyclization of such micelle forming compounds. Simultaneous separation and subsequent isolation of both the solubilized material and the surfactant is achieved by saturating the micellar solution prior to extraction with a salt of high solubility in water but of low solubility in polar organic solvents. While liquid-liquid extraction separates the solubilized compounds from the reaction mixture, the surfactant will precipitate and may be filtered, then purified for re-use by recrystallization from mostly polar organic solvents.

14. Electron Transfer in Transition Metal Ion Micelles

The simplest type of functional surfactant is one where the counterion is a participant in the redox reaction. For example, replacement of the Na^+ ions in sodium dodecyl sulfate (SLS) by Cu^{2+} yields assemblies in which Cu^{2+} ions constitute the counterion atmosphere of the micelle (Fig. 21).

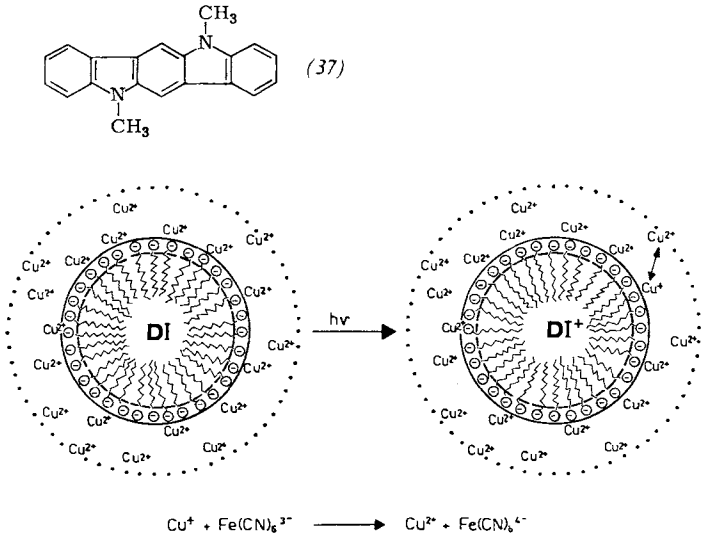


Fig. 21. Schematic representation of a $Cu(LS)_2$ micelle and of a photoinduced electron transfer of compound *(37)* (DI) in such a functional surfactant system.

These may be photoreduced to Cu^+ by suitable donor molecules incorporated in the micellar interior, *e.g.* by *N,N'*-dimethyl-5,11-dihydroindolo[3,2-*b*]carbazole (DI) *(37)*[24]. The absorption spectrum of an aqueous micellar solution of *(37)* is shown in Figure 22.

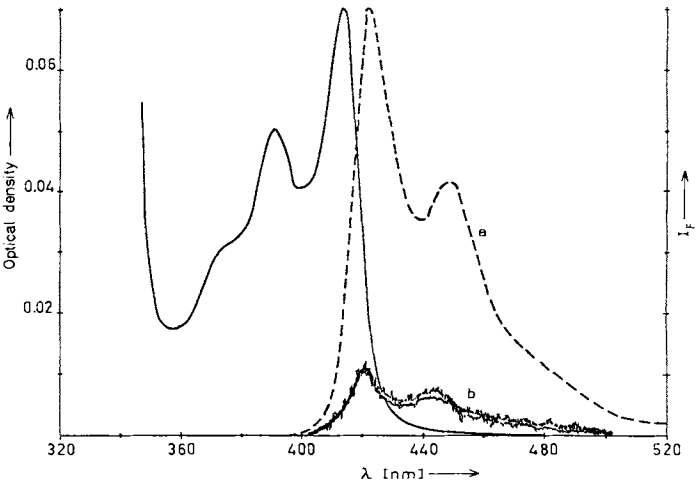


Fig. 22. Absorption and fluorescence spectra of *N,N'*-dimethyl-5,11-dihydroindolo[3,2-*b*]carbazole *(37)* (DI). a) Fluorescence of 3.7×10^{-5} M *(37)* in 0.2 M SLS; b) fluorescence of 5.1×10^{-5} M *(37)* in 0.1 M $Cu(LS)_2$.

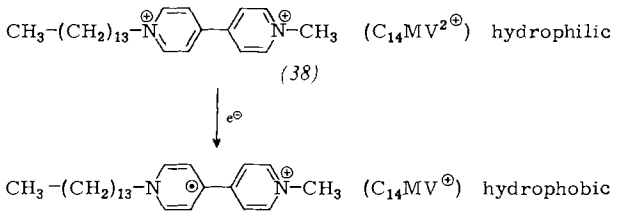
When dissolved in SLS micelles, *(37)* displays an intense fluorescence whose spectrum is also included in Figure 22. The fluorescence lifetime $\bar{\tau}_F$, measured by laser techniques, is 144 ns. Introduction of Cu^{2+} as counterion atmosphere induces a 300-fold decrease in the fluorescence yield and lifetime of *(37)*. The detailed laser analysis of this system showed that in $Cu(LS)_2$ micelles there is an extremely rapid electron transfer from the excited singlet state of *(37)* to the Cu^{2+} ions. This process occurs in less than a nanosecond and hence can compete efficiently with fluorescence and intersystem crossing. This astonishing result must be attributed to a pronounced micellar enhancement of the rate of the transfer reaction. It is of course a consequence of the fact that within such a functional surfactant unit regions with extremely high local concentrations of Cu^{2+} prevail. Theoretical estimates predict the counterion concentration in the micellar Stern layer to be between 3 and 6 M (see Section 10.2.)[52].

The significance of this functional organization becomes evident also when the back reaction of Cu^+ and DI^+ is considered. Previous studies[24,53] have shown that the intramicellar electron transfer from Cu^+ to DI^+, though thermodynamically high favorable, cannot compete kinetically with the escape of the cuprous ion from its native micelle into the aqueous phase. An efficient escape route is provided by the exchange with one of the Cu^{2+} ions present in high local concentration in the Gouy-Chapman layer. According to mere electrostatic arguments, the latter ion is $\exp(-e\psi/kT)$ times more likely to be absorbed on the micellar surface than Cu^+. Once in the aqueous phase, Cu^+ can be used for a second redox process such as the reduction of $Fe(CN)_6^{3-}$. The back reaction of the $Fe(CN)_6^{4-}$ with the oxidized donor, DI^+, is prevented by the negatively charged micellar surface. Hence, such a system is successful in storing light energy originally converted into chemical energy during a photoredox process.

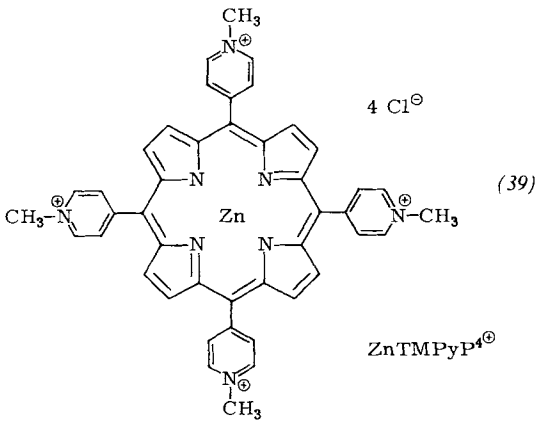
15. Micellar Systems Where the Surfactant Head Group Serves as an Electron Acceptor

15.1. Methylviologen Surfactant Assemblies

The encouraging results obtained with the simple surfactant systems enhanced our efforts to search for more developed molecular organizations suited for the conversion of light into chemical energy. We shall first consider assemblies containing the surfactant derivative of methylviologen as an electron acceptor. A characteristic feature of this species is that the oxidized form $C_{14}MV^{2+}$ has strongly hydrophilic properties while its reduced form is hydrophobic.



Consider now a solution containing $C_{14}MV^{2+}$ as an electron acceptor and the porphyrin derivative *(39)* as the photoactive electron donor. The concentration of $C_{14}MV^{2+}$ is



(39)

maintained below its CMC value, *i.e.* $<10^{-3}$ M. The reduction of the $C_{14}MV^{2+}$ by the triplet state of the porphyrin was studied by laser photolysis technique. Figure 23 shows the behavior of the optical absorption of a solution at 890 and 602 nm. The former is characteristic of the porphyrin triplet state while the latter reflects the production and disappearance of the redox products $ZnTMPyP^{5+}$ and $C_{14}MV^{+}$. Consider first a solution containing only $ZnTMPyP^{4+}$ and $C_{14}MV^{+}$. The reaction

$$ZnTMPyP^{4+} + C_{14}MV^{2+} \xrightarrow{h\nu} C_{14}MV^{+} + ZnTMPyP^{5+} \qquad (11)$$

occurs here reversibly: The decay of the triplet state is accompanied by the formation of redox products which, however, undergo a rapid back reaction (as shown in oscillogram b). In marked contrast to this behavior stand the results obtained in the presence of CTAC micelles. Here the forward electron transfer goes to completion without any subsequent

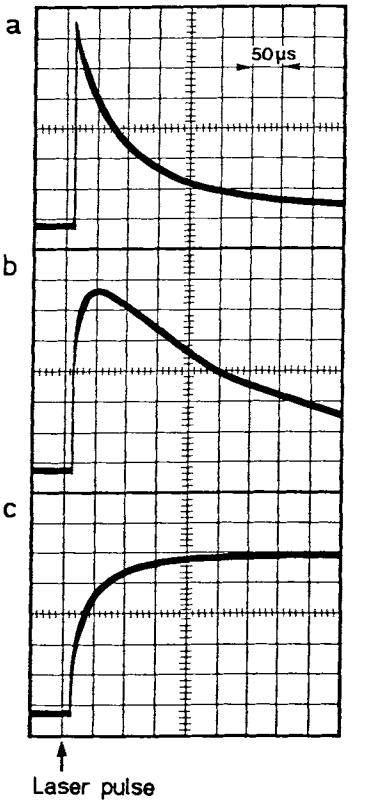


Fig. 23. Light-induced reduction of $C_{14}MV^{2+}$ by the triplet state of $ZnTMPyP^{4+}$. a) Triplet decay, $\lambda = 890$ nm; b) growth and decay of redox products in pure aqueous solution, $\lambda = 602$ nm; c) stabilization of redox products by CTAC micelles, $\lambda = 602$ nm. $[ZnTMPyP^{+}] = 5 \times 10^{-5}$ M, $[C_{14}MV^{2+}] = 10^{-3}$ M, $[CTAC] = 5 \times 10^{-2}$ M.

back reaction. In fact, the signal of $C_{14}MV^{+}$ and $ZnTMPyP^{5+}$ remains stable over many milliseconds. Detailed kinetic analysis shows that the back reaction is retarded by the CTAC micelles by at least a factor of 1000[63].

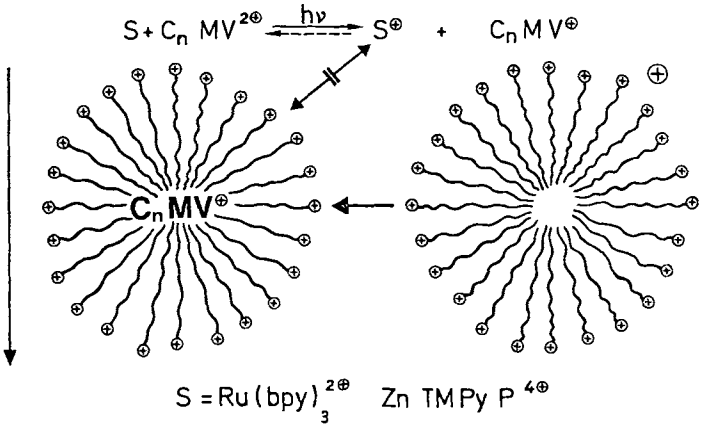


Fig. 24. Principle of charge separation by cationic micelles in the photoinduced reduction of amphiphilic viologen derivatives C_nMV^{2+}, *e.g. (38)*.

This charge separation effect induced by the micelles is explained schematically in Figure 24. The hydrophilic acceptor is mainly present in the aqueous phase and does not associate with the CTAC micelles. Upon reduction it acquires pronounced hydrophobic character. This leads to rapid solubilization in the cationic surfactant assemblies of CTAC. The

oxidized porphyrin is prevented from approaching the cationic micelles by their repulsive surface chearge. As the ζ-potential of CTAC micelles is about +100 mV the probability of encounter with $ZnTMPyP^{5+}$ is only 2×10^{-9}. This explains the effective micellar inhibition of the back reaction.

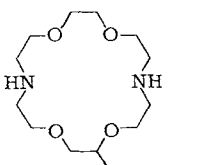
The $C_{14}MV^+$ produced in the photoredox reaction may be used to generate hydrogen from water. Recently, very active noble metal catalysts have been developed in our laboratory which can mediate the reaction:

$$2C_{14}MV^+ + 2H_2O \rightarrow 2C_{14}MV^{2+} + H_2 + 2OH^- \quad (12)$$

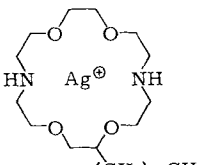
Continuous illumination of $ZnTMPyP^{4+}$ solutions containing $C_{14}MV^{2+}$, CTAC, and such a Pt catalyst leads to the production of hydrogen. In the initial experiments, EDTA or nicotinamides served as sacrificial donors to replenish the electron in $ZnTMPyP^{5+}$. However, more recently two nonsacrificial photochemical water-cleaving systems based on viologen derivatives have been introduced in our laboratory[64,65].

15.2. Reduction of Silver Ions in Aza-Crown Ether Surfactants

Macrocyclic compounds with a paraffinic chain were first described by *Cinquini et al.*[54]. In aqueous solution they readily form micelles with CMC values ranging between 10^{-5} and 10^{-3} M, depending on the exact nature of the head group and the chain length[55,56]. Crown ether surfactants are particularly suited as electron relays in redox events, since different metal ions covering a wide range of standard potentials may be inserted into the macrocyclic ring. Consider, for example, the crown 2-tetradecyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane *(40)*. Compound *(40)* strongly binds Ag^+ ions[57], the complexation constant being about 10^8.

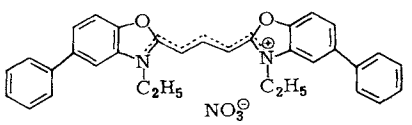


(40)



(41)

We shall now be concerned with the photoinduced reduction of the silver ion derivative *(41)*. This surfactant possesses a CMC value of 3×10^{-4} M. The micellar aggregates formed are relatively large, the molecular weight being 6.3×10^6 as determined by quasielastic light scattering technique. A variety of sensitizers when solubilized in aqueous micellar solutions of *(41)* were shown to be oxidatively bleached, with concomitant formation of Ag^0. Consider, for example, the cyanine dye *(42)*:



(42)

Its fluorescence emission is totally quenched ($\Phi_F < 10^{-6}$) in micellar solutions of *(41)*. On illumination with visible light,

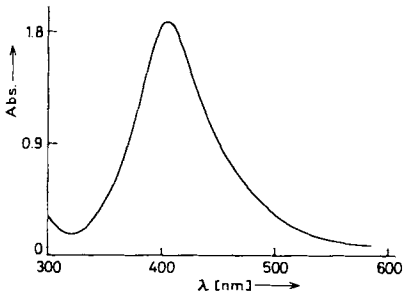


Fig. 25. Absorption spectrum of aza-crown ether *(40)* complexed and stabilized Ag^0 upon photolysis of the cyanine dye *(42)*.

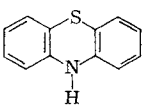
one observes a rapid bleaching of the cyanine and formation of a new stable absorption band with a maximum at $\lambda = 415$ nm (Fig. 25). This spectrum can be attributed to silver atoms stabilized by the macrocyclic ligand. It appears that in our system silver is prevented from aggregation by insertion in the crown ether cavity and hence preserved in the monoatomic state. The speed of Ag^0 formation is so rapid that it cannot be resolved by ns-laser photolysis techniques. Obviously, this effect has to be attributed to the close proximity of photoactive donor and Ag^+ sites on the surface of the micelle. The photoinduced reduction of Ag^+ can be performed with a number of other donor chromophores such as porphyrins, $Ru(bpy)_3^{2+}$, and pyrene. In all those cases no back reaction between oxidized donor and Ag^0 is observed. Apparently, through electrostatic interactions, the donor cation is ejected from the positively charged aggregates before back electron transfer can take place[58]. Once in the aqueous phase, the re-entry of the donor cation into the micelle is prevented by the repulsive surface charge. We conclude that in the photoinduced reduction of Ag^+ to silver atoms the functional macrocyclic surfactant serves three important purposes: high local concentration of the acceptor drastically accelerates the forward rate—and hence the yield— of reaction (13);

$$D^* + A \rightleftharpoons D^+ + A^- \quad (13)$$

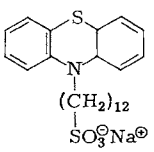
the Ag atom is stabilized by the macrocyclic ligand, and finally the back electron transfer is prevented by the microscopic electrostatic barrier provided by the lipid/water interface.

16. Functional Micelles with Attached Redox Chromophores

A significant development in the field of functional surfactants is the design of molecules where the redox chromophore is chemically linked to the hydrocarbon tail of the surfactant. It is expected that these "redox" micelles will play a fundamental role in light energy storing photoreactions. Consider, for example, the photoionization of phenothiazine (PTH) *(43)* which has been studied in anionic mi-



(43)



(44)

$$PTH \xrightarrow{h\nu} PTH^{\oplus\ominus} + e_{aq}^{\ominus} \quad (14)$$

celles[59,60,61]. Process (14) is monophotonic and leads to the formation of cation radicals and hydrated electrons. However, such a system is not suitable for use in the photoproduction of solvated electrons in an energy storing device since the solubility of *(43)* in the anionic micelles is limited ($<2\times10^{-4}$ M) and $PTH^{\oplus\ominus}$ is rapidly deprotonating. This renders the capacity of the system low. This problem is overcome when the functional PTH derivative sodium 12-(10′-phenothiazinyl)dodecylsulfonate *(44)* is used as the light absorbing chromophore. *(44)* micellizes readily at concentrations $>5\times10^{-4}$ M. An interesting cooperative effect was discovered with this redox chromophore[62]: When monomeric solutions of *(44)* are irradiated with low intensity light, no photoionization occurs. In contrast, above the CMC, hydrated electrons and cations are produced monophotonically in high yield. Moreover, the lifetime of the cation is hours to days in such a solution. This effect may be understood in terms of photoejection of electrons from the micellar into the aqueous phase and subsequent stabilization of the radical ions by the charged micelle water interface. The latter acts as a Schottky barrier, preventing the approach of hydrated electrons and parent ions (see Fig. 26).

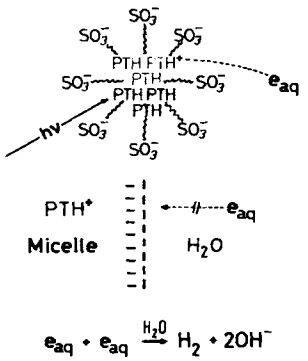


Fig. 26. Schematic illustration of the photoionization and charge separation processes in functional micelles formed by PTH—$SO_3^{\ominus}Na^{\oplus}$ *(44)* above the CMC. Re-entry of the electrons into the micelle is prevented by the potential barrier on its surface.

17. Conclusion

The conventional model of ionic micelles considers them as aggregates which form in aqueous solutions of detergents and that are capable of sequestering organic species. The photophysics of organic molecules that are solubilized by micelles provide information on the composition, structure and dynamics of the micellar environment. In turn, photochemical reactions in micelles display characteristics that distinguish them from comparable reactions in homogeneous solvents.

A number of specific examples of photoluminescence techniques are applicable and useful to probe the nature and behavior of micelles. For example, aggregation numbers, exit and entrance rates of solubilized species, and equilibrium distributions of solutes may be evaluated from photoluminescent probes. Information on structure and dynamics of micelles and the methods and strategy for obtaining this information, should be applicable to the investigation of more complex assemblies of biological interest such as membranes and cells.

The micellar aggregates may influence photophysical and photochemical properties of solutes in interesting ways as a result of the statistics, the restricted space, the local concentration effects, and the polar proximity of head groups and gegenions imposed upon species that are compartmentalized in a micellar aggregate. For example, phosphorescence efficiencies may be increased both by reduction of triplet quenching processes due to statistics and restricted space features of micelles and by the enhancement of phosphorescence rates by heavy atom gegenions. Excimer and exciplex formation may be greatly enhanced by local concentration effects. The lifetime of species produced by electron transfer may be lengthened by association with a micelle and by the stabilization of these highly reactive charged intermediates due to the proximate polar environment, which allows kinetic control of the important electron back transfer reactions. Photolyses which produce organic radical pairs in a micelle create high (0.1 M) local concentrations of organic radical pairs. These concentrations are maintained within the micelle's restricted space for relatively long time periods and allow for selectivity in the reactions of the radical pair. In effect, the micelle serves as a "super cage" for radical pairs and keeps them together in a restricted space for a time orders of magnitude longer than is possible in fluid homogeneous solution. Magnetic isotope and magnetic field effects of radical pairs are amplified in micellar systems.

Finally, the idea of "functionalized micelles", the strategy in which detergents themselves possess photophysically or photochemically active groups which are localized in the hydrophobic portion or in the ionic portion of the micellar structure, has provided novel information and has lead to unusual chemical processes. The extension of these ideas will surely be seen in current and future experimental investigations.

N. J. Turro thanks the National Institutes of Health (Grant CM-25523) for their generous support of this research. Acknowledgment is made to the Swiss National Foundation for supporting the work of M. Grätzel and A. M. Braun under grant No. 4.061.076.04 and 4.101.076.04, respectively. Both are also grateful to Ciba-Geigy Ltd., Basel, Switzerland, for financial and technical aid.

Received: October 22, 1979;
revised: June 26, 1980 [A 334 IE]
German version: Angew. Chem. 92, 712 (1980)

[1] For recent reviews of photoluminescence and photochemistry in micelles see: a) *J. K. Thomas*, Acc. Chem. Res. *10*, 133 (1977); b) *K. Kalyanasundaram*, Chem. Soc. Rev. *7*, 453 (1978); c) *M. Grätzel, J. K. Thomas* in *E. L. Wehry:* Modern Fluorescence Spectroscopy. Vol. 2. Plenum Press, New York 1976, p. 169; d) *K. L. Mittal:* Micellization, Solubilization, and Microemulsions. Vol. 1 and 2. Plenum Press, New York 1977; e) *C. Tanford:* The Hydrophobic Effect. Wiley, New York 1973; f) *J. H. Fendler, E. J. Fendler:* Catalysis in Micellar and Macromolecular Systems. Academic Press, New York 1975; g) for a recent review of photoluminescence and photochemistry see: *N. J. Turro:* Modern Molecular Photochemistry. Benjamin/Cummings, Menlo Park, California 1978.

[2] *N. E. Schore, N. J. Turro*, J. Am. Chem. Soc. 96, 306 (1974); 97, 2488 (1975).

[3] *N. J. Turro, K. C. Liu, M. F. Chow, P. Lee*, Photochem. Photobiol. *27*, 523 (1978).

[4] a) *K. Kalyanasundaram, F. Grieser, J. K. Thomas*, Chem. Phys. Lett. *51*, 507 (1977); b) *R. Humphry-Baker, Y. Moroi, M. Grätzel, ibid. 58*, 207 (1978).

[5] a) *G. Weber*, Annu. Rev. Biophys. Bioeng. *1*, 553 (1972); b) *M. Shinitzky, A. C. Dianoux, C. Gitler, G. Weber*, Biochemistry *10*, 2106 (1971).
[6] *H. J. Pownall, L. C. Smith*, J. Am. Chem. Soc. *95*, 3136 (1973).
[7] *P. P. Infelta, M. Grätzel, J. K. Thomas*, J. Phys. Chem. *78*, 190 (1974).
[8] a) *N. J. Turro, M. Aikawa, A. Yekta*, J. Am. Chem. Soc. *101*, 772 (1979); b) *J. Emert, C. Behrens, M. Goldenberg, ibid. 101*, 771 (1979); c) *K. Zachariasse*, Chem. Phys. Lett. *57*, 429 (1978).
[9] a) *R. R. Hautala, N. J. Turro*, Mol. Photochem. *4*, 545 (1972); b) *R. R. Hautala, N. E. Schore, N. J. Turro*, J. Am. Chem. Soc. *95*, 5508 (1973); c) *L. K. Patterson, E. Vicil*, J. Phys. Chem. *96*, 306 (1974).
[10] a) *A. Yekta, M. Aikawa, N. J. Turro*, Chem. Phys. Lett. *63*, 543 (1979); b) *P. P. Infelta, ibid. 61*, 88 (1979); c) *B. K. Selinger, A. R. Watkins, ibid. 56*, 99 (1978); d) *R. C. Dorrance, T. F. Hunter*, J. Chem. Soc. Faraday Trans. *70*, 1572 (1974).
[11] *N. J. Turro, A. Yekta*, J. Am. Chem. Soc. *100*, 5951 (1978).
[12] *M. Almgren, F. Grieser, J. K. Thomas*, J. Am. Chem. Soc. *101*, 2021 (1979).
[13] *M. Almgren, F. Grieser, J. K. Thomas*, J. Am. Chem. Soc. *101*, 279 (1979).
[14] *J. B. Birks:* Photophysics of Aromatic Molecules. Wiley, New York 1970; Organic Molecular Photophysics. Wiley, New York 1976, Vol. 1 and 2.
[15] *S. C. Wallace, J. K. Thomas*, Radiat. Res. *54*, 49 (1973).
[16] *M. Grätzel, J. K. Thomas*, J. Am. Chem. Soc. *96*, 1869 (1974).
[17] *J. S. Ham*, J. Chem. Phys. *21*, 756 (1953).
[18] a) *A. Nakajima*, Bull. Chem. Soc. Jpn. *44*, 32 (1971); b) Spectrochim. Acta *A 30*, 860 (1974); c) J. Mol. Spectrosc. *61*, 467 (1976).
[19] *K. Kalyanasundaram, J. K. Thomas*, J. Am. Chem. Soc. *99*, 2039 (1977).
[20] *Th. Förster, B. K. Selinger*, Z. Naturforsch. A *19*, 38 (1964).
[21] a) *R. C. Dorrance, T. F. Hunter*, J. Chem. Soc. Faraday Trans. I *68*, 1312 (1972); b) *73*, 1891 (1971).
[22] a) *B. B. Craig, K. Kirk, M. A. Rodgers*, Chem. Phys. Lett. *49*, 437 (1977); b) *U. Khuangu, B. K. Selinger, R. McDonald*, Aust. J. Chem. *24*, 1 (1976).
[23] *P. P. Infelta, M. Grätzel*, J. Chem. Phys. *70*, 179 (1979).
[24] *Y. Moroi, A. M. Braun, M. Grätzel*, J. Am. Chem. Soc. *101*, 567 (1979).
[25] *G. Rothenberger, P. P. Infelta, M. Grätzel*, J. Phys. Chem. *83*, 1871 (1979).
[26] *M. Hatley, J. Kozak, G. Rothenberger, P. P. Infelta, M. Grätzel*, J. Phys. Chem., in press.
[27] *M. Geiger, N. J. Turro*, Photochem. Photobiol. *22*, 273 (1975).
[28] *N. J. Turro, M. Aikawa, A. Yekta*, Chem. Phys. Lett. *64*, 473 (1979).
[29] *P. J. Wagner*, Acc. Chem. Res. *4*, 1681 (1971).
[30] *N. J. Turro, K. C. Liu, M. F. Chow*, Photochem. Photobiol. *26*, 413 (1977).
[31] *P. R. Worsham, D. W. Eaker, D. G. Whitten*, J. Am. Chem. Soc. *100*, 7091 (1978).
[32] *A. M. Braun, M. Krieg, N. J. Turro, M. Aikawa, G. A. Graf*, to be published.
[33] a) *R. Breslow, S. Kotabatake, J. Rothbard*, J. Am. Chem. Soc. *100*, 8156 (1978); b) *R. Breslow, J. Rothbard, F. Herman, M. L. Rodrigues*, ibid. *100*, 1213 (1978).
[34] *M. Mitani, T. Suzuki, H. Takenchi, K. Koyama*, Tetrahedron Lett. *1979*, 803.
[35] a) *P. S. Engel*, J. Am. Chem. Soc. *92*, 6074 (1970); b) *W. K. Robins, R. H. Eastman, ibid. 92*, 6076, 6077 (1970); c) *G. Quinkert, K. Opitz, W. W. Wiersdorf, J. Weinlich*, Tetrahedron Lett. *1963*, 1863.
[36] *N. J. Turro, W. R. Cherry*, J. Am. Chem. Soc. *100*, 7432 (1978).
[37] *P. de Mayo*, personal communication, February 1979.
[38] a) *N. J. Turro, B. Kraeutler*, J. Am. Chem. Soc. *100*, 7432 (1978); b) *R. S. Hutton, H. D. Roth, B. Kraeutler, W. R. Cherry, N. J. Turro, ibid. 101*, 2227 (1979).
[39] *A. M. Braun, K. Ramsteiner*, to be published.
[40] a) *I. Rico, M. T. Maurette, E. Oliveros, M. Rivière, A. Lattes*, Tetrahedron Lett. *1978*, 4795; b) *R. Fargues, M. T. Maurette, E. Oliveros, M. Rivière, A. Lattes*, Nouv. J. Chim. *3*, 487 (1979).
[41] *K. H. Lee, P. de Mayo*, J. Chem. Soc. Chem. Commun. *1979*, 493.
[42] *Y. Nakamura, Y. Imakura, T. Kato, Y. Morita*, J. Chem. Soc. Chem. Commun. *1977*, 887.
[43] *Y. Nakamura, Y. Imakura, Y. Morita*, Chem. Lett. *1978*, 965.
[44] *R. R. Hautala, R. L. Letsinger*, J. Org. Chem. *36*, 3762 (1971).
[45] *K. Yamada, K. Shigehiro, T. Kujozuka, H. Iida*, Bull. Chem. Soc. Jpn. *51*, 2447 (1978).
[46] *A. A. Gorman, G. Lovering, M. A. J. Rodgers*, Photochem. Photobiol. *23*, 399 (1976).
[47] *Y. Usui, M. Tsukada, H. Nakamura*, Bull. Chem. Soc. Jpn. *51*, 379 (1978).
[48] *N. J. Turro, A. Yekta, M. Aikawa*, Chem. Phys. Lett., in press.
[49] *R. Humphry-Baker, A. M. Braun, M. Grätzel*, to be published.
[50] *A. M. Braun, G. Nussberger, H. J. Pöschel* in *J. Cornelisse:* Organic Photochemical Synthesis. Vol. 3, in preparation.
[51] a) *M. P. Pileni, A. M. Braun, M. Grätzel*, Photochem. Photobiol. *31*, 423 (1980); b) *M. Krieg, M. P. Pileni, A. M. Braun, M. Grätzel*, to be published.
[52] a) *W. K. Mathews, J. W. Larsen, M. T. Pikal*, Tetrahedron Lett. *1972*, 513; b) *D. Stighter*, J. Phys. Chem. *68*, 3603 (1964).
[53] *Y. Moroi, P. P. Infelta, M. Grätzel*, J. Am. Chem. Soc. *101*, 573 (1979).
[54] *M. Cinquini, F. Montanari, P. Tundo*, J. Chem. Soc. Chem. Commun. *1975*, 393.
[55] *J. Le Moigne, P. Gramain, J. Simon*, J. Colloid Interface Sci. *60*, 565 (1977).
[56] *Y. Moroi, E. Promauro, M. Grätzel, E. Pelizzetti, P. Tundo*, J. Colloid Interface Sci. *64*, 341 (1974).
[57] For complexation of metal ions by aza-crown ethers, see: a) *J. M. Lehn, J. P. Sauvage, B. Dietrich*, J. Am. Chem. Soc. *92*, 2916 (1970); b) *H. K. Frensdorf, ibid. 93*, 600 (1971).
[58] *R. Humphry-Baker, M. Grätzel, P. Tundo, E. Pelizzetti*, Angew. Chem. *91*, 669 (1979); Angew. Chem. Int. Ed. Engl. *18*, 630 (1979).
[59] *S. A. Alkaitis, G. Beck, M. Grätzel*, J. Am. Chem. Soc. *97*, 5723 (1975).
[60] *S. A. Alkaitis, M. Grätzel, A. Henglein*, Ber. Bunsenges. Phys. Chem. *79*, 541 (1975).
[61] *S. A. Alkaitis, M. Grätzel*, J. Am. Chem. Soc. *98*, 3549 (1976).
[62] *M. Krieg, A. M. Braun, R. Humphry-Baker, M. Grätzel*, to be published.
[63] *P. A. Brugger, P. P. Infelta, A. M. Braun, M. Grätzel*, J. Am. Chem. Soc., in press.
[64] *K. Kalyanasundaram, M. Grätzel*, Angew. Chem. *91*, 759 (1979); Angew. Chem. Int. Ed. Engl. *18*, 701 (1979).
[65] *J. Kiwi, E. Borgarello, E. Pelizzetti, M. Visca, M. Grätzel*, Angew. Chem. *92*, 663 (1980); Angew. Chem. Int. Ed. Engl. *19*, 646 (1980).

The Structure of Simple Molecular Liquids

By Manfred D. Zeidler[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

Liquid structure is described by the pair-correlation function. If the liquid particles are molecules then the respective correlation function depends on distance and several angular variables; hence, for the sake of simplicity a symmetry-adapted representation must be used. The most important structural parameters of this molecular pair-correlation function can be determined approximately by a combination of several scattering experiments, such as neutron (employing different isotopes), X-ray and electron diffraction. Light scattering, dielectric, and nuclear magnetic relaxation experiments provide further, albeit less direct, access to such determinations. Some results obtained by measurements on chloroform are reported. Theoretical computations of these structural parameters are also discussed.

1. Introduction

The important role of liquids in chemical experiments can hardly be overemphasized, for most chemical reactions are carried out in the liquid phase. Apart from water, organic liquids are primarily used as solvents. The liquids of initial interest in chemistry are those which may be termed molecular liquids as distinct from atomic liquids (liquid rare gases).

Unfortunately, our theoretical understanding of the liquid state, occupying a position intermediate between the well-ordered solids and the disordered gases, is beset with considerable problems. During the last three decades remarkable progress could be made in the case of atomic liquids, whereas molecular liquids still give rise to many difficulties.

This explains why interest still centers on simple molecular liquids, *i.e.* molecules containing less than about ten atoms, exhibiting high symmetry, having no internal flexibility, and obeying the laws of classical statistical mechanics.

The aim of a theory of the liquid state is the calculation of thermodynamic data and of transport coefficients from given intermolecular potentials. The first task is more easily dealt with since we restrict ourselves to equilibrium properties (statistical thermodynamics), whereas transport coefficients have to be calculated within the framework of nonequilibrium statistical mechanics.

In relation to statistical mechanical theories the special importance of structural investigations follows from the fact that an intermediate experimental check can be made in going from the input of the potential to the output of the thermodynamical data: only those theories are acceptable which predict the correct structure.

2. The Intermolecular Potential

Even the input parameters for the theory cause remarkable difficulties. Clearly, the intermolecular potential depends on a whole series of parameters. Figure 1 shows the spatial arrangement of a pair of non-spherical molecules. A molecule-fixed coordinate system is assigned to each partner. In principle it may be chosen arbitrarily. However, it is convenient to

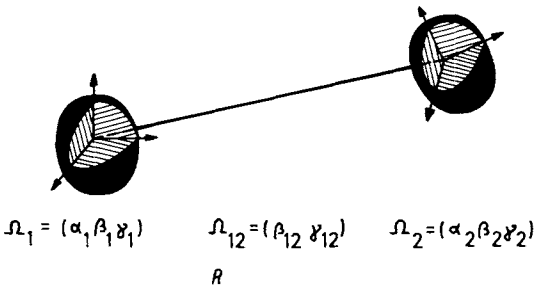


Fig. 1. Coordinates for a pair of non-spherical molecules.

define it in such a way that its axes coincide with the symmetry axes of the molecule. At a later stage the molecular symmetry may then be used to simplify the theoretical relations. As shown in Figure 1, two sets of Eulerian angles are needed to describe the orientation of both molecules in a reference system chosen arbitrarily (each set Ω consists of three angles α, β, γ). Moreover, a degenerate set of Eulerian angles (consisting of the two angles β and γ) is introduced to describe the orientation of the vector joining the molecular centers. An attentive reader will immediately notice that, strictly speaking, three Eulerian angles are redundant. Instead of an arbitrary choice of the reference system we are free to define the molecule-fixed coordinate system of one of the interaction partners as a reference system. However, our feeling for symmetry tells us that such a preference of a particular partner should be avoided. Otherwise, the symmetry inherent in the theoretical relations could be destroyed. Moreover, the arbitrary reference system may, if necessary, be identified with any system defined by the physical operation underlying the measurements. In any case it is clear that the intermolecular potential is a function of six independent parameters, *i.e.*, the distance R and five angles.

The question immediately arises as to how a function of so many variables can best be represented, if at all. This problem is generally associated with orientation dependent quantities: it always arises on going from spherical atoms to mole-

[*] Prof. Dr. M. D. Zeidler
Institut für Physikalische Chemie der Universität
Schlossplatz 4, D-4400 Münster (Germany)

On leave from the Institut für Physikalische Chemie und Elektrochemie der Universität
D-7500 Karlsruhe (Germany)

cules. A brief summing-up of the situation reveals that a tabulated representation is out of the question, since a rather more accurate documentation, *e.g.* using an angular grid of 5° for $0 \leq \beta \leq 180°$ and $0 \leq \alpha, \gamma \leq 360°$, and a radial grid of 0.1 for $0.8 \leq R/\sigma \leq 3$ (where σ is the distance at which the potential is just zero owing to mutual compensation of repulsive and attractive forces) would end up with 10^{10} entries. In theoretical treatises, however, one requires relatively clear and distinct analytical expressions.

To proceed further one introduces symmetry-adapted descriptions, as is usually done when confronted with complex problems. Obviously, the intermolecular potential does not depend on the absolute location of the molecular pair; in other words, it is totally symmetric with respect to infinitesimal rotations of the pair in three-dimensional space. Moreover, if the interaction partners exhibit an intrinsic molecular symmetry, *e.g.* if they are of tetrahedral shape, the intermolecular potential is also totally symmetric under the symmetry operations of these tetrahedrons. Again the symmetry operations involve rotations, but in contrast to the above situation these rotations are finite. However, all finite rotations may be regarded as sums of infinitesimal rotations. Apart from the orientations discussed above, also rotations in three-dimensional space can be described by Eulerian angles, because a rotation transforms a given orientation into a new one. A mathematical formulation of rotations is obtained by the introduction of transformation matrices, which relate the coordinates before and after a rotation. In principle, the coordinates, *i.e.* functions of the Eulerian angles, may be chosen arbitrarily. However, there exists a specially distinguished set of functions, characterized by the fact that the transformation matrix possesses the most simple structure. Those readers who are familiar with the mathematical theory of symmetry, the so-called group theory[1], will recognize that one chooses the basis for the irreducible representation of the continuous three-dimensional rotation group. These basis functions (whose explicit relations to the Eulerian angles are not needed here) may be written as $\Phi_{m_1 m_2}^{(l_1 l_2 l_{12})}(\Omega_1, \Omega_2, \Omega_{12})$. The indices l_i can take all integral values between 0 and ∞, the m_i all integral values from $-l_i$ to $+l_i$. In the construction of these functions the invariance of the potential with respect to the rotations of the molecular pair has already been taken into consideration; therefore, there appear only five instead of eight indices (corresponding to five or eight angles, respectively). A typical property of basis functions of irreducible representations in group theory is their orthogonality; consequently, it is also an important feature of these Φ-functions.

We next define potentials which are weighted with these Φ-functions and which are averaged over all orientations:

$$u_{m_1 m_2}^{(l_1 l_2 l_{12})}(R) = \iiint u(R, \Omega_1, \Omega_2, \Omega_{12}) \Phi_{m_1 m_2}^{(l_1 l_2 l_{12})}(\Omega_1, \Omega_2, \Omega_{12})^* \, d\Omega_1 \, d\Omega_2 \, d\Omega_{12} \quad (1)$$

where * denotes the complex conjugate (Φ may become complex). These quantities will be referred to as *u*-coefficients. Each coefficient, characterized by five indices, depends on the distance *R*, only. Knowledge of all these coefficients allows the reconstruction of the potential according to

$$u(R, \Omega_1, \Omega_2, \Omega_{12}) = \sum_{l_1 l_2 l_{12}} \sum_{m_1 m_2} u_{m_1 m_2}^{(l_1 l_2 l_{12})} \cdot \Phi_{m_1 m_2}^{(l_1 l_2 l_{12})} \quad (2)$$

One might immediately ask how many terms of this expansion are needed. The answer depends on the accuracy which is required for a characterization of the orientation dependence. It is known from group theory that the number of symmetry operations, summed up in definite classes, is equal to the number of irreducible representations in a symmetry group. To describe small differences in orientation, more rotational operations must of course be taken into account than are required in the case of rough differences, *i.e.* the expansion (2) involves more terms in the former case.

So far the above expansion corresponds to a Fourier transformation of the angular space. The more isotropic the potential, the faster the expansion converges. For a totally isotropic potential, only the term $u_{00}^{(000)}$ contributes. One may estimate from an uncertainity relation of the form

$$l_{max} = 2\pi/\Delta\varphi \quad (3)$$

up to which term with index l the expansion has to be considered, allowing an uncertainty $\Delta\varphi$ in the respective angle.

In order to obtain the final number of terms up to a given value l, some symmetry considerations are necessary, with which the vanishing terms can immediately be determined. As mentioned above, the pair potential has to be invariant under symmetry operations, in particular rotations, of both molecules. A suitable choice of the molecule-fixed axes facilitates such considerations. If the molecule possesses a K-fold symmetry axis, this may be chosen as the reference axis for the first Eulerian angle; then the index m (for molecule 1 or 2, respectively) must be an integral multiple of K. Thus, *e.g.*, for a three-fold axis all terms vanish, except those with $m = 0, 3, 6, 9 \ldots$; for rotation axes of infinite order (linear molecules) only terms with $m = 0$ contribute. Similar conditions hold for the second molecule-fixed axis, being orthogonal to the first axis discussed above. In the latter case the possible values of l are influenced. Considering *e.g.* linear molecules with a two-fold symmetry axis perpendicular to the axis of infinite order, l is limited to even numbers. We next consider a molecule possessing a rotation reflection axis. Then, m is determined by the order of the proper rotation axis, whereas the order of the rotation reflection axis determines the possible values of l. An instructive example is the tetrahedron, which exhibits a four-fold rotation reflection axis, coinciding with a proper two-fold axis. In this case both the sum $l + \frac{2m}{4}$ and m itself must be even. Finally, if we are dealing with identical molecules 1 and 2, the result must also be invariant with respect to an interchange of the indices l_1, l_2 and m_1, m_2, apart from the occurrence of a trivial factor $(-1)^{l_1 + l_2}$. Moreover, the possible values l_{12} are always restricted by the condition $|l_1 - l_2| \leq l_{12} \leq l_1 + l_2$; in addition, the sum $l_1 + l_2 + l_3$ must be even. The latter conditions follow from the invariance of the pair potential in the reference system.

These considerations show in which cases an expansion similar to eq. (2) will provide a useful representation of orientation dependent quantities. In any case, the number of data is manageable compared with the astronomically large number of entries in the aforementioned tabulation. An expansion according to eq. (2) was probably first introduced by *Jepsen* and *Friedman*[2], though similar but less general for-

mulations have been discussed in the earlier literature[3-5]. Detailed treatments may be found in references[6-9].

A calculation of u-coefficients is possible on the basis of certain models, one of the most popular and physically reasonable being the atomic model, where atoms are assumed as the interaction centers. This interaction is usually described by an empirical expression of the Lennard-Jones type:

$$u(R) \sim \varepsilon \left[\left(\frac{\sigma}{R}\right)^{\alpha} - \left(\frac{\sigma}{R}\right)^{\beta}\right] \tag{4}$$

where the four parameters ε, σ, α and β are the depth of the potential at its minimum, the distance at which the potential is zero, and the exponents characterizing repulsion and attraction. Frequently used values are $\alpha = 12$ and $\beta = 6$; at least the latter value can be established theoretically. With the above expression one then obtains for the u-coefficients of the molecular potential[9,10]:

$$u_{m_1 m_2}^{(l_1 l_2 l_{12})}(R) \sim \sum_{AB} Y_{m_1 m_2}^{(l_1 l_2)}(\theta_A, \varphi_A, \theta_B, \varphi_B) \times \varepsilon_{AB}\left[\left(\frac{\sigma_{AB}}{R}\right)^{\alpha_{AB}} X^{(l_1 l_2 l_{12})}\left(\alpha_{AB}, \frac{r_A}{R}, \frac{r_B}{r_A}\right) - \left(\frac{\sigma_{AB}}{R}\right)^{\beta_{AB}} X^{(l_1 l_2 l_{12})}\left(\beta_{AB}, \frac{r_A}{R}, \frac{r_B}{r_A}\right)\right] \tag{5}$$

Eq. (5) holds only in the range $R > r_A + r_B$; its application requires knowledge of the polar coordinates r, θ, φ in the molecule-fixed coordinate system. Summation runs over all pair-interactions AB. The functions X and Y are easily calculated; X contains a convergent series.

Obviously, the atom model suffers from the fact that shifts of the electrons due to the formation of chemical bonds are neglected. However, this effect can be accounted for by the addition of electric multipole interactions. This procedure is quite simple, because the multipole expansion is in accordance with the expansion in eq. (2). In particular, in the non-overlapping region the following relation holds[2,11]:

$$u_{m_1 m_2}^{(l_1 l_2 l_1 + l_2)}(R) \sim \frac{M_{l_1} \cdot M_{l_2}}{R^{l_1 + l_2 + 1}} \tag{6}$$

where M_l is the respective multipole moment (M_1 = dipole moment, M_2 = quadrupole moment, M_3 = octupole moment, *etc.*). In a similar way one can account for contributions due to induction and dispersion forces. If the multipole moments of the molecule are known from other sources, the respective calculations are easily performed.

An examination of the input potential on the basis of experimental quantities is only meaningful if the theoretical interrelationship is well established. This is true for the second virial coefficient, which only depends on pair interactions. The explicit relation is:

$$B(T) = 2\pi N_A \left(\frac{1}{8\pi^2}\right)^3 \int\int\int\int [1 - e^{-u(R,\Omega_1,\Omega_2,\Omega_{12})/kT}] R^2 \, dR \, d\Omega_1 \, d\Omega_2 \, d\Omega_{12} \tag{7}$$

On taking into consideration eq. (2) and integrating over all angles the second virial coefficient can be related to the u-coefficients.

3. Description of the Structure

In a solid the constituents are located at definite positions, resulting in a lattice, the structure of which may easily be described. In contrast the particles in a liquid can be arranged almost at random; only at some positions is there a slightly diminished or increased distribution. Consequently, a structural description of the type that is well established for solids is impossible. Instead, one adapts a concept known from statistics, the so-called correlation function. The correlation function yields the probability density of finding a given configuration of h coordinates. The coordinates themselves may consist of radial and orientational coordinates. If the sample consists of N particles, the N-particle correlation function is related to the potential energy *via* the Boltzmann factor:

$$g_N(q^N) \sim e^{-U(q^N)/kT} \tag{8}$$

q stands for the total set of single particle coordinates, and q^N denotes the total set of coordinates of all particles. If now a sub-set consisting of h particles of the total sample is considered, it is convenient to introduce reduced correlation functions

$$g_h(q^h) = \frac{1}{(N-h)!} \int g_N(q^N) \, dq^{N-h} \tag{9}$$

which are obtained by integration over all coordinates of the $(N - h)$ species not included in the sub-set.

In most applications the potential energy in eq. (8) is approximated by a sum over the two-particle potentials discussed in the preceding section. The sum covers all pairs AB, the number of which is quite obviously $(1/2)(N^2 - N)$. This fundamental assumption provides the basis for the so-called pair theory of liquids. At the present stage it is questionable whether extension to higher correlations is worthwhile. Of course, deviations from the pair approximation may occur within the limits of some percent, but these difficulties can be solved in a later refinement.

Clearly, in the pair theory the pair correlation function, *i.e.* the reduced correlation function with $h = 2$, plays an important role. Since we are concerned exclusively with this function, we drop the subscript 2. The relevant coordinates q are the same as discussed above for the pair potential, so we therefore denote the function by $g(R, \Omega_1, \Omega_2, \Omega_{12})$. All features of an orientation dependent quantity, discussed in the preceeding section, prove correct in this case, too. An analogous expansion to that in eq. (2) leads to g-coefficients, which form the basis for a quantitative description of the structure of a liquid[5-7].

4. From the Intermolecular Potential to the Structure

There exists only one reliable method for the calculation of g-coefficients from an input potential: computer simulation[12]. Of the two possible procedures, *i.e.* molecular dynamics and the Monte-Carlo method, the former is often preferred, because apart from equilibrium properties, transport coefficients can also be calculated. The procedure of

molecular dynamics is based on the numerical solution of Newton's equations of motion for a many-particle system (typically 4×3^3 up to 4×6^3 particles are accounted for). At first, the force acting on a particle is determined from the total potential energy, which is represented by a sum over all pair potentials. In the next step, accelerations, velocities, and positions are determined as a function of time, using optimum time increments. In spite of efficient programming and optimizing, especially in calculating the force, typical computer times of several minutes up to several hours are necessary per simulation of a molecular liquid on modern computers. Especially difficult is the calculation of rotational motion, since the relevant equations of motion, expressed by Eulerian angles, involve numerical instabilities. Various alternative treatments have therefore been attempted (for a review of the pertinent literature see [13]). A particularly attractive method has recently been developed by *Ryckaert et al.*[14]. The various atoms of a molecule are first assumed to move independently, *i.e.* they are allowed to undergo an independent translational motion. Thus, the well established computer-simulation procedures developed for atomic liquids can be used. Naturally, the molecules cannot decompose; therefore, one introduces additional constraints which preserve the intrinsic molecular geometry.

Interesting properties, such as the pair correlation function, are then obtained by evaluating the respective time averages. For this purpose one generates *e.g.* 2000 configurations; with a typical time increment of 5×10^{-15} s the course of the system with time is thus monitored over 10 ps. However, the average is only based on each 10th or 20th configuration, *i.e.*, one waits until marked changes have occurred in the system. In order to calculate g-coefficients according to eq. (1) one utilizes the fact that the ratio $g_{m_1m_2}^{(l_1l_2l_{12})}/g_{00}^{(000)}$ represents the angular average of the function $\Phi_{m_1m_2}^{(l_1l_2l_{12})}$ at the distance R (due to $\Phi_{00}^{(000)}=1$). The center-center distances R of all molecular pairs are then calculated for each configuration and likewise the functions $\Phi_{m_1m_1}^{(l_1l_2l_{12})}$ from the Eulerian angles. Then, within a discrete range ΔR, the results for the Φ-functions characterized by identical indices are added. Finally, the total sum over all considered configurations is calculated, and the result normalized in a suitable way. Thus, the sum in each range ΔR must be divided by $4\pi R^2 \Delta R$ in order to obtain the particle density, which on division by the 'macroscopic' number density of particles ρ yields the probability density.

So far, g-coefficients have been determined by the aid of computer simulations for the following model potentials: Two-center hard spheres[15], two-center Lennard-Jones potential neglecting[16,17], or accounting for quadrupolar interaction[18,19], three-center Lennard-Jones potential[20]. These potentials should approximate the behavior of the molecules N_2, F_2, Cl_2, Br_2, CO_2 and CS_2. Figure 2 shows the results obtained by *Singer* for Cl_2[17].

Apart from computer simulations several attempts have been made to find analytical methods for the calculation of g-coefficients, but with very little success. One should require, of course, that such methods are faster and more efficient than computer simulations. For atomic liquids there are well established analytical methods available. One therefore tries to extend such procedures to include molecular systems. The most reasonable way would appear to be *via* per-

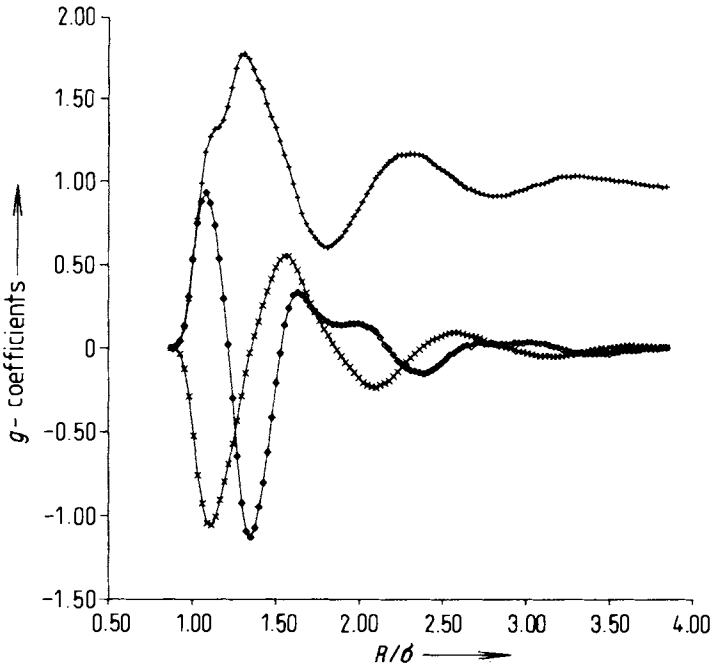


Fig. 2. g-Coefficients of the molecular pair correlation function, calculated by computer simulation. For the calculations a two-center Lennard-Jones potential has been used, $(r_A + r_B)/\sigma = 0.63$ (corresponding to Cl_2). The results are given for the density $\rho = 0.539\ \sigma^{-3}$ and the temperature $T \approx 1.00\ \varepsilon k^{-1}$.
(+—+) $g_{00}^{(000)}$;
(×—×) $\frac{1}{5} g_{00}^{(202)}$;
(◆—◆) $\frac{1}{5} g_{00}^{(220)} - \frac{2}{35} g_{00}^{(222)} + \frac{2}{35} g_{00}^{(224)}$
(after [17]).

turbation theories, in which the properties of the system of interest are developed from the known properties of a reference system. In order to guarantee the theory remaining simple, calculations should be limited to perturbations of the first order or, at most, second order.

For atomic liquids the following procedure has proven successful: A hard sphere liquid is chosen as reference system, the pair correlation function of which is very accurately known, also in its density dependence. Instead of resorting to tables, an empirical, analytical expression may be used which is based on the Percus-Yevick theory[21–23] and which can be empirically fitted to the results of computer simulations[24]. In order to obtain the pair correlation function of a Lennard-Jones liquid one first takes only the repulsive term u_R $(=(\sigma/R)^\alpha)$ of the potential given by eq. (4), since the structure is essentially determined only by this term. Figure 3 shows the exact type of separation; it was first suggested by *Weeks, Chandler,* and *Andersen*[25]. Next the diameter σ_{hs} of the hard spheres chosen as a reference is evaluated. The condition that the areas under the pair correlation functions of both systems (*i.e.* the reference system and the system of interest, the latter characterized by u_R) must be equal, may serve as an objective criterion. *Verlet* and *Weiss*[24] have developed a simple iteration procedure for the determination of this effective diameter. Finally, the resulting pair correlation function of the hard sphere system $g_{hs}(R)$ has to be multiplied by the Boltzmann factor $\exp[-u_R(R)/kT]$. Clearly, the Lennard-Jones system cannot have a discontinuity, in contrast to the hard sphere system, where $g_{hs}(R)$ drops discontinuously to zero at $R = \sigma_{hs}$. Therefore, one has to extra-

polate $g_{hs}(R)$ continuously to values $R<\sigma_{hs}$, before multiplying by the Boltzmann factor. This procedure, however, presents no difficulties[26]. Anyhow, the extrapolation range is small, since the Boltzmann factor itself rapidly approaches zero, due to the marked increase in u_R with decreasing R (see Fig. 3). All the steps of this procedure can easily be perform-

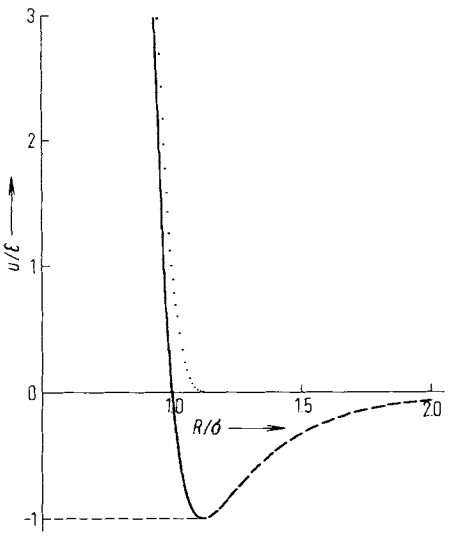


Fig. 3. Lennard-Jones potential (———) and its separation into a repulsive (·····) and attractive (– – – –) contribution; cf. eq. (4) (after [25]).

ed on a programmable pocket calculator[*]; the results can hardly be differentiated from those of a computer simulation. Figure 4 shows such results obtained for a Lennard-

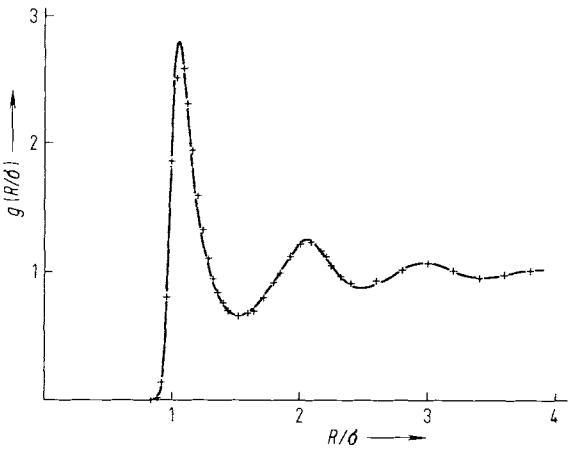


Fig. 4. Pair correlation function for a Lennard-Jones liquid at the temperature 1.273 εk^{-1} and the density 0.85 σ^{-3}. The curve has been calculated by the perturbation method described in the text, the crosses represent the results of a computer simulation [27].

Jones liquid ($\alpha=12$, $\beta=6$) at the density $\rho=0.85\,\sigma^{-3}$ and the temperature $T=1.273\,\varepsilon k^{-1}$; $g_{hs}(R)$ of the corresponding reference system has been calculated using the hard sphere diameter $\sigma_{hs}=1.0026\,\sigma$. For comparison, the results of a computer simulation[27] are also shown.

[*] If desired, a program for the TI-59 pocket calculator can be obtained from the author.

For molecular liquids, there lacks a method of comparable elegance. Previous attempts of similar treatments for molecular liquids should be briefly described (for a detailed summary see [28]). In most cases perturbation theories start from a spherical reference system so as to be able to apply the above procedures, originally developed for atomic systems. However, there is the disadvantage that the anisotropic systems of interest usually deviate too much from the isotropic reference system, so that first and second order pertubation theories may not suffice. In order to define a reference system one can separate $u_{00}^{(000)}$ in eq. (2) from the remaining terms. The respective pertubation theories for the pair correlation function have been treated up to second order[29]. An alternative choice of the reference system is obtained, if one replaces u in eq. (2) by the Boltzmann factor $\exp[-u/kT]=f$. The isotropic term $f_{00}^{(000)}$ can then be used again. One should note that $f_{00}^{(000)}$ does not only depend on $u_{00}^{(000)}$; inspection of eq. (1) shows that all other u-coefficients contribute, too. A reference system characterized by u_{ref} can be defined *via* the relation $f_{00}^{(000)}=\exp[-u_{ref}/kT]$. Pertubation calculations may then be performed in an analogous way[30]. Similarly to the atomic situation, considerations may be restricted to the repulsive term of the potential. With the aid of the corresponding term $f_{00}^{(000)}$ one can define an effective hard sphere potential, which then serves as reference[31]. The next logical step is the transition from spherical to non-spherical reference systems, but the additional numerical efforts are obvious: In order to calculate the final system, the pertubation theory has to be applied twice[32,33].

5. From the Structure to Thermodynamics

A further advantage of the expansion according to eq. (2) follows from the fact that the well known[34–40] statistical mechanical expressions for thermodynamical quantities can be used separately for each term of the expansion. As example the configurational contribution to the internal energy might be mentioned. Direct transfer of the well known relation yields

$$E_{m_1m_2}^{(l_1l_2l_{12})}=\frac{1}{2}N_A\cdot\rho\int_0^\infty u_{m_1m_2}^{(l_1l_2l_{12})}(R)\cdot g_{m_1m_2}^{(l_1l_2l_{12})}(R)\cdot 4\pi R^2\,dR \tag{10}$$

Addition of the various terms then provides the total internal energy. An analogous procedure can be used to calculate the pressure.

In some cases the thermodynamical quantity is determined by one single term of the expansion; in other words, there exist specific selection rules. This is true for expressions of the form

$$G^{(l)}-1\sim\rho\int_0^\infty[g_{00}^{(l10)}(R)-\delta_{l0}]\,4\pi R^2\,dR \tag{11}$$

In particular, $G^{(0)}/(\rho kT)$ is the isothermal compressibility, $G^{(1)}$ is the Kirkwood correlation factor, occurring in the theory of dielectrics[41], and $G^{(2)}$ is the Kerr correlation factor, occurring in the theoretical treatment of light scattering[42].

Normally, in the case of molecular liquids the higher terms of the expansion are of the same importance as the isotropic term in the case of atomic liquids.

6. Experimental Determinations of Structure

6.1. Neutron and X-ray Scattering

As is well known, in structural investigations the interference of waves can be used for measuring the distances between two diffraction centers. This method can be applied successfully, if the wavelength of the radiation is of the same order as that of the spacing. As shown in Figures 2 and 4, intermolecular distances are of the order of 10^{-10} m; thus X-ray and neutron radiation fulfill this condition. (Of course, this holds for intramolecular distances too, which, however, are not of interest here. They cause only additional disturbing interferences.) The wavelength λ of the neutrons depends on their velocity v or their energy E *via* the DeBroglie relation

$$h = \lambda \cdot mv = \lambda \cdot \sqrt{2mE} \tag{12}$$

m is the mass of the neutron. In order to obtain a wavelength of 7×10^{-11} m (which corresponds to the wavelength of the frequently used $Mo_{K\alpha}$ X-rays) the neutrons must have a velocity of 5651 ms^{-1} or an energy of 167 meV. This energy is markedly higher than the thermal energy at room temperature ($kT = 25$ meV at 298 K). These neutrons are therefore referred to as 'hot' neutrons. Consequently, the neutrons leaving a reactor must be accelerated. From a comparison of the velocities of neutrons and X-rays (the latter having the speed of light, *i.e.* 3×10^8 ms^{-1}) it is evident that structural determinations with neutrons are beset with difficulties, because molecular motions in liquids are characterized by velocities of similar magnitude. This ist the reason why one uses neutrons to study dynamic processes. One analyzes the change in energy of the scattered neutrons (inelastic scattering), which is a consequence of the Doppler effect, caused by the motion of the diffraction centers. In structural investigations with neutrons, one is not interested in the dynamics. Therefore, the energy is not recorded, rather one measures the number of scattered neutrons irrespective of their energy. Nevertheless, the energy transfer must be taken into account in the evaluation of the data; this is done by the so-called Placzek correction.

A further essential difference between scattering experiments with X-rays and those with neutrons arises as a result of the different nature of the scattering centers. X-rays are diffracted by the electron clouds, whereas neutrons penetrate as far as the nucleus and then are scattered. There are two consequences: 1) With atoms of the same nuclear charge, the scattering centers for X-rays are all equal, whereas, for neutrons they may behave differently due to the occurrence of different isotopes and also due to the possible existence of a nuclear spin, which can couple with the different spin states of the neutron spin. Unfortunately, different scattering centers partially destroy the interference of the radiation. Hence, the scattered radiation contains both coherent and incoherent contributions. Owing to their different origin, one distinguishes here between isotopic and spin incoherence; only the first effect can be suppressed (by working with isotopically pure samples), while if an isotope exhibits too strong a spin incoherence, its application is probably prohibitive. An important extreme case is the ^1H isotope, the scattering of which is about 98% incoherent *(vide infra)*. 2) The diffraction centers differ markedly in size. A comparison with the wavelengths of the radiations shows that the diffraction centers for X-rays are of comparable magnitude. In contrast, neutrons can be considered as point centers. This implies for the angular distribution of the scattered radiation, that X-rays scatter anisotropically, whereas neutrons scatter isotropically.

Scattering at the free atom is quantitatively described by the so-called scattering length, *i.e.* the range of interaction between the radiation and the center. For both types of radiation it is of the order of 10^{-15} m. Thus, it corresponds to the dimension of a (classical) electron or a nucleus. One distinguishes between coherent and incoherent scattering lengths, the former, denoted by f, are of particular interest for structural investigations. As discussed above in the case of neutrons f is a quantity independent of the angle, whereas in the case of X-rays it is an angular dependent quantity. The neutron scattering lengths of various isotopes (in the bound state) are collected in Table 1[43-45], while the scattering lengths for X-rays are shown in Figure 5[46].

On going from free atoms to atomic liquids the scattered neutron radiation is expected to be anisotropic too, owing to the possible occurrence of interferences. Thus, the angular distribution of the scattered radiation can be measured in order to determine the structure of the liquid. Figure 6 shows a schematic representation of the scattering experiment. The quanta, being generated by a monochromatic source, possess an incident momentum $\hbar\vec{k}_0$ and an incident energy E_0. They penetrate into the cyclindrically shaped sample, which is arranged perpendicular to the plane of the figure, and are scattered. After the scattering process their momentum is $\hbar\vec{k}$ and their energy E. The detector is positioned at the scattering angle 2θ. Instead of the transmission geometry shown in the figure, a reflection geometry is also frequently used in X-ray scattering experiments; the surface of the sample is thereby planar and the vector bisecting the angle between the inci-

Table 1. Scattering Lengths for Neutron Scattering.

Atomic Number	Isotope	Coherent Scattering Length f [a] [10^{-15} m]
1	^1H	−3.74
	^2H	6.67
6	^{12}C	6.65
	^{13}C	6.0
7	^{14}N	9.36
	^{15}N	6.44
8	^{16}O	5.80
	^{17}O	5.78
	^{18}O	6.00
9	^{19}F	5.66
15	^{31}P	5.13
16	^{32}S	2.80 [b]
	^{33}S	4.74
	^{34}S	3.48
17	^{35}Cl	11.70 [c]
	^{37}Cl	3.08
18	^{36}A	24.3
	^{40}A	1.82
35	^{79}Br	6.78 [d]
	^{81}Br	6.80
53	^{127}I	5.28

[a] In neutron scattering this scattering length for isotopes in the bound state is usually denoted by b. [b] *L. Koester, K. Knopf, W. Waschkowski*, Z. Phys. *A 289*, 399 (1979). [c] *L. Koester, K. Knopf, W. Waschkowski*, Z. Phys. *A 282*, 371 (1977). [d] *L. Koester*, private communication.

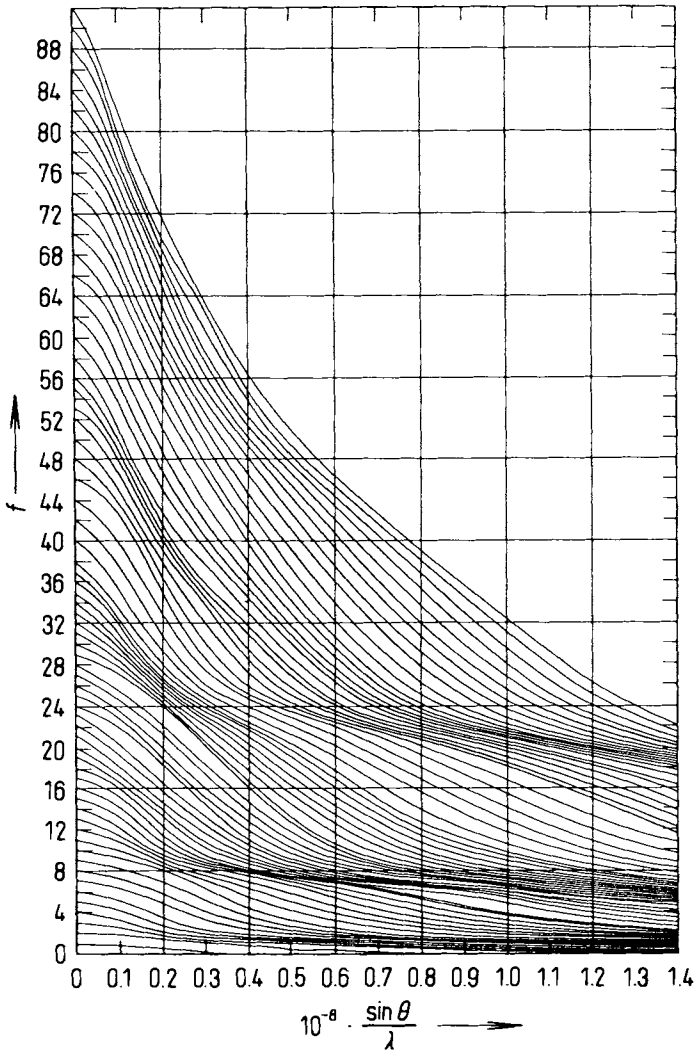


Fig. 5. Scattering lengths f of neutral atoms for X-ray scattering as a function of the scattering angle 2θ, or the wavelength λ, respectively. At $\theta = 0$, f is identical with the atomic number of the element, thus the curves can immediately be assigned to the elements. From reference [46].

dent and the reflected beam is oriented perpendicular to this surface. The corresponding arrangement is realized by synchronous rotations of the source and the detector, or, of the sample and the detector. The cuvette must be constructed in such a way that background scattering is minimal; a suitable cuvette material for neutron scattering is vanadium, for X-ray scattering beryllium. The intensity of the radiation, scattered into a differential angular cone defined by the size

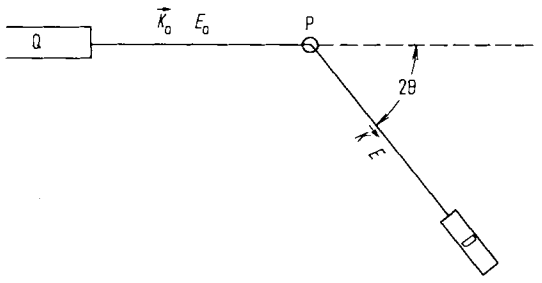


Fig. 6. General arrangement of a scattering experiment. Q: monochromatic radiation source, P: Sample , D: Detector, $\vec{K}_0$: wave vector of the incident beam, $\vec{K}$: wave vector of scattered beam, E_0: energy of the incident beam, E: energy of the scattered radiation, 2θ: scattering angle.

of the detector window, is now measured by moving the detector around the sample. One can save time by using detector banks consisting of several detectors, since the counting processes at the various detectors can be performed simultaneously at different angular positions. Figure 7 shows some results obtained for X-ray and neutron scattering experiments on dichloromethane[47].

If the energy transfer during the scattering process is neglected then the transfer of momentum on elastic scattering is given by

$$\hbar\vec{\kappa} = \hbar\vec{k}_0 - \hbar\vec{k} \tag{13}$$

The magnitude of the transfer of momentum ist obtained likewise, observing simple trigonometric rules, accounting for $k = k_0$ and introducing the DeBroglie relation (12):

$$\kappa = \frac{4\pi}{\lambda_0}\sin\theta \tag{14}$$

In the latter case the transfer of momentum would depend only on the wavelengths of the incident quanta and on the scattering angle. However, as mentioned above, the measur-

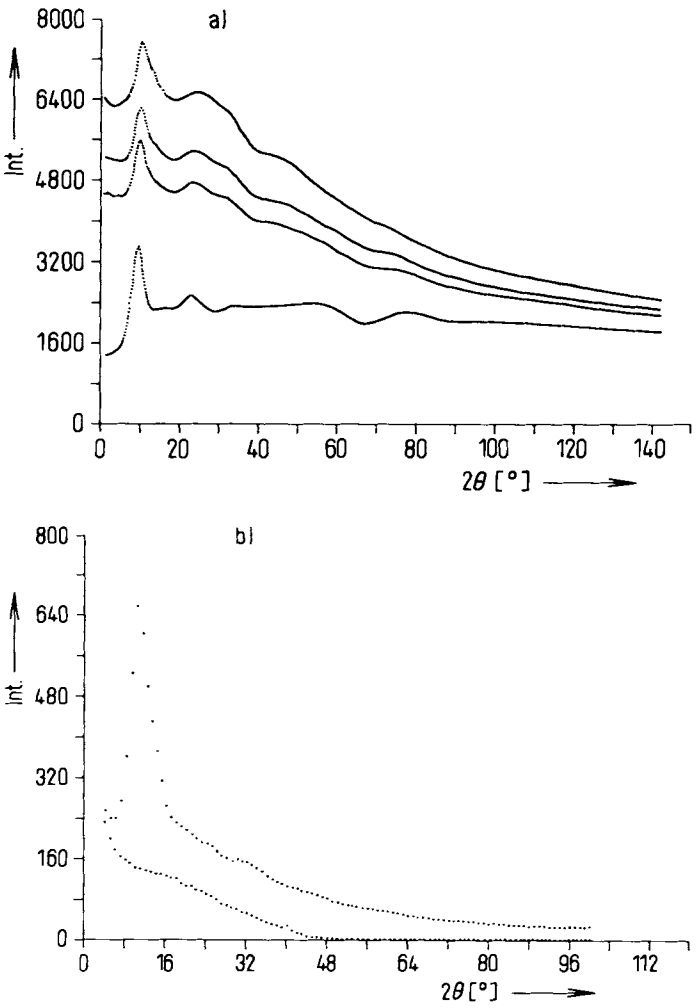


Fig. 7. Results a) for neutron and b) X-ray scattering on dichloromethane. The intensity is represented as a function of the scattering angle. a) The curves from top downwards refer to CH_2Cl_2, a mixture 0.64 CH_2Cl_2/0.36 CD_2Cl_2 (at this mixture composition the mean coherent scattering length of hydrogen vanishes), a mixture 0.5 CH_2Cl_2/0.5 CD_2Cl_2 (in mole fractions), and CD_2Cl_2. The strong intensity decay of the ^1H carrying samples with increasing scattering angle is caused by the inelastic effects, which are taken care of in the Placzek-correction. b) Upper curve: cuvette filled with CH_2Cl_2; lower curve: results for empty beryllium cuvette.

able energy changes in the neutron experiment give rise to the fact that measurements at a given scattering angle do not correspond to observations at a constant κ value. Therefore one has to account for the Placzek correction. With the identity (14) the scattering intensity can be represented as a function of the momentum transfer κ.

The general scattering theory for atomic liquids[43,45,46,48,49] relates this scattering intensity to the pair correlation function, which describes the structure of the liquid. The explicit relation is

$$I_{\mathrm{coh}}(\kappa) \sim f^2 \left\{ 1 + \rho \int_0^{\infty} [g(R) - 1] j_0(\kappa R)\, 4\pi R^2 \, \mathrm{d}R \right\} \tag{15}$$

Obviously, we are only interested in the coherent contribution of the scattered radiation (denoted by the index coh); the incoherent contribution has to be subtracted. It can be calculated from tables for incoherent scattering lengths. The expression in the curly brackets is termed the 'structure factor'; its second term modifies the atomic scattering, expressed by f^2. j_0 is the spherical Bessel function of zero order. The expression within the square brackets stands for the pair correlation function from which its asymptotic value at large R has been subtracted; the continuum contributes only at extremely small angles and cannot be measured, because the incident beam dominates at $2\theta = 0$.

We next consider molecular liquids. Here, one must distinguish between intramolecular and intermolecular contributions, because the scattering centers may belong to the same or to different molecules. Furthermore, there must exist a relation between the orientation dependent molecular pair correlation function $g(R, \Omega_1, \Omega_2, \Omega_{12})$ and the intermolecular coherent scattering intensity. An advantage of the expansion of the molecular pair correlation function (see eq. (2)) is that the relations well established for atomic liquids can be transferred for each single term. Therefore, using eq. (15) one arrives at the result[6,7,50,51]

$$I_{\mathrm{coh}(m_1 m_2)}^{(l_1 l_2 l_{12})} \sim a_{m_1}^{(l_1)}(\kappa)\, a_{m_2}^{(l_2)}(\kappa) \left\{ 1 + \rho \int_0^{\infty} [g_{m_1 m_2}^{(l_1 l_2 l_{12})}(R) - \delta(l, m; 0)] j_{l_{12}}(\kappa R)\, 4\pi R^2 \, \mathrm{d}R \right\} \tag{16}$$

The total scattering intensity is then given by a summation of the individual contributions. An interpretation analogous to eq. (15) shows that $a_m^{(l)}(\kappa)$ can be considered as the scattering length of the molecule. Owing to the comparable magnitudes of the wavelength of the radiation and the molecular size, in the case of neutron scattering $a_m^{(l)}$ is now also angular dependent. The two terms in the curly brackets are the intramolecular and the intermolecular contribution, respectively. Accounting only for the isotropic term $g_{00}^{(000)}$, eq. (16) reduces to eq. (15); only in this case is the Kronecker symbol $\delta(l, m; 0)$ unity, otherwise it vanishes. In order to obtain the molecular scattering length, one has to assume that the atomic scattering lengths do not change on going from the free atom to a molecule. This condition certainly holds in the case of neutron scattering, but it is questionable in the case of X-ray scattering, because X-rays are diffracted at the electron clouds. Thus, only the atomic scattering lengths and the coordinates of the atoms in the molecule-fixed coordinate system are needed to calculate $a_m^{(l)}$.

In order to obtain information on the liquid structure, one tries to determine as many g-coefficients as possible, using eq. (16). Apart from the usual, more or less established corrections for scattering experiments (corrections for background scattering, absorption, multiple scattering, and, in the case of neutrons, Placzek effects) a separation into intra- and intermolecular contributions is required. This separation is based on the fact that the molecular structure does not essentially change on going from the gas to the liquid state. Thus, the structure known from the gaseous phase is introduced to calculate the scattering intensity, which at large scattering angles must agree with the experimental value, since the intermolecular contribution has already vanished in this range. Discrepancies may be accounted for by allowing small changes in the molecular geometry.

The fact that the separated intermolecular coherent scattering intensity consists of a sum over many individual contributions, according to the second term in eq. (16), should not be discouraging. The number of g-coefficients depends on the distinctness of the orientations. The less pronounced they are, the more coefficients vanish. The reductions caused by symmetries have also already been discussed. In addition, the proportionality factors not explicitly written in eq. (16), and in particular the scattering lengths of the molecules, rapidly decrease with increasing indices. For example, it has proven correct that in the case of chloroform (possessing C_{3v} symmetry) the observed intensity is only influenced by four terms. For such a small number of important terms an experimental separation can be performed by an *equal* number of scattering experiments, if the scattering lengths of the molecules are varied from experiment to experiment. One is not, of course, allowed to change the structure of the liquid. There exist two possibilities: 1) application of different radiations (X-rays, neutrons and, recently, also electrons[52]). 2) Use of different isotopes in neutron scattering experiments. In the latter case the coherent scattering lengths of the isotopes should differ markedly. Inspection of Table 1 shows that, especially for organic liquids, there is only a limited number of suitable isotopes: chlorine is ideal, nitrogen is quite useful, carbon, oxygen and bromine cannot be used, fluorine, phosphorus and iodine consist only of one single isotope. ^{1}H presents difficulties owing to the strength of the incoherent contribution and to Placzek effects. This can easily be recognized from Figure 7; the scattering curves exhibit an increasing, monotonous drop to larger angles with increasing ^{1}H content due to inelastic scattering. Nevertheless, we cannot reject the application of this isotope due to the limited number of possibilities. In the case of chloroform successful measurements have recently been carried out with ^{1}H[53]. Obviously, the atomic concentration of the element in the molecule whose isotopes are varied, should be high, *i.e.* the less the scattering lengths of the isotopes differ, the higher should be the concentration. If all these conditions are favorable and the required number of scattering experiments can be performed, the individual contributions to the scattering intensity may be evaluated for each value κ, by solving the resulting system of simultaneous equations. However, eq. (16) shows that by this procedure only those terms can be separated whose scattering pre-factor can be varied independently. For this reason splitting of terms with equal indices l_1 and l_2 but different l_{12} is not possible.

So far, only a few scattering experiments aimed at a determination of g-coefficients have been performed in the liquid phase: water[52], acetonitrile[51], chloroform[53,54], the homologous series of methyl halides (chloride, bromide, iodide)[55] and dichloromethane[47]. Investigations on water have been performed using three different radiations[52,56]. In the author's group the main interest has been focussed on neutron scattering, using different isotopes. The following isotopic substitution experiments have been performed: ^{14}N and ^{15}N in acetonitrile[57,58]; ^{35}Cl and ^{37}Cl as well as ^{1}H and ^{2}H in chloroform[53], ^{1}H and ^{2}H in dichloromethane. In the case of methyl halides the gradual change in properties along the homologeous series has been exploited in order to separate the various contributions according to eq. (16). In all cases X-ray scattering experiments have also been carried out[47,51,55,60]. Obviously, the system most investigated is chloroform, where the results of five independent scattering experiments are available. One can also investigate mixtures of isotopes, as has been done in the case of chloroform[59]. The condition is that the system of simultaneous equations is linearly independent, which is still fulfilled in the case of three mixtures. However, the investigation of an additional mixture is only useful if the isotopes have very different scattering lengths, otherwise the differences between a pure isotope and a mixture are too small. In this context the chlorine isotopes are particularly favorable. In Figure 8 are shown the coefficients $g_{00}^{(000)}$, $g_{00}^{(101)}$, $g_{00}^{(110)}$ and $g_{00}^{(202)}$ determined for chloroform[53]. One should note, that $g_{00}^{(110)}$ still contains contributions due to $g_{00}^{(112)}$, which cannot be separated. Combination of the various experimental results, all of which show statistical deviations in the measured data, leads to the indicated error bars. It should be pointed out that such investigations can only be performed with the aid of a high flux reactor, and still one needs two or three days measuring time per isotope. Our measurements were carried out at the reactor of the Laue-Langevin Institute in Grenoble.

In the following, a qualitative interpretation of these results will be given. The coefficient $g_{00}^{(000)}$ describes the distribution of the molecular centers, or, more correctly, of the origins of the molecule-fixed coordinate systems, which, as discussed above, may be chosen arbitrarily. In the present example the origin is placed in the carbon atom of the chloroform molecule, the z-axis coincides with the three-fold axis pointing in the direction of the C—H bond. $g_{00}^{(000)}$ oscillates around unity. A first maximum is observed in the range of nearest neighbors at 4.5 Å, and a second (very weak) maximum can be recognized at 9 Å. The area under the first maximum, though not well defined, can serve as an estimate of the number of closest neighbors; for chloroform about six other molecules are found around a molecule selected at random. On the right of the first maximum a marked shoulder can be recognized, which is never observed in atomic liquids. The other g-coefficients provide information on orientational correlations. Similarly to $g_{00}^{(000)}$, where values larger than unity describe preferred configurations, positive products $g_{m_1m_2}^{(l_1l_2l_{12})} \cdot \Phi_{m_1m_2}^{(l_1l_2l_{12})}$ for the higher order terms occurring in eq. (2) indicate preferred orientations. (One should note, that only $g_{00}^{(000)}$ oscillates around unity, all other terms oscillate around zero.) Both factors must have the same sign, so that a positive product results. Therefore, knowledge of the sign of the angular function, in particular of the terms $\Phi_{00}^{(l01)}$ with $l=1$

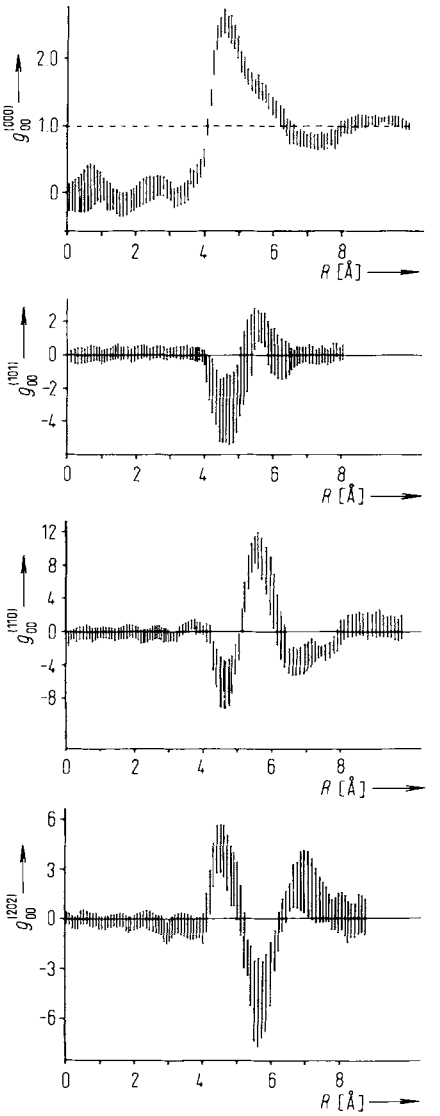


Fig. 8. g-Coefficients of the pair correlation function of chloroform at 298 K (after [53]).

and $l=2$ and $\Phi_{00}^{(l10)}$ with $l=1$, is required. If one denotes the angle between the z-axis and the intermolecular vector joining the molecular centers by β, there exist the simple relations

$$\Phi_{00}^{(101)} \sim -\cos\beta$$
$$\Phi_{00}^{(202)} \sim \tfrac{3}{2}\cos^2\beta - \tfrac{1}{2} \qquad (17)$$

Table 2. Orientational correlations in liquid chloroform, derived from results shown in Figures 8 and 9.

R-range [Å]	Sign of $g^{(101)}$	Sign of $g^{(202)}$	Angular range for β [°] [a]
4—5	−	+	0—55
5—6	+	−	90—125
6—7	?	+	0—55 or 125—180

R-range [Å]	Sign of $g^{(110)}$	Angular range for β [°] [b]
4—5	−	0—90
5—6	+	90—180
6—7	−	0—90

[a] Angle between the C_3-axis of the molecule and the intermolecular center-center vector. [b] Angle between the C_3-axes of two molecules.

which are displayed graphically in Figure 9. Identical expressions can also be derived for $\Phi_{00}^{(llO)}$, but in the latter case β describes the angle between the z-axes of the two molecules. A comparison with Figure 8 yields the results summarized in Table 2. Thus, already on a qualitative basis interest-

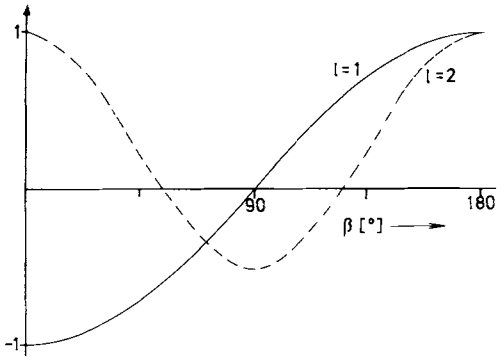


Fig. 9. The angular functions $\Phi_{(1)}^{(l_1l_2l)}$ and $\Phi_{(0)}^{(llO)}$ according to eq. (17) for l=1 and l=2.

ing conclusions may be drawn. For more quantitative interpretations, it is convenient to consider the ratios $g_{m_1m_2}^{(l_1l_2l_{(2)})} / g_{00}^{(000)}$, which represent the angular averages of the Φ-functions at varying distances from the reference molecule (see Section 4).

6.2. Light Scattering, Dielectric Measurements and Nuclear Magnetic Relaxation

Besides the scattering experiments with neutrons and X-rays, whose wavelengths are ideal for structural investigations, some further experimental methods have to be mentioned. However, these methods yield only integral structural quantities according to eq. (11). Here, the momentum transfer may be negligibly small due to too large a wavelength [see eq. (14)], as in the case of light scattering, or, no change of the momentum is experimentally observed, as in the measurements of the dielectric constant and in nuclear magnetic relaxation. A common disadvantage of light scattering and dielectric experiments, as well as X-ray scattering, is the fact that the electron clouds are involved. As a consequence, polarization effects can cause a complex change in the properties, thus affecting the corresponding measurable quantities. These are the dipole moment and the polarizability of the molecules, two properties which with respect to molecular rotations behave like the irreducible representations of the continuous three-dimensional rotation group with l=1 (dipole moment) or l=2 (polarizability). Therefore, it is possible to determine selectively the respective components in the expansion according to eq. (2). This fact can be characterized as an advantage of these methods. In contrast, nuclear magnetic relaxation involves no similar selectivity. In the latter case, and also in light scattering, additional difficulties arise due to molecular motions, as already discussed in the case of neutron scattering.

Light scattering occurs at wavelengths of about 5000 Å. One distinguishes between polarized experiments, where the polarization planes of the incident and the scattered light are parallel, and depolarized experiments. In the latter case the polarization vectors of the incident and the scattered light are perpendicular. The polarized scattering contains an *isotropic* component, caused by the rotationally invariant part of the molecular polarizability α_0. Owing to the spherical symmetry this component cannot depend on the orientation of the molecules, rather it has to be related to the $G^{(0)}$ term[6,42,61,62]:

$$I_{iso} \sim \alpha_0^2 G^{(0)} \tag{18}$$

I is the total scattering intensity, integrated over all frequencies. The *anisotropic* component of the molecular polarizability causes depolarized scattering. The total intensity I_{aniso} is given by an analogous expression, but now depending on $G^{(2)}$[42,62]

$$I_{aniso} \sim (\alpha_\perp - \alpha_\parallel)^2 G^{(2)} \tag{19}$$

if one is limited to molecules with a three-fold or higher symmetry axis. Then $a_\perp$ and $a_\parallel$ are the polarizability components perpendicular and parallel to these axes, respectively. A large number of studies on the total intensity I_{aniso} has been reported in the older literature. However the evaluation of these data is not so simple. A review of the respective difficulties and of the older literature has been given by *Pecora et al.*[63].

In the last few years it has been found that the occurrence of the term $G_{aniso}^{(2)}$ is not only restricted to the total intensity I_{aniso}. *Keyes* and *Kivelson*[64] could show that orientational pair correlations also enter into the frequency spectrum of depolarized light scattering. If the reorientational motions of the molecules in the liquid obey a rotational diffusion equation, the depolarized Raleigh-line possesses the form of a simple Lorentzian, characterized by a width at half height of

$$\Delta\tilde{\nu} = 1/(2\pi c \tau_{LS}) \tag{20}$$

(in wave numbers: cm^{-1}), where c is the speed of light. τ_{LS} is a correlation time describing the molecular reorientation. It is often referred to as the 'collective correlation time', because it involves contributions due to orientational correlations, in contrast to the correlation time τ_S which describes the reorientation of individual molecules. In the limit of a diffusive process τ_{LS} and τ_S are related by

$$\tau_{LS} = \frac{G(2)}{J^{(2)}} \cdot \tau_S \tag{21}$$

The factor $J^{(2)}$ accounts for dynamic correlations between neighboring molecules. For liquids consisting of small molecules and exhibiting no specific interactions such as hydrogen bonding, $J^{(2)}$ should be close to unity. Eq. (21) may then be used to determine $G^{(2)}$. For this purpose, two independent experiments must be performed, determining τ_{LS} from light scattering and τ_S from nuclear magnetic relaxation times or Raman experiments. A series of experimental results for $G^{(2)}$ has been compiled by *Pecora et al.*[63].

The dielectric constant is related to the term $G^{(1)}$ *via* the Kirkwood-Fröhlich equation[41]:

$$\frac{(\varepsilon - \varepsilon^{(\infty)}) \cdot (2\varepsilon + \varepsilon^{(\infty)})}{\varepsilon \cdot (\varepsilon^{(\infty)} + 2)^2} = \frac{1}{9} \cdot \frac{\rho}{\varepsilon_0 kT} \cdot G^{(1)} \mu_0^2 \tag{22}$$

It is not only necessary to know the static value of ε, usually obtained by capacity measurements at frequencies in the MHz region, but one has to determine also the high-frequency limit ε^{∞}, where the contributions to dipole reorientation have vanished, whereas those from molecular vibrations are still negligible. Clearly, it is not an easy matter to find the correct frequency. ε_0 is the permittivity (dielectric constant) of the vacuum, μ_0 is the dipole moment of the free molecule. A series of recent determinations of $G^{(1)}$ over a wide range of densities and temperatures can be found in reference[65].

Finally, the interrelationship between the nuclear magnetic relaxation time T_1[66] and the liquid structure should be mentioned. As already discussed in the case of scattering experiments, the desired information is contained in the intermolecular contribution, which can be separated by isotopic dilution experiments[67]. Owing to the smallness of the intermolecular contribution to the relaxation time of most nuclei, only the relaxation of protons needs further consideration. A disadvantage is the simultaneous dependence on structure and dynamics. A procedure similar to that employed in scattering experiments, *i. e.* an integration over all frequencies in order to eliminate the dynamic effects is impossible, since, owing to technical limitations, the interesting region of frequencies is not accessible (>10 GHz, the highest available NMR frequency for protons is at present 600 MHz). Therefore one is forced to introduce models for molecular motions. In the case of intermolecular relaxation such models become particularly complex, because both translational and rotational motions of the molecules have to be considered. By neglecting a coupling between rotational and translational motions and assuming a purely diffusive behavior, the intermolecular relaxation rate $1/T_1$ can be connected with the g-coefficients[68].

7. Conclusion

In this review of the structure of molecular liquids a consequent concept has been followed: Only such work has been discussed which is based on the total molecular pair correlation function, expressed by g-coefficients. This point of view should be acceptable, for this is a general description, from which partial results can always be deduced. An impressive advantage of the concept of g-coefficients is the simple application of the interconnections known from spherical systems to molecular (non-spherical) systems. Finally, a short account should be given of other methods used to describe the structure of molecular liquids.

Another obvious method is the retention of spherical orientation averaged atomic pair correlation functions in molecular liquids (the average over all orientations has to be formed at fixed atom-atom distance). For a molecule consisting of n non-equivalent atoms, there are $(1/2)\ (n^2+n)$ such functions. Knowledge of the g-coefficients allows the calculation of these functions[69]. The converse, however, is impossible. Sometimes the calculation of thermodynamic data using these functions proves to be very complicated, as shown *e. g.* by the relations describing the pressure[70]. Of course, atom pair correlation functions may also be obtained by computer simulations; then one extracts less complete information from the respective simulation. Apart from the publications cited above computer simulations of the systems H_2O, C_6H_6, NH_3, CCl_4 (all summarized in reference [71]) and CH_4[72] should be mentioned. If a hard sphere potential is chosen to describe the interatomic interactions, an analytical calculation of the atomic pair correlation functions is possible with the aid of a modified Percus-Yevick theory (RISM-theory)[73]. A comparison with X-ray and neutron experiments can easily be performed, because the formulas describing the scattering, if expressed by atomic pair correlation functions according to eq. (15), contribute additively to the total scattering intensity. The combination of various scattering experiments (electron, X-ray and neutron scattering), or, the use of different isotopes in neutron experiments, allows also in this case a separation into the individual contributions[52, 53, 56].

To obtain structural information from a single scattering experiment, or from one of the integral relations for $G^{(1)}$, $G^{(2)}$, or T_1, one needs very detailed models. The work concerned with the latter topics has not been discussed here. The reader is referred to recent reviews on the results from X-ray scattering experiments[74] and nuclear magnetic relaxation measurements[75].

A great deal of work has still to be done before our knowledge of molecular liquids is as detailed as our knowledge of atomic liquids. On the other hand, present activities in this field are promising. In particular, one may hope that simply applicable statistical mechanical methods for structural calculations will be developed, so that one is not entirely committed to computer simulations. Only then will more and more realistic potentials be developed by comparison with the previously described experiments, which then allow the calculation of all measurable quantities. At present, the situation is delightful for the experimentalists, for one cannot renounce their measurements.

Received: July 4, 1979 [A 328 IE]
German version: Angew. Chem. *92*, 700 (1980)

[1] *F. A. Cotton:* Chemical Applications of Group Theory. Wiley, New York 1971.
[2] *D. W. Jepsen, H. L. Friedman,* J. Chem. Phys. *38*, 846 (1963).
[3] *J. A. Pople,* Proc. Roy. Soc. London *A 221*, 498 (1954).
[4] *J. O. Hirschfelder, C. F. Curtiss, R. B. Bird:* The Molecular Theory of Gases and Liquids. Wiley, New York 1954.
[5] *W. A. Steele,* J. Chem. Phys. *39*, 3197 (1963).
[6] *L. Blum, A. J. Torruella,* J. Chem. Phys. *56*, 303 (1972).
[7] *L. Blum, A. H. Narten,* Adv. Chem. Phys. *34*, 203 (1976).
[8] *A. J. Stone,* Mol. Phys. *36*, 241 (1978).
[9] *J. Downs, K. E. Gubbins, S. Murad, C. G. Gray,* Mol. Phys. *37*, 129 (1979).
[10] *R. A. Sack,* J. Math. Phys. *5*, 260 (1964).
[11] *K. E. Gubbins, C. G. Gray, P. A. Egelstaff, M. S. Ananth,* Mol. Phys. *25*, 1353 (1973).
[12] *F. Vesely:* Computerexperimente an Flüssigkeiten. Physik Verlag, Weinheim 1978.
[13] *W. B. Streett, K. E. Gubbins,* Annu. Rev. Phys. Chem. *28*, 373 (1977).
[14] *J. P. Ryckaert, G. Ciccotti, H. J. C. Berendsen,* J. Comput. Phys. *23*, 327 (1977).
[15] *W. B. Streett, D. J. Tildesley,* Proc. R. Soc. London *A 348*, 485 (1976).
[16] *P. S. Y. Cheung, J. G. Powles,* Mol. Phys. *30*, 921 (1975).
[17] *K. Singer, A. Taylor, J. V. L. Singer,* Mol. Phys. *33*, 1757 (1977).
[18] *P. S. Y. Cheung, J. G. Powles,* Mol. Phys. *32*, 1383 (1976).
[19] *W. B. Streett, D. J. Tildesley,* Proc. R. Soc. London *A 355*, 239 (1977).
[20] *O. Steinhauser, M. Neumann,* Mol. Phys. *37*, 1921 (1979).
[21] *M. S. Wertheim,* Phys. Rev. Lett. *10*, 321 (1963).
[22] *G. J. Throop, R. J. Bearman,* J. Chem. Phys. *42*, 2408 (1965).
[23] *W. R. Smith, D. Henderson,* Mol. Phys. *19*, 411 (1970).
[24] *L. Verlet, J. J. Weis,* Phys. Rev. *A 5*, 939 (1972).
[25] *J. D. Weeks, D. Chandler, H. C. Andersen,* J. Chem. Phys. *54*, 5237 (1971).
[26] *D. Henderson, E. W. Grundke,* J. Chem. Phys. *63*, 601 (1975).
[27] *L. Verlet,* Phys. Rev. *165*, 201 (1968).
[28] *P. A. Egelstaff, C. G. Gray, K. E. Gubbins* in *A. D. Buckingham:* MTP International Review of Science. Serie II, Vol. 2. Butterworths, London 1975, p. 299.
[29] *K. E. Gubbins, C. G. Gray,* Mol. Phys. *23*, 187 (1972).

[30] *J. W. Perram, L. R. White,* Mol. Phys. *28*, 527 (1974).
[31] *S. Sung, D. Chandler,* J. Chem. Phys. *56*, 4989 (1972).
[32] *K. C. Mo, K. E. Gubbins,* J. Chem. Phys. *63*, 1490 (1975).
[33] *S. I. Sandler,* Mol. Phys. *28*, 1207 (1974).
[34] *P. A. Egelstaff:* An Introduction to the Liquid State. Academic Press, London 1967.
[35] *F. Kohler:* The Liquid State. Verlag Chemie, Weinheim 1972.
[36] *C. A. Croxton:* Introduction to Liquid State Physics. Wiley, London 1975.
[37] *J. P. Hansen, I. R. McDonald:* Theory of Simple Liquids. Academic Press, London 1976.
[38] *R. O. Watts, I. J. McGee:* Liquid State Chemical Physics. Wiley, New York 1976.
[39] *D. A. McQuarrie:* Statistical Mechanics. Harper & Row, New York 1976.
[40] *J. A. Barker, D. Henderson,* Rev. Mod. Phys. *48*, 587 (1976).
[41] *C. J. F. Böttcher:* Theory of Electric Polarization. Vol. I. Elsevier, Amsterdam 1973.
[42] *A. Ben-Reuven, N. D. Gershon,* J. Chem. Phys. *51*, 893 (1969).
[43] *B. T. M. Willis:* Chemical Applications of Thermal Neutron Scattering. Oxford University Press, London 1973.
[44] *K. Koester* in: Springer Tracts in Modern Physics. Vol. 80. Springer, Berlin 1977.
[45] *G. E. Bacon:* Neutron Diffraction. Clarendon Press, Oxford 1975.
[46] *H. P. Klug, L. E. Alexander:* X-Ray Diffraction Procedures. Wiley, New York 1974.
[47] *W. Jung,* Diplomarbeit, Universität Karlsruhe 1978.
[48] *A. C. Wright,* Adv. Struct. Res. Diffr. Methods *5*, 1 (1974).
[49] *W. Marshall, S. W. Lovesey:* Theory of Thermal Neutron Scattering. Clarendon Press, Oxford 1971.
[50] *W. A. Steele, R. Pecora,* J. Chem. Phys. *42*, 1863 (1965).
[51] *H. Bertagnolli, M. D. Zeidler,* Mol. Phys. *35*, 177 (1978).
[52] *E. Kálmán, G. Pálinkás, P. Kovács,* Mol. Phys. *34*, 505 (1977).
[53] *H. Bertagnolli,* Habilitationsschrift, Universität Karlsruhe 1979.
[54] *H. Bertagnolli, D. O. Leicht, M. D. Zeidler, P. Chieux,* Mol. Phys. *36*, 1769 (1978).
[55] *M. Fitzgerald,* Dissertation, Universität Karlsruhe 1979.
[56] *A. H. Narten,* J. Chem. Phys. *56*, 5681 (1972).
[57] *H. Bertagnolli, P. Chieux, M. D. Zeidler,* Mol. Phys. *32*, 759 (1976).
[58] *H. Bertagnolli, P. Chieux, M. D. Zeidler,* Mol. Phys. *32*, 1731 (1976).
[59] *H. Bertagnolli, D. O. Leicht, M. D. Zeidler, P. Chieux,* Mol. Phys. *35*, 199 (1978).
[60] *H. Bertagnolli, D. O. Leicht, M. D. Zeidler,* Mol. Phys. *35*, 193 (1978).
[61] *L. Blum, H. L. Frisch,* J. Chem. Phys. *55*, 1188 (1971).
[62] *B. J. Berne, R. Pecora:* Dynamic Light Scattering. Wiley, New York 1976.
[63] *D. R. Bauer, J. I. Brauman, R. Pecora,* Annu. Rev. Phys. Chem. *27*, 443 (1976).
[64] *T. Keyes, D. Kivelson,* J. Chem. Phys. *56*, 1057 (1972).
[65] *E. U. Franck* in *A. D. Buckingham, E. Lippert, S. Bratos:* Organic Liquids. Wiley, Chichester 1978.
[66] *T. C. Farrar, E. D. Becker:* Pulse and Fourier Transform NMR. Academic Press, New York 1971.
[67] *M. D. Zeidler:* Ber. Bunsenges. Phys. Chem. *69*, 659 (1965).
[68] *M. D. Zeidler,* Mol. Phys. *30*, 1441 (1975).
[69] *J. S. Hoye, G. Stell,* J. Chem. Phys. *65*, 18 (1976).
[70] *I. Aviram, D. J. Tildesley, W. B. Streett,* Mol. Phys. *34*, 881 (1977).
[71] *L. V. Woodcock* in *A. D. Buckingham, E. Lippert, S. Bratos:* Organic Liquids. Wiley, Chichester 1978.
[72] *S. Murad, D. J. Evans, K. E. Gubbins, W. B. Streett, D. J. Tildesley,* Mol. Phys. *37*, 725 (1979).
[73] *D. Chandler,* J. Chem. Phys. *59*, 2742 (1973).
[74] *H. W. Zimmermann* in *A. D. Buckingham, E. Lippert, S. Bratos:* Organic Liquids. Wiley, Chichester 1978.
[75] *H. G. Hertz,* Prog. Colloid Polym. Sci. *65*, 92 (1978).

COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Inductive, CC-Hyperconjugative, and Frangomeric Effects in Solvolytic Fragmentation Reactions

By *Cyril A. Grob, Martin Bolleter,* and *Walter Kunz*[*]

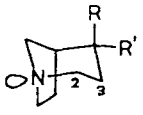
1-Azabicyclo[3.2.1]octyl *endo*-4-*p*-toluenesulfonate *(1a)*, 1-azabicyclo[3.3.1]nonyl *endo*-4-*p*-toluenesulfonate *(2a)*, and the equatorial[1] 4-bromo-1-azaadamantane *(3a)* undergo quantitative fragmentation in 80% ethanol to give the methyleneimmonium salts *(7)*, *(8)*, and *(9)*, respectively[2]. Moreover, they react some 10^3, 10^4, and 10^5 times faster than the nitrogen-free parent compounds *(4a)*, *(5a)*, and *(6a)*. This comparison demonstrates the pronounced frangomeric acceleration of the ionization of *(1a)*, *(2a)*, and *(3a)*[3]. The azabicyclics thus react by a concerted mechanism, as was to be expected from the antiperiplanar arrangement of the C(4)—R′ bond and the electron pair at N(1) relative to the C(2)—C(3) bond[3].

On the other hand, the axial[1] epimer *(1b)* in which this stereoelectronic condition is not fulfilled (cf. ref.[3]) reacts slower than the parent compound *(4b)*, giving the substitution and elimination products *(1c)*, *(1d)*, and *(12)*, respectively, along with the fragmentation product *(7)*. The fivefold slower reaction of *(1b)* relative to *(4b)* and the formation of several products suggest the intermediacy of the cation *(10)*, whose formation is rendered more difficult by the electron-withdrawing inductive ($-I$) effect of the nitrogen atom (SOH = solvent).

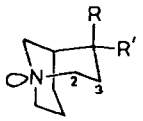
Surprisingly, the likewise axial[1] epimer *(2b)* reacts twice as fast, and *(3b) even 1230-times as fast* as *(5b)* and *(6a)*[5], respectively, although the stereoelectronic conditions for a concerted fragmentation are again not fulfilled[4]. In the case of *(2b)* and *(3b)*, fragmentation forming *(8)* and *(9)*, respectively, is accompanied by substitution giving *(2c)* and *(3c)*, and with *(2b)* by elimination giving the olefin *(13)*; this indicates occurrence of the cationic intermediates *(11)* and *(14)*, respectively. This assumption is supported by the observation that addition of ten mol. equiv. of sodium azide to an aqueous solution of *(3b)* hardly affects the reaction rate, while the yield of *(9)* falls from 75 to 58%. The question thus arises as to how the nitrogen atom accelerates the ionization of the axial bromide *(3b)* to form *(14)*.

[*] Prof. Dr. C. A. Grob, Dipl.-Chem. M. Bolleter, Dr. W. Kunz
Institut für Organische Chemie der Universität
St. Johanns-Ring 19, CH-4056 Basel (Switzerland)

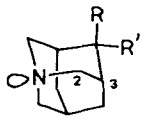
Fundamental studies by *Schleyer et al.*[6] have shown that nucleophilic participation of the solvent in the ionization of secondary *p*-toluenesulfonates (S_N2 with intermediate) is highly dependent upon steric hindrance at the rear of the reaction site. This hindrance is only slight in simple acyclic tosylates, significantly stronger in the cyclic compounds, and so strong in 2-adamantyl *p*-toluenesulfonate *(6b)* that nucleophilic participation of the solvent is no longer detectable[7]. This participation should therefore be practically ruled out in the ionization of the axial 4-bromo-1-azaadamantane *(3b)* but not in the case of *(1b)* and *(2b)*.



(1)



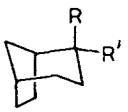
(2)



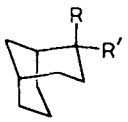
(3)

(a) R=H; R'=OTs
(b) R=OTs; R'=H
(c) R=H; R'=OH, OC_2H_5
(d) R=OH, OC_2H_5; R'=H

(a) R=H; R'=Br
(b) R=Br; R'=H
(c) R=H; R'=OH



(4)

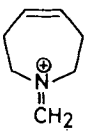


(5)

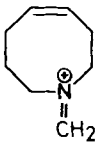


(6)

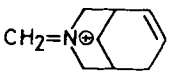
(a) R=Br
(b) R=OTs



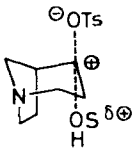
(7)



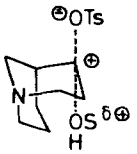
(8)



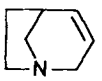
(9)



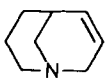
(10)



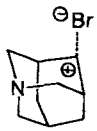
(11)



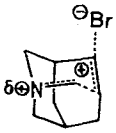
(12)



(13)



(14)



(15)

However, since the positive charge at the reaction site is largely transferred to the solvent by nucleophilic solvation, the electron deficiency at C(4) is only slight in the ion pairs *(10)* and *(11)* so that only the $(-I)$ effect of the nitrogen atom should be effective. But if access of solvent is hindered, as in *(14)*, then the positive charge spreads over the molecule, and particularly to the nitrogen atom if, as in *(15)*[8], it is hyperconjugated *via* a CC single bond with the cationic site at C(4)[9]. This also applies to the equatorial epimers *(1a)*, *(2a)*, and *(3a)*, in which nucleophilic solvation is likewise hindered but which can undergo concerted fragmentation. Thus exclusion of solvent triggers a reaction-promoting hyperconjugative or frangomeric effect. However, the stereoelectronic requirements for CC hyperconjugation are evidently less rigorous than for concerted fragmentation, and also less rigorous than conventional orbital models would suggest.

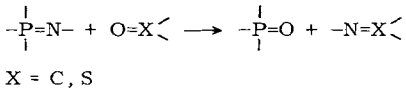
Received: April 30, 1980 [Z 547 IE]
German version: Angew. Chem. *92*, 734 (1980)

[1] "Equatorial" and "axial" relative to the piperidine ring.
[2] Or their products formaldehyde and secondary amine; cf. *C. A. Grob, W. Kunz, P. R. Marbet*, Tetrahedron Lett. *1975*, 2613; *E. Kräuchi*, Dissertation, Universität Basel 1977.
[3] Cf. review: *C. A. Grob*, Angew. Chem. *81*, 543 (1969); Angew. Chem. Int. Ed. Engl. *8*, 535 (1969).
[4] Unusual behavior is also observed with 6-*exo*-amino-2-*exo*-norbornyl *p*-toluenesulfonate (cf. *W. Fischer, C. A. Grob, G. von Sprecher, A. Waldner*, Tetrahedron Lett. *1979*, 1901) and 2-chloro-2,3,3-trimethyl-1-butanol (cf. *W. Fischer, C. A. Grob*, Helv. Chim. Acta *61*, 2336 (1978)).
[5] Owing to the plane of symmetry there is only one isomer of *(6)*.
[6] *T. W. Bentley, P. von R. Schleyer*, J. Am. Chem. Soc. *98*, 7658 (1976); *F. L. Schadt, T. W. Bentley, P. von R. Schleyer, ibid. 98*, 7667 (1976).
[7] This steric hindrance probably accounts for the fact that *(4b)* and *(5b)* react *ca.* 500 times faster than *(6b)* in 80% ethanol.
[8] The electron shift is indicated in only one of the equivalent bridges for the sake of clarity.
[9] *C. A. Grob*, Angew. Chem. *88*, 621 (1976); Angew. Chem. Int. Ed. Engl. *15*, 569 (1976); *W. Fischer, C. A. Grob*, Helv. Chim. Acta *61*, 1588 (1978); *C. A. Grob, A. Waldner, ibid. 62*, 1736 (1979); *W. Fischer, C. A. Grob, G. von Sprecher, A. Waldner*, Tetrahedron Lett. *1979*, 1905.

$(R_2NPO)_3$: A Novel Heterocycle with λ^3-Phosphorus by Trimerization of an Aminooxophosphane[**]

By *Edgar Niecke, Hans Zorn, Bernt Krebs*, and *Gerald Henkel*[*]

The Staudinger iminophosphorane/carbonyl reaction and its sulfinyl variant[1] are of preparative importance for the coupling of nitrogen-carbon and nitrogen-sulfur double bonds, respectively.



X = C, S

In the case of iminophosphanes, however, this reaction provides a possible approach for the generation of phosphorus compounds with $p_\pi(P)$—$p_\pi(O)$ bonding. This class of compounds is gaining more and more interest in connection with investigations on highly reactive species containing element-element multiple bonds[2].

We report here on a pseudo-Wittig reaction of the iminophosphane *(1)*, which leads to the previously unknown 1,3,5-trioxa-2λ^3,4λ^3,6λ^3-triphosphorin system.

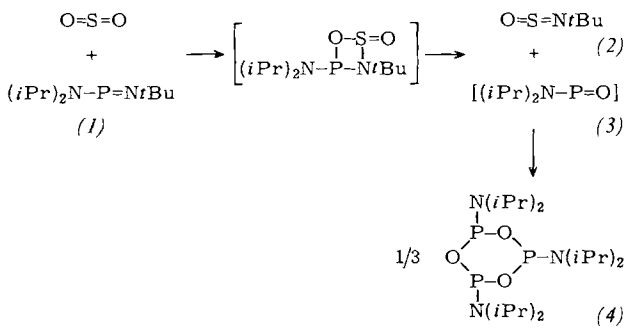
Diisopropylamino-*tert*-butyliminophosphane *(1)* already reacts with sulfur dioxide at $-25\,^\circ C$[3] to give *tert*-butyliminosulfur oxide *(2)* and a product of the composition

[*] Prof. Dr. E. Niecke, Dipl.-Chem. H. Zorn
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)
Prof. Dr. B. Krebs, Dr. G. Henkel
Anorganisch-Chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

[**] Phosphazanes of Coordination Number 2 and 3, Part 18. This work was supported by the Fonds der Chemischen Industrie. We thank Dr. *T. Wirthlin*, Varian AG, Zug/Switzerland for carrying out the NMR measurements.—Part 17: *E. Niecke, D.-A. Wildbredt*, Chem. Ber. *113*, 1549 (1980).

"R_2NPO", which proved to be the trimer *(4)* of the aminooxophosphane (phosphinidene oxide) *(3)*.

Presumably, in the initial step of the reaction a [2+2]-cycloaddition product is formed, which decomposes to kinetically labile *(3)*. Compound *(3)* is stabilized by coordinative saturation at the phosphorus to give the trioxatriphosphorin *(4)*—a reaction which can be formally compared with the observed cyclization in the isoelectronic XSN-system ($3XSN \rightarrow (XSN)_3$[4]).



The phosphorus-oxygen heterocycle *(4)* is a colorless, crystalline solid (m.p. 109 °C), sensitive to atmospheric moisture and oxygen. The composition and structure are secured by elemental analysis, mass spectrum[5], and NMR data, as well as by X-ray structure analysis (Fig. 1).

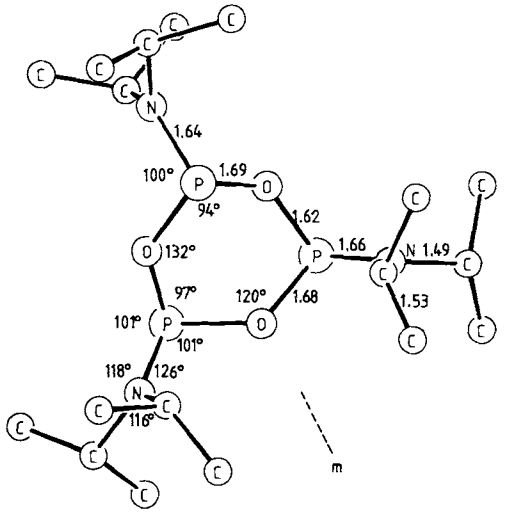


Fig. 1. $P_3O_3[N(i\text{-}C_3H_7)_2]_3$ *(4)* in the crystal, with average bond lengths [Å] and angles (σ *ca.* 0.012 Å and ca. 1.0°, resp.). *(4)*: space group $P2_1/n$, $a = 10.092(4)$, $b = 36.848(15)$, $c = 7.484(3)$ Å, $\beta = 106.54(3)°$, $Z = 4$ (at −133 °C).

The $^{31}P\{^1H\}$-NMR spectrum (30% solution in C_6D_6; H_3PO_4 ext.; 25 °C) shows the preferred population of only one isomer (>98%)[6] with two types of stereochemically different phosphorus atoms ($\delta A = 140.3$, $\delta B_2 = 131.3$, $^2J_{P_AP_B} = 13.5$ Hz), whose signals lie in the same region as those of 2-amino-1,3,2-dioxaphosphorinanes[7]. In accord with the ^{31}P-NMR spectrum, the ^1H-NMR spectrum (30% solution in CH_2Cl_2: TMS int.; 25 °C) shows two multiplets, each (2:1) for the methyl- and methine-protons: $\delta = 1.21$ ($^3J_{HH} = 6.8$ Hz), 3.59 ($|^3J_{HP_B} + {}^5J_{HP_B}| = 10.8$ Hz $[P_BN(CHMe_2)_2]$), 1.24 ($^3J_{HH} = 6.8$ Hz), 3.83 ($^3J_{HP_A} = 11.5$ Hz $[P_AN(CHMe_2)_2]$).

In the solid state the heterocycle *(4)* has, to a close approximation, C_s-symmetry. The sterically homogeneous molecules are disordered in the unit cell. Surprisingly, the heterocycle has almost ideal boat conformation in the crystal, whereby the transannular P...O distance (3.01 Å) between the ring atoms in the mirror plane of the molecule can possibly be seen as an indication of a 1,4-dipole-dipole interaction. The ligands take up the equatorial position at the phosphorus atoms, in which both a 1,3 repulsion of the ligands is minimized and a more effective $p_\pi(N)$—$d_\pi(P)$ interaction is achieved. The transfer of electrons from the nitrogen to the phosphorus manifests itself in the relatively short P—N bonds (1.64 and 1.66 Å) as well as in the planar arrangement of the ligands at the nitrogen atoms.

The molecule *(3)* can be trapped by complexation[8].

Procedure

About 180 mmol SO_2, dried with $CaCl_2$, is passed into a solution of *(1)* (9.5 g, 47 mmol) in ether (15 ml) at −25 °C under N_2. Immediately after passage of SO_2 is complete the excess SO_2 is removed under further cooling. The reaction solution is then warmed up to room temperature, and the solvent and any *(2)* that is formed are removed. Finally, the solid product is recrystallized twice from benzene; yield 2.8 g *(4)* (41%), colorless needles, m.p. 107 °C.

Received: October 18, 1979 [Z 542a IE]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 737 (1980)

[1] *H. Staudinger, E. Hauser*, Helv. Chim. Acta *4*, 861 (1921).
[2] *H. Quast, M. Heuschmann*, 2nd Int. Symposium on Inorganic Ring Systems, Göttingen 1978; Angew. Chem. *90*, 921 (1978); Angew. Chem. Int. Ed. Engl. *17*, 867 (1978); *H. Tomioka, Y. Izawa*, J. Org. Chem. *42*, 582 (1977); *U. Schmidt*, Angew. Chem. *87*, 535 (1975); Angew. Chem. Int. Ed. Engl. *14*, 523 (1975).
[3] Carbonyl compounds react only under stronger conditions; so far only polymers could be obtained.
[4] *O. Glemser, H. Perl*, Naturwissenschaften *48*, 620 (1961); *O. Glemser, H. Meyer, A. Haas*, Chem. Ber. *98*, 446 (1965).
[5] MS (70 eV): $m/e = 441$ (12%, M^+), 89 (100%, $OPNCHMe^+$).
[6] The possible existence of at least one further isomer (<2%) which is in equilibrium with *(4)* could be ascertained ^{31}P-NMR spectroscopically.
[7] *W. G. Bentrude, Han-Wan Tan*, J. Am. Chem. Soc. *95*, 4666 (1973).
[8] *E. Niecke, M. Engelmann, H. Zorn, B. Krebs, G. Henkel*, Angew. Chem. *92*, 738 (1980); Angew. Chem. Int. Ed. Engl. *19*, 710 (1980).

Complex-Stabilization of an Aminooxophosphane (Phosphinidene Oxide)[**]

By *Edgar Niecke, Monika Engelmann, Hans Zorn, Bernt Krebs*, and *Gerald Henkel*[*]

While stable methylenephosphanes *(1)* and iminophosphanes *(2)* have been reported recently, the existence of the phosphorus-oxygen $(p\text{-}p)_\pi$ bond, such as in *(3)*, has not been verified, although trapping reactions would indicate the formation of such a species[2]. Recently, reaction of aminoiminophosphane *(4)* and sulfur dioxide yielded the trioxatriphosphorine *(6)*, which is presumably formed by stereospe-

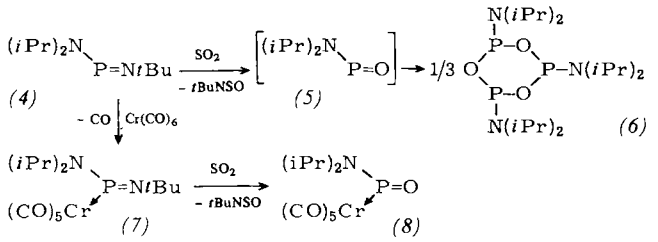
−P=C< −P=N− −P=O
(1) *(2)* *(3)*

[*] Prof. Dr. E. Niecke, M. Engelmann, Dipl.-Chem. H. Zorn
Fakultät für Chemie der Universität
Postfach 8640, D-4800 Bielefeld 1 (Germany)
Prof. Dr. B. Krebs, Dr. G. Henkel
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

[**] Phosphazenes of Coordination Number 2 and 3, Part 19. This work was supported by the Fonds der Chemischen Industrie.—Part 18: [1].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0909-0710 $ 02.50/0

cific cycloaddition of the intermediate aminooxophosphane (phosphinidene oxide) *(5)*[1]. By application of the SO_2-reaction to the iminophosphane complex *(7)* we have now succeeded in trapping the aminooxophosphane as complex *(8)*.



The compounds *(7)* and *(8)* are pale yellow crystalline solids which are sensitive to atmospheric moisture and oxygen. Their composition and constitution are confirmed by elemental analysis, IR, Raman, NMR and mass spectral data, and by complete X-ray structure analyses.

The mass spectrum (Varian 311A, 70 eV, direct sample introduction) of *(7)* (L = $(iPr)_2NPNtBu$) and of *(8)* (L = $(iPr)_2NPO$) show the molecular ion $LCr(CO)_5^+$ [*m/e* = 394 (3%) and 339 (4%), resp.] and the fragments $LCr(CO)_n^+$ (*n* = 4—0) resulting from successive cleavage of CO, with the LCr^+ fragment (*m/e* = 257 and 199, resp.) as base peak. In the IR and Raman spectra (Table 1) of *(7)* and *(8)* five bands appear in the expected ν(CO) range which can be considered as resulting from a strong perturbation of the local C_{4v} symmetry of the $Cr(CO)_5$ group. The frequency shift to high wave numbers observed in the case of *(8)* is possibly due to the stronger π-acceptor properties of the aminooxophosphane ligand.

Table 1. Characteristic IR [a] and Raman data [b] of compounds *(7)* and *(8)*.

(7) IR	*(7)* Raman	*(8)* IR	*(8)* Raman	For (C_{4v})	
2072 s	2072 m-s	2080 s	2082 m-s		A_1^1
1984 s	1986 vs	1995 m	1996 vs		B_1
1960 sh	1960 m	1985 s	1985 m-s	ν(CO)	A_1^2
1952 vs	1950 sh	1965	1963 s		E
1940 sh	1937 s	1935 vs	1940 w		
1340 m, br.	1344 s, br. [c]	1198 m	1203 s [d]		

[a] Nujol mull. [b] Solid. [c] ν(P=N). [d] ν(P=O).

The broad intense Raman line at 1344 cm^{-1} in *(7)*, as in the case of other iminophosphane complexes[3], can be ascribed to strengthening of the P=N-bonding [in *(2)*: 1242 cm^{-1}[4]] by coordination. In *(8)* a Raman band of comparable intensity appears at 1200 cm^{-1}; accordingly, it should arise from a stretching vibration with predominant P=O character.

The ^1H- and $^{13}C\{^1H\}$-NMR spectra of *(7)* and *(8)* show the expected groups of signals (Table 2). In the ^{31}P-NMR spectrum of *(7)* the coordination of the iminophosphane results in an upfield shift of the ^{31}P resonance signal[3,5] [δ = 224.0; for comparison, 295.2 in *(4)*]. On the other hand, the replacement of the *tert*-butyl imino-group in *(7)* by oxygen as in *(8)* leads to strong deshielding of the phosphorus atom (δ = 319.2), from which it can be concluded that the phosphorus in *(7)* is considerably more electrophilic than in *(4)*. These findings are consistent with an extremely reactive "free" aminooxophosphane.

Figure 1 shows the molecular structure of the complex *(8)*[6]. The central phosphorus atom is trigonal-planar

Table 2. ^{31}P-, ^1H- and ^{13}C-NMR data of the compounds *(7)* and *(8)* [a].

	(7)	*(8)*
$\delta(^{31}P)$	224.0	319.2
$\delta(^1H)$ (J_{HP} [Hz])		
*t*Bu	1.40	—
*i*Pr	1.17, 3.77 [b] (15.3)	1.23, 3.25 [b] (13.5)
$\delta(^{13}C)$ (J_{CP} [Hz])		
*t*Bu	33.5 (5.9), 57.0 (1.9)	—
*i*Pr	22.2 (3.3), 48.9 (9.6)	22.4 (3.3), 50.2 (10.3)
CO_{eq}	215.1 (16.0)	213.9 (18.7)
CO_{ax}	220.3 (3.6)	218.2

[a] 20% solution in $CDCl_3$; H_3PO_4 ext. (^{31}P) or TMS (^1H, ^{13}C) int.; 25 °C. [b] $^3J_{HH}$ = 6.7 *(7)*, 5.9 Hz *(8)*.

coordinated, as it is in the complexes $(CO)_5CrL$ [L = $(Me_3Si)_2NP{=}NtBu$, $tBuHNP{=}NSiMe_3$][3c], whose structures were analyzed previously. The extremely short $P—N_{amine}$ distance[7] and the P=O bond length, which is comparable with that in trimethylphosphane oxide[8], are compatible with a pseudoallylic $R_2\overset{+}{N}\cdots P\cdots\bar{O}$ interaction.

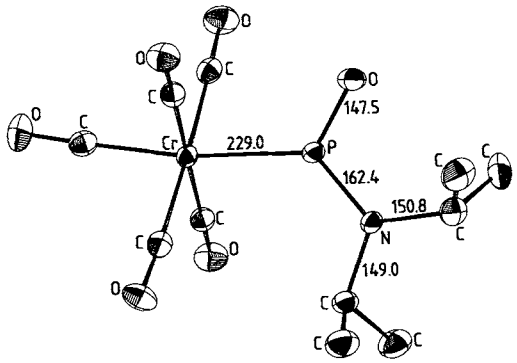


Fig. 1. Molecular structure of *(8)* (without H atoms; vibration ellipsoids with 50% probability) with important bond lengths (pm; σ = 0.2 pm). Further bond data: O—P—N 120.6(1)°, O—P—Cr 111.4(1)°, N—P—Cr 128.0(1)°; Cr—C_{ax} 188.4(2) pm, Cr—C_{eq} 190.2—191.4(2) pm.

This is in accord with an almost planar arrangement of the C_2N—P=O moiety; the dihedral angle between the C_2N- and NPO-plane is only 1.6°. The P—Cr distance is significantly shorter than in the corresponding iminophosphane complexes[3c], which should be attributed to better π-acceptor properties of the aminooxophosphane ligand. These properties result from the higher orbital electronegativity of the phosphorus in *(8)* in comparison with that in the iminophosphanes.

Procedure

All reactions are carried out in anhydrous solvents under N_2. *(7)*: A solution of *(4)* (4.4 g, 22 mmol) and $Cr(CO)_6$ (5.0 g, 23 mmol) in tetrahydrofuran (THF) (250 ml) is irradiated in a photoreactor at −5 °C until about 2/3 of the calculated amount of CO has been formed. The solution is then concentrated to 50 ml and unreacted $Cr(CO)_6$ is filtered off. The residue after removal of solvent is recrystallized twice from *n*-hexane; yield 2.8 g (32%) *(7)*, m.p. 95—98 °C (dec.).

(8): About 15 mmol SO_2, dried over $CaCl_2$, is passed into a solution of *(7)* (2.1 g, 5.3 mmol) in ether (20 ml) at −30 °C. Unreacted SO_2 is removed at −30 °C and the reaction solution warmed to room temperature. The crude product [*ca.* 80% *(8)*] after removal of solvent and any *t*BuNSO that is

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/0909-0711 $ 02.50/0

formed is purified by sublimation at 50 °C/0.1 torr; yield 0.9 g (43%) *(8)*, m.p. 93—96 °C (dec.).

Received: January 9, 1980 [Z 542b IE]
supplemented: April 8, 1980
German version: Angew. Chem. *92*, 738 (1980)

CAS Registry numbers:
(4), 63950-84-5; *(6)*, 74563-07-8; *(7)*, 74592-15-7; *(8)*, 74592-16-8; SO_2, 7446-09-5; *t*-BuNSO, 38662-39-4; $Cr(CO)_6$, 13007-92-6

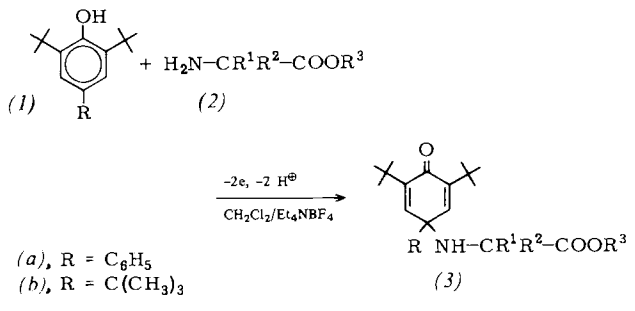
[1] *E. Niecke, H. Zorn, B. Krebs, G. Henkel,* Angew. Chem. *92*, 737 (1980); Angew. Chem. Int. Ed. Engl. *19*, 709 (1980).
[2] *H. Quast, M. Heuschmann,* 2nd Int. Symposium on Inorganic Ring Systems, Göttingen 1978; Angew. Chem. *90*, 921 (1978); Angew. Chem. Int. Ed. Engl. *17*, 867 (1978), and references cited therein.
[3] *E. Niecke, R. Kröher, G. Ringel,* Chemiedozententagung, Marburg 1977; *G. Ringel,* Dissertation, Universität Göttingen 1977; *S. Pohl,* J. Organomet. Chem. *142*, 185, 195 (1977); *E. Niecke, G. Ringel, S. Pohl,* unpublished.
[4] *H. Zorn,* Diplomarbeit, Universität Göttingen 1975.
[5] *O. J. Scherer, N. Kuhn, H. Jungmann,* Z. Naturforsch. B *33*, 1321 (1978).
[6] *(8)* crystallizes monoclinically, space group $P2_1/n$, $a = 1126.2(3)$, $b = 2186.4(5)$, $c = 632.6(2)$ pm, $\beta = 100.65(3)°$, $V = 1530.8 \times 10^6$ pm^3, $Z = 4$ (at −130 °C). Refinement with the structure factors of 2661 observed reflections converged to the unweighted R value of 3.5%.
[7] A comparable bond length is observed in ions of the type [N═P═N]$^+$: *S. Pohl,* Z. Naturforsch. *B 32*, 1342 (1977); *A. H. Cowley, M. C. Cusher, J. S. Szobota,* J. Am. Chem. Soc. *100*, 7784 (1978).
[8] *D. E. C. Corbridge:* The Structural Chemistry of Phosphorus. Elsevier, Amsterdam 1974.

An Amino-Protecting Group for Use in Peptide Synthesis Which Can Be Introduced Electrochemically[**]

By *Mohamed Hassen Khalifa, Günther Jung,* and *Anton Rieker*[*]

In acetonitrile, sterically hindered phenols of type *(1)* can be electrochemically oxidized to phenyloxylium ions which form *p*-quinols or *p*-quinol derivatives in the presence of nucleophiles (water, alcohols and amines)[1,2]. The specificity and yield of this synthesis are usually far higher than normally attained in chemical oxidation.

We now report the application of electrochemical oxidation of 2,4,6-trisubstituted phenols to the synthesis of new *N*-protected amino acids and peptide derivatives. A suitable reagent is 3,5-di-*tert*-butyl-4-biphenylol *(1a)* which is readily accessible by reaction of 2,6-di-*tert*-butyl-1,4-benzoquinone with phenylmagnesium bromide and subsequent reduction with zinc/HCl[3,4]. Introduction of the new protecting group 3,5-di-*tert*-butyl-4-oxo-1-phenyl-2,5-cyclohexadienyl (PCHd)



(a), R = C_6H_5
(b), R = $C(CH_3)_3$

is accomplished by anodic oxidation of *(1a)* in dichloromethane in the presence of the free amino acid esters *(2)* at an anode potential of +1300 mV *vs* Ag/0.01 M $Ag^{\oplus}$ at a platinum electrode in an undivided cell.

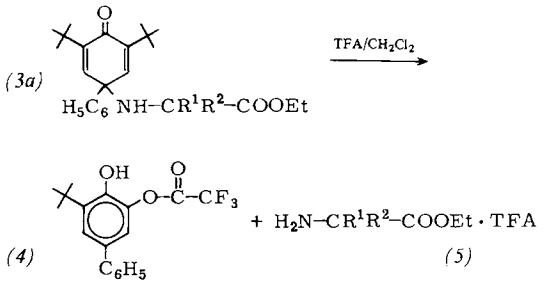
The *N*-(PChd)-amino acid esters *(3a)* (Table 1) are usually formed cleanly, with high selectivity, and without racemization. Polyfunctional amino acids have to be completely blocked except for the amino group to be protected.

Table 1. Yields and physical data of selected PChd-protected amino acids *(3a)* and peptides derivatives.

N-PChd derivative	Yield [%]	M.p. [°C]	$[\alpha]_D^{20}$ [e]	R_F [g]
PChd-Gly-OH	90 [a]	167—168	—	0.30 (II)
PChd-L-Ala-OH	94 [a]	181—183	−125.9	0.45 (II)
PChd-Aib-OEt	97 [b]	88—89	—	0.26 (I)
PChd-Aib-OH	94 [c]	169—171	—	0.48 (II)
PChd-L-Leu-OBzl	89 [b]	86—87	−169.5	0.41 (I)
PChd-L-Leu-OH	60 [c]	131—133	−185.3	0.69 (II)
PChd-L-Pro-OBzl	59 [b]	144—145	+ 55.3	0.29 (I)
PChd-L-Pro-OH	57 [c]	81—82	+183.8	0.56 (II)
PChd-L-Leu-Gly-NH_2	85 [d]	148	+ 51.3 [f]	0.58 (II)
PChd-L-Pro-L-Leu-Gly-NH_2	75 [d]	116—118	+ 70.5	0.54 (II)

[a] Based on *(1a)* after hydrolysis of *(3)*. [b] Based on *(1a)* (on reaction of H-Aib-OEt with *(1a)* in a molar ratio of 1:1 the yield is 82%). [c] Based on hydrolysis of *(3)*. [d] Based on coupling of PChd-Leu-OH and PChd-Pro-OH, respectively. [e] $c = 1$, ethanol. [f] $c = 0.4$. [g] (I) Dichloromethane/light petroleum (3:2), (II) chloroform/methanol (8:1).

The alkali-stable PChd group can be quantitatively removed by 50% trifluoroacetic acid (TFA) in dichloromethane within 15 min at 25 °C. The protecting group regenerates a phenol *(4)*[5] which can easily be separated from the amino acid ester *(5)* by extraction with diethyl ether.



These mild acidolysis conditions permit selective use of this protecting group alongside benzyloxycarbonyl, benzyloxy, and benzyl ester protecting groups, even in syntheses involving repeated coupling and deblocking steps.

Particularly useful is the quantitative hydrogenolytic removal with Pd/C (10%) in methanol which regenerates the protecting group in its original form *(1a)*. This method of removal permits its use alongside all hydrogenolysis-stable protecting groups, *e.g.* the Boc group.

The applicability of the PChd protecting group in peptide synthesis has been tested in the case of the MSH inhibitor H-L-Pro-L-Leu-Gly-NH_2[6] (see Table 1). Coupling of PChd-L-Leu-OH with H-Gly-NH_2 by the DCC/HOBt method afforded PChd-L-Leu-Gly-NH_2. The H-L-Leu-Gly-NH_2 generated both by acidolysis as well as hydrogenolysis was then reacted with PChd-L-Pro-OH by the same method to give well-crystalline, unequivocally characterized PChd-L-Pro-L-Leu-Gly-NH_2 which, on hydrogenolysis, gave chromatographically pure, racemate-free H-L-Pro-L-Leu-Gly-NH_2. Thus the new protecting group fulfils the requirements of unequivocal peptide syntheses[7]. The PChd group also facilitates ready fast monitoring of the course of reaction by means of UV detection. Easy recovery of the phenol *(1a)* after hydro-

[*] Dr. M. H. Khalifa, Prof. Dr. G. Jung, Prof. Dr. A. Rieker [†]
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)
[†] To whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

genolytic removal of the protecting group should prove valuable, above all when working on a large scale.

Anodic oxidation of the phenol *(1b)* in the presence of amino acid esters *(2)* afforded *N*-(1,3,5-tri-*tert*-butyl-4-oxo-2,5-cyclohexadienyl)amino acid esters; however, the yield obtained is lower (<50%). Removal of this protecting group can only be accomplished by catalytic hydrogenation. Finally, the PChd group can also be introduced electrochemically to protect the carboxy group of *N*-protected amino acids.

General procedure

(1a) (2.82 g, 10 mmol), *(2)* (20 mmol), and 2,6-dimethylpyridine (2.14 g, 20 mmol) are dissolved in dichloromethane (150 ml) which is 0.1 M in Et_4NBF_4. After saturation with N_2 the mixture is electrolyzed at Pt gauze electrodes in an undivided cell[2]. The initial anode potential is chosen (*ca.* +1000 mV *vs* Ag/0.01 M $Ag^{\oplus}$) such that the current lies below 130 mA. In the course of electrolysis the current falls off; the electrode potential is then increased stepwise to +1300 mV and the reaction continued until *(1a)* has been completely consumed. The solvent is removed *in vacuo* and the residue washed repeatedly with diethyl ether. The oily residue of PChd-amino acid ester *(3a)* and 2,6-dimethylpyridine, obtained after removal of the ether, can be separated by a single filtration over silica gel (light petroleum 60—90 °C/dichloromethane 2:1 as eluent) and crystallization from alcohol. Oily PChd-amino acid esters (Gly, Ala) can also be hydrolyzed with 0.2 N NaOH in CH_3OH/H_2O (4:1) immediately upon extraction.

Received: March 3, 1980 [Z 543 IE]
German version: Angew. Chem. *92*, 739 (1980)

CAS Registry numbers:

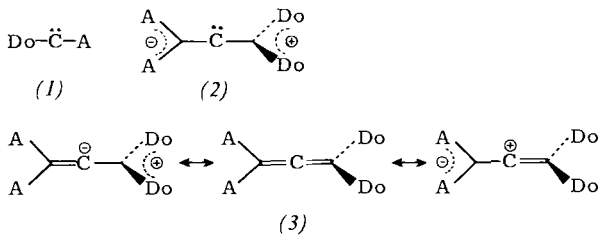
(1a), 2668-47-5; H-Gly-OH, 56-40-6; L-H-Ala-OH, 56-41-7; H-Aib-OEt, 1113-49-1; H-Aib-OH, 62-57-7; L-H-Leu-OBzl, 1738-69-8; L-H-Leu-OH, 61-90-5; L-H-Pro-OBzl, 41324-66-7; L-H-Pro-OH, 147-85-3; L-H-Leu-Gly-NH_2, 39705-58-3; L-H-Pro-L-Leu-Gly-NH_2, 2002-44-0; PChd-Gly-OH, 74763-73-8; PChd-L-Ala-OH, 74763-74-9; PChd-Aib-OEt, 74763-75-0; PChd-Aib-OH, 74763-76-1; PChd-L-Leu-OBzl, 74763-77-2; PChd-L-Leu-OH, 74763-78-3; PChd-L-Pro-OBzl, 74763-79-4; PChd-L-Pro-OH, 74763-80-7; PChd-L-Leu-Gly-NH_2, 74763-81-8; PChd-L-Pro-L-Leu-Gly-NH_2, 74763-82-9; 2,6-di-*tert*-butyl-1,4-benzoquinone, 719-22-2; phenyl bromide, 108-86-1

[1] *A. Ronlán, V. D. Parker*, J. Chem. Soc. *C 1971*, 3214.
[2] *A. Rieker, E.-L. Dreher, H. Geisel, M. H. Khalifa*, Synthesis *1978*, 851.
[3] *A. Rieker, P. Ziemek*, Z. Naturforsch. *B 20*, 640 (1965).
[4] *A. Rieker, K. Scheffler*, Justus Liebigs Ann. Chem. *689*, 78 (1965).
[5] Cf. *A. Nishinaga, K. Nakamura, T. Matsuura, A. Rieker, D. Koch, R. Griesshammer*, Tetrahedron *35*, 2943 (1979).
[6] *R. A. Boissonnas, St. Guttmann, P. A. Jaquenoud, J.-P. Waller*, Helv. Chim. Acta *38*, 1491 (1955).
[7] *E. Wünsch* in Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit., Vol. XV/1. Thieme, Stuttgart 1974.

The Ambiphilicity of 1,1-Diethoxy-4,4,4-trifluoro-3-(trifluoromethyl)-1,2-butadiene[**]

By *Rolf W. Saalfrank, Winfried Paul,* and *Heide Liebenow*[*]

Electron-rich or electron-deficient allenes, *e.g.* tetrakis(dimethylamino)allene or allenetetracarboxylic acid tetraethyl ester, respectively react at the central atom C^2 with electrophiles or nucleophiles to give dipolar products[1]. Ambiphilic carbenes, *e.g.* chloro(methoxy)carbene, exhibit electrophilic and nucleophilic selectivity, respectively, towards electron-rich and electron-deficient olefins[2]. If the donor substituent (Do) in an ambiphilic carbene *(1)* is replaced by a stabilized



(1) *(2)* *(3)*

anion, and the acceptor substituent (A) is replaced by a stabilized cation, then one obtains a dipolar carbene *(2)* which can also be regarded as allene *(3)*. We have now found that such donor/acceptor-substituted allenes are likewise ambiphilic, *i.e.* can react at the central atom C^2 both electrophilically as well as nucleophilically.

Reaction of hexafluoroacetone *(4)* with (2,2-diethoxyvinylidene)triphenylphosphorane *(5)* affords the thermally surprisingly stable 3-(diethoxymethylene)-2,2,2-triphenyl-4,4-bis(trifluoromethyl)-1,2λ^5-oxaphosphetane *(6)*[3] (yield 92%; m.p. 109 °C, dec.), which only decomposes above 100 °C into triphenylphosphane oxide and 1,1-diethoxy-4,4,4-trifluoro-3-(trifluoromethyl)-1,2-butadiene *(7)*. The characterization of *(6)* as a derivative of pentavalent phosphorus was achieved $^{31}P\{^1H\}$-NMR spectroscopically (Table 1). The $^{13}C\{^1H\}$-NMR spectrum contains only four signals (Table 1) for the three phenyl groups. The equilibration of the apical and equatorial positions of the trigonal-bipyramidal structure *(6)* already takes place rapidly (^{13}C-NMR time scale) at room temperature by a ligand-rearrangement process.

Table 1. Some characteristic spectroscopic data of the compounds *(6)—(12)* [a].

(6), ^1H-NMR: 0.63 (t, 3H, CH_3), 1.29 (t, 3H, CH_3), 3.33 (q, 2H, CH_2), 3.92 (q, 2H, CH_2), 7.15 to 7.80 (m, 15H, phenyl-H); $^{13}C\{^1H\}$-NMR: 164.38 (d, $=C(OEt)_2$, $^2J_{PC}=12.2$), 140.45 (d, 3 phenyl-C, $^1J_{PC}=100.7$), 133.08 (d, 6 phenyl-C, $^2J_{PC}=10.6$), [b], 128.94 (d, 3 phenyl-C, $^4J_{PC}=2.3$), 127.45 (d, 6 phenyl-C, $^3J_{PC}=13.0$), 106.66 (d, =C—P, $^1J_{PC}=144.9$), 66.62 (s, CH_2), 66.37 (s, CH_2), 14.14 (s, CH_3), 13.95 (s, CH_3); ^{19}F-NMR: 5.86 (s, 6F, CF_3); $^{31}P\{^1H\}$-NMR: −49.09

(7), ^1H-NMR: 1.39 (t, 6H, CH_3), 3.64 (q, 4H, CH_2); $^{13}C\{^1H\}$-NMR: 199.57 (m, =C=), 160.26 (s, $=C(OEt)_2$), 118.82 (q, CF_3, $^1J_{FC}=275.6$), 109.36 (sept, $=C(CF_3)_2$, $^2J_{FC}=37.3$), 68.89 (s, CH_2), 14.23 (s, CH_3); ^{19}F-NMR: −14.52 (s, 6F, CF_3); IR (Film): ν(C=C=C) = 1965 cm^{-1}

(8a), ^1H-NMR: 1.18 (t, 3H, CH_3), 1.30 (t, 3H, CH_3), 3.88 (q, 2H, CH_2), 3.99 (q, 2H, CH_2), 7.12 to 7.70 (m, 5H, phenyl-H); $^{13}C\{^1H\}$-NMR: 158.53 (s, $=C(OEt)_2$), 157.15 (qt, $=CF_2$, $^1J_{FC}=300.5$, $^3J_{FC}\approx4.0$), [b], 89.49 (s, =CPh), 87.42 (m, $=CCF_3$); ^{19}F-NMR: −0.75 (quin, dq), 1F, =CF, $^2J_{FF}=11.0$, $^4J_{FF}=11.0$), −2.18 (dq, 1F, =CF, $^2J_{FF}=11.0$, $^4J_{FF}=17.1$), −19.44 (dd, 3F, CF_3, $^4J_{FF}=11.0$, $^4J_{FF}=17.1$)

(8b), ^1H-NMR: 1.23 (t, 3H, CH_3), 1.28 (t, 3H, CH_3), 1.73 (s, 3H, CH_3), 3.80 (q, 2H, CH_2), 3.88 (q, 2H, CH_2); $^{13}C\{^1H\}$-NMR: 156.38 (s, $=C(OEt)_2$), 156.16 (qt, $=CF_2$, $^1J_{FC}=297.5$, $^3J_{FC}\approx4.0$), 123.25 (ddq, CF_3, $^1J_{FC}=271.6$, $^3J_{FC}\approx5.0$), 87.00 (m, $=CCF_3$), 84.88 (s, $=CCH_3$); ^{19}F-NMR: 18.67 (dd, 3F, CF_3, $^4J_{FF}=11.5$, $^4J_{FF}=20.0$), 0.60 to −1.45 (m, 2F, $=CF_2$)

(9b), ^1H-NMR: 1.24 (t, 9H, CH_3), 3.55 (q, 6H, CH_2), 6.66 (s, broad, 1H, =CH); $^{13}C\{^1H\}$-NMR: 143.46 (m, =CH), [b], 120.89 (q, CF_3, $^1J_{FC}=276.1$), 119.55 (q, CF_3, $^1J_{FC}=276.1$), 110.74 (s, $C(OEt)_3$); ^{19}F-NMR: −14.32 (dq, 3F, F_3C^a (?), $^4J_{FF}=8.2$, $^4J_{HF}=1.5$), −20.57 (q, 3F, F_3C^b, $^4J_{FF}=8.2$)

(10), ^1H-NMR: 1.36 (t, 3H, CH_3), 3.38 (q, 2H, CH_2), 6.95 (s, broad, 1H, =CH); $^{13}C\{^1H\}$-NMR: 162.02 (s, COOEt), 132.82 (m, =CH), [b], 120.34 (q, CF_3, $^1J_{FC}=274.1$), 119.63 (q, CF_3, $^1J_{FC}=275.5$); ^{19}F-NMR: −13.27 (dq, 3F, F_3C^a (?), $^1J_{FF}=6.8$, $^4J_{HF}=1.4$), −17.50 (q, 3F, F_3C^b, $^4J_{FF}=6.8$)

(11), ^1H-NMR: 1.36 (t, 6H, CH_3), 3.65 (q, 4H, CH_2), 7.20 to 7.93 (m, 5H, phenyl-H); $^{13}C\{^1H\}$-NMR: 156.53 (s, C=O), 153.07 (s, $=CC(OEt)_2$), [b], 119.93 (q, CF_3, $^1J_{FC}=275.4$), 119.41 (q, CF_3, $^1J_{FC}=276.9$), 109.84 (s, $C(OEt)_2$); ^{19}F-NMR: −17.13 (q, 3F, CF_3, $^4J_{FF}=7.8$), −20.32 (q, 3F, CF_3, $^4J_{FF}=7.8$)

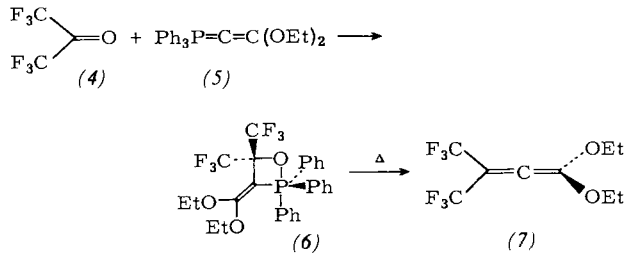
(12), ^1H-NMR: 1.36 (t, 3H, CH_3), 4.43 (q, 2H, CH_2), 7.16 to 7.90 (m, 6H, phenyl-H and NH); $^{13}C\{^1H\}$-NMR: 161.90 and 157.05 (two s, CONH and COOEt), 142.42 (s, $=CCOOEt$), [b], 119.99 (q, 2 CF_3, $^1J_{FC}=277.0$); ^{19}F-NMR: 17.88 (q, 3F, CF_3, $^4J_{FF}=7.7$), −18.75 (q, 3F, CF_3, $^4J_{FF}=7.7$)

[a] $CDCl_3$, δ values, J [Hz]: ^1H-NMR (60.00 MHz) and $^{13}C\{^1H\}$-NMR (25.15 MHz) TMS int.; ^{19}F-NMR (94.09 MHz) F_3CCOOH ext. and $^{31}P\{^1H\}$-NMR (40.48 MHz) H_3PO_4 ext. [b] The positions of CF_3 and/or $C(CF_3)_2$ are not clear.

[*] Univ.-Doz. Dr. R. W. Saalfrank, Dipl.-Chem. W. Paul, H. Liebenow
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

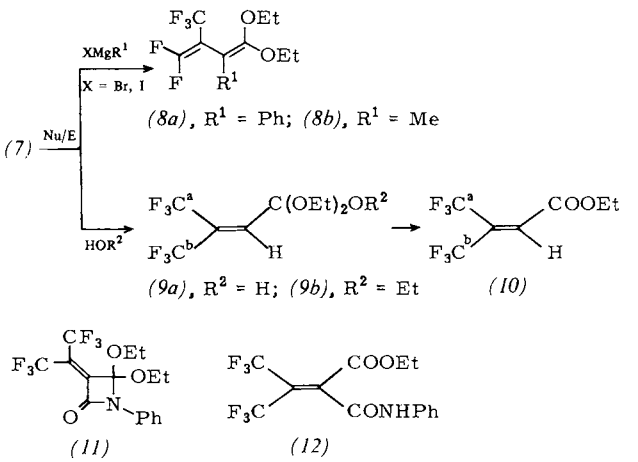
[**] Donor/Acceptor-Substituted Allenes, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 4: *R. W. Saalfrank, E. Ackermann, H. Winkler, R. Böhme*, Chem. Ber., in press.

A simplified flash thermolysis of the primary product *(6)* opens a facile entry to the allene *(7)* (yield 79%; m.p. $\approx -5\,^{\circ}C$), which is storable in the cold for some time, but rapidly ($\tau_{1/2} \approx 5$ min) forms a crystalline center-center dimer[4] at room temperature. The spectral data of *(7)* (Table 1) confirm the proposed structure.



Characteristic for the ambiphilic donor/acceptor allene *(7)* is the finding that it can be attacked both nucleophilically as well as electrophilically at the carbon atom C^2. For example, nucleophilic attack with Grignard reagents and subsequent elimination of a fluoride ion affords the 1,3-butadiene derivatives *(8)* [*(8a)* and *(8b)*: yield 66% and 70%, resp.; b.p. 87 and 35 °C/0.5 torr, resp.], while electrophilic attack with water or ethanol furnishes the addition products *(9)*. *(9a)* spontaneously loses ethanol to give the ethyl 4,4,4-trifluoro-3-trifluoromethylcrotonate *(10)* [yield 78%; b.p. 127 °C (126—127 °C[5])], whereas the ethyl 4,4,4-trifluoro-3-trifluoromethylorthocrotonate *(9b)* (yield 74%; b.p. 30 °C/0.3 torr) can be isolated.

Addition of phenyl isocyanate to the allene *(7)* affords the 1:1 cycloadduct *(11)* (yield 64%; m.p. 48 °C). As in other similar cases, a polar two-step process[6] is assumed for this [2+2]-cycloaddition of an electrophilic reagent to an electron-rich π-system. The ^{1}H-NMR spectrum of the β-lactam *(11)* shows two equivalent ethyl groups, the ^{19}F-NMR spectrum two non-equivalent trifluoromethyl groups (Table 1).



Further proof of the structure of *(11)* is provided by its acid hydrolysis to the ester *(12)* (yield 75%; m.p. 142 °C).

Procedure

(6): 1.7 g (10.0 mmol) of *(4)* is fed into a solution of *(5)*[7] (3.8 g, 10.0 mmol) in anhydrous ether (40 ml) at −78 °C in the absence of moisture. After warming to room temperature the solvent is distilled off and the residue [*(6)*] recrystallized from dichloromethane/ethyl acetate (1/10).

(7): *(6)* (5.4 g, 10.0 mmol) is decomposed in a Schlenk tube by immersion in an oil-bath heated to 150 °C at 0.5 torr; the allene *(7)* that distils over is frozen in a trap cooled to −78 °C.

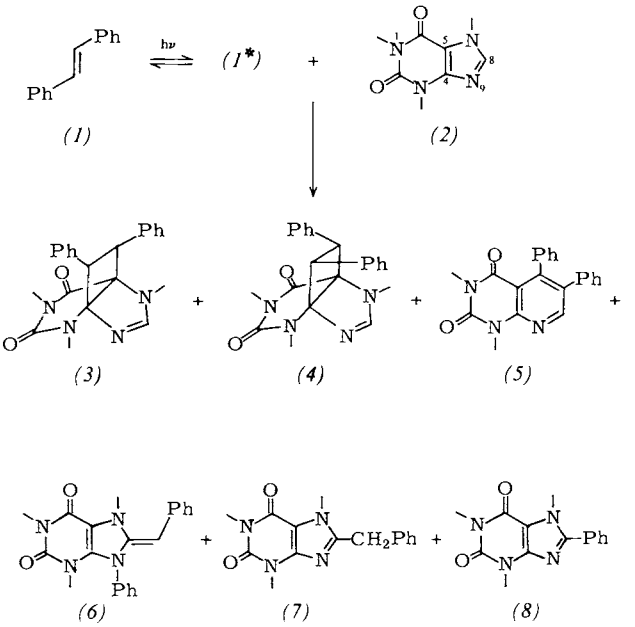
Received: February 18, 1980 [Z 544 IE]
German version: Angew. Chem. 92, 740 (1980)

[1] *R. Gompper, U. Wolf*, Justus Liebigs Ann. Chem. *1979*, 1406.
[2] *R. A. Moss, M. Fedorynski, W.-C. Shieh*, J. Am. Chem. Soc. *101*, 4736 (1979).
[3] *H. J. Bestmann, K. Roth, R. W. Saalfrank*, Angew. Chem. *89*, 915 (1977); Angew. Chem. Int. Ed. Engl. *16*, 877 (1977); *H. J. Bestmann*, J. Pure Appl. Chem. *51*, 515 (1979); *H. J. Bestmann, K. Roth, E. Wilhelm, R. Böhme, H. Burzlaff*, Angew. Chem. *91*, 945 (1979); Angew. Chem. Int. Ed. Engl. *18*, 876 (1979).
[4] *R. W. Saalfrank, W. Paul*, unpublished.
[5] *W. J. Middleton*, J. Org. Chem. *30*, 1307 (1965).
[6] *R. W. Hoffmann*, Angew. Chem. *84*, 306 (1972); Angew. Chem. Int. Ed. Engl. *11*, 324 (1972).
[7] *H. J. Bestmann, R. W. Saalfrank, J. P. Snyder*, Chem. Ber. *106*, 2601 (1973).

Photoreactions of Stilbene with Caffeine: Known, and New Types of Reactions[**]

By *Gerd Kaupp* and *Heinz-Willi Grüter*[*]

The kinetic, spectroscopic and stereochemical detection of diradicals in cyclovinylogous additions (or reversions)[1] enabled a planned search for new types of reactions. It is to be expected that diradicals not only stabilize themselves by cycloadditions (or cycloreversions)[1] and H-shifts[2], but also by substituent migrations and fragmentations with carbene formation. We report on three new types of reactions which occur alongside the usual [2+2]-[3] and [4+2]-photocycloadditions[4] and which are particularly easy to detect because of the ^{1}H-NMR key signals of the methyl groups when caffeine *(2)* traps electronically excited stilbene *(1*)*. The products *(3)*, *(4)* ([2+2]-addition), *(5)* ([4+2]-addition followed by methylamine elimination), *(6)*, *(7)*, and *(8)* are formed in the



[*] Prof. Dr. G. Kaupp, H.-W. Grüter
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Wissenschaftliche Gesellschaft Freiburg i. Br. We thank Dr. *D. Hunkler* for recording the NMR spectra.

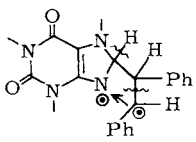
ratio 28:6:3:43:10:10 (see Procedure; m.p. and NMR data, see Table 1)[5].

Table 1. Melting points and NMR data of the compounds *(3)*—*(8)* [5].

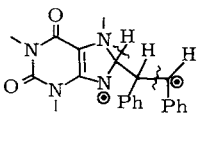
Cpd.	M.p. [°C]	^{1}H-NMR [^{13}C-NMR] ($CDCl_3$, δ, J [Hz])
(3)	176.5—	(250 MHz) 7.38—7.17 (10H, m), 7.02 (1H, s), 4.26 (1H,
[a]	177.5	AB, J=10), 3.96 (1H, BA, J=10), 3.18 (3H, s), 3.16 (3H, s), 3.12 (3H, s); [163.4, 159.2 (d, J=195), 151.3, 136.8, 136.0, 129.0 (2C), 128.7 (2C), 128.4 (2C), 128.1, 127.8 (2C), 127.7, 84.6, 66.7, 57.6 (d, J=130), 52.6 (d, J=135), 30.3 (q, J=139), 29.3 (q, J=140), 27.5 (q, J=142)] [b]
(4)	60—65	(250 MHz) 7.46—7.28 (10H, m), 7.19 (1H, br. s, $\Delta\nu_{1/2}$
[a]	(sinters)	=4), 4.35 (1H, AB, J=10), 4.21 (1H, BA, J=10), 3.37 (3H, s), 2.56 (3H, s), 2.45 (3H, s)
(5)	206	(60 MHz) 8.71 (1H, s), 7.6—7.0 (10H, m), 3.94 (3H, s), 3.55 (3H, s)
(6)	80—82	(250 MHz) 7.44 (1H, s), 7.42—7.22 (8H, m), 6.99—6.92
[c]	(sinters)	(2H, m), 3.61 (3H, s), 3.51 (3H, s), 3.44 (3H, s); [155.7
	116—118	(q, J=2.5), 151.9 (heptet, J=3), 151.0 (dq, J=12, 3.5), 148.8 (q, J=3), 138.8 (m), 135.6 (m), 135.3 (dt, J=155, 4.5), 129.1 (2C, m), 129.0 (2C, m), 128.9 (m), 128.8 (m), 128.5 (2C, m), 126.6 (2C, m), 107.7 (q, J=2.5), 32.3 (q, J=143), 30.0 (q, J=143), 28.0 (q, J=142.5)]
(7)	159—160	(250 MHz) 7.38—7.17 (5H, m), 4.18 (2H, s), 3.82 (3H, s), 3.61 (3H, s), 3.40 (3H, s) [d]
(8)	176—178	(90 MHz) 7.75—7.50 (5H, m), 4.06 (3H, s), 3.64 (3H, s);
	[e]	3.44 (3H, s)

[a] Irradiation (λ=250; 290 nm) at 293 K and 83 K rapidly leads to decomposition to *(1)* and *(2)*. [b] Without resolution of the long-range couplings. [c] On irradiation the *Z*-isomer absorbing at longer wavelengths is formed photoreversibly. [d] Consistent with data in the literature (*K. Bhushan, J. H. Lister*, Aust. J. Chem. *29*, 891 (1976)). [e] M.p. 176—178 °C (*H. Goldner, G. Dietz, E. Carstens*, Justus Liebigs Ann. Chem. *692*, 134 (1966)); 185 °C (*F. Yoneda, T. Nagamatsu*, J. Chem. Soc. Perkin I *1976*, 1547; we thank Prof. *Yoneda* for communicating his ^{1}H-NMR data, which are in complete agreement with ours).

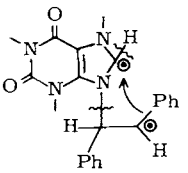
The formation of *(6)* [substitutive addition with phenyl migration and cleavage of the double bond of *(1)*], of *(7)* [substitutive addition with the cleavage of the double bond of *(1)*] and of *(8)* [intermolecular exchange of vinyl substituents] are without precedence. Their formulation is especially simple and clear if one assumes initial formation of 1,4-diradicals *(9)*, *(10)* and *(11)*, as in the cycloadditions[1] to give *(3)*, *(4)* (initial attack at C-4 or C-5)[3] and *(5)* (initial attack at C-5 or C-8)[4]. The indicated rearrangements and bond cleavages would then have to take place in order to form the products[6].



(9)



(10)



(11)

The experimental results show that hitherto unknown types of reactions predominate and enable the synthesis of interesting products such as that of the oxidizable and acylatable *(6)* from the rare class of enediamines, without well-known reactions such as the formation of [4.3.2]propellanes[3] [*(3)* and *(4)*] being completely suppressed[7]. The new types of reactions are applicable to other heterocycles. Thus, the photoreaction of *(1)* with benzothiazole leads predominantly to 2-benzylidene-3-phenylbenzothiazoline [analogous to *(6)*] and 2-(1,2-diphenylethyl)benzothiazole (H-migration) in the ratio 1:1[7].

Procedure

A solution of *(1)* (1.0 g, 5.5 mmol) and *(2)* (10 g) in dichloromethane (150 ml) under N_2 is irradiated for four days with a mercury high-pressure lamp (Philips HPK 125 W) using a Solidex filter (λ>300 nm)[8]. The solvent is removed by evaporation and the residue is extracted with 3 × 100 ml hot benzene. Unreacted *(2)*, which precipitates on cooling the combined extracts, is filtered off and the residue from the mother liquor (2.3 g) is separated by preparative TLC on 300 g SiO_2, firstly with cyclohexane [400 mg *cis*-stilbene, 95 mg unreacted *(1)*, 70 mg stilbene dimers[2]] and finally with ethyl acetate. 350 mg (17%) of *(6)*, 230 mg (11%) of *(3)* and 60 mg (4%) of *(7)* were isolated (cryst. in heptane and isopropanol). Repeated preparative TLC furnishes 60 mg (4%) *(8)* and 20 mg (1%) *(5)* (cryst. in methanol). *(4)* (50 mg, 2.5%) is purified by preparative HPLC [pre-packed column (Knauer: length 25 cm, diameter 32 mm, 10 μm-LiChrosorb RP-18), 73% methanol] (cryst. in heptane).

Received: January 18, 1980 [Z 545 IE]
revised: April 10, 1980
German version: Angew. Chem. *92*, 735 (1980)

CAS Registry numbers:
(1), 103-30-0; *(2)*, 58-08-2; *(3)*, 74744-23-3; *(4)*, 74806-53-4; *(5)*, 74752-29-7; *(6)*, 74744-24-4; *(7)*, 5426-88-0; *(8)*, 6439-88-9

[1] *G. Kaupp, E. Teufel, H. Hopf*, Angew. Chem. *91*, 232 (1979); Angew. Chem. Int. Ed. Engl. *18*, 215 (1979); *G. Kaupp, ibid. 83*, 361 (1971) and *10*, 340 (1971); Justus Liebigs Ann. Chem. *1973*, 844, and references cited therein.

[2] Houben-Weyl-Müller: Methoden der Organischen Chemie. Thieme, Stuttgart 1975, Vol. IV/5a, p. 278ff., 360ff.; numerous examples therein.

[3] *G. Kaupp, M. Stark*, Angew. Chem. *90*, 803 (1978); Angew. Chem. Int. Ed. Engl. *17*, 758 (1978), and references cited therein.

[4] *G. Kaupp, H.-W. Grüter*, Angew. Chem. *91*, 943 (1979); Angew. Chem. Int. Ed. Engl. *18*, 881 (1979); Chem. Ber. *113*, 1458 (1980), and references cited therein.

[5] All products gave correct elemental analyses; the UV spectra are consistent with the given structures. Other products detectable by HPLC are formed in yields of <1%; these were not subjected to further investigation.

[6] The stoichiometrically required carbene fragments presumably occur in the decomposition reactions; for the reaction behavior of *(9)* cf. the conversion of a carbene into a 1,3-diradical (*M. S. Platz*, J. Am. Chem. Soc. *101*, 3398 (1979)).

[7] *G. Kaupp, H.-W. Grüter*, lecture at the Chemiedozententagung in Erlangen, March 24—28, 1980, and lecture at the VIIIth IUPAC-Symposium on Photochemistry in Seefeld (Austria), July 13—19, 1980.

[8] The same products are formed on more selective irradiation (λ>315 nm), but the reaction is hindered because the content of *cis*-stilbene [in photoequilibrium with *(1)*] increases.

1,2,3,5,6,7-*s*-Hydrindacenehexone and 1,2,3,6,7,8-Pyrenehexone—Two New Strong Acceptors[**]

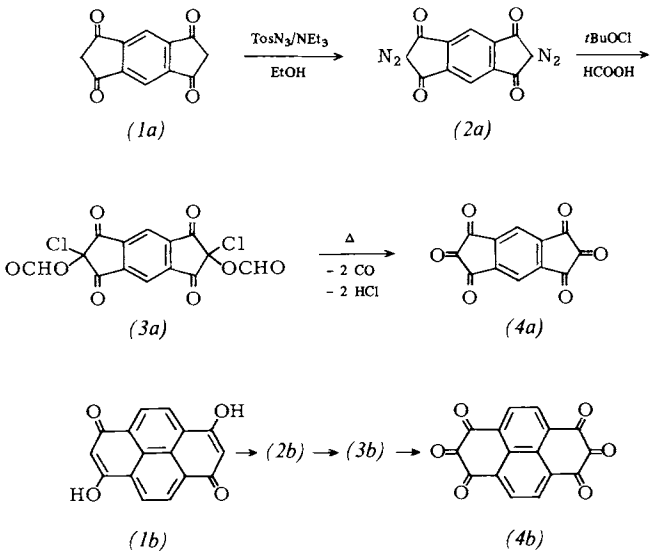
By *Rolf Gleiter* and *Peter Schang*[*]

Dedicated to Professor David Ginsburg on the occasion of his 60th birthday

The properties of vicinal triketones[1] suggest that compounds containing two or more vicinal tricarbonyl groups should be strong acceptors. In order to test this hypothesis, we have synthesized 1,2,3,5,6,7-*s*-hydrindacenehexone *(4a)* and 1,2,3,6,7,8-pyrenehexone *(4b)* from the tetraoxo com-

[*] Prof. Dr. R. Gleiter
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
Dipl.-Ing. P. Schang
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



pounds *(1a)* and *(1b)*, respectively[2], which were transformed into the bis(diazo) compounds *(2a)* and *(2b)*[3], respectively.

The reaction of *(2a)* and *(2b)* with formic acid and *tert*-butyl hypochlorite[4] afforded the bis(α-chloro-α-formyloxy) β-diketones *(3a)* and *(3b)*. Pyrolysis of *(3a)* and *(3b)* gave the bis(triketones) *(4a)* and *(4b)*, which were characterized by elemental analysis and their IR, UV/VIS, and mass spectra (see Table 1).

Table 1. Physical data of the new compounds *(4a)* and *(4b)*.

Cpd. Yield [a]	UV [b] λ [nm] (log ε)	IR [c] [cm^{-1}]	$\varepsilon_{1/2}^{-}$ [d] [V]
(4a) 53%	620 sh (1.72), 265 (4.43), 246 (4.31), 217 (4.14)	1782, 1750, 1728	0.15
(4b) 60%	533 sh (2.10), 355 (4.15), 342 (4.15), 266 (4.04), 234 (4.67), 203 (4.36)	1746, 1703, 1690	0.11

[a] Overall yield starting from *(1a)* and *(1b)*. [b] In acetonitrile. [c] In KBr. [d] In acetonitrile *vs.* SCE.

The half-wave potentials measured on polarographic reduction (see Table 1) provide an indication of the good acceptor properties of *(4a)* and *(4b)*. The values found resemble that of tetracyanoquinodimethane ($\varepsilon_{1/2}^{-}=0.19$ V)[5]. 1:1 complexes of pyrene and *(4a)* and *(4b)* have been isolated[6].

Procedure

(4a): Compound *(1a)* (2.0 g, 9.3 mmol) is dissolved in ethanol (500 ml) + triethylamine (2.8 ml, 20 mmol) and treated with tosyl azide (4.0 g, 20 mmol). After 48 h *(2a)* is obtained as grayish-blue crystals[7], yield 2.2 g (89%). Reaction of *(2a)* (2.0 g, 7.5 mmol) in formic acid (60 ml) with *tert*-butyl hypochlorite (1.8 g, 16.5 mmol) with cooling in an ice bath affords *(3a)*[8] (2.35 g, 85%). Vacuum pyrolysis (0.01 torr/180–200 °C) of *(3a)* gives *(4a)* in *ca.* 70% yield.

Received: April 1, 1980 [Z 546 IE]
German version: Angew. Chem. *92*, 768 (1980)

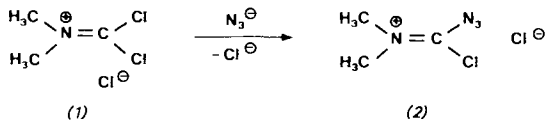
CAS Registry numbers:
(1), 74725-70-5; *(2)*, 39571-81-8; *(3)*, 53910-13-7; *(4)*, 74725-71-6; *(5)*, 74725-72-7; *(6)*, 74725-71-6; *(7)*, 74725-73-8; *(8)*, 74725-74-9

[1] *M. Rubin*, Chem. Rev. *75*, 177 (1975), and references cited therein.
[2] a) *I. Davies*, Dissertation, University of Pacific, Stockton, Calif. 1962; Chem. Abstr. *59*, 9917a (1963); *O. Neilands, M. Vavere*, J. Gen. Chem. USSR *33*, 1032 (1963); b) *H. Vollmann, H. Becker, M. Corell, H. Streck*, Justus Liebigs Ann. Chem. *531*, 1 (1937).
[3] Review: *M. Regitz*, Synthesis *1972*, 531.
[4] Analogous procedure: *M. Regitz, H. G. Adolph*, Justus Liebigs Ann. Chem. *723*, 47 (1969); *B. Eistert, P. Donath*, Chem. Ber. *106*, 1537 (1973).
[5] *M. E. Peover*, Trans. Faraday Soc. *58*, 2370 (1962).
[6] Pyrene + *(4a)*, IR [cm^{-1}]: 1773, 1744, 1728, 856, 714; UV, λ_{max} [nm] ($\log\varepsilon_{max}$): 590 (2.36), 334 (4.69), 272 (4.82), 240 (4.98), 231 (4.70). Pyrene + *(4b)*, IR [cm^{-1}]: 1735, 1700, 1688, 851, 714; UV, λ_{max} [nm] ($\log\varepsilon_{max}$): 488 (2.52), 361 (4.04), 333 (4.76), 271 (4.72), 239 (5.02), 230 (4.85).
[7] IR [cm^{-1}]: $\tilde{\nu}(CN_2)=2125$, $\tilde{\nu}(CO)=1669$.
[8] IR [cm^{-1}]: $\tilde{\nu}(CO)=1775$, 1750, 1723.

Iminium-Activated Azides—New Reagents for the Transfer of Diazonium or Diazo Groups[**]

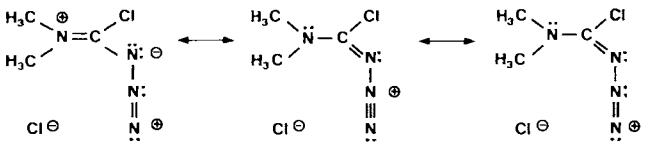
By *Bruno Kokel* and *Heinz Günter Viehe*[*]

Replacement of chlorine in the phosgeniminium salt *(1)* by the N_3-group affords (azidochloromethylene)dimethylammonium chloride *(2)*[2], whose reaction with primary amides to give aminotetrazoles has been described[2].



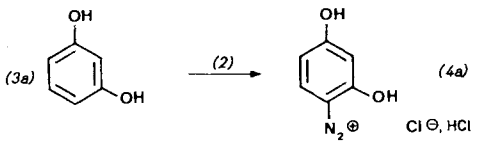
(1) *(2)*

As the limiting structures of *(2)* show, this compound is expected to react as a powerful ambident electrophile either on the iminium carbon or on the azide-nitrogen.

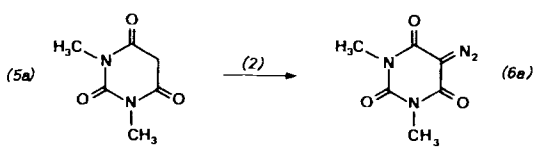


(2)

We have found that *(2)* reacts with a variety of CH-acidic compounds by diazo- or diazonium group transfer. Thus, resorcin *(3a)* in dichloromethane produces already at room temperature the diazonium chloride *(4a)* in almost quantitative yield.



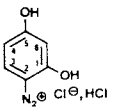
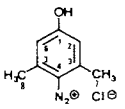
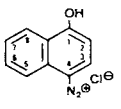
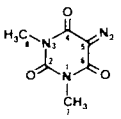
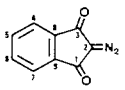
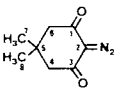
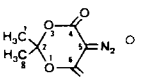
Compounds with carbonyl-activated methylene groups such as *N,N*-dimethyl barbituric acid *(5a)* readily react at room temperature with *(2)* to give good yields of the corresponding diazo compounds such as *(6a)*.



[*] Prof. Dr. H. G. Viehe, Dr. B. Kokel
Laboratoire de Chimie Organique, Université de Louvain
Lavoisier, Place Louis Pasteur 1
B-1348 Louvain-la-Neuve (Belgium)

[**] Phosgeniminium Chemistry, Part 26. We thank Prof. Dr. *M. Regitz* for valuable discussions.—Part 25: [1].

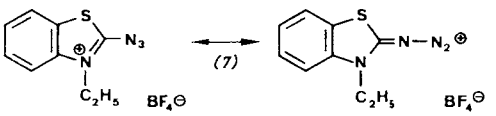
Table 1. Diazonium compounds *(4)* and diazo compounds *(6)* synthesized from *(3)* and *(5)* in CH_2Cl_2.

Product		Yield [%]	M.p. [°C] solvent	Conditions	IR (KBr) [cm^{-1}] [c]	^{1}H-NMR [d]	MS	Ref.	^{13}C-NMR [d]
	*(4a)*	90—92	130 (dec.) CH_3COOH	8 h, 20 °C [a]	2205	6.55 (dd, H-4), 6.70 (d, J=1.8, H-6), 6.9 (br., 2OH), 7.98 (d, J=9.0, H-3), DMSO	136 (M^+), 108, 80		86.5 (S, m, C-2), 103.0 (D, d, C-5), 171.4 (S, d, d, C-1), DMSO d, C-5), 171.4 (S, d, d, C-1), DMSO
	*(4b)*	53—55	194—196 (dec.) CH_3COOH	5—6 h, 20 °C	2210, 2230	2.58 (s, $2CH_3$), 6.4 (br., OH), 6.9 (s, H-2, 6), DMSO	148 (M^+), 120, 107, 91, 77		21.7 (Q, m, C-7, 8), 103.9 (S, m, C-4), 121.7 (D, m, C-2, 6), 151.9 (S, q, C-3, 5), 172.3 (S, t, C-1), D_2O
	*(4c)*	57—58	140—144 (dec.) *i*PrOH or CH_3COOH	8 h, 20 °C	2160, 2200	6.92 (d, J=9.5, H-2), 6.95 (br., OH), 7.5—7.8 (m, H-5, 6, 7), 8.29 (d, m, H-8), 8.53 (d, J=9.5, H-3), DMSO	170 (M^+), 142, 114		
	*(6a)*	87—88	158 *i*PrOH	4 h reflux [b]	2160	3.3 (s), $CDCl_3$	182 (M^+), 154, 97, 69	[4]	28.5 (Q, s, C-7, 8), 71.7 (S, br., C-5), 150.6 (S, m, C-2), 158.2 (S, q, C-4, 6), $CDCl_3$
	*(6b)*	73—75	148 *i*PrOH	4 h reflux	2130	7.55 (s), $CDCl_3$	172 (M^+), 144, 88	[3]	70.0 (S, C-2), 122.2 (D, C-5, 6), 134.8 (D, C-4, 7), 137.2 (S, C-8, 9), 182.2 (S, C-1, 3), CD_3NO_2
	*(6c)*	78—80	108 *i*PrOH	4 h reflux	2150, 2200	1.1 (s, $2CH_3$), 2.4 (S, $2CH_2$), $CDCl_3$	166 (M^+), 151, 138, 108, 95		28.3 (Q, m, C-7, 8), 31.1 (S, m, C-5), 50.6 (T, m, C-4, 6), 83.5 (S, m, C-2), 189.7 (S, t, C-1, 3), $CDCl_3$
	*(6d)*	62—64	88—90 *i*PrOH	4 h reflux	2180	1.76 (s, $2CH_3$), $CDCl_3$	170 (M^+), 155	[3]	27.2 (Q, C-7, 8), 67.2 (S, C-5), 108.0 (S, C-2), 159.2 (S, C-4, 6), DMSO

[a] In the dark. [b] In $CHCl_3$. [c] *(4)*: ν(—N$\equiv$); *(6)*: ν(=N_2). [d] δ values, J [Hz]; S (singlet), D (doublet), T (triplet), Q (quadruplet): couplings *via* one bond; s, d, t, q, ... m: couplings two and more bonds.

Table 1 illustrates the potential of this new reagent in the well-known field of diazo group transfer[3], which generally occurs under basic or neutral conditions.

To our knowledge, the only diazo group transfer reagents which work under acidic conditions are the less readily accessible azidinium salts such as *(7)*[4,5]. *(7)*, like *(2)*, belongs to the class of reactive but stable heterosubstituted (azidomethylene)ammonium salts.



(7)

Experimental

(4): *(3)* (10 mmol) is added to a solution of *(2)* (12 mmol) in 100 ml of CH_2Cl_2. After 5—8 hours' stirring at room temperature the salt *(4)* precipitates out.

(6): *(5)* (10 mmol) is added to a solution of *(2)* (12 mmol) in 100 ml of CH_2Cl_2. This solution is refluxed with stirring for about 4 h. After removal of the greater part of the solvent, the residue is treated with ether, filtered, and evaporated down. After rubbing the oily residue with 2-propanol, *(6)* is isolated and dried.

Received: March 21, 1980 [Z 548 IE]
German version: Angew. Chem. 92, 754 (1980)

CAS Registry numbers:
(3a), 108-46-3; *(4a)*, 74808-87-0; *(4b)*, 74808-88-1; *(4c)*, 74808-89-2; *(5a)*, 769-42-6; *(6a)*, 74808-90-5; *(6b)*, 1807-49-4; *(6c)*, 1807-68-7; *(6d)*, 7270-63-5; 3,5-dimethylphenol, 108-68-9; 1-naphthalenol, 90-15-3; 1*H*-indene-1,3(2*H*)-dione, 606-23-5; 5,5-dimethyl-1,3-cyclohexanedione, 126-81-8; 2,2-dimethyl-1,3-dioxane-4,6-dione, 2033-24-1

[1] *D. Van Broeck, Z. Janousek, R. Merényi, H. G. Viehe*, Angew. Chem. *91*, 355 (1979); Angew. Chem. Int. Ed. Engl. *18*, 333 (1979).
[2] *H. G. Viehe, P. George*, Chimia *29*, 209 (1975).
[3] *M. Regitz*, Angew. Chem. *79*, 786 (1967); Angew. Chem. Int. Ed. Engl. *6*, 733 (1967).
[4] *F. F. Blicke, H. C. Godt, Jr.*, J. Am. Chem. Soc. *76*, 2798 (1954).
[5] *H. Balli, F. Kersting*, Justus Liebigs Ann. Chem. *647*, 11 (1961); *H. Balli, R. Löw, V. Muller, H. Rempfler, A. Sezen-Gezgin*, Helv. Chim. Acta *61*, 97, 104, 108 (1978).

Photochemical Reductive *cis*-Elimination in *cis*-Diazidobis(triphenylphosphane)platinum(II) Evidence of the Formation of Bis(triphenylphosphane)platinum(0) and Hexaazabenzene[**]

By *Arnd Vogler, Robin E. Wright,* and *Horst Kunkely*[*]

Reductive *cis*- and *trans*-eliminations in transition metal complexes not only take place thermally, but also photochemically. Two $X^{\ominus}$ ligands are oxidized, which, in the first step of the photoreaction split off, either as $X^{\odot}$ radicals or cleave directly as a new energy-poorer molecule X_2. On steric grounds, in *trans*-eliminations the formation of radicals $X^{\odot}$ should be favored, in *cis*-eliminations, on the other hand, the departure of X_2. Both types of reaction have been observed. Irradiation of *trans*-$[Pt(CN)_4(N_3)_2]^{2\ominus}$ leads to $[Pt(CN)_4]^{2\ominus}$ and $N_3^{\odot}$ radicals, which were detected by ESR spectroscopy[1]

[*] Prof. Dr. A. Vogler, Dr. R. E. Wright, Dr. H. Kunkely
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 2 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

and flash photolysis[2]. In contrast *cis*-$[IrClH_2(PPh_3)_3]$ photolyzes directly to $[IrCl(PPh_3)_3]$ and H_2 without the intermediary formation of H atoms[3].

We have now been able to show that the complex *cis*-$[Pt(N_3)_2(PPh_3)_2]$ also undergoes a photochemical *cis*-elimination. At the same time evidence was also found that the azide ligands are cleaved off as N_6 molecule (hexaazabenzene) with concomitant formation of $[Pt(PPh_3)_2]$.

It was already known that $[Pt(C_2O_4)(PPh_3)_2]$ undergoes reductive photoelimination. The bidentate oxalate ligand is oxidized to CO_2, and $[Pt(PPh_3)_2]$ is formed. This was detected, not directly but only as the stable dimer $[Pt(PPh_3)_2]_2$[4].

Irradiation[5] of *cis*-$[Pt(N_3)_2(PPh_3)_2]$[6] at room temperature with shortwave light ($\lambda = 280$ nm)[7] in solvents such as ethanol or tetrahydrofuran likewise leads to $[Pt(PPh_3)_2]_2$, with evolution of N_2. To gain an insight into the reaction behavior, low-temperature photolyses were carried out. For analysis of the photoproducts in glasses of organic solvents at 77 K, ESR and luminescence spectroscopy were resorted to. The latter is especially suited for the identification of platinum(0)-phosphane complexes[8].

Irradiation of *cis*-$[Pt(N_3)_2(PPh_3)_2]$ and $[Pt(C_2O_4)(PPh_3)_2]$ in ethanol or methyltetrahydrofuran at 77 K leads to photoproducts which fail to give ESR signals, but in both cases an intense emission peak is observed at $\lambda = 445$ nm. On warming the photolyzed glasses to room temperature $[Pt(PPh_3)_2]_2$ was formed, which was identified by its intensely red luminescence ($\lambda_{max} = 665$ nm) at 77 K. In the low-temperature photolysis of the oxalate complex the organic glass remained colorless, whereas in the case of the azide complex a yellow coloration rapidly occurred (absorption maximum at $\lambda = 380$ nm), which on warming the matrix immediately disappeared with simultaneous evolution of N_2.

On the basis of these observations we suggest that the photolysis of the azide complex proceeds according to the equation

$$cis\text{-}[Pt(N_3)_2(PPh_3)_2] \rightarrow [Pt(PPh_3)_2] + N_6$$

Oxalate and azide complex form a common photoproduct (emission at $\lambda = 445$ nm) stable only at low temperatures; this can only be $[Pt(PPh_3)_2]$. On warming and melting the glasses it affords the stable dimer $[Pt(PPh_3)_2]_2$[4]. The reactive complex $[Pt(PPh_3)_2]$ is assumed to occur as intermediate in many reactions of platinum-triphenylphosphane complexes, but has so far not been isolated[9]. However, other $[Pt(PL_3)_2]$ complexes containing sterically demanding ligands L have been isolated[10].

While the ESR spectra of the products of low-temperature photolysis of *trans*-$[Pt(CN)_4(N_3)_2]^{2\ominus}$ clearly indicated that azide radicals were formed[11], the formation of such radicals from *cis*-$[Pt(N_3)_2(PPh_3)_2]$ could not be demonstrated. In analogy to the H_2-elimination from *cis*-$[IrClH_2(PPh_3)_3]$[3] we therefore assume that the azide ligands are cleaved from *cis*-$[Pt(N_3)_2(PPh_3)_2]$ as a N_6-molecule. We ascribe the yellow coloration to N_6, which is stable only at low temperatures and decomposes to N_2 on heating the matrix.

As extension of our studies in this field we carried out flash photolyses of *cis*-$[Pt(N_3)_2(PPh_3)_2]$ in ethanol and methyltetrahydrofuran at room temperature. Although no $N_3^{\odot}$ radicals[11] could be detected, an intermediate was observed which absorbed at $\lambda = 380$ nm and decomposed according to a reaction of first order with $k = 1.66 \times 10^2\ s^{-1}$ (Fig. 1).

The possible existence of N_6 (hexaazabenzene) has been discussed in a number of theoretical papers[12]. The lability of N_6 is generally regarded as being due to compensation of the resonance stabilization of an aromatic N_6-ring by repulsion of the lone pairs of electrons at the N atoms. According to one published paper, N_6 should decompose without activation energy[12c]. Other calculations lead to the conclusion

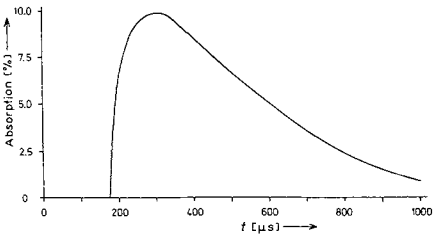


Fig. 1. Decomposition curve of a transient ($\lambda_{abs} = 380$ nm) in the flash photolysis of *cis*-$[Pt(N_3)_2(PPh_3)_2]$ (7×10^{-5} mol/l) in ethanol; flash energy 900 J.

that N_6 is slightly stabilized[12b] and therefore can certainly be stable at low temperatures.

Received: November 7, 1979 [Z 549 IE]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 745 (1980)

CAS Registry numbers:
cis-$[Pt(N_3)_2(PPh_3)_2]$, 34275-32-6; $[Pt(C_2O_4)(PPh_3)_2]$, 15377-00-1; $[Pt(PPh_3)_2]_2$, 11128-10-2; $[Pt(PPh_3)_2]$, 15094-61-8; N_6, 7616-35-5

[1] *A. Vogler, A. Kern, J. Hüttermann*, Angew. Chem. *90*, 554 (1978); Angew. Chem. Int. Ed. Engl. *17*, 524 (1978); *A. Vogler, A. Kern, B. Fusseder*, Z. Naturforsch. *B 33*, 1352 (1978).
[2] *H. Kunkely*, unpublished results.
[3] *G. L. Geoffroy, R. Pierantozzi*, J. Am. Chem. Soc. *98*, 8054 (1976).
[4] *D. M. Blake, C. J. Nyman*, J. Am. Chem. Soc. *92*, 5359 (1970).
[5] All photochemical investigations were performed in carefully dried and O_2-free solvents.
[6] a) *W. Beck, W. P. Fehlhammer, P. Pöllmann, E. Schuierer, K. Feldl*, Chem. Ber. *100*, 2335 (1967); b) *P. H. Kreutzer, K. T. Schorpp, W. Beck*, Z. Naturforsch. *B 30*, 544 (1975).
[7] Longwave irradiation ($\lambda > 300$ nm) leads to other photoproducts.
[8] *R. F. Ziolo, S. Lipton, Z. Dori*, Chem. Commun. *1970*, 1124.
[9] *L. Abis, A. Sen, J. Halpern*, J. Am. Chem. Soc. *100*, 2915 (1978), and references cited therein.
[10] *S. Otsuka, T. Yoshida, M. Matsumoto, K. Nakatsu*, J. Am. Chem. Soc. *98*, 5850 (1976).
[11] *G. Ferraudi, J. F. Endicott*, Inorg. Chem. *12*, 2389 (1973).
[12] a) *M. H. Palmer, A. J. Gaskell, R. H. Findlay*, Tetrahedron Lett. *1973*, 4659; J. Chem. Soc. Perkin Trans. II *1974*, 778; b) *J. S. Wright*, J. Am. Chem. Soc. *96*, 4753 (1974); Theor. Chim. Acta *36*, 37 (1974); c) *M. S. J. Dewar*, Pure Appl. Chem. *44*, 767 (1975).

Carbonates and Polycarbonates from Urea and Alcohol[**]

By *Peter Ball, Heinz Füllmann*, and *Walter Heitz*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

Carbonates and polycarbonates are conventionally prepared by reaction of alcohols and diols, respectively, with phosgene.

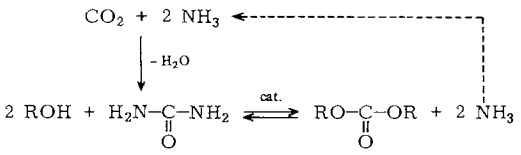
$$2\,ROH + COCl_2 + 2\,NaOH \rightarrow RO{-}CO{-}OR + 2\,NaCl + 2\,H_2O$$

This reaction creates safety problems (use of phosgene) and is energetically unfavorable: the chlorine required for the synthesis of phosgene ends up in NaCl.

[*] Prof. Dr. W. Heitz, Dr. P. Ball, Dipl.-Chem. H. Füllmann
Fachbereich Physikalische Chemie, Fach Polymere, der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by Bayer AG, the Fonds der Chemischen Industrie, and the Federal German Ministry of Research and Technology.

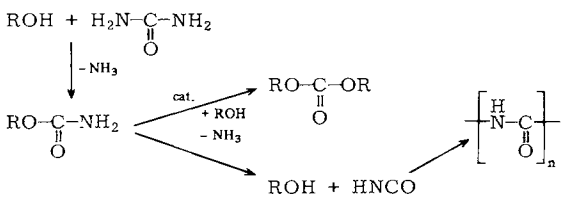
In order to circumvent these disadvantages an attempt could be made to use CO_2[1–4] or another derivative of carbonic acid as starting material. Urea (Scheme 1) reacts with alcohols to form carbonates and ammonia. The industrial synthesis of urea starts from CO_2 and ammonia, *i.e.* the ammonia liberated in the carbonate synthesis can be recycled and only CO_2 and alcohol are therefore consumed.



Scheme 1

In the reaction of esters with amides, the equilibrium is largely on the side of the amides. However, if amides are treated at high temperatures with alcohols and the resulting ammonia is removed from the reaction mixture then the synthesis of esters can be successfully accomplished.

Paquin discovered that alcohols react with urea to form carbamic esters[5]. Yields of 50 to 90% are obtained on catalysis with zinc acetate. On use of the catalysts reported by *Paquin* small amounts of carbonate can be detected by gas chromatography if the reaction time is prolonged. Many catalysts effect loss of more than the amount of ammonia corresponding to formation of carbamic ester; but reaction products of isocyanic acid—cyamelide and cyanuric acid—are also formed. In other words, the carbamic ester decomposes to isocyanic acid and alcohol. We have found that combinations of a weak Lewis acid and a Lewis base accelerate carbonate formation to such an extent that the competing liberation of isocyanic acid is suppressed (Scheme 2). Examples are shown in Table 1.



Scheme 2

Table 1. Catalysts for reaction of 2-ethyl-1-hexanol and urea to give bis(2-ethylhexyl) carbonate (see Scheme 2).

Catalyst [a]	Amount [b]	Yield [%] [c]
$Mg(OCH_3)_2/PPh_3$	3/3	41
$Fe(acac)_3/PPh_3$	3/3	76
$CeCl_3 \cdot 3H_2O/PPh_3$	3/3	36
$LaCl_3 \cdot 7H_2O/PPh_3$	3/3	40
$CoCl_2 \cdot 6H_2O/PPh_3$	3/3	54
$Cd(OAc)_2/PPh_3$	3/3	64
$Al(iBu)_2H/PPh_3$	0.5/0.5	87
$Al(iBu)_2H/P(OPh)_3$	1.5/0.95	90
$Al(iBu)_2H/P(OPh)_3$	3/1.6	94
$Al(iBu)_2H/P(NMe_2)_3$	1.5/2.0	94

[a] Both compounds in equimolar amounts. [b] Mol.-% of catalyst component relative to urea. [c] Based on urea.

Kinetic studies have shown that the reaction proceeds in two steps. 50% of the ammonia are liberated fast, *i.e.* the carbamic ester is formed fast. Even on raising the temperature from 165 to 180 °C the rate of the second step remains much lower than that of the first.

The carbamic esters can also be treated directly with alcohols to form carbonates; the same catalysts prove effective. The catalysts differ in the nature of the by-products obtained. The principal side reaction is ether formation. Use of diisobutylaluminum hydride/tributyl phosphite leads in the case of 2-ethyl-1-hexanol to the formation of 3.5% of bis(2-ethylhexyl) ether; the ether content increases with increasing Al/P ratio in the catalyst.

On treatment with urea primary and secondary alcohols can be converted into carbonates (Table 2). With low boiling alcohols the required reaction temperature can be attained, without altering the pressure, by addition of the alcohol.

Table 2. Reaction of alcohols with urea to give carbonates; diisobutylaluminum hydride/triphenylphosphane as catalyst.

ROH	Yield [%] [a]	RO—CO—OR B. p. [°C/torr]
1-Pentanol	81	115/12 [c]
Cyclohexanol	78	
3-Methylcyclohexanol	82	
2-Ethyl-1-hexanol	87	168—170/12
Isononyl alcohol [b]	73	

[a] Based on urea. [b] Isomeric mixture of primary isononanols. [c] 127 °C/15 torr [6].

The reaction is also suitable for the preparation of polycarbonates. It was applied to long-chain primary aliphatic diols and primary cycloaliphatic diols. Addition of monofunctional alcohols initially generates oligomeric carbonates whose low viscosity permits quantitative separation of the ammonia. The molecular weight of the product is then increased by transesterification. The reaction temperatures of up to 270 °C show that aliphatic polycarbonates are more stable than reported in the literature.

Procedure

Dipentyl carbonate: Urea (24 g), 1-pentanol (35.3 g), triphenylphosphane (0.795 g) and DIBAH-T solution (2.5 ml; 20% solution of diisobutylaluminum hydride in toluene (Schering)) are heated together at 135—150 °C for 5 h. The NH_3 escaping *via* a Vigreux column is collected by titration or by freezing. The temperature is increased to 185 °C during the following 2 h. 1-Pentanol (35.3 g) is added, the mixture is heated to 185—197 °C for 10 h, and the product is isolated by distillation.

Bis(2-ethylhexyl) carbonate: Dry urea (180 g), 2-ethyl-1-hexanol (1200 g), triphenylphosphane (4 g), and DIBAH-T solution (18 ml) are heated together to *ca.* 160 °C. The liberated ammonia is collected in a cold trap. The reaction temperature is raised to 270 °C in the course of 16 h. The cold trap than contains 93 g of NH_3 (91% yield). After removal of the excess alcohol by distillation, 743 g of the product remains.

Poly(oxycarbonyloxymethylene-1,4-cyclohexylenemethylene): Urea (15 g), cyclohexanedimethanol (30.3 g), isononyl alcohol (34 g), triphenylphosphane (0.34 g), and DIBAH-T solution (1.2 ml) are heated together to 170 °C; the temperature is then raised to 225 °C within 45 min and subsequently to 260 °C at a steady rate over 2.5 h. Excess isononyl alcohol, some diol, and diisononyl carbonate are distilled off under water pump vacuum and then oil pump vacuum. The polycarbonate (32.8 g) is not crystalline; $M_n = 11\,000$ (determined by vapor pressure osmometry), $\eta_{rel} = 1.26$ (measured as a 0.5% solution in CH_2Cl_2, 25 °C).

Received: February 13, 1980;
supplemented: March 31, 1980 [Z 550 IE]
German version: Angew. Chem. 92, 742 (1980)

[1] *W. J. Peppel*, Ind. Eng. Chem. *50*, 767 (1958).
[2] *W. Muenster, E. Dreher*, DBP 1169459 (1960), BASF.
[3] *S. Sakai, T. Fujinama, T. Yamada, S. Furusawa*, Nippon Kagaku Kaishi *10*, 1789 (1975).
[4] *N. Yamazaki, S. Nakahama, F. Higashi*, Polym. Prepr. *20*, (1), 146 (1979).
[5] *A. Paquin*, Z. Naturforsch. *1*, 518 (1946).
[6] *S. Bowden, E. Buther*, J. Chem. Soc. *1939*, 78.

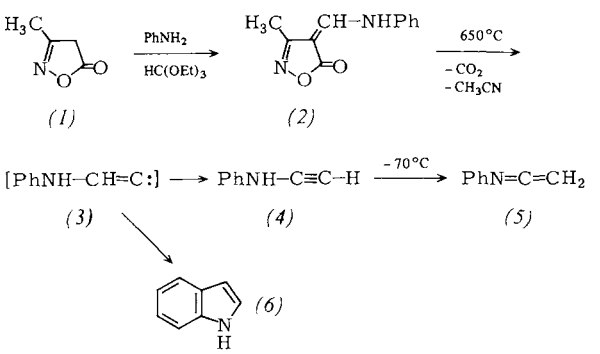
N-Ethynylamines of the Type R—NH—C≡C—H[**]

By *Hans-Wilhelm Winter* and *Curt Wentrup*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

Aminoacetylenes carrying secondary or primary amino-groups were previously unknown because of their tautomerization to ketenimines and nitriles, respectively. We have now developed a method which permits the preparation of such compounds, and report here on the first examples.

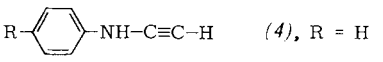
Flash vacuum pyrolysis of 4-methyleneisoxazol-5(4*H*)-ones is known to produce vinylidenes, which rearrange efficiently to acetylenes[1]. The starting material required for the preparation of *N*-ethynylaniline *(4)*, 4-(anilinomethylene)-3-methylisoxazol-5(4*H*)-one *(2)* has been obtained[2] by reaction of 4-benzylideneisoxazol-5(4*H*)-one with *N,N'*-diphenylformamidine. However, enamines of the type *(2)* can be obtained in a much simpler and general manner by reaction of the free isoxazolone *(1)* with amines and ortho-esters[3].



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

Thus, *(2)* was obtained in 70% yield in less than 5 min by heating an equimolar mixture of *(1)* and aniline in triethyl orthoformate. The initial pyrolyses of *(2)* were carried out using an externally heated quartz tube (32 × 2 cm) as previously described[4]. *(2)* was stable toward pyrolysis up to *ca.* 450 °C (10^{-5} torr). Between 450 and 650 °C increasing amounts of CO_2 and acetonitrile were formed and identified by IR spectroscopy of the volatile pyrolysis products. Work-up of the products at room temperature afforded *N*-phenylketenimine *(5)* (50% at 650 °C/4 × 10^{-5} torr). *(5)* was identified by IR and NMR spectroscopy, and by hydrolysis to acetanilide. Furthermore, a 4.5% yield of indole *(6)* was isolated from the 650 °C pyrolysis. The formation of *(6)* is ascribed to a cyclization of the vinylidene (carbene) *(3)*. Similar cyclizations of other vinylidenes have been reported[5].

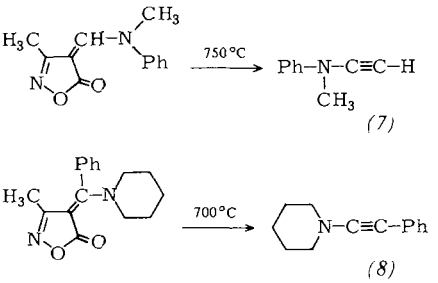
The isolation of *(5)* from the above pyrolyses indicated that *N*-ethynylaniline *(4)* had been formed initially. In order to isolate and observe *(4)* a pyrolysis apparatus equipped for IR spectroscopy was used[6]. This consisted of a quartz tube incorporating a 5-cm sublimation zone and a 10-cm pyrolysis zone, mounted in a water-jacketed stainless steel housing. The pyrolysis products were condensed directly on a KBr target attached to a turnable liquid nitrogen cryostat and housed in a vacuum shroud equipped with KBr windows[7]. In this manner, the pyrolysis of *(2)* at 650 °C/10^{-5} torr gave *(4)*, which was stable at −196 °C and identified by strong IR absorptions at 2120 (C≡C) and 3290 (C≡C—H) cm^{-1}; the latter absorption was superimposed by a broad NH-band at *ca.* 3200—3300 cm^{-1}. These absorptions disappeared on warming the sample to *ca.* −70 to −60 °C, when new, strong signals due to the ketenimine *(5)* at 2020 and 2040 cm^{-1} appeared in their place.



(4), R = H

(4a-d), R = CH_3, OCH_3, OC_2H_5, NO_2

Other aminoacetylenes related to *(4)* have been obtained in a similar manner [*(4a)*: 2125 cm^{-1}; *(4b)*: 2123 cm^{-1}; *(4c)*: 2125 cm^{-1}; *(4d)*: 2136 cm^{-1}] and isomerized to the corresponding ketenimines on warming[8]. The tautomerization to ketenimines can, of course, be prevented by using *N,N*-disubstituted 4-(aminomethylene)-3-methylisoxazol-5(4*H*)-ones[3] as starting materials. Examples of pyrolysis products are the acetylenes *(7)* (2130 cm^{-1}) and *(8)* (2220 cm^{-1}).



(7) *(8)*

Experimental

(5): 670 mg of *(2)* was pyrolyzed at 650 °C/4 × 10^{-5} torr by sublimation from a sample flask held at 125 °C. The products were collected in a U-tube cooled in liq. N_2. After pyrolysis was complete, distillation of the products *in vacuo* below 0 °C afforded CO_2 and acetonitrile. Further distillation at 25 °C afforded *(5)* (50%): IR (CCl_4): 2040 vs, 2020 vs, 1600 s, 1500 s, 700 s cm^{-1}; ^{1}H-NMR (CCl_4): δ = 3.4 (s, 2H), 7.2 (m, 5H). *(5)* was identical with a sample prepared according to *Staudinger*[9].—In a separate experiment, the cold pyrolysis products were treated with 50 ml of 10% HCl and then allowed to stand for 2 h at room temperature. The mixture was extracted with ethyl acetate, the extract washed with water, dried over $MgSO_4$, concentrated, and chromatographed on SiO_2/$CHCl_3$. Elution with $CHCl_3$ followed by $CHCl_3$/CH_3OH (9:1) gave indole (4.5%), starting material *(2)* (13%), and acetanilide (43%).

Received: March 10, 1980 [Z 551 IE]
German version: Angew. Chem. 92, 743 (1980)

CAS Registry numbers:
(1), 1517-96-0; *(2)*, 40538-65-6; *(4)*, 42540-72-7; *(4a)*, 74808-95-0; *(4b)*, 74808-96-1; *(4c)*, 74808-97-2; *(4d)*, 74808-98-3; *(6)*, 120-72-9; *(7)*, 4231-31-6; *(8)*, 53968-70-0; 1-benzylidenisoxazol-5(4*H*)-one 31681-56-8; *N,N'*-diphenylformamidine, 622-15-1

[*] Prof. Dr. C. Wentrup, Dipl.-Chem. H.-W. Winter
Fachbereich Chemie, Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are indebted to Miss *A. Damerius, L. A. J. Köhler*, and *K.-P. Netsch* for technical collaboration.

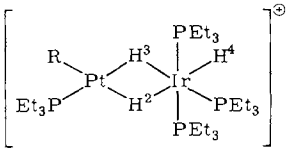
[1] *C. Wentrup, H.-W. Winter*, Angew. Chem. *90*, 643 (1978); Angew. Chem. Int. Ed. Engl. *17*, 609 (1978); *C. Wentrup, W. Reichen*, Helv. Chim. Acta *59*, 2615 (1976).

[2] *F. B. Dains, E. L. Griffin,* J. Am. Chem. Soc. *35*, 959 (1913).
[3] *H.-J. Wollweber,* Dissertation, University of Marburg 1980.
[4] *N. M. Lân, C. Wentrup,* Helv. Chim. Acta *59*, 2068 (1976).
[5] *J. Becker, C. Wentrup, E. Katz, K.-P. Zeller,* J. Am. Chem. Soc. *102*, 5110 (1980); *R. F. C. Brown, F. W. Eastwood, G. P. Jackman,* Aust. J. Chem. *30*, 1757 (1977).
[6] *H.-W. Winter, L. A. J. Köhler, C. Wentrup,* unpublished.
[7] Manufacturer: Air Products, Allentown, Pa. The distance between the exit of the pyrolysis tube and the KBr target was *ca.* 1 cm.
[8] Experiments in collaboration with *H. Briehl.*
[9] *H. Staudinger, E. Hauser,* Helv. Chim. Acta *4*, 887 (1921). For spectral data, see also *J. K. Crandall, W. W. Conover,* J. Org. Chem. *39*, 63 (1974).

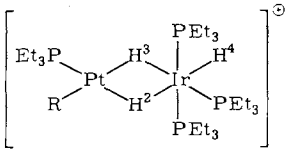
New Dihydrido-Bridged Binuclear Platinum-Iridium Complexes[**]

By *Attilio Immirzi, Alfredo Musco, Paul S. Pregosin,* and *Luigi M. Venanzi*[*]

Carbonyl complexes having bridging hydrogen atoms are rather common in transition metal chemistry[1]. Recently, bridging hydrido complexes not containing CO ligands have received considerable attention[2]. Whereas a number of hydrido-bridged bi-homometallic complexes have been reported[1], only few examples of heterometallic complexes are known[3,4]. We report here the synthesis and structural characterization of the stable mixed Pt—Ir cations *(1)* and *(2)* containing double hydrido bridges.



(1a), R = C_6H_5; *(2a)*, R = H[1]



(1b), R = C_6H_5; *(2b)*, R = H[1]

The cations *(1)* and *(2)* are formed as follows:

$$trans\text{-}[PtR(CH_3OH)(PEt_3)_2]^+ + [IrH_5(PEt_3)_2] \rightarrow (1) \text{ or } (2) + H_2$$

As shown in the above equation the reaction occurs with transfer of a phosphane ligand from platinum to iridium, a rather uncommon phenomenon in the absence of free ligand[5] The rather novel nature of the above complexes prompted us to undertake the X-ray structure determination of *(1a)* [BPh_4] (Fig. 1)[6]. The molecular geometry of the cation *(1a)* is consistent with a square planar Pt^{II} and an octahedral Ir^{III} with two bridging H atoms between them and one terminal H atom on Ir. The atoms Pt, P1, C1, Ir and P2 are nearly coplanar with P1 and P2 in a cisoid arrangement. The axial ligands Et_3P3 and Et_3P4 are slightly bent towards the bridging hydrogens thus reducing the steric interaction with the equatorial phosphane ligand Et_3P3. The Pt···Ir distance is practically identical with the Pt···Pt distance (2.692(3) Å) in $[(Cy_3P)(Me_3Si)Pt(\mu\text{-}H)_2PT(Me_3Si)(Cy_3P)]$ (Cy = cyclohexyl)[7] and slightly longer than the Ir···Ir distance (2.518 Å) in $[(Ph_3P)_2(H)Ir(\mu\text{-}H)_3Ir(H)(Ph_3P)_2][PF_6]$[8], as expected for a compound with three bridging hydrogens.

Support for the presence of the terminal and bridging hydride ligands in *(1)* and *(2)* is provided by ^{1}H-NMR spectroscopy. The ^{1}H and ^{31}P-NMR spectra of *(1a)* in CD_2Cl_2, *dissolved and measured at −60 °C,* are assigned as follows: δ = −7.05 (H2, ^1J(PtH) = 671 Hz), −9.04 (H3, ^1J(PtH) = 662 Hz), −15.27 (H4); 16.3 (P1, ^1J(PtP1) = 3656 Hz,

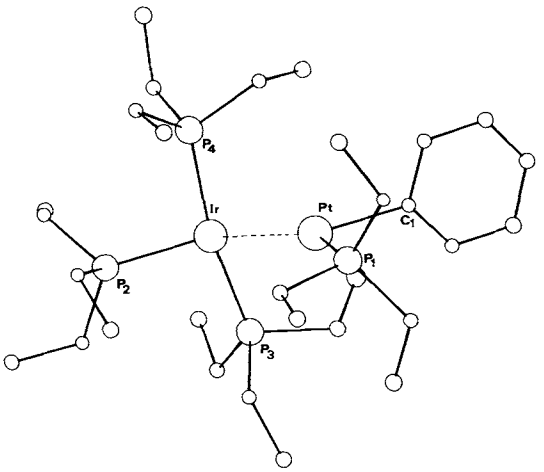


Fig. 1. Molecular structure of the cation *(1a)*. Bond lengths [Å]: Pt···Ir 2.687(2), Pt—C 2.08(2), Pt—P1 2.213(6), Ir—P2 2.323(5), Ir—P3 2.354(6), Ir—P4 2.341(6); bond angles [°]: Pt—Ir—P2 138.2(1), Pt—Ir—P3 86.6, Pt—Ir—P4 91.2(1), Ir—Pt—C1 133.0(3), Ir—Pt—P1 140.7(1), P2—Ir—P3 96.6, P2—Ir—P4 94.5(2), P3—Ir—P4 165.7(1); torsion angles (°, avg. error ~1°): P1—Pt—Ir—P2 −2, P1—Pt—Ir—P3 94, P1—Pt—Ir—P4 −100; P2—Ir—Pt—C1 −178, P3—Ir—Pt—C1 −82, P4—Ir—Pt—C1 84.

^4J(P1P2) = 43 Hz, ^4J(P1P3) = 4 Hz), 6.0 (P2, ^2J(P2P3) = 18 Hz), −4.5 (P3, ^3J(PtP3) = 40 Hz). On warming to −30 °C a new set of signals appear and these are assigned to isomer *(1b)*: δ = −4.18 (H2 or H3, ^1J(PtH2 or H3) = 826 Hz), −11.64 (H3 or H2, ^1J(PtH3 or H4) = 525 Hz), −14.61 (H4), 18.7 (P1, ^1J(PtP1) = 3349 Hz), ^4J(P1P3) = 4 Hz), 5.6 (P2, ^2J(P2P3) = 18 Hz), −2.3 (P3, ^3J(PtP3) = 36 Hz). At this temperature a 1:1 mixture of *(1a)* and *(1b)* is obtained in *ca.* one hour. The same isomeric composition is observed at room temperature. Of special interest in isomer *(1a)* is that: (a) the appearance of H3 immediately allows its assignment since this hydrogen is *trans* to *two* PEt_3 groups and therefore, shows two large ^2J(P1H3) and ^2J(P2H3) values (66 Hz)[9] and (b) H2 does not show large (>20 Hz) ^2J(P1H2 or P2H2) couplings. In isomer *(1b)*, however, both H2 and H3 show *one* strong ^2J(PH) coupling (*ca.* 74 Hz).

Similar spectral observations and structural assignments have been made for *(2a)* and *(2b)*.

Experimental

(1a) [BPh_4]: A solution of $AgBF_4$ (0.143 g, 0.73 mmol) in 3 ml of methanol was added to a suspension of *trans*-$[PtCl(C_6H_5)(PEt_3)_2]$ (0.400 g, 0.73 mmol) in 5 ml of methanol and the AgCl filtered off. $[IrH_5(PEt_3)_2]$ (0.319 g, 0.73 mmol) in 5 ml of methanol was added to the colorless filtrate. The resulting yellow solution was treated with a solution of $NaBPh_4$ (0.252 g, 0.73 mmol) in 5 ml of methanol. A yellow microcrystalline solid *(1a)* [BPh_4] precipitated and was collected by filtration (0.663 g, 72% yield). *(1a)* may be recrystallized from CH_2Cl_2/CH_3OH. *(2a)* [BPh_4] was prepared in a similar fashion starting from *trans*-$[PtCl(H)(PEt_3)_2]$.

[*] Prof. L. M. Venanzi, Dr. A. Musco, and Dr. P. S. Pregosin
Laboratorium für Anorganische Chemie, ETH-Zentrum
CH-8092 Zürich (Switzerland)
Dr. A. Immirzi
Instituto di Chimica delle Macromolecole del C.N.R.
Via A. Corti 12, Milano (Italy)

[**] This work was supported by the Swiss National Science Foundation. The Authors wish to thank the C.N.R. (Rome) for a leave of absence to A. M.

Received: March 26, 1980 [Z 552 IE]
German version: Angew. Chem. *92*, 744 (1980)

[1] *R. Bau, R. G. Teller, S. W. Kirtley, T. F. Koetzle,* Acc. Chem. Res. *12*, 176 (1979).

[2] *G. Bracher, D. M. Grove, P. S. Pregosin, L. M. Venanzi,* Angew. Chem. *91*, 169 (1979); Angew. Chem. Int. Ed. Engl. *18*, 155 (1979) and references cited therein.

[3] *N. W. Alcock, O. W. Howarth, P. Moore, G. E. Morris,* J. Chem. Soc. Chem. Commun. *1979*, 1160.

[4] *J. P. C. M. Van Dongen, C. Masters, J. P. Visser,* J. Organomet. Chem. *94*, C 29 (1975).

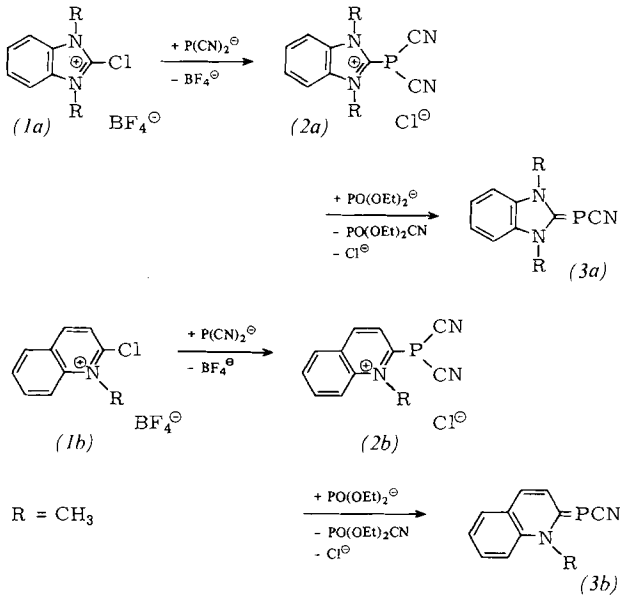
[5] *R. Huis, C. Masters,* J. Chem. Soc. Dalton Trans. *1976*, 1796.

[6] *(1a)* [BPh_4] is monoclinic, space group $P2_1/a$; $a = 20.578(3)$, $b = 15.046(3)$, $c = 18.222(3)$ Å, $\beta = 94.52(2)°$, $Z = 4$. 6852 reflections ($d > 0.95$ Å) were measured by an automatic counter diffractometer (Philips PW-1100) using $Cu_{K\alpha}$ radiation. The 5603 reflections having $I_{net} > 3\sigma$ were used in the structure determination. Atomic positions were obtained by the Patterson-Fourier method and refined using the least squares procedure with unitary weight factors, isotropic thermal vibration and 4×4 block diagonal approximation down to $R = 9.1\%$.

[7] *M. Ciriano, M. Green, J. A. K. Howard, J. Proud, J. L. Spencer, F. G. A. Stone,* J. Chem. Soc. Dalton Trans. *1978*, 801.

[8] *R. H. Crabtree, H. Felkin, G. E. Morris, T. J. King, J. A. Richards,* J. Organomet. Chem. *113*, C 7 (1976).

[9] *J. P. Jesson* in *E. L. Muetterties:* Transition Metal Hydrides. Marcel Dekker, New York 1971.



The =PCN Group as a Pseudochalcogen; Cyanophosphinidene-Substituted Heterocycles[**]

By *Alfred Schmidpeter, Wolfgang Gebler, Franz Zwaschka,* and *William S. Sheldrick*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

The "cyano displacement principle"[1a] suggests the $-P(CN)_2$ group to have the character of a pseudohalogen, and the =PCN group to have the character of a pseudochalcogen. The pseudohalogen character has been shown in the ions $P(CN)_2^-$, $P(CN)_2Br_2^-$, and $P(CN)_2I_2^-$[1]; we sought to establish the pseudochalcogen character by means of cyanophosphinidene analogues *(3)* of the oxo- or thioxo derivatives of nitrogen heterocycles. The synthesis of these new compounds can be accomplished *via* the dicyanophosphide ion by reductive removal of CN developed for the production of $P(CN)_2^-$[1a]. In the case of *(3a)* this reaction starts initially from benzimidazolone, so that *(3a)* really is formed by O/PCN exchange, not just formally.

The tetrafluoroborates *(1)*[2] obtained by methylation of the 2-chloroheterocycles with $HC(OMe)_2BF_4$ react with [18]crown-6-sodium dicyanophosphide or triethylammonium dicyanophosphide[1] to give the respective 2-(dicyanophosphino) chlorides *(2)* (Table 1). Treatment with sodium diethylphosphite generates the cyanophosphinidene-heterocycles *(3)*.

The cyanophosphinidene-heterocycles *(3)* (Table 1) occupy a connecting position between the phosphamethinecyanine cations synthesized by *Dimroth* as the first (—P=C—) compounds[3] and the dicyanophosphide anion[1a]. In a metathetic reaction these ions afford the salts *(4)* (Table 1) which have the same composition as compounds *(3)*. They are stable as crystals, but surprisingly rearrange in solution even at room temperature, *e.g.* on attempted recrystallization, affording *(3)*. The exchange could proceed *via* a diphosphetane betaine *(5)*[4].

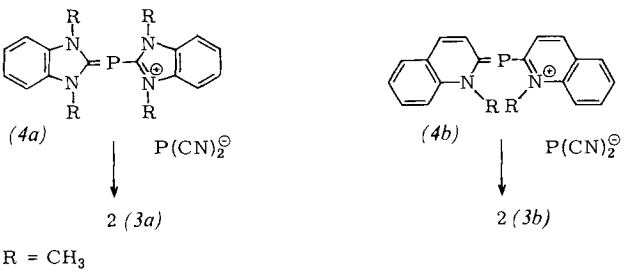
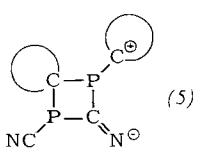


Table 1. Compounds of types *(2)*, *(3)*, and *(4)*.

Cpd.	Color	M.p. [°C]	ν_sCN	ν_{as}CN [cm^{-1}]	λ_{max} [nm]	$\delta(^{31}P)$ [a]	$\delta(^1H)$ [b]
(2a)	vermilion	130—132	2195	2180			
(2b)	greenish yellow	106—109	2190	2165		− 44	
(3a)	yellow	155—157		2105	356	−133	3.87
(3b)	brick red	162 (dec)		2115	448	− 38	3.77 [c]
(4a)	yellow	122—123			415	−103, −193	
(4b)	brown	248—252			588	56.5, −193	

[a] In CH_3CN; *(3a, b)* in tetrahydrofuran. [b] Methyl protons. [c] $^4J_{PH} = 2.5$ Hz.

The cyanophosphinidene-heterocycles *(3)* form air-stable acicular crystals. The ^{31}P chemical shifts lie roughly in the middle between those of $P(CN)_2^-$ and those of the corresponding phosphamethine cyanine cation, *i.e.* between the two $\delta(^{31}P)$ values of *(4)*. Their CN stretching vibration is shifted by about 75 cm^{-1} to longer wavelengths relative to that of cyanophosphines but is close to that of $P(CN)_2^-$[1a] and



[*] Prof. Dr. A. Schmidpeter, Dipl.-Chem. F. Zwaschka, W. Gebler
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Priv.-Doz. Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[**] Cyanophosphorus Compounds, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 5: *W. S. Sheldrick, A. Schmidpeter, F. Zwaschka, K. B. Dillon, A. W. G. Platt, T. C. Waddington,* J. Chem. Soc. Dalton Trans., in press.

thus indicates a negative charge of the PCN group. This negative charge corresponds to a positive charge of the heterocycle, as is manifested in the chemical shift of the N-methyl protons which lies half way between that in the neutral and in the cationic heterocycle.



The considerable contribution of the resonance formula *(B)* is underscored by the interatomic distances found on X-ray structure analysis of *(3a)* (Fig. 1). *(3a)* forms orthorhombic crystals, space group $Pna2_1$, $Z=4$[5]; the cyano group is disordered (occupation factors = 0.50). The arrangement of the methyl protons rules out the possibility that the molecule lies on a crystallographic symmetry plane (as would be required for Pnam).

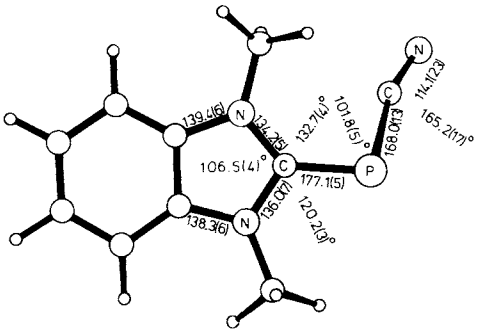


Fig. 1. Structure, bond lengths [pm], and bond angles of 2-(cyanophosphinidene)-1,3-dimethylbenzimidazoline *(3a)* (average values are given for the disordered PCN group) [5].

In contrast to what is suggested by resonance formula *(A)* without formal charges, the PC bond in the PCN group is considerably shorter than the $PC_{imidazole}$ bond. However, this observation should not be regarded as evidence for a conjugational dependence of the two parts of the molecule, which the resonance *(A)*↔*(B)* seems to suggest. The two moieties (PCN and P-heterocycle) are actually not coplanar in *(3a)*[6]; their PC distances resemble those in the dicyanophosphide ion (167—169 pm[7]) and in the phosphamethinecyanines (176—181 pm[3]). The consistently strong bond in the PCN unit confirms its classification as pseudochalcogen.

Procedure

(2): *(1)* (10 mmol) and [18]crown-6-$NaP(CN)_2$[1a] (10 mmol), each in CH_3CN (10 ml each) are cooled to −20 °C and united. *(2)* precipitates in 70—90% yield.

(3): Compound *(2)* (10 mmol) is suspended in a solution of an equimolar amount of $NaPO(OEt)_2$ in tetrahydrofuran (20 ml) and stirred for 12 h. Compound *(3)* crystallizes from the concentrated filtrate; yield 20—40%.

(4): To a solution of [18]crown-6-$NaP(CN)_2$[1a] (10 mmol) in CH_3CN (40 ml) is added an equimolar amount of the corresponding phosphamethinecyanine tetrafluoroborate in CH_3CN (125 ml). *(4)* is obtained in about 50% yield. The rest of the mixture is converted into *(3)* and can be separated from the mother liquor by concentration. *(4)* is transformed into *(3)* on attempted recrystallization from CH_3CN or CH_2Cl_2.

Received: April 8, 1980;
supplemented: May 9, 1980 [Z 553 IE]
German version: Angew. Chem. 92, 767 (1980)

CAS Registry numbers:
(1a), 18116-10-4; *(1b)*, 16843-24-6; *(2a)*, 74763-83-0; *(2b)*, 74763-84-1; *(3a)*, 74763-85-2; *(3b)*, 74763-86-3; *(4a)*, 74792-73-7; *(4b)*, 74792-75-9; [18]crown-6-$NaP(CN)_2$, 63731-77-1

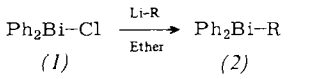
[1] a) *A. Schmidpeter, F. Zwaschka*, Angew. Chem. *89*, 747 (1977); Angew. Chem. Int. Ed. Engl. *16*, 704 (1977); b) *ibid. 91*, 441 (1979) and *18*, 411 (1979), respectively.
[2] *N. Greif*, Dissertation, Universität Marburg 1967.
[3] *K. Dimroth*, Fortschr. Chem. Forsch. (Top. Curr. Chem.) *38*, 1 (1973).
[4] Cf. the recently synthesized 1,3-diphosphetanimines; *G. Becker, O. Mundt, W. Uhl*, Chemiedozententagung, Erlangen 1980, B 18.
[5] $a=1648.4(4)$, $b=912.0(2)$, $c=705.6(1)$ pm, $\rho_{calc}=1.27\ g\cdot cm^{-3}$; 697 independent reflections ($Cu_{K\alpha}$, $3.5° \leqq \theta \leqq 135.0°$, empirical absorption correction), $R=0.049$, $R_w=0.035$.
[6] In dicyanodiamide, the corresponding parts of the molecule, which are however linked *via* a common nitrogen atom, are coplanar: *E. W. Hughes*, J. Am. Chem. Soc. *62*, 1258 (1940).
[7] According to a new structure analysis; *W. S. Sheldrick, A. Schmidpeter, F. Zwaschka*, unpublished.

The Diphenylbismuthyl Group—A Potential New Auxiliary Group in Organic Synthesis[**]

By *Fritz Steinseifer* and *Thomas Kauffmann*[*]

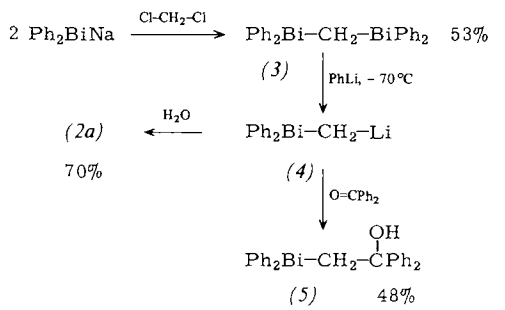
Organoelement groups have acquired considerable importance in organic synthesis as "mobile functional groups"[1]. Our own observations suggest that the diphenylbismuthyl group is also suitable for this purpose:

1) Alkyldiphenylbismuthanes *(2)*, which to our knowledge have not been previously reported[2], could now be synthesized in very good yields. Although air-sensitive, compounds *(2)* show surprising thermal stability (can be distilled almost without decomposition at 100—190 °C) and differ from trialkylbismuthanes by not being pyrophoric.



(2a), R = CH_3, 0 °C, 89%
(2b), R = n-C_4H_9, −70 °C, 91%
(2c), R = n-C_6H_{13}, −70 °C, 91%

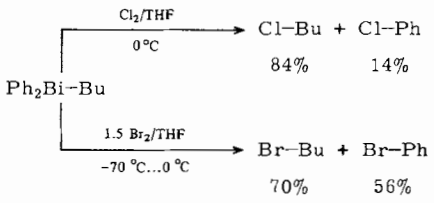
2) The diphenylbismuthyl group can be introduced into organic compounds by means of Ph_2BiNa and $Ph_2Bi—CH_2Li$ *(4)*. The Ph_2Bi/Li exchange reaction *(3)*→*(4)* reveals that the diphenylbismuthyl group can stabilize a carbanionic center like other organo-heavy metal groups[3].



[*] Prof. Dr. Th. Kauffmann, Dipl.-Chem. F. Steinseifer
Organisch-Chemisches Institut der Universität
Orléans-Ring 33, D-4400 Münster (Germany)

[**] New Reagents, Part 16. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 15: *A. Rensing, K.-J. Echsler, Th. Kauffmann*, Tetrahedron Lett. *1980*, 2807.

3) Whereas halogenolysis of alkyldiphenylarsanes or -stibanes or of alkyl phenyl selenides (alkyl = CH_2R) requires relatively high temperatures (*e.g.* bromolysis: 130 °C[4], 220 °C[5], and 80 °C[6], respectively), halogens cleave alkyldiphenylbismuthanes below 0 °C. Bromine and, in particular, chlorine selectively rupture the Bi-alkyl bond, thus favoring applications in organic synthesis[7].



4) As shown by the reactions *(3)*→*(4)*→*(2a)*, the diphenylbismuthyl group can be replaced by lithium—provided the resulting lithium compound is stabilized[8]—or hydrogen under mild conditions.

The diphenylbismuthyl group therefore offers a combination of favorable properties that is so far unique.

The structures of the new compounds (Table 1) have been confirmed by elemental analysis, ^{1}H-NMR and mass spectrometry.

Received: April 18, 1980 [Z 554 IE]
German version: Angew. Chem. 92, 747 (1980)

CAS Registry numbers:
(1), 39248-62-9; *(2a)*, 74724-75-7; *(2b)*, 74724-76-8; *(2c)*, 74724-77-9; *(3)*, 74724-78-0; *(4)*, 74724-79-1; *(5)*, 74724-80-4; ClBu, 109-69-3; ClPh, 108-98-7; BrBu, 109-65-9; BrPh, 108-86-1

6-Oxoverdazyls[**]

By *Franz A. Neugebauer* and *Hans Fischer*[*]

The reaction of 2,4-dimethylcarbonohydrazide *(1)*[1] with aldehyde *(2)* in the molar ratio 1:1 gives colorless hexahydro-*s*-tetrazines *(3)* as major product. The structural assignment is based on ^{1}H-NMR spectra. Dehydrogenation of *(3)* (*e.g.* with Ag_2O, $K_3Fe(CN)_6$, PbO_2) afforded stable monomeric radicals, *viz.* 6-oxoverdazyls *(4)*. The radical *(4a)* crystallizes from ligroin as yellow needles. Figure 1 shows the ESR spectrum (benzene): $a(N_{2,4}) = 6.50$, $a(N_{1,5}) = 5.19$, $a(H_{CH_3}) = 5.45$ (6 H), $a(H_{CH}) = 0.78$ G, $g = 2.0036$. *(4b)* forms red crystals from methanol: ESR (benzene): $a(N_{2,4}) = 6.5$, $a(N_{1,5}) \approx a(H_{CH_3}) \approx 5.3$ G, $g = 2.0036$.

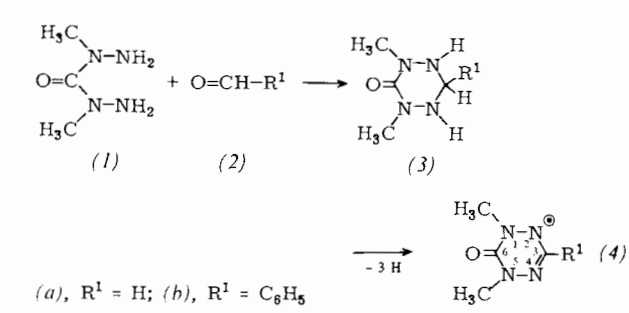


Table 1. Physical data of the new compounds.

Cpd.	M.p. [°C] b.p. [°C/torr]	^{1}H-NMR [b]	MS (*m/e*) [c]
(2a)	105—110/ 0.2	1.45 (s; 3H, CH_3), 7.1—7.6 (m; 6H) and 7.6—8.0 (m; 4H, aromatic H)	378 (M^+, 0.1%), 363 (18), 316 (4), 301 (13), 286 (15), 224 (7), 209 (100), 154 (3), 77 (9)
(2b)	128—130/ 0.02	0.86 (t, J=7 Hz; 3H, CH_3), 1.36 (sext, J=7 Hz; 2H, CH_2—CH_3), 1.8—2.4 (m; 4H, Bi-CH_2—CH_2), 7.1—7.6 (m; 6H) and 7.6—8.0 (m; 4H, aromatic H)	420 (M^+, 0.3%), 364 (2), 363 (54), 343 (4), 287 (8), 286 (18), 266 (9), 209 (100), 78 (4)
(2c)	135—140/ 0.02	0.86 (t, J=6 Hz; 3H, CH_3), 1.30 (m; 6H, $(CH_2)_3$—CH_3), 1.8—2.4 (m; 4H, Bi-CH_2—CH_2), 7.1—7.6 (m; 6H) and 7.6—8.0 (m; 4H, aromatic H)	456 (0.06), 448 (M^+, 0.3%), 371 (4), 364 (6), 363 (41), 294 (8), 287 (10), 286 (22), 209 (100), 154 (3), 85 (4)
(3)	91 [a]	2.70 (s; 2H, CH_2), 7.1—7.6 (m; 12H) and 7.6—8.0 (m; 8H, aromatic H)	740 (M^+, 0.003%), 649 (1), 495 (1), 363 (3), 286 (15), 209 (100), 154 (1)
(5)	118—120 [a]	2.2—2.5 (s; 1H, OH), 3.19 (s; 2H, CH_2), 7.1—8.0 (m; 20H, aromatic H)	418 (16%), 406 (32), 380 (10), 364 (52), 363 (10), 303 (38), 287 (46), 286 (100), 225 (38), 209 (100)

[a] From light petroleum (60—90 °C). [b] δ values, in $CDCl_3$, TMS. [c] 70 eV.

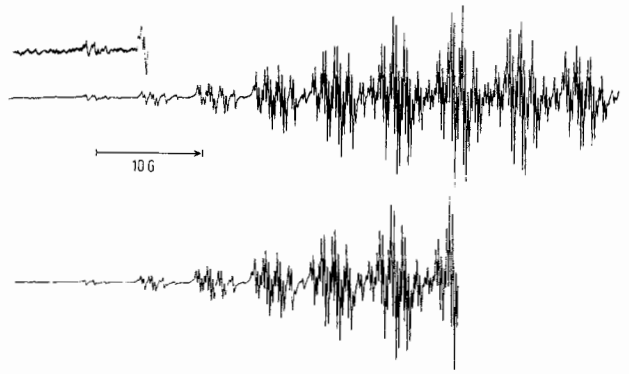
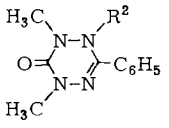


Fig. 1. ESR spectrum of *(4a)* in benzene at room temperature. Below, simulated spectrum (line width 0.16 G).

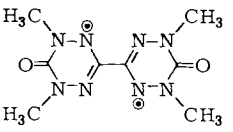
[1] *A. H. Davidson, P. K. G. Hodgson, D. Howells, S. Warren*, Chem. Ind. (London) *1975*, 455.
[2] Earlier attempted syntheses (*F. Challenger*, J. Chem. Soc. *105*, 2210 (1914); *109*, 250 (1916); *F. Challenger, C. F. Allpress, ibid. 119*, 913 (1921)) by reaction of diphenylbismuthyl chloride failed at the high temperatures employed, probably due to phenyl/alkyl exchange.
[3] *Th. Kauffmann, B. Altepeter, K.-J. Echsler, J. Ennen, A. Hamsen, R. Joussen*, Tetrahedron Lett. *1979*, 501.
[4] *Th. Kauffmann, R. Joussen, A. Woltermann*, Angew. Chem. *89*, 759 (1977); Angew. Chem. Int. Ed. Engl. *16*, 709 (1977).
[5] *R. Joussen*, Dissertation, Universität Münster 1979.
[6] *Th. Kauffmann, H. Ahlers, H.-J. Tilhard, A. Woltermann*, Angew. Chem. *89*, 760 (1977); Angew. Chem. Int. Ed. Engl. *16*, 710 (1977).
[7] MPh_3 groups (M = Pb, Sn, Ge, Si) are very unfavorable in this respect.
[8] Bi—C bonds are cleaved by thiols in such a way that an H atom goes to the C atom: *H. Gilman, J. F. Nelson*, J. Am. Chem. Soc. *59*, 935 (1937).

[*] Prof. Dr. F. A. Neugebauer, H. Fischer
Max-Planck-Institut für Medizinische Forschung
Abteilung Organische Chemie
Jahnstrasse 29, D-6900 Heidelberg (Germany)

[**] Verdazyls. Part 28. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 27: *F. A. Neugebauer, H. Fischer, P. Meier*, Chem. Ber. *113*, 2049 (1980).



(5b), R^2 = H; *(6b)*, R^2 = CH_3



(7)

Hydrogenation of the radicals *(4)* (0.5 mol H_2, Pd) leads to the leuco compounds *(5)* which are again dehydrogenated to *(4)* on exposure to air. Alkylation of *(5)*, *e.g.* methylation, yields stable tetrahydro-*s*-tetrazine derivatives *(6)*.

This radical preparation is not limited to monoaldehydes such as *(2)*. Analogous reaction of *(1)* with glyoxal bis(sodium hydrogen sulfite) hydrate gave the C-3, C-3′ linked diradical *(7)*, as black crystals from chloroform. On the basis of its ESR half-field resonance, *(7)* is seen to have a zero field splitting parameter of $D' \approx 320$ G.

The 6-oxoverdazyls *(4)* and *(7)* are sufficiently soluble in water for ESR studies. Their isolation demonstrates that the *N*-aryl substituents of the verdazyls[3] can be replaced by methyl groups without any significant loss of stability.

Selected physical data of the compounds synthesized are listed in Table 1.

Table 1. Compounds *(3)* to *(7)*. All the compounds gave a molecular peak of 100% intensity in their mass spectra.

Cpd.	M.p. [°C]	Yield [%]	^{1}H-NMR [a]
(3a)	110—111	73	2.91 (s, 6H, CH_3), 3.68 (t, $J \approx 9$ Hz, 2H, CH_2), 4.28 (t, 2H, NH)
(3b) [2]	138—139	76	2.97 (s, 6H, CH_3), 4.93 (br. s, 1H, CH), 5.64 (br. s, 2H, NH), 7.2—7.7 (m, 5H, aromatic H)

Cpd.	M.p. [°C]	Yield [%]	UV [b]
(4a)	52—53	33	429 (3.08), 374 (3.13)
(4b)	72—73	80	492 (2.68), 413 (3.21), 248 (4.46)
(5b) [c]	83—84		
(6b)	60—61		317 (3.74), 260 (4.09)
(7)	258—260 (dec.)		500 (3.02), 420 (3.34), 383 (3.58), 241 (4.44)

[a] δ values, in [D_6]-dimethyl sulfoxide. [b] λ_{max} [nm] (lgε), in dioxane. [c] IR [cm^{-1}], in KI: $\tilde{\nu}$ = 3200, 3160 (NH).

Received: January 21, 1980 [Z 555 IE]
German version: Angew. Chem. *92*, 766 (1980)

CAS Registry numbers:
(1), 13782-38-2; *(2)* (R′ = H), 50-00-0; *(2)* (R′ = C_6H_5), 100-52-7; *(3a)*, 74808-99-4; *(3b)*, 74809-00-0; *(4a)*, 74809-01-1; *(4b)*, 74809-02-2; *(5b)*, 74809-03-3; *(6b)*, 74809-04-4; *(7)*, 74809-05-5

[1] *L. Raphaelian, H. Hooks, G. Ottmann*, Angew. Chem. *79*, 315 (1967); Angew. Chem. Int. Ed. Engl. *6*, 363 (1967).

[2] *(3b)* has already been synthesized [1] but was regarded as 1-benzylidene-2,4-dimethylcarbonohydrazide [1]; however, this assignment is incompatible with the ^{1}H-NMR spectrum (see Table 1).

[3] *F. A. Neugebauer*, Angew. Chem. *85*, 485 (1973); Angew. Chem. Int. Ed. Engl. *12*, 455 (1973).

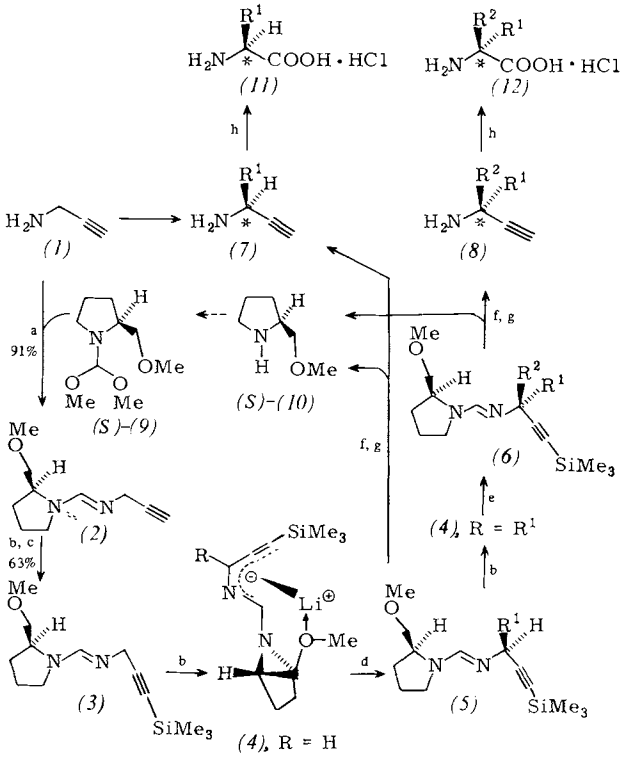
Asymmetric Synthesis of Amines by Carbon-Carbon Coupling in the α-Position to Nitrogen

By *Michael Kolb* and *Jacqueline Barth*[*]

We recently reported on the asymmetric synthesis of α-substituted α-amino acids with (*S*)-1-(dimethoxymethyl)-2-(methoxymethyl)pyrrolidine [SDMP, *(9)*] as chiral agent[1]. We describe here the use of *(9)* for the asymmetric synthesis of the amines *(7)* and *(8)* and their secondary products. The key reaction is the diastereoselective coupling of the carbon-carbon bond at the α-position to the amine nitrogen.

Propargylamine *(1)* is first converted into the amidine *(2)*[2a] (colorless oil). H/Li exchange at the acetylene function in *(2)* with *n*-butyllithium (5 min) leads, after addition of freshly distilled trimethylsilyl chloride, to the 3-silylated propargylamine derivative *(3)*[2b]. The so protected amine *(3)* is metalated with *n*-butyllithium to *(4)* (30 min). After addition of the electrophile R^1X at −78 °C, the reaction mixture is allowed to warm to room temperature. Aqueous workup affords the substituted amidines *(5)*. The completely alkylated derivative *(6)* is obtained from *(5)* by repeating the metalation and alkylation with R^2X (see Scheme 1). ^{1}H-NMR and IR spectra show that *(4)* reacts regioselectively with RX at C-1. Neither allene products (alkylation at C-3) nor enyne products (alkylation at the amidine C) were observed.

The α-substituted propargylamines *(7)* and *(8)* are obtained from *(5)* and *(6)*, respectively, by hydrolysis of the amidine function with hydrazine hydrate and cleavage of the silyl protecting group with sodium methoxide (see Scheme 1). The pyrrolidine derivative (*S*)-*(10)* liberated from *(5)* and *(6)* can be reconverted into *(9)*.



Scheme 1. a) *(1)*:*(9)* = 1:1; without solvent, 3 h, 80 °C oilbath temperature. b) *(2)*: *n*-BuLi = 1:1.1; in tetrahydrofuran (THF), −78 °C. c) 1.1 equiv. Me_3SiCl, 5 min at −78 °C, then 30 min at 25 °C. d) *(4)*: R^1X = 1:1.1. e) *(5)*: R^2X = 1:1.1. f) *(5)* or *(6)*: $H_2NNH_2 \cdot H_2O$ = 1:5—10; in anhydrous ethanol, 2—4 h, reflux. g) 1 equiv. CH_3ONa in CH_3OH, 2—3 h, 25 °C. h) RuO_2, $NaIO_4$.

The yield and optical rotation of the reaction products are collected in Table 1. The enantiomeric purity of the amines *(7)* and *(8)* was determined by oxidation to the corresponding amino acids *(11)* and *(12)*, respectively[3]. The asymmetric induction increases with increasing size of the electrophile (see Table 1, α-methylphenylalanine and α-methylnorleucine). As to be expected, the preferred configuration at the asymmetrically substituted carbon atom in *(8)* changes if the electrophiles R^1X and R^2X are added in the reverse order.

[*] Dr. M. Kolb, J. Barth
Centre de Recherche Merrell International
16 rue d'Ankara, F-67084 Strasbourg (France)

Table 1. Chiral propargylamines *(7)* and *(8)* and their protected precursors *(5)* and *(6)*; enantiomeric excess (e.e.) of the amino acids *(11)* and *(12)* obtained from *(7)* and *(8)*, respectively.

R^1X		*(5)*		*(7)*		*(11)*·HCl
		Chem. yield [%] [a]	$[\alpha]_D^{20}$ [b]	Chem. yield [%] [a]	$[\alpha]_D^{20}$	e.e. [%] Config.
CH_3I		84		[6]		
n-C_4H_9I		85	−39	55	+1.3 [c]	9 (*S*) [d]
C_6H_5—CH_2Br		66		72	−1.9 [c]	15 (*S*) [e]
R^1X	R^2X	*(6)*		*(8)*		*(12)*·HCl
		Chem. yield [%] [a]	$[\alpha]_D^{20}$ [b]	Chem. yield [%] [a]	$[\alpha]_D^{20}$	e.e. [%] Config.
CH_3I	C_2H_5I	76	−29.5	68	+5.0 [f]	(*S*) [7, 8]
CH_3I	n-C_4H_9I	71 [g]	−27	86	+8.1 [c, g]	(*S*) [8]
CH_3I	C_6H_5—CH_2Br	75	+22	84	−5.6 [f]	84 (*S*) [9]
n-C_4H_9I	CH_3I	77 [g]	−36	56	−4.9 [c, g]	(*R*) [8]
C_6H_5—CH_2Br	CH_3I	79		77	+4.5 [e]	67 (*R*) [9]

[a] Yield of isolated, analytically pure product. [b] $c = 2$, benzene. [c] $c = 2$, H_2O. [d] L-norleucine·HCl: $[\alpha]_D^{20} = +13.8$ ($c = 2$, H_2O). [e] L-phenylalanine: $[\alpha]_D^{20} = -12.5$ ($c = 2$, H_2O). [f] $c = 1$, H_2O. [g] The yield in the alkylation step and in the asymmetric induction does not change if the solution of *(4)* in THF prepared at −78 °C is stirred for 20 min at 25 °C before addition of the electrophile.

The propargylamine derivatives *(7)* and *(8)* synthesized are configuratively related, since the chelates *(4)* in the configuration depicted in Scheme 1 are preferably alkylated from the upper side. This is in complete contrast to the described asymmetric synthesis of α-alkylated α-amino acids with the same reagent SDMP, whereby preferred alkylation from the lower side has been observed[1].

The method described here for the preparation of the optically active propargylamines *(7)* and *(8)* is not only of importance for the enantioselective synthesis of α-alkylated α-amino acids. The ethynyl group in the products corresponds to a d^1/d^2-synthon[4], *i.e.* an extremely versatile function[5], which in combination with the asymmetric synthesis describe here offers numerous possibilities for the enantioselective preparation of nitrogen compounds.

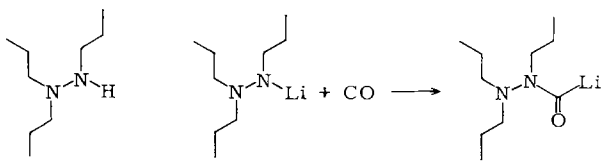
Received: September 7, 1979 [Z 556 1E]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 753 (1980)

[1] *M. Kolb, J. Barth*, Tetrahedron Lett. *1979*, 2999.
[2] a) B.p. 78—80 °C/0.05 torr; ^{1}H-NMR ($CDCl_3$/TMS): $\delta = 7.73$ (s, N=CH); IR ($CHCl_3$): 3320 (H—C—C), 1660 (N=CH) cm^{-1}; $[\alpha]_D^{20} = -56.2$ ($c = 2$, C_6H_6); b) b.p. 105—108 °C/0.05 torr; ^{1}H-NMR ($CDCl_3$/TMS): $\delta = 7.70$ (s, N=CH), 0.20 [s, $Si(CH_3)_3$]; IR (CCl_4): 2170 (C—C), 1650 (N=CH) cm^{-1}; $[\alpha]_D^{20} = -47.3$ ($c = 2$, C_6H_6).
[3] *H. Gopal, A. J. Gordon*, Tetrahedron Lett. *1971*, 2941.
[4] *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).
[5] *V. Jäger, H. G. Viehe* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th edit., Vol. V/2a. Thieme, Stuttgart 1977; *R. A. Raphael*: Acetylenic Compounds in Organic Synthesis. Butterworth, London 1955.
[6] Optically pure (*R*)-(+)-1-methylpropargylamine was obtained in 2% yield on resolution of the racemic mixture; *A. Lindquist, B. Ringdahl, U. Svensson, R. Dahlbom*, Acta Chem. Scand. *B 30*, 517 (1976); *A. Marszak-Fleury*, Ann. Chim. (Paris) *13*, 656 (1958).
[7] Optically pure (*S*)-(+)-1-ethyl-1-methylpropargylamine was obtained in 14% yield on resolution of the racemic mixture. *B. Ringdahl, R. Dahlbom*, Acta Chem. Scand. *B 30*, 993 (1976).
[8] *K. Weinges, B. Stemmle*, Chem. Ber. *106*, 2291 (1971).
[9] *S. Terashima, K. Achiwa, S. Yamada*, Chem. Pharm. Bull. *14*, 1138 (1966).

Tripropylcarbazoyllithium

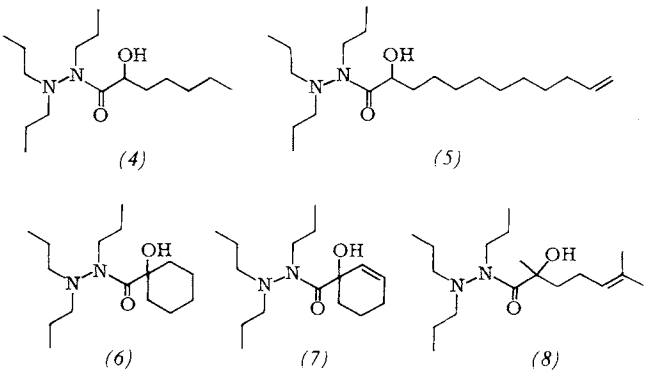
By *Valentin Rautenstrauch* and *François Delay*[*]

Can structural modifications lead to synthetically useful acyllithiums[1]? To answer this question further[2] we have investigated the preparation and reactions of tripropylcarbazoyllithium *(3)*.



(1) *(2)* *(3)*

(3) is readily obtained by carbonylation of lithium tripropylhydrazide *(2)* in tetrahydrofuran (THF)/hexane solution[3] (*ca.* 0.5 M) at *ca.* −75 °C and normal pressure, as demonstrated by its reactions. *(2)* is prepared by lithiation of tripropylhydrazine *(1)*[4] with *n*-butyllithium. *(3)* is inert towards CO (cf. [1c]), but reacts rapidly[5] and cleanly, at −75 °C, with aldehydes and ketones: Addition of the reactants [0.7—1.2 mol per mol of *(1)*] to the solution of *(3)* and subsequent hydrolysis leads to the hydroxycarbohydrazides *(4)*—*(8)* [high-boiling oils, yields 60—85%]. Under these simplest experimental conditions [*e.g.* without inverse addition of *(3)*], *(3)* does *not* react with the hydrazide function of the



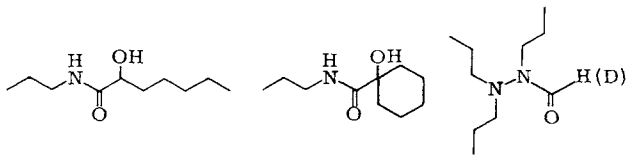
(4) *(5)* *(6)* *(7)* *(8)*

alcoholates of *(4)*—*(8)* (cf. [1c]). Although the hydrazide function of the adducts *(4)*—*(8)* is greatly hindered, they can be smoothly cleaved, by reaction with lithium in liquid NH_3/THF and subsequent hydrolysis, to give the unhindered propylamides [cf. [1d], *e.g. (4)*→*(9)*, m.p. 88—89 °C, yield *ca.* 90%; *(6)*→*(10)*, m.p. 105—106 °C, yield *ca.* 85%].

Addition of water to the solution of *(3)* gives the formohydrazide *(11)* and addition of D_2O gives the labeled hydrazide

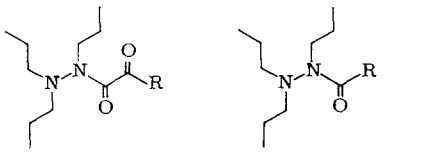
[*] Dr. V. Rautenstrauch [+], Dr. F. Delay
Firmenich SA, Laboratoires de Recherche
b.p. 239, CH-1211 Genève 8 (Switzerland)
[+] Author to whom correspondence should be addressed.

[D_1]-*(11)*, along with traces of *(11)* [[D_1]-*(11)*:*(11)* = 94:6[6a], yields of *(11)*, [D_1]-*(11)* *ca.* 40%].



(9) *(10)* *(11)*/[D_1]-*(11)*

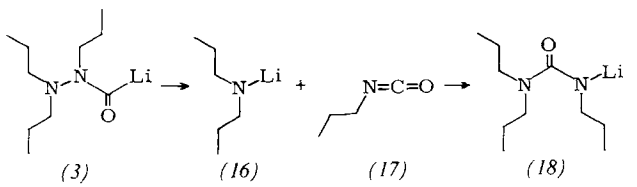
(3) reacts in a 1:1 molar ratio with esters: addition of 1.1 equiv. of ethyl acetate or isobutyrate to the solution of *(3)* at *ca.* −75 °C and work up with water gives the oxocarbohydrazides *(12)* [yield *ca.* 35%, unidentified minor products] and *(13)* [yield *ca.* 55%], respectively.



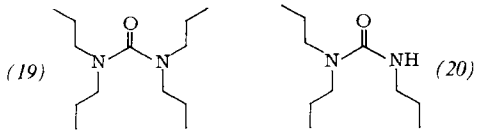
(12), R = CH_3 *(14)*, R = CH_3

(13), R = $(CH_3)_2CH$ *(15)*, R = n-C_3H_7

Methyl iodide (1.1 equiv.) methylates *(3)* slowly[5] (4 h) at *ca.* −75 °C to give the acetohydrazide *(14)* [yield *ca.* 60%]. Propyl iodide alkylates *(3)* very slowly[5] at *ca.* −75 °C to give the butyrohydrazide *(15)* [*ca.* 30% conversion in 15 h]; hydrolysis with D_2O shows that, in parallel, *(3)* slowly[5] reacts with the medium to give *(11)* [→[D_1]-*(11)* + *(11)*, 78:22[6b]]. In the alkylations, *(3)* does not react with *(14)* and *(15)* (cf. [1c]). Addition of hexamethylphosphoramide (2 equiv.) at *ca.* −75 °C accelerates the alkylations, but also, and more strongly, the reaction with the medium to give *(11)*; hydrolysis with D_2O shows that *(3)* does not survive [→unlabeled *(11)*[6b]].



(3) *(16)* *(17)* *(18)*



(19) *(20)*

The alkylations cannot be accelerated by raising the temperature, because *(3)* rearranges to give the *N*-lithiourea *(18)*. In the presence of *e.g.* propyl iodide, mixtures of tetrapropylurea *(19)* and the hydrazide *(15)* are then formed. In the absence of an alkylating agent, warming the solution of *(3)* to 0—5 °C for 2 h and subsequent hydrolysis affords tripropylurea *(20)* as the main product, along with some *(11)* and many unidentified minor products; hydrolysis with D_2O shows that *(11)* is again partially formed by prior reaction of *(3)* with the medium [→[D_1]-*(11)* + *(11)*, 69:31[6b]]. Presumably, *(3)* dissociates to give lithium dipropylamide *(16)* and propyl isocyanate *(17)* and the pair *(16)*/*(17)* then recombines to give *(18)*.

(3) can also be obtained by lithiation of the formohydrazide *(11)* with lithium diisopropylamide at *ca.* −75 °C (cf. [1a]), but the equilibrium seems to be unfavorable: exposure of *(11)* to 1.2 equiv. of the base [in the medium used for the carbonylation of *(2)*, starting concentration of *(11)* *ca.* 0.4 M, 10 min—5 h] and subsequent hydrolysis with D_2O affords a 63:37 mixture[6b] of [D_1]-*(11)* and *(11)*. The carbonylation of *(2)* is the better method.

Procedures

Solutions of *(3)*: A hexane solution (1.5—1.6 M) of *n*-butyllithium (3.2 mmol) is added to a solution of *(1)*[4] (3.2 mmol) in 5 ml THF [or 2.5 ml THF and 2.5 ml 1,2-dimethoxyethane (DME)[3]] at *ca.* −75 °C under an inert gas and after 5 min stirring, CO is passed (*ca.* 3 l/h) at *ca.* −75 °C for 4 h through the stirred solution.

Reaction of *(3)* with aldehydes, ketones, and esters: The reactants (0.7—1.2 equiv.) are added at once to the solution of *(3)*. After 1—2 h stirring at *ca.* −75 °C, H_2O (*ca.* 22 °C) is added.

Hydrolysis of *(3)* with D_2O: 1 ml of D_2O (*ca.* 22 °C) is added to the solution (*ca.* −75 °C) of *(3)* [from 3.2 mmol of *(1)*]. After 3 min stirring in an ice-bath, the mixture is diluted with H_2O.

Cleavage of the hydroxycarbohydrazides: A solution of the educt (0.8 mmol) in 6 ml THF is added dropwise with stirring to 6 ml of liquid NH_3 at *ca.* −75 °C. Li (3.1 mmol) is then added to the mixture (blue solution or suspension) which is then warmed with stirring until the blue color disappears (*ca.* −50 °C). More Li (3.1 mmol) is then added, and the mixture is kept at reflux for 30 min (blue solution or suspension), and is finally treated with NH_4Cl (20 mmol). The NH_3 is then evaporated and H_2O is added.

All compounds are isolated by extraction with ether, concentration, and distillation. Analytically pure samples are obtained by gas chromatography or recrystallization.

Received: November 29, 1979 [Z 557 IE]
German version: Angew. Chem. *92*, 764 (1980)

CAS Registry numbers:
(1), 67398-42-9; *(2)*, 74809-06-6; *(3)*, 74809-07-7; *(4)*, 74809-08-8; *(5)*, 74809-09-9; *(6)*, 74809-10-2; *(7)*, 74809-11-3; *(8)*, 74825-02-8; *(9)*, 74809-12-4; *(10)*, 74809-13-5; *(11)*, 74809-14-6; *(12)*, 74809-15-7; *(13)*, 74809-16-8; *(14)*, 74809-17-9; *(15)*, 74809-18-0; *(16)*, 4111-53-9; *(17)*, 110-78-1; *(18)*, 74809-19-1; *(19)*, 13149-88-7; *(20)*, 74809-20-4; ethyl acetate, 141-78-6; ethyl isobutyrate, 97-62-1; methyl iodide, 74-88-4; propyl iodide, 107-08-4

[1] a) Preparation by lithiation of formamides with lithium diisopropylamide: the unhindered dimethylcarbamoyllithium *(21)* is not persistent [*B. Bánhidai, U. Schöllkopf*, Angew. Chem. *85*, 861 (1973); Angew. Chem. Int. Ed. Engl. *12*, 836 (1973)]; the hindered diisopropylcarbamoyllithium *(22)* is persistent

(21) $(CH_3)_2N—CO—Li$ $[(CH_3)_2CH]_2N—CO—Li$ *(22)*

but the equilibrium seems to be unfavorable [*R. R. Fraser, P. R. Hubert*, Can. J. Chem. *52*, 185 (1974)]; b) preparation of *(22)* by lithiation of the corresponding formamide with *tert*-butyllithium: the lithiation has to be carried out at *ca.* −95 °C and in dilute solution (*ca.* 0.08 M) [*A. S. Fletcher, K. Smith, K. Swaminathan*, J. Chem. Soc. Perkin Trans. I *1977*, 1881]; c) preparation by carbonylation of lithium dialkylamides: even the hindered *(22)* reacts with CO [*V. Rautenstrauch, M. Joyeux*, Angew. Chem. *91*, 72 (1979); Angew. Chem. Int. Ed. Engl. *18*, 83 (1979)]; d) the amides obtained by reaction of the hindered *(22)* with electrophiles are extremely unreactive, *e.g.* on attempted hydrolysis.

[2] *U. Schöllkopf, H. Beckhaus*, Angew. Chem. *88*, 296 (1976); Angew. Chem. Int. Ed. Engl. *15*, 293 (1976).

[3] In most of the experiments, we used a THF/DME/hexane mixture according to our first procedure[1c]. Later we found that THF/hexane alone can also be used.

[4] *(1)* was prepared in low yield, but very simply, from propyl chloride and hydrazine [*O. Westphal*, Ber. Dtsch. Chem. Ges. *74*, 759 (1941)]; purification by fractionation, b. p. 60—63 °C/12 torr; impurities: *ca.* 5% tetrapropyl- and 1,1-

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/0909-0727 $ 02.50/0*

dipropylhydrazine. Triisopropylhydrazine can be obtained analogously [*F. Klages, G. Nober, F. Kircher, M. Bock*, Justus Liebigs Ann. Chem. *547*, 1 (1941)]. More efficient but less simple methods for the preparation of trialkylhydrazines are available [Houben-Weyl: Methoden der Organischen Chemie. 4th edit., Vol. X/2. Thieme, Stuttgart 1967].

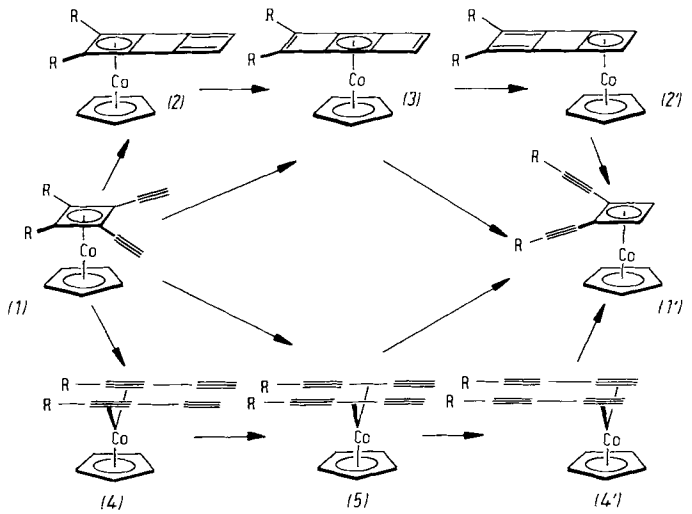
[5] Not quantitatively investigated.

[6] a) Analysis by high-resolution mass spectrometry. Estimated analytical error ± 3. b) Analysis by combination of high- and low-resolution mass spectrometry. Estimated analytical error ± 5. We thank Prof. *A. Buchs*, Université de Genève, for recording the high-resolution mass spectra.

A Theoretical Investigation of the Diethynylcyclobutadiene(cyclopentadienyl)cobalt Rearrangement[**]

By *Peter Hofmann* and *Thomas A. Albright*[*]

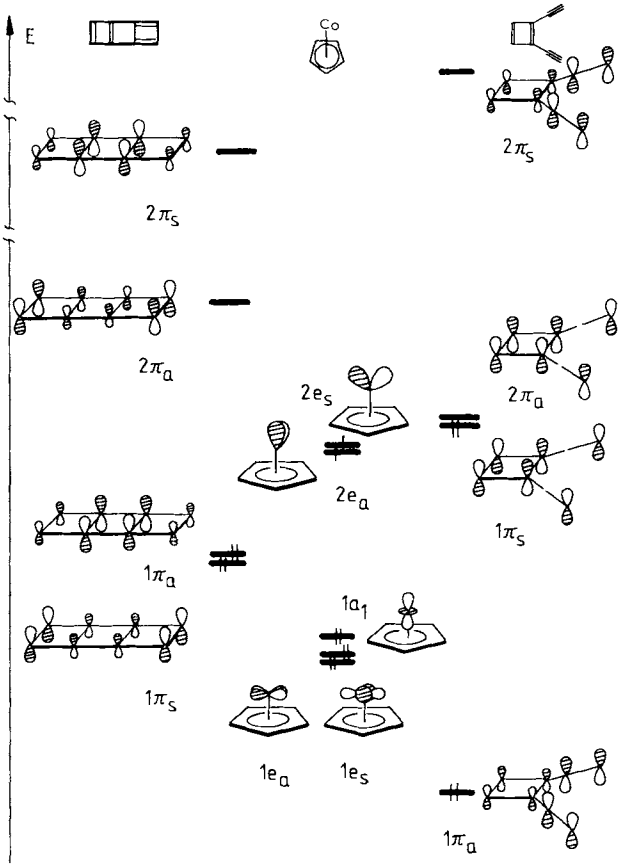
A recent fascinating development in the area of alkyne metathesis has been the synthesis and interconversion of η^4-dialkynylcyclobutadiene-η^5-cyclopentadienylcobalt complexes by *Vollhardt* and *Fritch*[1]. Subjected to flash pyrolysis conditions, such compounds [*(1)* in scheme 1, R = $SiMe_3$] isomerize to *(1')*. This rearrangement[1b] has been proposed to occur by intervention of a novel complex *(2)*[1a], which could undergo a haptotropic shift[2] of the CoCp fragment leading first to *(2')* and finally to the observed product *(1')*.



Scheme 1. Possible rearrangement pathways of η^4-diethynylcyclobutadiene-η^5-cyclopentadienylcobalt complexes (Ref. [1a]).

Another conceivable process (Scheme 1, lower part) involves the retrocycloaddition of *(1)* to a bis-alkadiyne complex *(4)* and a shifting of the CoCp fragment *via (5)* to *(4')*; cycloaddition again would yield *(1')*. We show here that, based on theoretical results, both mechanistic alternatives are highly improbable. This forms part of a general theoretical analysis for the propensity of an ML_n unit to migrate in polyene-ML_n complexes[3]. Along with these haptotropic rearrangements we have initiated an investigation of the electronic requirements of retrocycloaddition *(1)*→*(4)* as well as of the cycloadditions *(1)*→*(2)* and *(4')*→*(1')* which are closely related to the mechanism of alkyne metathesis and of transition metal catalyzed alkyne oligomerizations. Our MO calculations are of the Extended Hückel type[4].

The relevant orbitals of tricyclo[4.2.0.$0^{2,5}$]octa-1(6),2,4,7-tetraene ("bicyclobutadienylene"), the CoCp-fragment[5] and of diethynylcyclobutadiene are presented in Scheme 2.



Scheme 2. Relevant valence orbitals of tricyclooctatetraene (left), CoCp (middle) and diethynylcyclobutadiene (right).

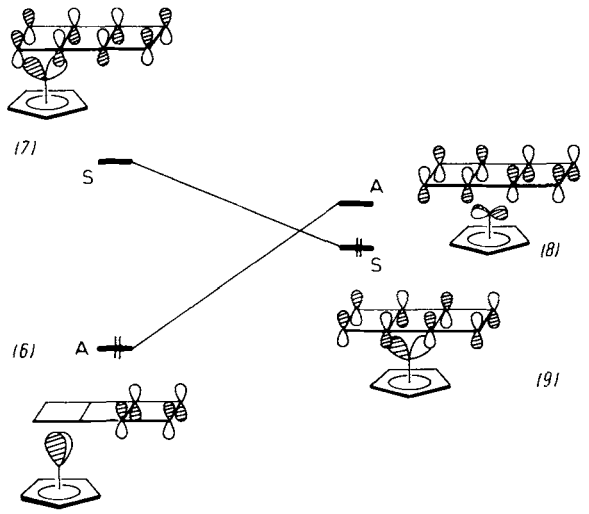
For structure *(2)*, the $2e_s$ and $2e_a$ frontier orbitals of the CoCp unit make the dominant contribution to the bonding of the polyene ligand. $2e_s$ finds a good match in symmetry and energy to interact with the $1\pi_s$ orbital of the tricyclooctatetraene ligand. The situation with $2e_a$ is a bit more complicated: $2e_a$ forms a bonding combination with $1\pi_a$, sending $1\pi_a$ to lower energy, the antibonding combination of $1\pi_a$ and $2e_a$ strongly mixes into itself $2\pi_a$, the LUMO of the tricyclooctatetraene. This mixing takes place in a bonding way with respect to $2e_a$, forming *(6)* as an occupied but practically nonbonding orbital. The $1a_1$, $1e_s$ and $1e_a$ orbitals of the CoCp fragment are largely nonbonding levels, localized at the cobalt center.

A shift *(2)*→*(3)* of the CoCp fragment as a plausible step of the interconversion *(1)*→*(1')* causes an orbital crossing between the HOMO *(6)* of the complex and its LUMO *(7)*, the antibonding combination of $1\pi_s$ and $2e_s$. In other words, the conversion *(2)*→*(2') via (3)* is symmetry forbidden. To see how this comes about note that it is the bonding combination of $2\pi_a$ with $2e_a$ which keeps the HOMO *(6)* from rising to a

[*] Priv.-Doz. Dr. P. Hofmann
Institut für Organische Chemie I der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)
Prof. Dr. T. A. Albright
Department of Chemistry, University of Houston
Houston, Texas 77004 (USA)

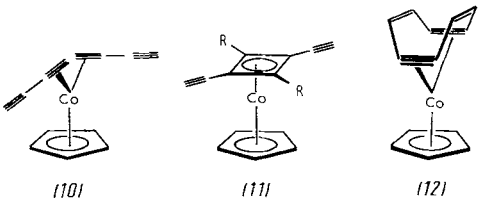
[**] Haptotropic Rearrangements of Polyene-ML_n Complexes, Part 1. This collaboration was made possible by a NATO Scientific Affairs Grant. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie (P. H.), the Robert A. Welch Foundation and the Petroleum Research Foundation (T. A. A.). T. A. A. is Camille and Henry Dreyfus Scholar Teacher (1979–1984).

high energy. For geometry *(3)* this interaction is lost by symmetry and, thus, during the CoCp transit, *(6)* rises to high energy, ultimately becoming MO *(8)* of structure *(3)* (predominantly $2\pi_a$ in character). On the other hand, the antibonding between $2e_s$ and $1\pi_s$ vanishes so that the LUMO *(7)* is lowered in energy and in addition begins to mix into itself $2\pi_s$ in a bonding fashion with respect to $2e_s$, so that finally MO *(9)* results.



The symmetry imposed barrier of the CoCp migration is calculated as 47 kcal/mol. The relatively high temperatures used in the experiments and the fact that the CoCp unit need not remain on the mirror plane bisecting the tricyclooctatetraene (which technically avoids the HOMO-LUMO correlation) would still make the pathway *via (3)* an attractive process. However, the conversion of *(1)* to *(2)* is also strongly symmetry forbidden. The orbitals of the diethynylcyclobutadiene ligand are shown on the right side of Scheme 2. Of these $1\pi_s$ and $2\pi_a$ form ideal bonding combinations with $2e_s$ and $2e_a$, respectively. The π-orbitals of both valence isomers of the pure ligand correlate with each other nicely during the cycloaddition and, therefore, they must as well in the CoCp-complexes. The problem lies in the orthogonal ("in plane") π- and π^*-orbitals of the two ethynyl groups of *(1)*, the S and A combinations of which are easily constructed. Of these orbitals two are important, the S-combination of the π^*-levels and the A-combination of the π-levels. As the two ethynyl groups approach each other to cycloadd to a four membered ring, the symmetric combination of the π^* orbitals finally becomes a bonding σ-orbital, the A-combination of the alkyne π-MO's correlates to an antibonding σ^*-orbital of the new ring. The transformation of *(1)* into *(2)* therefore is not unlike the symmetry forbidden $[{}_{\pi}2_s + {}_{\pi}2_s]$ dimerization of ethylene[6]. The activation barrier found for the rearrangement *(1)*→*(1')* of 37 kcal/mol[1b] seems to be too small for the process to occur by way of *(2)* and *(3)*. It can also be shown, that the direct conversion of *(1)* into *(3)* [CoCp migration and simultaneous ring closure] is doubly symmetry forbidden: two occupied A-levels become empty, while two unoccupied MO's of S symmetry correlate to occupied orbitals of the product.

The direct retrocycloaddition of *(1)* to *(4)* is also strongly symmetry forbidden. A σ^*-orbital of the cyclobutadiene ring develops into a filled π-level of the alkyne ligands, a σ-MO correlates to π^* orbitals. The reverse of this process has been treated by *Mango et al.* in qualitative terms[7]. Our preliminary calculations furthermore put a higher barrier on going from *(4)* to *(4')* (60 kcal/mol) than that for the rotation of an alkyne ligand *via (10)* (23 kcal/mol). Thus, one would expect, that if the energy manifold leading from *(1)* to *(4)* were accessible, then "cross products" of the type given by *(11)* should be observed. Such is not the case for $R = D$[1a], and when $R = SiMe_3$[1b] *Vollhardt* and *Fritch* find *(11)* to be formed with a higher activation energy than that for the *(1)*→*(1')* rearrangement. The reason for the enormous energetic requirements of a CoCp shift *(4)*→*(4')* lies in the fact, that all dominant frontier orbital interactions in *(4)* between $2e_s$ and $2e_a$ of CoCp and the highest occupied π and the lowest unoccupied π^* orbitals of two diacetylenes break down for symmetry reasons in *(5)*.



(10) (11) (12)

Our preliminary results therefore make all pathways of a diethynylcyclobutadiene-CoCp rearrangement as shown in Scheme 1 appear rather improbable.

A further mechanistic hypothesis for this unusual reaction could involve the direct conversion of *(1)*, $R = H$, to *(12)*, mentioned as "structural and electronic counterpart" of *(3)* by *Vollhardt* and *Fritch*[1a].

Received: January 14, 1980 [Z 558 IE]
German version: Angew. Chem. *92*, 747 (1980)

CAS Registry number:
(1), 67378-04-5

[1] a) *J. R. Fritch, K. P. C. Vollhardt*, J. Am. Chem. Soc. *100*, 3643 (1978); b) Angew. Chem. *91*, 439 (1979); Angew. Chem. Int. Ed. Engl. *18*, 409 (1979).

[2] *N. T. Anh, M. Elian, R. Hoffmann*, J. Am. Chem. Soc. *100*, 110 (1978).

[3] a) *T. A. Albright, P. Hofmann*, unpublished; b) *T. A. Albright, P. Hofmann, R. Hoffmann, P. Lillya, P. Dobosh*, in preparation; c) *P. Hofmann, R. Hoffmann*, J. Am. Chem. Soc. *98*, 598 (1976).

[4] *R. Hoffmann*, J. Chem. Phys. *39*, 1397 (1963). H_{ij}-matrix elements: *J. H. Ammeter, H.-B. Bürgi, J. C. Thibeault, R. Hoffmann*, J. Am. Chem. Soc. *100*, 3686 (1978). Parameters and geometrical details: *P. Hofmann et al.*, unpublished.

[5] Valence orbitals of a CoCp unit: *M. Elian, M. M. L. Chen, D. M. P. Mingos, R. Hoffmann*, Inorg. Chem. *15*, 1148 (1976).

[6] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[7] *F. D. Mango*, Fortschr. Chem. Forsch. *45*, 39 (1974); *F. D. Mango, J. H. Schachtschneider*, J. Am. Chem. Soc. *91*, 1030 (1969); *F. D. Mango*, Tetrahedron Lett. *1973*, 1509.

Characterization by Mössbauer Spectroscopy of Iron Carbide Phases in a Highly Active Carbon Matrix Catalyst for Medium Pressure Fischer-Tropsch Synthesis[**]

By *Hartwig Schäfer-Stahl*[*]

As crucial intermediates in the synthesis of hydrocarbons from CO and H_2 on heterogeneous catalysts containing iron, cobalt, and nickel (Fischer-Tropsch synthesis), the formation of metal carbide phases was reported as long ago as the 1920's by *F. Fischer et al.*[1], partly on the basis of results of

[*] Dr. H. Schäfer-Stahl
Fakultät für Chemie der Universität
Postfach 5560, D-7750 Konstanz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. I wish to thank Prof. Dr. *H. H. Brintzinger* for valuable discussions.

hydrolysis experiments with such catalysts (cf. also [2]). This concept is still a matter of controversy[3,4]. We now report observations on a highly active matrix catalyst which show that the catalytically active sites are formed at iron carbide crystallites.

Reduction of iron halide-graphite intercalation compounds leads to destruction of the ordered host lattice, giving a carbon layer matrix with a greatly increased surface area in which highly dispersed iron particles are embedded whose diameter is shown by Mössbauer spectroscopy and electron microscopy[5,6] to be smaller than 2000 pm (20 Å). This matrix catalyst mediates Fischer-Tropsch synthesis at temperatures as low as 140 °C in the medium pressure range[7].

Under these conditions the original iron particles undergo complete transformation. Superparamagnetic iron oxide and, above all, ferromagnetic ε- and χ-iron carbide phases are recognizable in the Mössbauer spectrum. If the temperature of Fischer-Tropsch synthesis is raised to 185 °C then the unstable iron oxide phases disappear and only magnetically ordered ε- and χ-iron carbide phases are present in the catalyst. The activity of the catalyst increased concomitantly. Subsequent heating to 320 °C in a gas mixture having a high concentration of H_2 effects complete phase transition to the χ-iron carbide phase (magnetically ordered at room temperature) which is then also stable at 140 °C (Fig. 1). This χ-iron carbide phase is the most active form of the investigated matrix catalyst in the temperature range around 140 °C. Since the phase is magnetically ordered at room temperature but fails to show sharp X-ray reflections, the particle diameter can be estimated as between several tens and several hundreds of Å.

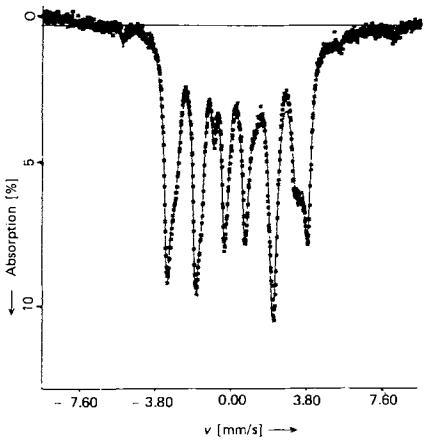


Fig. 1. Mössbauer spectrum of the matrix catalyst after 600 h operation at 140 °C in its most active form. Almost the entire iron content is present in the form of ferromagnetic χ-carbide. (Recorded under protective gas with an ELSCINT AME40 instrument, calibration with Ne-He laser interferometer and α-Fe foil. Chemical shift relative to center of gravity of the α-Fe spectrum.)

However, if the catalyst is heated to 320 °C in a gas mixture having a low H_2 content then the χ-iron carbide phase is partly degraded to ferromagnetic Fe_3O_4; it no longer exhibits Fischer-Tropsch activity at 140 °C. A residual catalytic activity can be detected at 185 °C; in the course of several days the χ-iron carbide phase is regenerated with a concomitant increase in catalytic activity. A similar increase in activity is observed when the partially oxidized catalyst is reduced with hydrogen before it is re-used. After such regeneration small amounts of ferromagnetic Fe_3O_4 and of α-Fe are recognizable in the Mössbauer spectrum. Accordingly, the original activity of the pure χ-iron carbide phase is not quite reached. This oxidation-reduction cycle is reproducible.

The correlation between catalytic activity and content of iron carbide phases, and particularly the χ-iron carbide phase, observed in all the operations described above can be regarded as unequivocal proof that such carbide phases are the actual catalytically active component, at least below 200 °C.

The matrix catalyst under investigation is particularly suitable for a structure-reactivity correlation. Owing to the extremely low diameter of the particles, which are essentially isolated from one another by the disordered carbon layer matrix and the exceptionally low reaction temperatures thus possible, the formation, transformation, and growth of the reactive phases can be recognized from the sequence of magnetically disordered iron, superparamagnetic iron oxide alongside ε-iron carbide, iron carbide mixtures, and ultimately pure χ-iron carbide. Our results differ in this point from those of similar studies on α-Fe particles[3,8] whose larger diameters necessitated higher formation temperatures, at which the temperature-dependent sequential formation of oxide and carbide phases and their varying catalytic activities are unobservable.

The high proportion of surface atoms in the highly dispersed particles described above also has the effect that the periphery of the particles makes a significant contribution to the Mössbauer spectra relative to the bulk. Since none other than carbide phases, and especially no α-Fe phase[3,8], can be observed at maximum activity, it may be assumed that χ-iron carbide is also present in the periphery of the reactive particles. It remains to be established how the carbide centers activate the CO molecule for reduction and chain propagation reactions and whether analogies exist with recently described reactions of CO at iron carbide clusters in homogeneous solution[9].

Procedure

All operations were performed in an argon atmosphere with exclusion of air and moisture. Flattened and comminuted lithium wire (11 g) and biphenyl (65 g) are stirred in tetrahydrofuran (THF) (500 ml) at −80 °C until dissolution is complete. $FeCl_3 \cdot C_{6.8}$ (50 g) is cautiously added with further cooling. If the green color of the solution disappears further lithium wire is added until the green color is retained. After 10 minutes' stirring at room temperature the solvent and volatile components are stripped off *in vacuo* and sublimed off up to 100 °C, respectively.—Some 20 $cm^3 = 10$ g of the matrix catalyst prepared with biphenyllithium and having an iron content of 0.98 g (≙ 0.0175 mol Fe) is examined with regard to its catalytic activity.

The Fischer-Tropsch reaction was carried out in a differential reactor with a membrane pump in the external synthesis gas cycle at pressures between 10 and 32 bar and a flow rate of 18 l/h. The reactivity of the matrix catalyst follows from the decrease in pressure of the synthesis gas with time. The product spectrum (GC-MS) was similar to that obtained on use of standard precipitation catalysts; it did not alter significantly during the catalyst transformations described above.

Received: February 13, 1980;
supplemented: June 18, 1980 [Z 560 IE]
German version: Angew. Chem. *92*, 761 (1980)

CAS Registry numbers:
No compounds indexed

[1] *F. Fischer, H. Tropsch*, Ber. Dtsch. Chem. Ges. *59*, 830 (1926); *F. Fischer, H. Bahr*, Gesammelte Abh. Kennt. Kohle *8*, 255, 269 (1924—27).
[2] *M. Ritschel, W. Vielstich*, Chem.-Ing.-Tech. *52*, 327 (1980).
[3] *D. J. Dwyer, G. A. Somorjai*, J. Catal. *52*, 291 (1978).

[4] *G. Henrici-Olivé, S. Olivé*, J. Catal. *60*, 481 (1979); *R. J. Madon, ibid. 60*, 485 (1979); *P. A. Jacobs, H. H. Nijs, J. J. Verdonck, J. B. Uytterhoeven*, Preprints, Symposia Anaheim, CA 23, 469, ACS Div. Petrol. Chem.; *H. Kölbel, D. Schneidt*, Erdöl, Kohle, Erdgas, Petrochem. *30*, 139 (1977).
[5] *B. Cleveland, C. R. Guarnieri, J. C. Walker*, Bull. Am. Phys. Soc. *15*, 108 (1970).
[6] *H. Schäfer-Stahl*, Chem.-Ing.-Tech., in press.
[7] Increasing temperature, synthesis gas composition $2H_2/CO$ (30 bar). For comparison: Fischer-Tropsch catalysts based on graphite intercalation compounds reduced with potassium at 300 °C are catalytically active only above 300 °C; *M. Ichikawa, M. Sudo, M. Soma, T. Onishi, K. Tamaru*, J. Am. Chem. Soc. *91*, 1538 (1969); *V. J. Mashinskii, V. A. Postnikov, Yu. N. Novikov, A. L. Lapidus, M. E. Vol'pin, Ya. T. Eidus*, Izv. Akad. Nauk SSSR, Ser. Khim. *1976*, 2018; *S. Parkash, S. K. Chakrabartty, J. G. Hooley*, Carbon *15*, 307 (1977).
[8] *J. A. Amelse, J. B. Butt, L. H. Schwartz*, J. Phys. Chem. *82*, 558 (1978); *G. B. Raupp, W. N. Delgass*, J. Catal. *58*, 337, 348, 361 (1979).
[9] *J. S. Bradley, G. B. Ansell, E. W. Hill*, J. Am. Chem. Soc. *101*, 7417 (1979).

Facile Synthesis of α- and β-*O*-Glycosyl Imidates; Preparation of Glycosides and Disaccharides[**]

By *Richard R. Schmidt* and *Josef Michel*[*]

Glycosides and saccharides are largely synthesized *via* haloses and their activation by heavy metal salts—especially silver salts[1,2]. The disadvantages of this method are self-evident. Simplification of this approach should come from the synthesis of sterically pure, readily isolable intermediates with other leaving groups not requiring activation by heavy metal salts[2,3]. Suitable candidates would seem to be, *e.g.*, α- and β-glycosyl imidates, since β-glycosyl imidates—prepared from α-haloses with silver salts—undergo acid-catalyzed reaction to give good chemical and stereochemical yields of α-glycosides and α-saccharides[4]. Thus a facile synthesis of α- and β-glycosyl imidates is called for[5].

Ketenimines and nitriles containing electron-withdrawing substituents are known to afford imidates directly on reaction with alcohols[6]. We shall now demonstrate for the case of the C-1-unprotected glucopyranose *(1)* that this reaction can be applied to cyclic hemiacetals. Use of sodium hydride as base and aryl-substituted ketenimines gave exclusively the β-imidates *(2)*—*(5)* whereas the same reaction both with benzyl- and with acetyl-protected glucopyranose *(1)* and trichloroacetonitrile led diastereospecifically to the α-imidates *(6)* and *(7)* (Table 1). Both the β-imidates and the α-imidates, now prepared for the first time, could be conveniently isolated.

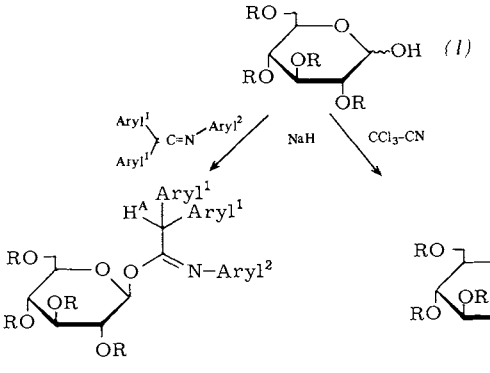
Table 1. *O*-Glycosyl imidates *(2)*—*(7)* prepared [a].

	Yield [%] [b]	^{1}H-NMR [c] H-1	H^A	$J_{1,2}$	IR [d] $\nu_{C=N}$	$[\alpha]_{578}^{20}$	*c* [e]
(2)	84	6.11	5.22	7.0	1670	+ 33.0	2.0
(3)	83	6.11	5.22	7.0	1650	+ 33.0	1.75
(4)	93	6.05	5.04	7.2	1670	+ 34.5	1.88
(5)	38	6.11	5.30	7.5	1670	+ 68.7	1.6
(6)	96	6.56	8.60	3.5	1670 (ν_{NH}: 3320)	+ 61.5	1.0
(7)	85	6.60	8.77	3.5	1680 (ν_{NH}: 3330) (ν_{CO}: 1755)	+103.0	1.2

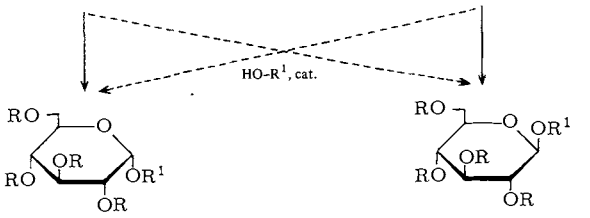
[a] Abbreviations: Ac = acetyl; Bn = benzyl. All compounds gave correct elemental analyses. [b] Isolated yields. [c] 80 MHz spectra in $CDCl_3$ with tetramethylsilane as internal standard; δ values, coupling constants in Hz. [d] [cm^{-1}], film between NaCl plates. [e] In $CHCl_3$.

[*] Prof. Dr. R. R. Schmidt, Dipl.-Chem. J. Michel
Fakultät für Chemie der Universität
Postfach 5560, D-7750 Konstanz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



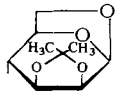
(2): R = Bn, $Aryl^1 = C_6H_5$, $Aryl^2 = p\text{-}CH_3\text{-}C_6H_4$ *(6)*: R = Bn
(3): R = Bn, $Aryl^1 = Aryl^2 = C_6H_5$ *(7)*: R = Ac
(4): R = Bn, $Aryl^1 = Aryl^2 = p\text{-}Cl\text{-}C_6H_4$
(5): R = Bn, $Aryl^1 = C_6H_5$, $Aryl^2 = p\text{-}(CH_3)_2N\text{-}C_6H_4$



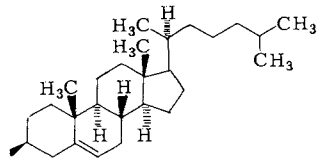
(8a)–*(8e)*, *(8h)*: R = Bn
(9c)–*(9h)*: R = Bn
(9i)–*(9k)*: R = Ac

(a): $R^1 = -CO-CH_3$
(b): $R^1 = p\text{-}C_6H_4\text{-}CH_3$

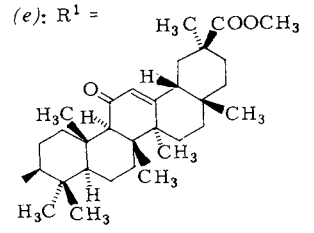
(c): R^1 =



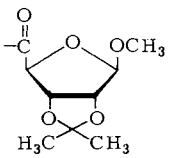
(d): R^1 =



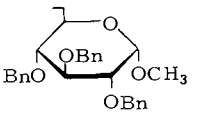
(e): R^1 =



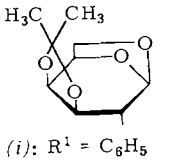
(f): R^1 =



(g), *(k)*: R^1 =

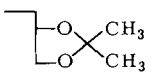


(h): R^1 =



(i): $R^1 = C_6H_5$

(j): R^1 =



As expected, the benzyl-protected β-imidates *(2)*—*(5)* undergo acid-catalyzed reaction with hydroxy components in dichloromethane to form mainly or exclusively the α-linkage product *(8)* while the α-imidate *(6)* correspondingly affords the β-linkage product *(9)* (see Table 2). The use of carboxylic acids [→*(8a)*, *(9f)*], *p*-cresol [→*(8b)*], steroid alcohols [→*(8d)*, *(9d)*; *(8e)*, *(9e)*], and carbohydrates [→*(8c)*, *(9c)*; *(9g)*; *(8h)*, *(9h)*] demonstrates the considerable scope of this simple method of glycosidation; however, the stereochemical result has not yet been optimized in all cases. The particularly readily accessible acetyl-protected α-imidate *(7)* reacts on ca-

Table 2. Reactants, reaction conditions, and products of glycoside and disaccharide synthesis. Dichloromethane as solvent [a].

Reactant	Cat.	Ratio [Reactant]:[HO—R¹]:[Cat.]	Conditions T [°C]	t [h]	Yield (8)+(9) [%] [b]	(8):(9)		Physical data of products ¹H-NMR [c] H-1	$J_{1,2}$	m.p. [°C]	$[\alpha]_{578}^{20}$	c [d]
(2)	—	1 :4 —	20	6	87	>19:1 [d]	(8a) [e]	6.36 (d)	3.5	oil	—	
(2)	TsOH	1.2:1:1	20	6	83	5:1	(8b)	5.43 (d)	3.5	oil	+ 63.7	1.5 [f]
(4)	TsOH	1.4:1:1	20	18	58	3:1	(8c)	4.86 (d)	3.5	oil	+ 21.0	1.3
							(9c)	[g]			− 16.3	1.0
(5)	TsOH	1.5:1:1	20	96	84	3:1	(8d) [e]	[g]		140—142	+ 47.3	1.5
							(9d) [e]	[g]		102—103	+ 0.6	1.6
(5)	TsOH	1.3:1:1	20	96	76	5:1	(8e)	5.02 (d)	3.5	oil	+126.0	1.15
							(9e)	4.45 (d)	7.5	oil	+ 98.2	1.0
(6)	—	1 :1 —	20	4	66	< 1:19 [d]	(9f) [e]:	5.63 (d)	7.0	oil	− 9.2	1.5
(6)	$BF_3 \cdot Et_2O$	1.3:1:1.3	−20	2	90	< 1:19 [d]	(9g) [e]	[g]		133—134	+ 17.9	1.0
(6)	TsOH	1.1:1:0.2	20	96	66	1:2	(8h)	[g]		oil	+ 29.0	1.52
							(9h)	[g]		oil	− 7.4	1.7
(7)	$BF_3 \cdot Et_2O$	1 :1:2.4	20	24	75	< 1:19 [d]	(9i) [e]	[g]		123—125	− 24.0	1.0
(7)	$BF_3 \cdot Et_2O$	1 :1:0.25	20	1	58	< 1:19 [d]	(9j) [e]	4.61 [d]	7.5	115—117	− 18.8	1.0
(7)	$BF_3 \cdot Et_2O$	1 :1:1	20	1.5	44	< 1:19 [d]	(9k)	[g]		61—64 [h]	+ 3.6	1.1

[a] Abbreviations: Bn = benzyl, TsOH = *p*-toluenesulfonic acid. All compounds gave correct elemental analyses. [b] Isolated yields based on the limiting reactant. [c] 80 MHz spectra in $CDCl_3$ with tetramethylsilane as internal standard; δ values, multiplicity in parentheses; H-1 of the glucopyranosyl group, coupling constants in Hz. [d] Only *(8a), (9f), (9g), (9i), (9j), (9k)* could be detected by chromatography; detection limit < 1:19. [e] The data of compounds reported in the literature are in agreement with those given; *(8a): P. W. Austin, F. E. Hardy, J. G. Buchanan, J. Baddiley*, J. Chem. Soc. *1964*, 2128; *(8d), (9d): G. Wulff, U. Schröder, J. Wichelhaus*, Carbohydr. Res. *72*, 280 (1979); *(9f): J. Michel*, Diplomarbeit, Universität Konstanz 1978; *(9g):* see [3]; *(9i): I. Karasawa, R. Onishi*, Nippon Nogei Kagaku Kaishi, *35* (8), 707 (1971); Chem. Abstr. *63*, 5729e (1965); *(9j): T. Ogawa, K. Katano, M. Matsui*, Carbohydr. Res. *70*, 37 (1979). [f] Rotation of the 5:1 mixture. [g] Cannot be determined from the ¹H-NMR spectrum. [h] Amorphous product.

talysis by boron trifluoride-ether to give exclusively the β-glycosides and β-disaccharides *(9i)—(9k)*. Thus a facile method is now also available for the synthesis of β-glucopyranosides.

Procedure

(2)—(7): Ketenimine (10 mmol) and sodium hydride (0.1–0.2 mol), or trichloroacetonitrile (3.5 ml) and sodium hydride (10 mmol), are added to a solution of *(1)* (10 mmol) in dichloromethane (50 ml) at room temperature. After some time [*(2)*, 35 h; *(3)*, 24 h; *(4)*, 5 h; *(5)*, 3 d; *(6)*, 2 h; *(7)*, 20 min] the mixture is filtered, concentrated, and filtered over a short column [*(2)—(5)*, basic alumina (activity grade I), eluant, dichloromethane/ether 1:1; *(6)*, silica gel, light petroleum (low boiling)/ether 3:2; *(7)*, silica gel, ether]. Compound *(5)* is also purified by column chromatography on silica gel (light petroleum (low boiling)/ether = 3:2).

Received: February 15, 1980 [Z 559 IE]
German version: Angew. Chem. *92*, 763 (1980)
Publication delayed at authors' request

CAS Registry numbers:
(1) (R = Bn), 38768-81-9; *(1)* (R = Ac), 40437-08-9; *(2)*, 74808-05-2; *(3)*, 74808-06-3; *(4)*, 74808-07-4; *(5)*, 74808-08-5; *(6)*, 74808-09-6; *(7)*, 74808-10-9; *(8a)*, 56822-49-2; *(8b)*, 74808-11-0; *(8c)*, 74808-12-1; *(8d)*, 41736-89-4; *(8e)*, 74808-13-2; *(8h)*, 74824-34-3; *(9c)*, 74808-14-3; *(9d)*, 70753-59-2; *(9e)*, 74824-28-5; *(9f)*, 74808-15-4; *(9g)*, 56632-57-6; *(9h)*, 74808-16-5; *(9i)*, 4468-72-8; *(9j)*, 34382-09-7; *(9k)*, 74808-17-6

[1] *G. Wulff, G. Röhle*, Angew. Chem. *86*, 173 (1974); Angew. Chem. Int. Ed. Engl. *13*, 157 (1974).
[2] Disaccharide formation by 1-*O*-alkylation, which requires neither haloses nor heavy metal salts, is fundamentally different: *R. R. Schmidt, M. Reichrath*, Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 466 (1979).
[3] See also *S. Shoda, T. Mukaiyama*, Chem. Lett. *1979*, 847.
[4] *J. R. Pougny, J.-C. Jaquinet, M. Nassr, M. L. Milat, P. Sinay*, J. Am. Chem. Soc. *99*, 6762 (1977).
[5] *J. Michel*, investigations for doctoral thesis.
[6] *D. G. Neilson* in *S. Patai*: The Chemistry of Amidines and Imidates. Wiley, London 1975, p. 385.

N-Sulfinylnonafluorobutanesulfonamide—A Supernucleophile[**]

By *Reinhard Bussas* and *Günter Kresze*[*]

A few years ago we had found that sulfinyl-*p*-toluenesulfonamide *(2)* is a very reactive enophile[1]. In the meantime

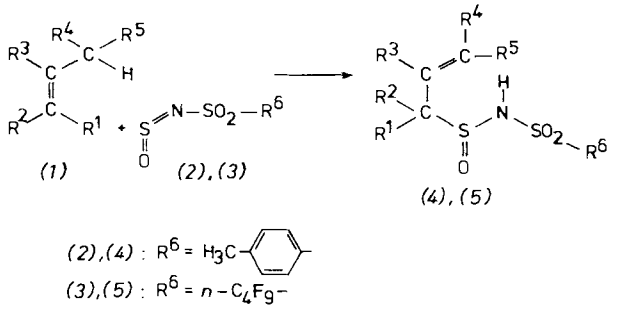


Table 1. Comparison of the ¹H-NMR spectroscopically determined half-lives ($\tau_{1/2}$) [a] in the ene-reaction of alkenes *(1a—g)* with *N*-sulfinylnonafluorobutanesulfonamide *(3)* and with *N*-sulfinyl-*p*-toluenesulfonamide *(2)*.

(1)	R^1	R^4	R^2	R^3	R^5	$\tau_{1/2}$ [min] (3)	(2)
(a)	—$(CH_2)_3$—		H	H	H	1	600
(b)	—$(CH_2)_4$—		H	H	H	1	600
(c)	—$(CH_2)_5$—		H	H	H	1	600
(d)	Cl	H	H	CH_3	H	1	≫6000
(e)	H	H	H	Cl	H	5	12000
(f)	H	H	H	Br	H	5	12000
(g)	H	CH_2OCOCH_3	H	H	H	5	15000

[a] In each case determined in a 3 M $CDCl_3$ solution of *(1)* and *(3)* or *(2)* at 20 °C.

[*] Prof. Dr. G. Kresze, Dipl.-Chem. R. Bussas
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] Reactions of *N*-Sulfinyl Compounds, Part 13. This work was supported by the Fonds der Chemischen Industrie. We thank Bayer AG, Leverkusen, for supplying us with nonafluorobutanesulfonyl fluoride.—Part 12: [4].

Déléris et al.[2] and *Sharpless et al.*[3] have independently published analogous results and presented some interesting possible applications of the 2-alkenesulfinamides *(4)* they have synthesized. In a systematic investigation[4] of the structure-reactivity relations of the enophiles of type *(2)* and the ene components *(1)* we have now found that the enophilicity of *(2)* and similar *N*-sulfinylsulfonamides can be further markedly enhanced by incorporation of strongly electron-attracting groups R^6.

A. Laporterie, J. Dubac, G. Manuel, G. Déléris, J. Kowalski, J. Dunoguès, R. Calas, Tetrahedron *34*, 2669 (1978); *J.-P. Pillot, G. Déléris, J. Dunoguès, R. Calas,* J. Org. Chem. *44*, 3397 (1979); *G. Déléris, J. Dunoguès, R. Calas,* Tetrahedron Lett. *1979*, 4835.

[3] *T. Hori, S. P. Singer, K. B. Sharpless,* J. Org. Chem. *43*, 145 (1978).

[4] *G. Kresze, R. Bussas,* Justus Liebigs Ann. Chem. *1980*, 843.

[5] *H. W. Roesky,* Inorg. Nucl. Chem. Lett. *6*, 807 (1970).

[6] *R. S. Glass, D. L. Smith,* J. Org. Chem. *39*, 3712 (1974); *J. B. Hendrickson, P. L. Skipper,* Tetrahedron *32*, 1627 (1976).

[7] *K. Laping, M. Hanack,* Tetrahedron Lett. *1979*, 1309; *M. Hanack, K. Laping, ibid. 1977*, 4493; *M. Hanack, F. Massa, ibid. 1977*, 661.

Table 2. Characteristic data of the *N*-(nonafluorobutanesulfonyl)-2-alkenesulfinamides *(5)* [a].

(5)	Reaction time [h]	Yield [%]	M.p. [b] [°C]	IR [cm^{-1}] [c] ν_{NH}	^{1}H-NMR [d] *H*—CSO	*H*C=C (2H)	N—H (1H)	^{13}C-NMR [e] *C*—SO—N
(a) [f]	0.5	73	113	3100—2800	3.88 mc (1H)	$ABXY_2$ system: 5.7—6.8 and 6.2—6.3	9.74 s	63.0 63.2
(b) [f]	0.5	76	104	3100—2800	3.96 mc (1H)	$ABXY_2$ system: 5.6—5.8 and 6.1—6.3	9.56 s	67.5 67.7
(c) [f]	0.5	88	79	3100—2800	4.20 mc (1H)	$ABXY_2$ system: 5.4—5.8 and 6.0—6.2	10.00 s	64.2 64.9
(d)	1	79	74	3300—2900	5.80 s (1H)	degenerate AB-system: 5.52 and 5.62	10.0—11.0	84.0
(e)	2	86	86	3500—3100	4.20 "s" (2H)	degenerate AB-system: 5.67 "s"	10.05 s	66.6
(f)	2	89	73	3500—3100	4.48 "s" (2H)	degenerate AB-system: 6.08 and 6.33	10.40 s	68.4
(g)	0.5	83	63	3500—3000	3.90 ("d", J = 7.5 Hz) (2H)	ABX_2Y_2 system: 5.77 and 6.07	8.0—9.0	59.7

[a] All compounds *(5)* gave correct analyses. [b] Start of melting (intervals generally 1 K; as a rule decomposition with evolution of gas and red coloration). [c] KBr disk. [d] δ values, measuring frequency in the case of *(5a)—(5c)* and *(5g)*: 200 MHz; in the case of *(5f)*: 60 MHz; solvent in the case of *(5a)—(5e)* and *(5g)*: CD_3CN; in the case of *(5d)*: $(CD_3)_2CO$, in the case of *(5e)—(5f)*: $CDCl_3$ (internal standard: TMS). [f] Mixture of diastereoisomers.

Thus, *N*-sulfinylnonafluorobutanesulfonamide *(3)*[5] (obtained from nonafluorobutanesulfonyl fluoride in three steps) is about 10^3—10^4 times more reactive than *(2)* (see Table 1).

This finding has parallels in the dramatic increase in dienophilicity of C=C and C≡C bonds by trifluoromethanesulfonyl-[6] or nonafluorobutanesulfonyl-substitution[7]. A surprising feature is the extremely marked effect of varying the residue R^6, which is "insulated" from the reaction center by the sulfonyl group. With *(3)*, very "electron-deficient" alkenes *(1)* can also undergo the ene-reaction which do not react any further [*e.g. (1d)*] or only very slowly and in moderate yields [like *e.g. (1c)* and *(1f)*] with *(2)*. Some characteristic data of 2-alkenesulfonamides *(5)* synthesized so far are given in Table 2.

Procedure

(5): A solution of *(3)* (3.45 g, 10 mmol) in anhydrous tetrachloromethane (5 ml) is treated at −20 °C under dry N_2 with 11 mmol *(1)*. After the requisite reaction time (Table 1) either the precipitate is filtered off under N_2 or the reaction mixture is treated with anhydrous pentane until clouding occurs and the product brought to crystallization at −78 °C. Purification is achieved by dissolution in diethyl ether at 20 °C, addition of pentane, and cooling to −78 °C. The products *(5)* can be stored for a few months at −20 °C in the absence of moisture.

Received: April 18, 1980 [Z 561a IE]
German version: Angew. Chem. *92*, 748 (1980)

[1] *N. Schönberger, G. Kresze,* Justus Liebigs Ann. Chem. *1975*, 1725; *G. Kresze* in *C. M. Stirling:* Organic Sulfur Chemistry. Butterworths, London 1975, p. 65ff.

[2] *G. Déléris, J. Kowalski, J. Dunoguès, R. Calas,* Tetrahedron Lett. *1977*, 4211;

3-Oxa-Ene Reactions of *N*-Sulfinylnonafluorobutanesulfonamide with Alkanones—General Synthesis of 2-Oxoalkanesulfinic Acid Derivatives[**]

By *Günter Kresze* and *Reinhard Bussas*[*]

We have found that *N*-sulfinylnonafluorobutanesulfonamide *(2)* reacts with alkyl-substituted alkanones and cycloalkanones within minutes at 20 °C, and with 1-aryl-2-alkanones within a few hours (direct ^{1}H-NMR spectrometric observations) to give *N*-(nonafluorobutanesulfonyl)-2-oxoalkanesulfinamides *(3)* (see Table 1, cf. [1a]). This finding is of interest, *inter alia*, in connection with the mechanism of oxidation of carbonyl compounds and alkenes with SeO_2[1b].

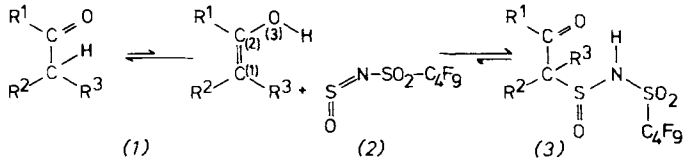
We propose that the enol form of *(1)* reacts in a 3-oxa-ene reaction with *(2)*. This hypothesis is supported by the following observations:

Non-enolizable alkanones such as diphenylmethanone, 1,1,1,3,3,3-hexachloro-2-propanone, and 1-phenyl-2,2,2-trifluoro-1-ethanone do not react with *(2)* at 20 °C[2].

The C—H acidity of *(1)* and analogous compounds[3], which would be decisive in the alternative mechanism of an HX addition[4], plays no significant role, since compounds much more strongly acid than the alkanones presented here

[*] Prof. Dr. G. Kresze, Dipl.-Chem. R. Bussas
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Reactions of *N*-Sulfinyl Compounds, Part 14. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft. We thank Bayer AG, Leverkusen, for supplying nonafluorobutanesulfonyl fluoride.—Part 13: [1a].



(1) (2) (3)

	R^1	R^2	R^3
(a)	C_2H_5	CH_3	H
(b)	C_6H_5	H	H
(c)	C_6H_5	CH_3	H
(d)	C_6H_5	C_2H_5	H
(e)	C_6H_5	Br	H
(f)	4-Br—C_6H_4	H	H
(g)	4-Cl—C_6H_4	H	H
(h)	4-O_2N—C_6H_4	H	H
(i)	3-O_2N—C_6H_4	H	H
(k)	α-Naphthyl	H	H
(l)	C_6H_5	CH_3	CH_3
(m)	—$(CH_2)_3$—		H
(n)	—*o*-CH_2—C_6H_4—$(CH_2)_2$—		H
(o)	—$(CH_2)_4$—		H
(p)	—*o*-CH_2—C_6H_4—$(CH_2)_2$—		H
(q)	—$(CH_2)_5$—		H
(r)	—$(CH_2)_{10}$—		H

The formation of *(3)* is reversible: on allowing a solution of the product *(3)* to stand, the signals of the educts *(1)* appear in the NMR spectrum.

3-Oxa-ene reactions have previously been observed on only few occasions, *e.g.* in the cyclization of alkenones[5], in the reaction of 1-(1,3,5-triazin-2-yl)-2-propanone with enophiles[6], and in the reaction of 1,3-dicarbonyl compounds with 2-oxopropanedinitrile[7]. In our opinion the formation of *N*-fluorosulfonyl-β-oxocarboxamides from α-methylene ketones and fluorosulfonyl isocyanate can also be regarded as a 3-oxaene reaction[8].

The isolation of product *(3)* now confirms the possibility of such a mechanism also for the oxidation of *(1)* with SeO_2; moreover, the reaction *(1)*→*(3)* opens up a facile entry to 2-oxoalkanesulfinic acid derivatives which were previously reported unobtainable[9a] or only obtainable in certain cases (without α-H atom)[9b].

Procedure

(3): A solution of *(2)* (3.45 g, 10 mmol) in anhydrous CCl_4 (5 ml) is treated with 11 mmoles of *(1)* at 20 °C [in the case of *(1a)*, *(1m)*, *(1o)*—*(1r)* at 0 °C] under dry nitrogen. After the requisite reaction time (Table 1) either the precipitate is filtered off under N_2 or the reaction mixture is treated with anhydrous pentane until clouding occurs and then brought to crystallization at −78 °C. Purification is achieved by recrystallization from diethyl ether/pentane. The products *(3)* can be stored for months at −20 °C in the absence of moisture.

Table 1. Characteristic data of the *N*-(nonafluorobutanesulfonyl)-2-oxoalkanesulfinimides *(3)*.

(3)	Reaction time [h]	Yield [%]	M.p. [a] [°C]	IR [cm^{-1}] [b] $\nu_{C=O}$	IR [b] ν_{NH}	^{1}H-NMR [c] *H*—CSO	^{1}H-NMR [c] N—*H* (1H)	^{13}C-NMR [d] —*C*—SO—N	^{13}C-NMR [d] *C*=O
(a) [e]	0.5	86	82	1710	3500—3000	4.34 (q, J=7)	9.79 s	70.5	206.7
						4.40 (q, J=7) (1H)		71.9	207.7
(b)	1.5	82	108	1680	3500—3000	4.97 s (2H)	10.14 s	65.8	192.6
(c) [e]	4	91	112	1670	3400—2900	5.27 (q, J=7)	9.86 s	67.7	196.0
						5.34 (q, J=7) (1H)		68.6	197.3
(d) [e]	20	83	88	1670	3500—3000	5.26 (t, J=7)	9.92 s	72.7	196.3
						5.29 (t, J=7) (1H)		74.3	197.1
(e) [e]	140	77	101	1680	3500—3100	6.52 (s)	10.12 s	61.5	190.5
						6.69 (s) (1H)		65.6	191.2
(f)	5	93	128	1675	3500—2800	4.928 [f]	10.14 s	65.5	191.7
						4.933			
(g)	5	95	125	1675	3500—2900	4.933 [f]	10.13 s	65.6	191.7
						4.938			
(h)	15	89	106	1685	3500—2900	5.003 [f]	10.14 s	66.0	193.1
						5.008			
(i)	10	84	82	1690	3500—3000	5.034 [f]	10.17 s	65.6	191.2
						5.046			
(k)	3.5	92	110	1670	3500—2900	5.10 s (2H)	10.21 s	65.7	192.3
(l)	20	80	112	1665	3200—2900	[1.97 s (6H)] [g]	9.20 s	80.8	198.9
(m) [e]	0.5	94	84	1740	3500—3000	3.94 (t, J=11)	10.11 s	68.4	211.3
						3.99 (t, J=9)		72.5	215.0
(n) [e]	0.5	90	111	1700	3500—3000	4.47 mc (1H)	10.23 s	67.5	198.0
								71.3	200.7
(o) [e]	0.5	85	104	1700	3500—3000	4.12 (t, J=6)	9.81 s	74.5	206.4
						4.17 (t, J=6)		75.4	206.7
(p) [e]	1	79	94	1670	3500—2800	4.40 mc (1H)	9.96 s	70.6	192.5
								72.5	193.2
(q) [e]	0.5	87	96	1685	3500—3000	4.35 mc (1H)	9.84 s	76.7	209.0
								77.3	209.3
(r) [e]	0.5	91	100	1705	3500—3100	4.49 mc (1H)	9.85 s	76.0	206.3
								77.3	206.6

[a] Beginning of melting (interval generally 1 K; as a rule, decomposition with evolution of gas and red coloration). [b] KBr disk. [c] δ values, measuring frequency: 200 MHz; solvent: CD_3CN (internal standard: DMS); couplings in Hz. [d] δ values, measuring frequency: 15 MHz; solvent CD_3CN (internal standard: DMS). [e] Mixture of diastereomers. [f] 2H, diastereotopism. [g] $(H_3C)_2C$—SO—N.

(*e.g.* nitroalkanes or malonodinitrile) do not react with *(2)* under analogous conditions.

The observed autocatalysis of the reaction—once formed, *(3)* as strong acid (NH acidified by sulfonyl- and sulfinyl-group) catalyzes enol formation—also supports the proposed mechanism.

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/0909-0738 $ 02.50/0 Angew. Chem. Int. Ed. Engl. 19 (1980) No. 9

Received: April 18, 1980 [Z 561 b IE]
German version: Angew. Chem. 92, 750 (1980)

[1] a) *R. Bussas, G. Kresze*, Angew. Chem. *92*, 748 (1980); Angew. Chem. Int. Ed. Engl. *19*, 732 (1980); b) *K. B. Sharpless, K. M. Gordon*, J. Am. Chem. Soc. *98*, 300 (1976); *L. M. Stephenson, D. R. Speth*, J. Org. Chem. *44*, 4683 (1979).

[2] Fluoride ions catalyze the reaction of hexafluoropropanone with *N*-sulfinylaniline: *Yu. V. Zeifman, E. G. Ter. Gabrielyan, D. P. Del'tsora, N. P. Gambaryan*, Izv. Akad. Nauk SSSR *2*, 396 (1979); aldehydes and α-diketones react with *N*-sulfinyl-*p*-toluenesulfonamide with evolution of SO_2 to give imines: *G. Kresze, R. Albrecht*, Angew. Chem. *74*, 781 (1962); Angew. Chem. Int. Ed. Engl. *1*, 595 (1962); *R. Albrecht, G. Kresze, B. Mlakar*, Chem. Ber. *97*, 483 (1964); *G. Kresze, D. Sommerfeld, R. Albrecht, ibid. 98*, 601 (1965); *R. Albrecht, G. Kresze, ibid. 98*, 1431 (1965).

[3] *F. G. Bordwell*, Pure Appl. Chem. *49*, 963 (1977).

[4] *G. Kresze, W. Wucherpfennig*, Angew. Chem. *79*, 109 (1967); Angew. Chem. Int. Ed. Engl. *6*, 149 (1967).

[5] *R. Block, P. LePerchec, F. Rouessac, J.-M. Conia*, Tetrahedron *24*, 5971 (1968).

[6] *Y. Bessière-Chrétien, H. Serne*, J. Heterocycl. Chem. *11*, 317 (1974).

[7] *K. Kociolek, M. T. Leplawy*, Synthesis *1977*, 778; *K. Kociolek, M. Leplawy*, Rocz. Chem. *49*, 1841 (1975).

[8] *J. Sander, K. Clauss*, Angew. Chem. *92*, 138 (1980); Angew. Chem. Int. Ed. Engl. *19*, 131 (1980); cf. also *K. Clauss, H. Jensen, ibid. 85*, 965 (1973) and *12*, 869 (1973).

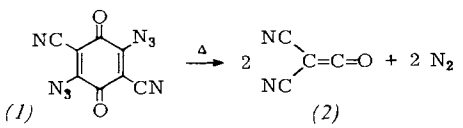
[9] a) *E. J. Corey, T. Durst*, J. Am. Chem. Soc. *90*, 5548 (1968); b) *R. P. Gupta, J. S. Pizey*, Phosphorus Sulfur *7*, 325 (1979).

Direct Detection of Dicyanoketene in the Gas Phase[**]

By *Alfred Hotzel, Richard Neidlein, Reinhard Schulz*, and *Armin Schweig*[*]

Cyanoketenes are exceptionally reactive and are therefore regarded as highly unstable[1]. Evidence for their existence could only be gained indirectly by trapping reactions, except in the case of sterically stabilized *tert*-butyl- and *tert*-pentylcyanoketenes. Dicyanoketene itself was also postulated in 1978 on the basis of trapping products[2].

We now wish to report the generation of free dicyanoketene *(2)* in the gas phase and its characterization by UV photoelectron spectroscopy and mass spectrometry.



(1) *(2)*

On slow warming of 2,5-diazido-3,6-dicyano-1,4-benzoquinone *(1)*[3] to 60 °C *in vacuo* ($p < 5 \times 10^{-2}$ mbar) a gas mixture could be pumped off over a longer period of time whose PE spectrum (Fig. 1) showed it to contain not only nitrogen and a small amount of carbon dioxide[4] but also a further compound having the vertical ionization energies ① 10.56 eV, ② 13.25 eV and 13.49 eV. Band ① is split into partial vibrational bands separated by 1150 cm^{-1} and its shape resembles that of the lowest-energy $^2B_1$ PE band of ketene[5].

The high intensity of band ② is attributable to superposition of several ionizations. PERTCI calculations[6] with MNDO wave functions[7] permit assignment of the bands ①/$^2B_1(\pi)$ and ②/$^2B_2(\sigma)$, $^2A_1(\sigma)$, $^2A_2(\pi)$, and $^2B_2(\sigma)$ to ionizations of dicyanoketene *(2)*.

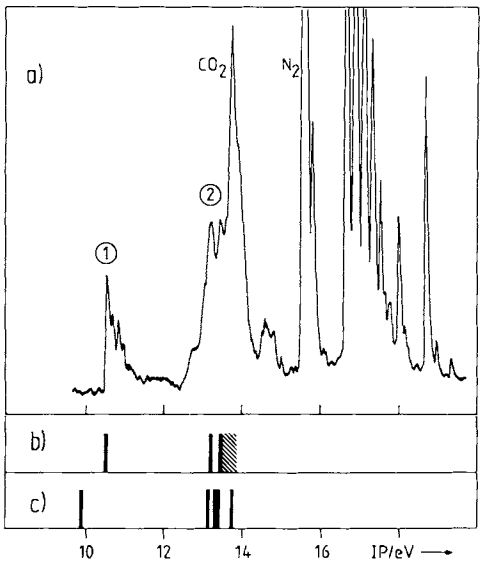


Fig. 1. a) He-I photoelectron spectrum of the gaseous product mixture obtained on heating 2,5-diazido-3,6-dicyano-1,4-benzoquinone *(1)* to 60 °C/$< 5 \times 10^{-2}$ mbar; b) experimental, and c) calculated (MNDO-PERTCI) vertical ionization energies of dicyanoketene *(2)*.

In view of the unusual reaction conditions—the highly reactive dicyanoketene is pumped off from the surface of the decomposing quinone *(1)* which does not itself go into the gas phase even in a high vacuum—further independent evidence appeared desirable.

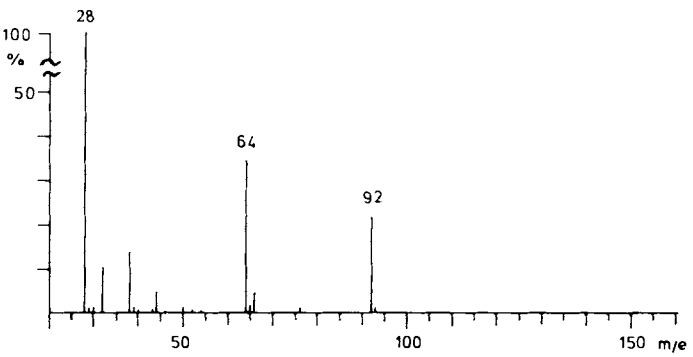
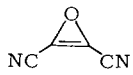


Fig. 2. 100-eV mass spectrum of the dicyanoketene *(2)* obtained together with nitrogen on heating 2,5-diazido-3,6-dicyano-1,4-benzoquinone *(1)* to 85 °C in the ion source.

To this end we slowly heated the quinone *(1)* in the ion source of a mass spectrometer until vigorous evolution of nitrogen occurred (85 °C). The mass spectrum (Fig. 2) unequivocally confirms the formation of dicyanoketene *(2)*. High resolution spectra of the two characteristic peaks at the mass numbers 92 (M^+) and 64 ($M^+ - CO$) afforded the empirical formula C_4N_2O (calc. 92.0011, exp. 92.0011) and C_3N_2 (calc. 64.0061, exp. 64.0060). Fragmentation of the molecular cation with loss of CO is characteristic of ketenes[8] and rules out the two C_4N_2O isomers *(3)* and *(4)* as possible competing products in the decomposition of *(1)*. This is in agreement with MNDO calculations (standard enthalpies of formation: *(2)* 52 kcal/mol; *(3)* 118 kcal/mol; *(4)* 101 kcal/mol).

[*] Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)
Prof. Dr. R. Neidlein, Dr. A. Hotzel
Pharmazeutisch-chemisches Institut der Universität
Im Neuenheimer Feld 364, D-6900 Heidelberg (Germany)

[**] Part 89 of Theory and Application of Photoelectron Spectroscopy. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 88: *R. Schulz, A. Schweig, C. Wentrup, H.-W. Winter*, Angew. Chem., in press

(3)  NC–≡–O–CN (4)

Thus dicyanoketene (2), like dicyanothioketene[9], is stable at low pressure in the gas phase.

Received: February 29, 1980 [Z 562a IE]
German version: Angew. Chem. 92, 751 (1980)

CAS Registry numbers:
(1), 66563-24-4; (2), 4361-47-1; (3), 74408-85-8; (4), 74408-84-7

[1] R. C. De Selms, Tetrahedron Lett. 1969, 1179; H. W. Moore, W. Weyler, H. R. Shelden, ibid. 1969, 3947; H. W. Moore, W. Weyler, J. Am. Chem. Soc. 92, 4132 (1970); W. Weyler, W. G. Duncan, H. W. Moore, ibid. 97, 6187 (1975).

[2] R. Neidlein, E. Bernhard, Angew. Chem. 90, 395 (1978); Angew. Chem. Int. Ed. Engl. 17, 369 (1978).

[3] We are grateful to Dr. R. Gartner for the preparation of 2,5-dichloro-3,6-dicyano-1,4-benzoquinone, from which (1) was obtained according to [2]. The premature deflagration of (1) in the experiments described could be suppressed by preparation of (1) in the presence of roughly twice the amount of finely divided calcium carbonate ("solid state dilution"). The mixture of (1) and $CaCO_3$ was thoroughly dried at 0 °C and 10^{-6} mbar prior to each experiment.

[4] It could be demonstrated by mass spectrometry that carbon dioxide is formed on thermal decomposition of the (di- or polymeric?) byproducts. This reaction becomes increasingly pronounced with rising temperature, but plays only a minor role below 100 °C. Increasing temperature considerably strengthened the mass peak at $m/e = 44$ after that at $m/e = 92$ had disappeared almost completely.

[5] D. Hall, J. P. Maier, P. Rosmus, Chem. Phys. 24, 373 (1977).

[6] H. L. Hase, G. Lauer, K.-W. Schulte, A. Schweig, Theor. Chim. Acta 48, 47 (1978); the geometry was optimized by MNDO [7].

[7] M. J. S. Dewar, W. Thiel, J. Am. Chem. Soc. 99, 4899 (1977).

[8] J. Seibl: Massenspektrometrie. Akademische Verlagsgesellschaft, Frankfurt am Main 1974.

[9] R. Schulz, A. Schweig, Angew. Chem. 92, 752 (1980); Angew. Chem. Int. Ed. Engl. 19, 740 (1980).

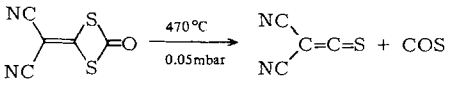
Direct Detection of Dicyanothioketene in the Gas Phase[**]

By *Reinhard Schulz* and *Armin Schweig*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

Dicyanothioketene (2) has been formulated as an intermediate on several occasions[1]; however, all attempts to isolate this species or to detect it by spectroscopy have so far failed. Not even monocyanothioketenes have yet been identified directly[2].

We have now succeeded in directly detecting this apparently highly reactive molecule by variable temperature photoelectron spectroscopy (VTPES)[3] on gas phase pyrolysis of 2-(4-oxo-1,3-dithietan-2-ylidene)malonitrile (1)[1a]. A previous attempt to generate (1) in the gas phase by this reaction and to isolate it in solution at low temperature afforded only dimeric and polymeric material[4].



(1) (2)

The reaction (1)→(2) was performed in a flash pyrolysis reactor (stainless steel tube, 20 × 0.6 cm; *ca.* 5×10^{-2} mbar) directly above the ionization region of a modified PS 18 photoelectron spectrometer and went to completion at 470 °C. The PE spectrum of the starting material (1) (Fig. 1a) shows bands at ① 10.00 eV/$^2B_1(\pi)$, ② 10.95—11.10 eV/$^2A_2(\pi)$ and $^2B_2(n)$, ③ 12.80 eV/$^2B_1(\pi)$, ④ 13.08 eV/$^2B_2(\sigma)$ and $^2A_1(\sigma)$ and ⑤ 13.70 eV/$^2A_2(\pi)$[5]. The PE spectrum of the pyrolysis products (Fig. 1b) contained not only the known bands of carbon oxide sulfide[6] but also the new bands at ① 9.94 eV/$^2B_1(\pi)$, ② 12.79 eV/$^2B_2(\sigma)$, ③ 13.00—13.8 eV/$^2B_1(\pi)$, $^2B_2(\sigma)$, $^2A_1(\sigma)$ and $^2A_2(\pi)$[5a]. Band ① is split into vibrational partial bands separated by 1500 cm^{-1} and expectedly[7]

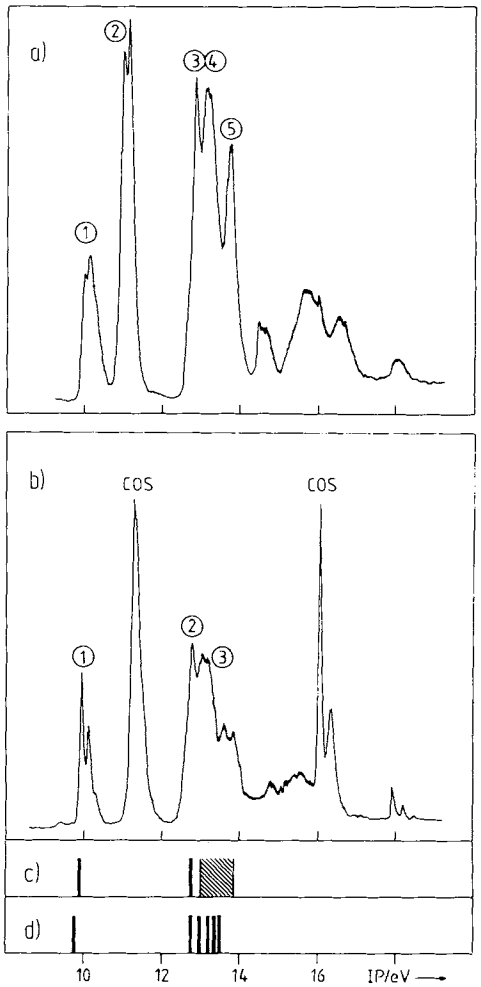
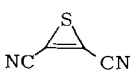


Fig. 1. He-I photoelectron spectrum of a) the starting material (1) and b) its pyrolysis products at 470 °C; c) experimental and d) calculated (MNDO-PERTCI) vertical ionization energies of dicyanothioketene (2).

shows the same fine structure as the energetically lowest-lying $^2B_1(\pi)$ band in the PE spectrum of thioketene[8]. The identity of dicyanothioketene (2) follows not only from the extremely clear-cut reaction but also from the good agreement between the experimental vertical ionization energies and those predicted by MNDO[9a]-PERTCI[9b] calculations (Fig. 1). The ionization energies are expectedly smaller than for dicyanoketene[10]. The energy difference between the $^2B_1(\pi)$ states of dicyanoketene and dicyanothioketene (0.7 eV) is in excellent agreement with the corresponding difference in the case of the ketene/thioketene pair[8].

(3)  NC–≡–S–CN (4)

[*] Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

[**] Part 90 of Theory and Application of Photoelectron Spectroscopy. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 89: [10].

Among the three isomers *(2)*, *(3)*, and *(4)*, MNDO calculations with optimized molecular geometries show dicyanothioketene *(2)* to have the lowest energy content (standard enthalpies of formation: *(2)* 110 kcal/mol; *(3)* 134 kcal/mol; and *(4)* 122 kcal/mol). These values suggest that it might well be possible to generate thiirenedicarbonitrile *(3)* by photochemical methods.

Like dicyanoketene[10], free dicyanothioketene *(2)* is stable in the gas phase at low pressure. Unlike dicyanoketene, however, *(2)* can readily be generated continuously over a prolonged period in a flow system by gas phase pyrolysis.

Received: February 29, 1980 [Z 562b IE]
German version: Angew. Chem. *92*, 752 (1980)

CAS Registry numbers:
(1), 13157-38-5; *(2)*, 54856-36-9; *(3)*, 74808-29-0; *(4)*, 74808-30-3

[1] a) *K. Dickoré, R. Wegler*, Angew. Chem. *78*, 1023 (1966); Angew. Chem. Int. Ed. Engl. *5*, 970 (1966); b) *R. Neidlein, H. G. Reuter*, Arch. Pharm. (Weinheim) *308*, 189 (1975).

[2] *E. Schaumann, J. Ehlers, H. Mrotzek*, Justus Liebigs Ann. Chem. *1979*, 1734.

[3] *A. Schweig, H. Vermeer, U. Weidner*, Chem. Phys. Lett. *26*, 299 (1974); *W. Schäfer, A. Schweig*, Z. Naturforsch. *A 30*, 1785 (1975); *R. Schulz, A. Schweig*, Angew. Chem. *92*, 52 (1980); Angew. Chem. Int. Ed. Engl. *19*, 69 (1980).

[4] *G. Seybold, Ch. Heibl*, Chem. Ber. *110*, 1225 (1977).

[5] Assignment according to MNDO [9a]-PERTCI [9b] calculations with optimized molecular geometries; b) assignment by comparison of He-I with He-II intensities; cf. *P. Dechant, A. Schweig, W. Thiel*, Angew. Chem. *85*, 358 (1973); Angew. Chem. Int. Ed. Engl. *12*, 308 (1973).

[6] *D. W. Turner, C. Baker, A. D. Baker, C. R. Brundle:* Molecular Photoelectron Spectroscopy. Wiley-Interscience, London 1970.

[7] The PE band of the lowest-energy $^2B_1(\pi)$ state of dicyanoketene has the same fine structure as the corresponding band of ketene [10].

[8] *P. Rosmus, B. Solouki, H. Bock*, Chem. Phys. *22*, 453 (1977).

[9] a) *M. J. S. Dewar, W. Thiel*, J. Am. Chem. Soc. *99*, 4899 (1977); *M. J. S. Dewar, M. L. McKee, H. S. Rzepa, ibid. 100*, 3607 (1978); b) *H.-L. Hase, G. Lauer, K.-W. Schulte, A. Schweig*, Theor. Chim. Acta *48*, 47 (1978).

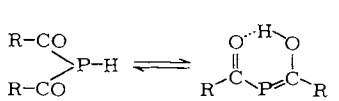
[10] *A. Hotzel, R. Neidlein, R. Schulz, A. Schweig*, Angew. Chem. *92*, 751 (1980); Angew. Chem. Int. Ed. Engl. *19*, 739 (1980).

Lithium Dibenzoylphosphide · 1,2-Dimethoxyethane —A New 2-Phospha-1,3-dionate[**]

By *Gerd Becker, Matthias Birkhahn, Werner Massa*, and *Werner Uhl*[*]

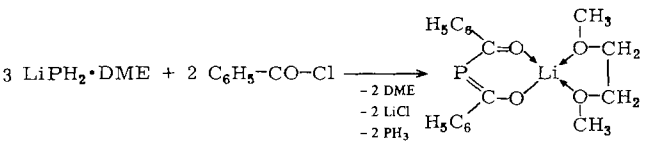
Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

The diacylphosphanes *(1)*, $R = CH_3$, $(CH_3)_3C$, synthesized so far show a remarkable keto-enol tautomerism and resemble 1,3-diketones in their properties[1]. According to X-ray structure analyses of nickel bis(dipivaloylphosphide)·DME[2] (DME = 1,2-dimethoxyethane) and of aluminum tris(dibenzoylphosphide)[3a] this similarity is also shown by 2-phospha-1,3-dionates; the metal ions are not coordinated to the phosphorus atoms but in chelate rings to the oxygen atoms of the anions.



(1)

In order to synthesize the hitherto unknown dibenzoylphosphane *(1)*, $R = C_6H_5$, we treated monolithium phosphide·DME[4] with benzoyl chloride in DME. However, instead of the expected monobenzoylphosphane, lithium dibenzoylphosphide·DME *(2)* was formed with slow evolution of phosphane.



(2)

The reaction course can be rationalized by assuming formation of the monosubstituted compound, subsequent lithium/hydrogen exchange, and renewed reaction with an excess of benzoyl chloride. The resulting dibenzoylphosphane reacts with lithium phosphide to form *(2)*.

Compound *(2)* was characterized by elemental analysis and by its NMR and IR data. The ^{31}P- and ^{13}C-NMR signals of the C—P—C group show a downfield shift[5] as has been observed in similar compounds[1b,3]. Since the poor solubility in apolar solvents containing no DME precluded determination of the molecular size and constitution, we investigated *(2)* by an X-ray structure analysis (see Fig. 1).

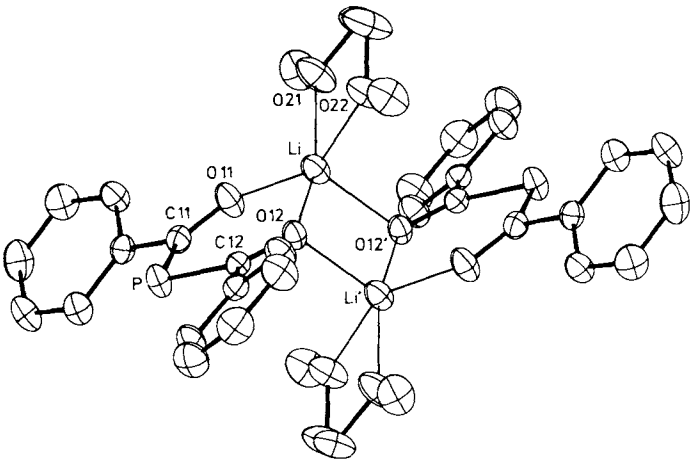


Fig. 1. ORTEP plot of the molecular structure of dimeric lithium dibenzoylphosphide·1,2-dimethoxyethane. The vibrational ellipsoids correspond to 50% probability. *(2)*, space group $P2_1/c$, with $a = 1907.1(7)$, $b = 762.6(7)$, $c = 1259(2)$ pm; $\beta = 104.5(1)°$; 4 formula units. 1907 independent, observed ($F > \sigma$) reflections recorded on an automatic four-circle diffractometer CAD4 (Enraf-Nonius) at $-80\,°C$ ($Mo_{K\alpha}$ radiation, $4° < 2\theta < 48°$) and corrected in the conventional way; $R_w = 0.034$.

(2) exists as 2-phospha-1,3-dionate; the lithium ion is bonded to all oxygen atoms of the ligands. No monomer is present in the solid state; by the inversion as a crystallographic symmetry operation the molecules are linked pairwise to form dimers (Fig. 1). The coordination number of lithium is raised to 5 by bonding to a further oxygen atom O12′ belonging to the inverse dibenzoylphosphide ion; the two lithium atoms of the dimer are located 45 pm above the basal planes of two edge-linked, somewhat distorted square pyramids of O atoms. Although the Li—Li distance (283 pm) is shorter than in the element (304 pm)[6a], metal-metal interaction can be ruled out at a covalent radius of 134 pm[6b]. Similar association is observed in other 1,3-dionates[6c].

[*] Prof. Dr. G. Becker, M. Birkhahn, Dr. W. Massa, Dipl.-Chem. W. Uhl
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] Part 14 of Acyl- and Alkylidenephosphanes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. 13. Mitteilung: *G. Becker, W. Uhl*, Z. Anorg. Allg. Chem., in press.

As in phosphamethinecyanines, λ^3-phosphorins[7], and phosphaferrocenes[8], the third valence of the phosphorus is involved in partial double bonds in the conjugated system of *(2)*. The bond lengths and angles (Table 1) in the dibenzoylphosphide ion are similar to those of the aluminum compound[3a]. The larger ionic radius of the lithium ion (59 pm), however[9], results in an increase of the intramolecular O11—O12 distance ("bite") to 279 pm. The bond lengths of the differently coordinated oxygen atoms O11 and O12 differ only slightly. As expected, the formally singly negatively charged phosphide anion is bound by shorter bonds to the lithium than the uncharged DME. Both chelate rings are not planar; lithium (72 pm) and phosphorus (11 pm) are located above the plane of the six-membered ring formed by the atoms C11, O11, O12, and C12.

Table 1. Selected structural parameters of *(2)*. For clarity, in Figure 1 the carbon atoms of the phenyl groups as well as C8n and C9n of the DME ligand have not been labeled. Atoms from the inverse molecule are marked with an apostrophe.

Bond lengths [pm]			Bond angles [°]	
	n=1	n=2		
P—C1n	181.5(3)	179.6(3)	C11—P—C12	101.8(1)
C1n—C2n	152.0(4)	151.1(4)	P—C11—O11	128.4(2)
C1n—O1n	125.4(3)	127.4(2)	P—C12—O12	128.4(2)
O1n—Li	194.4(5)	201.5(4)	C11—O11—Li	136.0(2)
O2n—Li	215.2(5)	210.4(5)	C12—O12—Li	132.4(2)
C8n—O2n	140.0(4)	138.0(4)	O11—Li—O12	89.7(2)
C81—C82	146.8(5)	—	O11—Li—O21	89.5(2)
O2n—C9n	141.3(4)	142.7(5)	O12—Li—O22	94.6(2)
Li—O12′	204.4	—	O21—Li—O22	75.6(2)
Li—Li′	283.2	—	O11—Li—O22	147.3(3)
			O12—Li—O21	159.7(3)

Procedure

All operations must be performed under highly pure Ar with dry (Na, $LiAlH_4$) solvents.—A solution of monolithium phosphide·DME (20.3 g, 156 mmol) in DME (200 ml) is added dropwise to a stirred, cooled (−35 °C) solution of benzoyl chloride (14.6 g, 104 mmol) in DME (50 ml). The mixture is then warmed to +20 °C and stirring is continued until evolution of phosphane has ceased (*ca.* 12 h). The precipitated lithium chloride is filtered off and washed with small amounts of DME. The solvent is vacuum distilled from the filtrate and the residue is dissolved in DME. At −25 °C, air-stable, orange-red, hexagonal prisms crystallize from the solution: yield 15.1 g (44.7 mmol, 86%), dec. p. 308 °C (under argon).

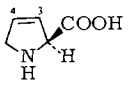
Received: March 10, 1980 [Z 563 IE]
German version: Angew. Chem. *92*, 756 (1980)

[1] a) *G. Becker*, Allg. Prakt. Chem. *23*, 73 (1972); *G. Becker, H. P. Beck*, Z. Anorg. Allg. Chem. *430*, 77 (1977); b) *G. Becker, M. Rössler, ibid.*, in press.
[2] *G. Becker, O. Mundt, M. Rössler*, Z. Anorg. Allg. Chem., in press.
[3] a) *G. Becker, H. P. Beck*, Z. Anorg. Allg. Chem. *430*, 91 (1977); b) *G. Becker, O. Mundt, ibid. 443*, 53 (1978).
[4] *H. Schäfer, G. Fritz, W. Hölderich*, Z. Anorg. Allg. Chem. *428*, 222 (1977).
[5] ^{13}C-NMR (C_6D_6 with small amounts of DME): δ=225, $^1J_{P,C}$=86.5 Hz; ^{31}P-NMR (DME): δ=64.0 (downfield shift).
[6] a) International Tables for X-Ray Crystallography. Vol. 3. Kynoch Press, Birmingham 1968, p. 278; b) *J. E. Huheey*: Inorganic Chemistry. Harper and Row, New York 1972, p. 184; c) *R. C. Mehrotra, R. Bohra, D. P. Gaur*: Metal β-Diketonates and Allied Derivatives. Academic Press, London 1978.
[7] *K. Dimroth*, Fortschr. Chem. Forschung *38*, 1 (1973).
[8] *F. Mathey, A. Mitschler, R. Weiss*, J. Am. Chem. Soc. *99*, 3537 (1977).
[9] *R. D. Shannon, C. T. Prewitt*, Acta Crystallogr. *B 25*, 925 (1969).

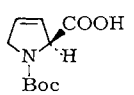
Direct Method for the Synthesis of *N*-Boc-L-3,4-didehydroproline[**]

By *Jean-Robert Dormoy, Bertrand Castro, Georges Chappuis, Ulrich Stefan Fritschi*, and *Peter Grogg*[*]

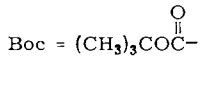
The incorporation of L-3,4-didehydroproline *(1)* into biologically active peptides very seldom results in loss of activity[1-3]; in fact, in some cases the activity even increases, with reduced toxicity of the product[3,4]. Deuterium and tritium can also be incorporated into biologically active peptides *via* dehydroproline[1,3].



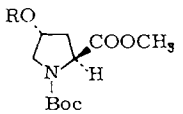
(1)



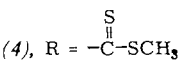
(2)

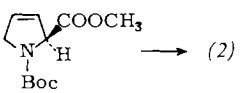


Hitherto, *(1)* had to be prepared by resolution[1,5] from the technically difficultly accessible racemic educt[6]. We have now succeeded in synthesizing *N*-Boc-L-3,4-didehydroproline *(2)* directly from the naturally occurring L-4-hydroxyproline.



(3), R = H

(4), R = 



(5)

N-Boc-L-4-hydroxyproline methyl ester *(3)*[7] was converted (90%) into the *S*-methyl xanthogenate *(4)*[8], which on Tschugaeff pyrolysis[9] gave the protected 3,4-didehydro ester *(5)* in 64% yield together with some protected 4,5-didehydro ester (3—5%) and educt *(3)* (5—9%). Hydrolysis of *(5)* afforded *(2)* in (70%) yield (see Procedure).—The 250-MHz ^{1}H-NMR spectra of the compounds *(4)* and *(5)* and of the 4,5-didehydro ester are given in Table 1.

Table 1. 250-MHz ^{1}H-NMR shifts of the ring protons in the compounds *(4)*, *(5)* and in the 4,5-didehydro isomer of *(5)* (δ values, in $CDCl_3$, TMS int., multiplets).

Cpd.	H-2 (1H)	H-3	H-4 (1H)	H-5
(4) [b]	4.39 [a] 4.47	2.27 [a] 2.33 (2H)	5.96	3.82 (2H)
(5)	4.95 [a] 5.01	5.74 (1H)	6.01	4.23 (2H)
(5)-isomer	4.61	3.06 (2H)	4.93	6.52 [a] 6.63 (1H)

[a] In some cases the conformers could be recognized by separate signals. *H. L. Maia, K. G. Orrell, H. N. Rydon*, Chem. Commun. *1971*, 1209; *J. Savrda* in *A. Loffet*: Peptides 1976, Brussels 1976, p. 653. [b] SCH_3: δ=2.56 (s, 3H).

Procedure

(4): *(3)* (10 mmol), tetrabutylammonium hydrogen sulfate (10 mmol) and CS_2 (12 mmol) were dissolved in benzene (20

[*] Prof. Dr. B. Castro, Dr. J. R. Dormoy
Laboratoire de Chimie Organique II, Université de Nancy I
Case officielle 140, F-54037 Nancy (France)
Dr. G. Chappuis, U. S. Fritschi, Dr. P. Grogg
Bachem Feinchemikalien AG
CH-4416 Bubendorf (Switzerland)

[**] Dehydroamino Acids, Part 1.

ml) at room temperature. 20 ml of 50% NaOH was added dropwise to the vigorously stirred solution; after a further 5 min the solution turned yellowish-brown. The solution was treated with 11 mmol of methyl iodide, stirred for 10 min, and then poured into an ether/ice mixture (150 ml/50 g). The aqueous phase was separated off and extracted with ether. The combined organic extracts were dried over $MgSO_4$, treated with activated charcoal, filtered, and the solvent removed in a vacuum. A yellowish oily residue crystallized on cooling. Recrystallization from ether/*n*-hexane furnished *(4)* in 90% yield as colorless crystals of m.p. 73—75 °C.

(2): 1 g (2.98 mmol) of *(4)* was completely decomposed (*ca.* 4—6 h) by Tschugaeff pyrolysis[9] (170—180 °C/12 torr). Column chromatographic separation (ethylacetate/*n*-hexane 1:3) afforded *(5)* (64%) as colorless oil and its 4,5-didehydro isomer (5%) together with some *(3)* (6%).—A solution of *(5)* (0.5 g, 2.2 mmol) in 15 ml H_2O/dioxane (1:1) was hydrolyzed (2 hours) with 5 ml of 50% NaOH. The solvent was removed in a vacuum and the crude product recrystallized from ether/*n*-hexane; yield 0.328 g *(2)*, m.p. 92—95 °C; $[\alpha]_D^{20} = -249.8$ ($c = 1.04$ in MeOH)[1].

Received: April 10, 1980 [Z 564 IE]
German version: Angew. Chem. *92*, 761 (1980)

[1] *A. M. Felix, Ch. Wang, A. A. Liebman, Ch. M. Delaney, T. Mowles, B. A. Burghardt, A. M. Charnecki, J. Meienhofer,* Int. J. Pept. Protein Res. *10*, 299 (1977).
[2] *Ch. R. Botos, C. W. Smith, Y.-L. Chan, R. Walter,* J. Med. Chem. *22*, 926 (1979).
[3] *G. H. Fisher, W. Ryan,* FEBS Lett. *107*, 273 (1979).
[4] *S. Natarajan, M. E. Condon, M. S. Cohen, J. Reid, D. W. Cushman, B. Rubin, M. A. Ondetti:* 6th American Peptide Symposium. June 17—22, Abstract E3, 62 (1979).
[5] *S. S. Kerwar, A. M. Felix, R. J. Marcel, I. Tsay, R. A. Salvador,* J. Biol. Chem. *251*, 503 (1976).
[6] *A. Corbella, P. Gariboldi, G. Jommi, F. Mauri,* Chem. Ind. (London) *1969*, 583.
[7] *(3)*, m.p. 97—98 °C, $[\alpha]_D^{22} = -79 \pm 0.5$ ($c = 1.03$ in MeOH) is obtainable from Bachem Feinchemikalien AG, CH-4416 Bubendorf, Switzerland.
[8] *P. Dicesare, B. Gross,* Synthesis, in press.
[9] *C. H. De Puy, R. W. King,* Chem. Rev. *60*, 431 (1960); *H. R. Nace,* Org. React. *12*, 57 (1962).

Dehydroxylation of Hydrogen Zeolites: Conditions for the Preparation of Thermally Stable Catalysts

By *Laszlo Marosi*[*]

Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

Hydrogen zeolites of Y type are finding increasing use as industrial catalysts for transformations of hydrocarbons; they are produced by thermal decomposition of the ammonium form[1]. However, catalytically inactive products may also arise. One possible reason for the loss of activity might be the elimination of the catalytically active hydroxyl groups (as water) together with ammonia on heating. The mechanism of this scientifically and industrially important dehydroxylation process is still a matter of controversy. In particular, it is unclear whether elimination of water in a shallow bed involves formation of tricoordinated (Si^+Al) sites or of oxoaluminum cations[2]. Our studies on the thermal dehydroxylation of HX and HY zeolites showed that elimination of water *in vacuo* or under shallow bed conditions[3] proceeds in two steps with formation of Lewis acid centers having different properties.

The first step affords partially dehydroxylated zeolites whose properties are compatible with the presence of tricoordinated silicon and aluminum in the crystal lattice.

In the second step framework aluminum atoms migrate into the intracrystalline pore system. This can give rise to a variety of products having differing crystallinity and ion exchange capacity, including products resembling deep bed-calcined Y zeolites in their thermal properties.

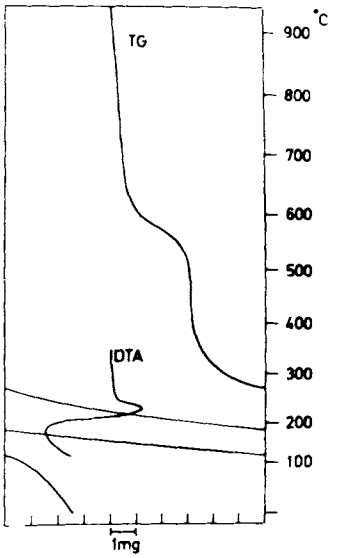


Fig. 1. Thermogravimetric diagram for the thermal decomposition of NH_4Y zeolite (Si/Al = 2.0).

Up to about 320 °C, physically bound water and ammonia are liberated, affording the hydrogen zeolite. Only a slow loss of weight is observed in the first dehydroxylation step from 320 to 550 °C. No changes are seen in the X-ray diffraction pattern. Nevertheless, precise evaluation of the thermogravimetric diagram (Fig. 1) shows that 40% of the hydroxy groups are eliminated in this step.

The second dehydroxylation step is characterized by a fast elimination of water at 550 to 630 °C. The lattice constant decreases from 24.70 to about 24 Å. Moreover, lattice distortions occur, leading to complete disruption of the crystal lattice on further increasing the temperature.

For detailed studies NaX and NaY zeolites with different Si/Al ratios were prepared by known methods[4], transformed into the ammonium form, and calcined under shallow-bed conditions at a temperature below that of lattice destruction (Fig. 2).

The residual content of hydroxy groups (α) decreases with increasing aluminum content, and the lattice constant remains unchanged. The ion exchange capacity after partial dehydroxylation, determined by fourfold exchange with a 0.1 M solution of $AgNO_3$, always corresponds to the sum of the sodium content and the residual proton content.

The resulting Lewis acid centers do not possess ion exchange properties. The contribution of this step to the overall dehydroxylation can be estimated from a simple scheme: the faujasite structure consists of cuboctahedra made up of six four-membered rings of tetrahedra. At a molar ratio of Si/Al = 3, *i.e.* the composition of the silicon-richest Y zeolite, each of the four-membered rings contains an aluminum

[*] Dr. L. Marosi
Ammoniaklaboratorium der BASF AG
D-6700 Ludwigshafen (Germany)

atom. Replacement of further silicon atoms leads to neighboring pairs of aluminum atoms in opposite corners of the four-membered rings whose contribution increases with increasing aluminum content. It can be deduced from the experimental results shown in Figure 2 that for HX and HY

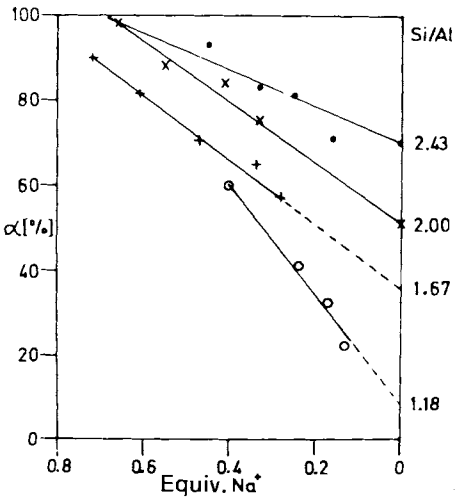


Fig. 2. Decrease in content of hydroxy groups (α) on heating of sodium-containing NH_4 zeolite: 60 h at 470 °C (●); 15 h to 470 °C (×); 8 h to 470 °C (+); 4 h to 530 °C (○).

zeolites the number of eliminated water molecules in the first dehydroxylation step is in agreement with the number of pairs of aluminum atoms for a given Si/Al ratio (Table 1).

Table 1. Relationships between the calculated amount of neighboring aluminum atoms and the experimentally determined extent of dehydroxylation for HX and HY zeolites having various Si/Al molar ratios.

Si/Al	Neighboring Al atoms [%]	Dehydroxylation [%]
3.0	0	
2.43	28.50	30
2.0	50	50
1.67	66	63
1.18	91	90

It must therefore be assumed that in the first dehydroxylation step water is eliminated from those hydroxy groups which are coordinated to neighboring framework aluminum atoms. Remarkably, the same number of hydroxy groups prove to be non-acidic on amine titration[5].

The second step of dehydroxylation always involves migration of framework aluminum atoms into the intracrystalline pore system. This leads to products having an ion exchange capacity considerably greater than their respective sodium content; this suggests formation of AlO^+ ions during the elimination of water (see Fig. 3).

The elimination of water becomes increasingly slower with increasing sodium content; even after complete dehydroxylation the samples are still crystalline. The influence of the dehydroxylation rate on the crystallinity can also be demonstrated for Si-rich HY zeolites. For instance, if the sample is heated at a rate of 0.1 °C/min between 500 and 600 °C then the crystal structure is retained to over 1000 °C. Samples of this kind obtained by controlled dehydroxylation resemble deep-bed calcined Y zeolites in their properties[3]. They possess a high thermal stability and—as demonstrated by the hatched region in Figure 3—exhibit a considerable ion exchange capacity. Their lattice constant lies between 24.30 and 24.50 Å.

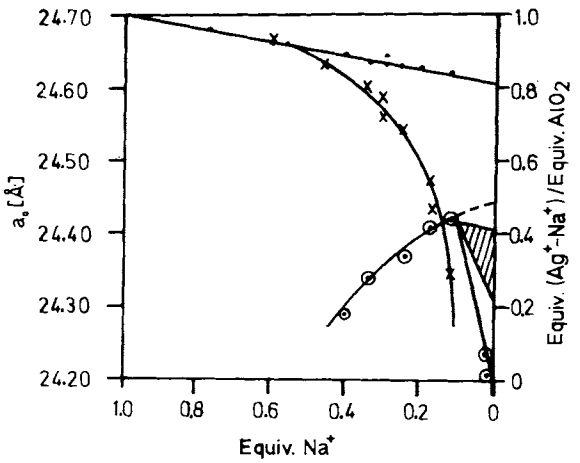
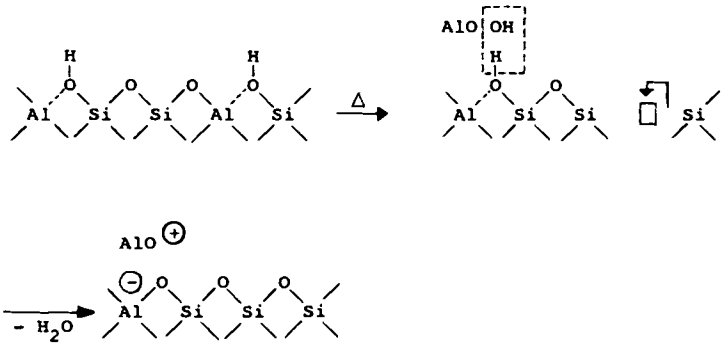


Fig. 3. Lattice constant a_0 of NaHY zeolite (Si/Al = 2.43) (●) and the corresponding completely dehydroxylated products (×) and the increase in ion exchange capacity (○). The sample was heated to 750 °C for dehydroxylation. Hatched: ion exchange capacity.

Since the migration of the framework aluminum atoms into the intracrystalline pore system also takes place *in vacuo* it cannot be interpreted as a result of hydrolysis. It appears more likely that the AlO(OH) skeletal units swing out in the course of their thermal motion and under subsequent cationization according to the following scheme. (The vacancy at the AlO(OH) is occupied by silica, *e.g.* from peripheral regions.)



Whether, and to what extent, the AlO(OH) groups are cationized depends upon the relative rate of swinging and cationization. Too fast a heat-up rate between 500 and 600 °C causes most of the aluminum atoms to leave the crystal framework. The lattice then collapses. Depending upon the rate of dehydroxylation a variety of products can arise which differ in their crystallinity and ion exchange capacity and also contain defect sites. By a suitable choice of calcination conditions it is possible to balance these two processes such that the products have a particularly high thermal stability. This mechanism of water elimination in the second dehydroxylation step can also be applied to shallow-bed and deep-bed dehydroxylation and thus permits a coherent view of the processes occurring under different dehydroxylation conditions.

Received: January 2, 1980;
revised: June 16, 1980 [Z 565 IE]
German version: Angew. Chem. 92, 759 (1980)

CAS Registry numbers:
No compounds indexed

[1] *H. A. Szymanski, C. N. Stamires, G. R. Lynch*, J. Opt. Soc. Am. *50*, 1323 (1960).
[2] *J. B. Uytterhoeven, L. G. Christner, W. K. Hall*, J. Phys. Chem. *69*, 2117 (1965); *G. H. Kühl* in *J. B. Uytterhoeven:* Molecular Sieves. Leuven University Press, Leuven 1973, p. 227; *D. W. Breck, G. W. Skeels*, ACS Symp. Ser. *40*, 271 (1977); *P. A. Jacobs, H. K. Beyer*, J. Phys. Chem. *83*, 1174 (1979); *J. V. Smith*, Adv. Chem. Ser. *101*, 183 (1971).
[3] *G. T. Kerr*, J. Catal. *15*, 200 (1969).
[4] *R. M. Milton*, US-Pat. 2882244 (1959); *D. W. Breck*, US-Pat. 3130007 (1964).
[5] *R. Beaumont, D. Barthomeuf, Y. Trambonze*, Adv. Chem. Ser. *102*, 327 (1971).

Amorphous Zeolites

By *John M. Thomas* and *Leslie A. Bursill*[*]

Crystalline zeolites possess a wide range of properties that make them industrially important. It is less widely known that imperfectly-ordered (quasi-crystalline or semiamorphous) zeolites also exist, and that these, too, possess potentially attractive properties. There is, however, some difficulty in characterizing these amorphous variants; and it is rather puzzling that a material which lacks long-range order can nevertheless exhibit marked cation-exchange capacity and catalytic activity, which in the case of the crystalline varieties, arise because of the unit-cell level porosity of the aluminosilicate. Our communication focuses on these two points; and, in particular, describes how high resolution electron microscopy (h.r.e.m.) helps rationalize these problems.

We have recently shown[1] that it is possible, notwithstanding their beam-sensitivity, to record direct structural images, at a resolution close to 3 Å, of crystalline zeolites such as Na-A, Na-X, Na-Y and ZSM 5. During the course of examination the zeolites gradually become amorphous; but advantage may be taken of this fact since both the course of the process of amorphization as well as the various degrees of quasicrystallinity may be analyzed by direct (real-space) imaging. (The reliability of the images taken by h.r.e.m., both for crystalline and amorphous materials, is known from computer simulation procedures that are described fully elsewhere[2,3].)

Considerable insight is gained from the study of amorphous zeolites in this way. This is illustrated with reference to Fig. 1 which is a high-resolution image of a dehydrated crystal of Na-A (idealized formula $Na_{12}Al_{12}Si_{12}O_{48}$) that has been appreciably converted to an amorphous condition[4]. There are several noteworthy features:

(i) A 'raft' (*ca.* 10^4 Å^2 in projected area) of crystalline material consisting of an ordered array of so-called supercages[2]—*ca.* 10^2 in all—is surrounded by essentially amorphous aluminosilicate.
(ii) A smaller 'raft' (*ca.* 3×10^3 Å^2 in area), less well-ordered than the other and not in registry with it, consisting of some 30 supercages, is also surrounded by amorphous material.
(iii) Several isolated supercages, one of which is arrowed, may be identified in the amorphized background.

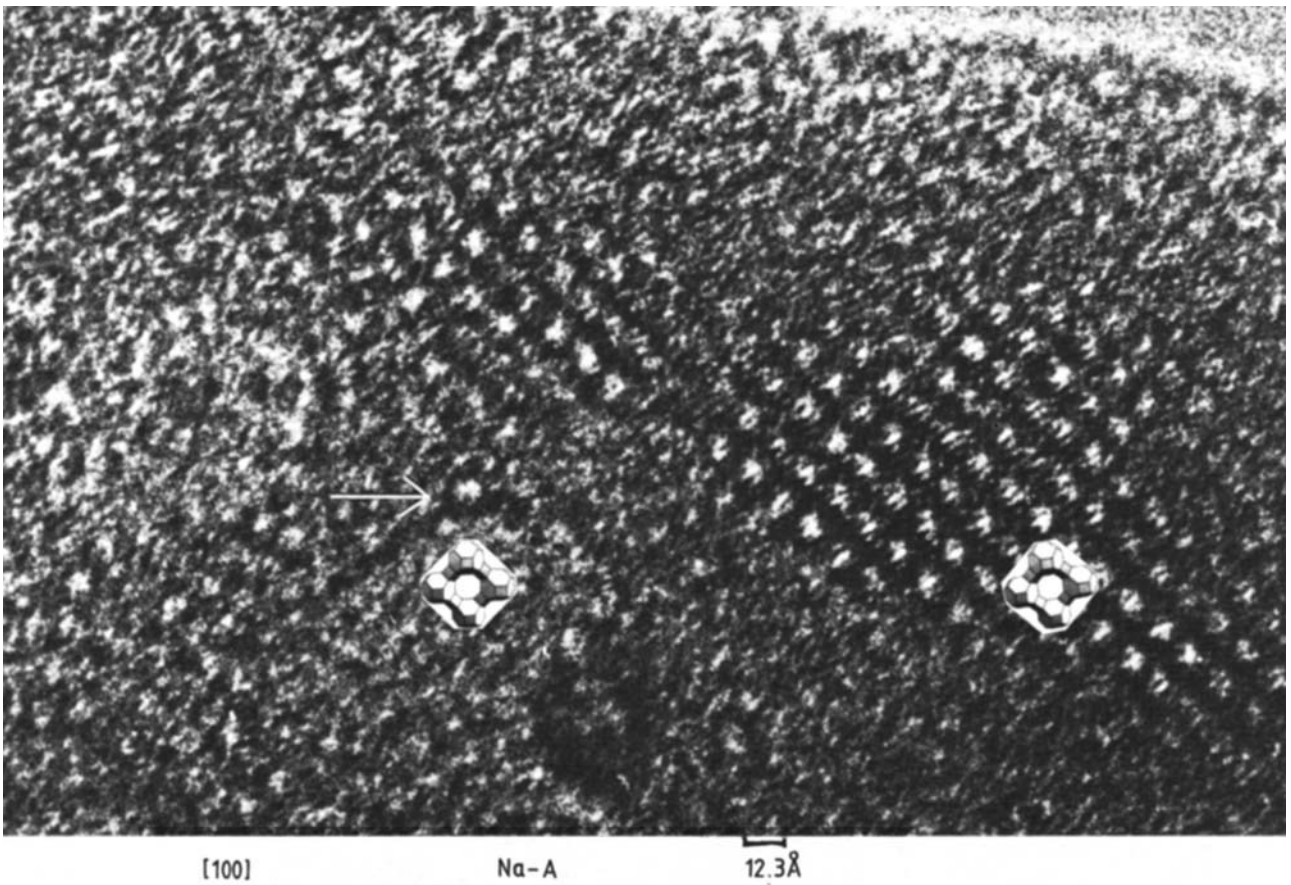


Fig. 1. High resolution electron micrograph of a thin film (<40 Å thick) of quasi-crystalline zeolite A, showing the supercages as white dots. For details see text.

[*] Prof. Dr. J. M. Thomas, Dr. L. A. Bursill [**]
Department of Physical Chemistry, University of Cambridge
Lensfield Road, Cambridge, CB2 1EP (England)
[**] On leave from Department of Physics, University of Melbourne (Australia)

We may now appreciate how amorphous zeolites can retain much of their cation-exchange capacity: even though clusters of sodalite cages (which circumscribe the supercage—see inset) are detached from the parent crystal, thereby generating

a structure the long-range order of which is disrupted, these sub-unit cell fragments still possess the basic attribute that confers upon them their exchange capacity and catalytic activity.

Clearly h.r.e.m. can play a useful role in the characterization of microcrystalline and amorphous zeolites, more so perhaps than other solids since the individual units (in this case the cubo-octahedra) are more readily discernible, and hence the interpretation of image detail more straightforward.

Received: June 13, 1980 [Z 566 IE]
German version: Angew. Chem. 92, 755 (1980)

CAS Registry numbers:
No compounds indexed

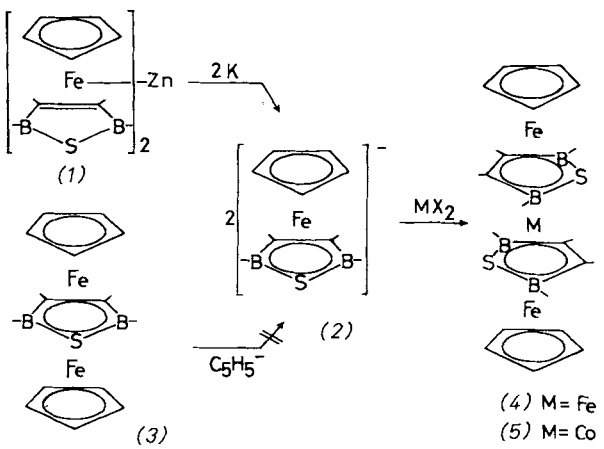
[1] *L. A. Bursill, E. A. Lodge, J. M. Thomas,* Nature *286,* 111 (1980); *J. M. Thomas, G. R. Millward, L. A. Bursill,* Phil. Trans. Roy. Soc., in press; *L. A. Bursill, E. A. Lodge, J. M. Thomas,* J. Chem. Soc. Chem. Commun., in press.
[2] *J. M. Cowley,* Diffraction Physics. North-Holland, Amsterdam 1975.
[3] *D. A. Jefferson, G. R. Millward, J. M. Thomas,* Acta Cryst. *A 32,* 823 (1976); *J. M. Thomas, D. A. Jefferson,* Endeavour (New Series) *2,* 127 (1978).
[4] *R. M. Barrer,* Zeolites and Clay Minerals as Sorbents and Catalysts. Academic Press, New York 1978.

Bis(η-cyclopentadienyliron-μ,η-thiadiborolene)iron—Structure of a η-C_5H_5 Tetradecker Sandwich Complex[**]

By *Walter Siebert, Christian Böhle,* and *Carl Krüger*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

Triple-decker complexes with terminal carbon monoxide or thiaborolene ligands are cleaved by cyclopentadienide into anionic mononuclear compounds which form tetradecker complexes with transition-metal halides[1]. An analogous cleavage of the η-cyclopentadienyl triple-decker sandwich *(3)*[2] fails because of its short Fe...Fe distance. By reacting the compound $[(C_5H_5)Fe(C_8H_{12})]_2Zn$, recently described by *Jonas et al.*[3], with 1,2,5-thiadiborolene to give the trinuclear complex *(1)* (58% yield) we have now found a route for the synthesis of the long-sought sandwich anion *(2)*[4]. We report here on the first η-cyclopentadienyl-μ-thiadiborolene tetradecker sandwich complexes *(4)* and *(5)* which we obtained in 53 and 42% yield, respectively, from the anion *(2)* and $FeCl_2$ and $CoCl_2$.



Direct reaction of *(1)* with $CoCl_2$ leads, as a result of ligand exchanges, to $(C_5H_5)Co(C_2B_2S)$ (83%), $(C_5H_5)_2Fe$ (70%) and traces of *(3)*. Reaction of *(1)* with $FeCl_2$ in boiling tetrahydrofuran (THF) affords besides *(3)* and *(4)* (19%) the hydride complex $[(C_5H_5)Fe(H)(C_2B_2S)]$, which contains a Fe—H—B 3z/2e bond [$\delta^{11}B(CS_2) = 0.3$ (br. s, 1), 34.7 (s, 1)]. This compound is also obtained on reaction of *(1)* with HCl-gas; the isomeric hydride complex $[(C_5H_5)(C_2B_2S)Fe—H]$ [$\delta^{11}B(CS_2) = 25.3$ (s, 1), 38.7 (s, 1); $\delta^1H(CS_2) = -7.4$ (Fe—H)] is formed initially and is then converted thermally into the compound with the Fe—H—B bridge[4].

The constitution of *(4)* follows from the spectroscopic data [$\delta^1H(CS_2) = 3.52$ (s, 10), 3.1 (m, 4), 1.9 (m, 4), 1.79 (s, 12), 1.22 (t, 12); $\delta^{11}B(CS_2) = 19.2$; MS: $m/e = 630$ (M^+, 100%) (70 eV)]. The ^{11}B signal indicates four equivalent boron atoms as well as bifacial coordination of the thiadiborolene ligands. The B—CH_3 signal is consistent with a *trans* arrangement of the μ-ligands, which, as for the trinuclear complexes $[(CO)_3Mn(C_2B_2S)]_2Fe$[5] and $[(C_2B_2S)Co(C_2B_2S)]_2Fe$[1], is confirmed by the crystal structure analysis[6] (Fig. 1).

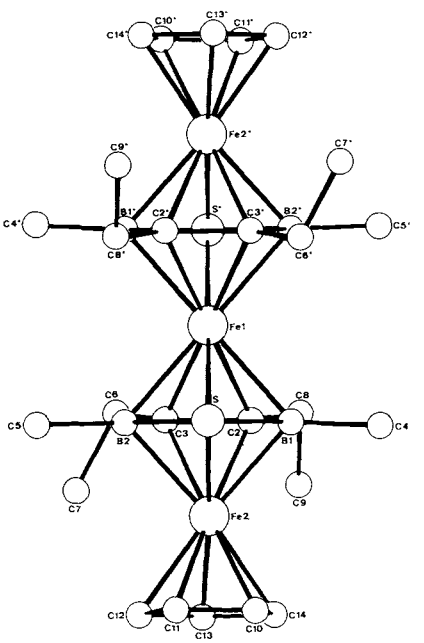


Fig. 1. Molecular structure of the complex *(4)* in the crystal.

The distances between the ring atoms in the μ-ligands are C—C = 1.461(3), B—C = 1.564(3), 1.556(3) and B—S = 1.909(2), 1.913(2) Å, and in the η-ligands C—C = 1.405(4)—1.417(4) Å. Fe1 occupies an inversion center, the Fe1—Fe2 distance (3.272(1) Å) is only slightly longer than in *(3)* (3.236(1) Å).

The distances between the metal atoms and the best planes of the ligands (D) [Fe—D(C_5H_5) = 1.67, Fe—D(C_2B_2S) = 1.63, and Fe1—D(C_2B_2S) = 1.64 Å] are similar. In contrast, strongly deviating distances (1.69, 1.60, and 1.93 Å) were found in the tetradecker sandwich complex

[*] Prof. Dr. W. Siebert, Dr. C. Böhle
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)
Present address:
Anorganisch-Chemisches Institut der Universität
Im Neuenheimer Feld 270
D-6900 Heidelberg 1 (Germany)
Priv.-Doz. Dr. C. Krüger
Max-Planck-Institut für Kohlenforschung
Lembkestrasse 5, D-4330 Mülheim-Ruhr 1 (Germany)

[**] Tetradecker Complexes, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 2: [1].

$[(C_2B_2S)Co(C_2B_2S)]_2Fe$ *(6)*[1]. The different influence of the d^7 fragments $(C_5H_5)Fe$ and $(C_2B_2S)Co$ on the $(C_2B_2S)Fe(C_2B_2S)$ unit is manifested in the expansion of the central sandwich from 3.28 in *(4)* to 3.86 Å in *(6)*; the expansion reflects the enhanced acceptor character of the terminal thiadiborolene ligands. Consequently, there are no drastic changes in the ligand/metal bonding relationships on incorporation of the 12-valence-electron "stack" $[(C_2B_2S)Fe]$ into the tripledecker *(3)* to give the tetradecker *(4)*. Therefore $(C_5H_5)Fe[(C_2B_2S)Fe]_n(C_5H_5)$ complexes with $n>2$ should also be stable.

(4), with a $(4\times\pi^6+3\times d^6)$ arrangement, is the parent member of the series of tetradecker sandwich complexes (42 to 48 valence electrons). The cobalt compound *(5)* with a total of 43 valence electrons is accordingly paramagnetic and has an 8-line ESR spectrum ($\langle g\rangle=2.087$, $\bar{a}(^{59}Co)=45$, 2 G).

Procedure

(1): A mixture of $[(C_5H_5)Fe(COD)]_2Zn$[3] (1.9 g, 3.63 mmol) and 3,4-diethyl-2,5-dimethyl-1,2,5-thiadiborolene (1.9 g, 11.4 mmol) in *n*-hexane (25 ml) is heated under reflux for 1 h. After filtration through a frit the solution is concentrated by evaporation to 10 ml and cooled to −78 °C. The red crystals which are formed are washed with ether and dried in a high vacuum. Yield 1.35 g *(1)* (58%); m.p. 182—184 °C; $\delta^{11}B(CS_2)=14.6$; MS: $m/e=639$ (M^+, 15%).

(4): A solution of *(1)* (0.95 g, 1.49 mmol) in THF (25 ml) is allowed to react with mirror potassium (0.22 g, 5.64 mmol) for 64 h. Excess potassium is separated off and the solution treated with 0.4 g (1.49 mmol) $FeCl_2\cdot 2THF$. After 16 hours' stirring and removal of THF, the residue is taken up in toluene (20 ml), filtered, evaporated down to 5 ml, and allowed to stand for 16 h at −78 °C. Yield 0.5 g (53%) *(4)* as black needles, m.p. 209—211 °C (dec.). *(5)* is obtained analogously (0.4 g, 42%): m.p. 218 °C (dec.).

Received: April 18, 1980 [Z 567 IE]
German version: Angew. Chem. *92*, 758 (1980)

[1] *W. Siebert, W. Rothermel, C. Böhle, C. Krüger, Y.-H. Tsay, D. J. Brauer*, Angew. Chem. *91*, 1014 (1979); Angew. Chem. Int. Ed. Engl. *18*, 949 (1979).
[2] *W. Rothermel*, Dissertation, Universität Marburg 1979.
[3] *K. Jonas, L. Schieferstein*, Angew. Chem. *91*, 590 (1979); Angew. Chem. Int. Ed. Engl. *18*, 549 (1979); *K. Jonas, L. Schieferstein, C. Krüger, Y.-H. Tsay, ibid. 91*, 590 (1979) and *18*, 550 (1979).
[4] *C. Böhle*, Dissertation, Universität Marburg 1980.
[5] *W. Siebert, C. Böhle, C. Krüger, Y.-H. Tsay*, Angew. Chem. *90*, 558 (1978); Angew. Chem. Int. Ed. Engl. *17*, 527 (1978).
[6] Crystallographic data: $a=8.142(1)$, $b=8.754(1)$, $c=10.973(1)$ Å, $\alpha=95.978(6)$, $\beta=97.938(6)$, $\gamma=112.674(8)°$. Space group $P\bar{1}$, $Z=1$, 4076 reflections, 457 unobserved (2σ); $R=0.034$ ($R_w=0.040$).

BOOK REVIEWS

Integriertes Organisches Praktikum. By *S. Hünig, G. Märkl,* and *J. Sauer*. Verlag Chemie, Weinheim 1979, xlvii, 739 pages, bound, DM 112.00.

It is comforting to know that students taking organic chemistry will bear the imprint of the practical hand book that they use, and that in comparison with this any reforms bandied about at official levels are only of marginal importance. After generations of students trained on "Gattermann", the "Organikum" appeared in the mid-sixties and its design still determines the character of a practical organic handbook. However, it would be a miracle if after almost two decades new demands were not made for a "modern" book, and above all for the application of the now routine spectroscopic methods. This is where the "Integriertes Organisches Praktikum" comes in.

"Integrated" should mean the equal and simultaneous treatment of synthesis, isolation in pure form, and structure determination. This statement of the aims defines a new type of practical handbook that of necessity cannot replace the textbook. Thus, at the beginning of each chapter there is a short general introduction, and at the end a block with an index of working methods used. Each experiment is divided into sections as follows: theoretical preparations (with information on the subjects to be studied), performance of the reaction, isolation, and purification, realization of the experiment, evaluation of the results, and conclusions. With the aid of a formal summary that he must complete and augment, the student learns to view the experimental results within a broader context. Interspersed exercises, problems, and questions should stimulate further thought on the subject.

The external appearance of the book is characterized by many illustrations of the IR and NMR spectra of educts and products and by apparatus symbols, which do more to illustrate every working step than a lengthy description. Sources of danger are particularly indicated and hints on first aid are appended (many an unnecessary repetition could be easily avoided by the consistent use of "pointing hands").

The present book can switch the points. It has succeeded in its aim, is well thought out, is complete in itself, and is impressive in the sheer elegance of its didactic construction. The authors' years of experience and their love of detail are palpable on every page. Its scope corresponds to a single-semester course, and the book thus fits well into the study plans currently under discussion. Provided that adequate assistance is available—which is particularly important with this more school-oriented practical handbook—the student will know in his bones "what organic chemistry is" after this relatively short period. He learns very early to proceed in the manner that will be demanded of him later in his undergraduate and postgraduate studies. The intellectual requirement is greater and the attractiveness—the book is not like a collection of cooking recipes—correspondingly higher. However, it is necessary not to waste the advantages of the earlier practical groundwork (syntheses performed in accordance with the universally held "Organikum" precepts) by anchoring them more firmly in a subsequent advanced practical course.

The present book offers a chance and deserves a positive response. The spirit of an "Integrated Organic Practical Handbook" will prevail sooner or later, and the practical instructors are called upon to test to what extent the new concept is becoming established in their field.

One obstacle should not be underestimated: the call is to seek out *new* paths. Can this hurdle be overcome? Let us hope so.

Günther Maier [NB 518 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Gas Chromatography with Glass Capillary Columns. 2nd Edit. By *W. Jennings.* Academic Press, New York 1980. xiii, 320 pp., bound, $ 25.00.—ISBN 0-12-384360-X

Pyrolytic Methods in Organic Chemistry. Organic Chemistry, Vol. 41. By *R. F. C. Brown.* Academic Press, New York 1980. xii, 347 pp., bound, $ 38.50.—ISBN 0-12-138050-5

Catalysis in Organic Syntheses. Edited by *W. H. Jones.* Academic Press, New York 1980. viii, 314 pp., bound, $ 29.50.—ISBN 0-12-389050-0

Radiationless Transitions. Edited by *Sheng Hsien Lin.* Academic Press, New York 1980. xi, 425 pp., bound, $ 48.50.—ISBN 0-12-450650-X

NMR of Chemically Exchanging Systems. By *J. I. Kaplan* and *G. Fraenkel.* Academic Press, New York 1980. xi, 165 pp., bound, $ 19.50.—ISBN 0-12-397550-6

Physical Chemistry of High Temperature Technology. By *E. T. Turkdogan.* Academic Press, New York 1980. xvi, 447 pp., bound, $ 49.50.—ISBN 0-12-704650-X

Physicochemical Methods for Water and Wastewater Treatment. Edited by *L. Pawlowski.* Pergamon Press, Oxford 1980. vii, 327 pp., bound, £ 22.50.—ISBN 0-08-024013-5

Intellectual Property Law Review—1979. Vol. 11. Edited by *G. Rose.* Clark Boardman Company, New York 1980. civ, 450 pp., bound, £ 32.00.—ISBN 0-87632-145-7

Catalysis. Vol. 3. Senior Reporters *C. Kemball* and *D. A. Dowden.* The Chemical Society, London 1980. xiii, 285 pp., bound, DM 122.50.—ISBN 0-85186-720-0.—A volume of the series "Specialist Periodical Reports"

Photoelectrochemistry. By *Yu. Ya. Gurevich, Yu. V. Pleskov,* and *Z. A. Rotenberg.* Consultants Bureau, New York 1980. xv, 239 pp., bound, $ 39.50.—ISBN 0-306-10963-0

Spectroscopic Techniques for Organic Chemists. By *J. W. Cooper.* John Wiley & Sons, New York 1980. xv, 376 pp., bound, £ 11.50.—ISBN 0-471-05166-7

Synthetic Methods of Organic Chemistry. Edited by *W. Theilheimer.* S. Karger, Basel 1980. xx, 524 pp., bound, DM 597.00.—ISBN 3-8055-0327-X

Organic Chemistry. By *D. S. Kemp* and *F. Vellaccio.* Worth Publishers, New York 1980. xiii, 1422 pp., bound, $ 21.95.—ISBN 0-87901-123-8

Electrophoresis '79. Advanced Methods Biochemical and Clinical Applications. Edited by *B. J. Radola.* Walter de Gruyter & Co., Berlin 1980. xv, 858 pp., bound, DM 185.00.—ISBN 3-11-008154-7

Untersuchung der Beschaffenheit von Glasoberflächen mit Hilfe der Sorptionstechnik. By *L. Žagar, D. H. Höfgen, H. F. Jordan,* and *H. J. Kubuschok.* Westdeutscher Verlag, Opladen 1980. iii, 60 pp., brochure, DM 15.00.—ISBN 3-531-02941-X

Principles and Applications of Homogeneous Catalysis. By *A. Nakamura* and *M. Tsutsui.* John Wiley & Sons, New York 1980. ix, 204 pp., bound, £ 18.80.—ISBN 0-471-02869-X

Nucleotide Analogs. Synthesis and Biological Function. By *K. H. Scheit.* John Wiley & Sons, New York 1980. xi, 288 pp., bound, DM 16.00.—ISBN 0-471-04854-2

27th International Congress of Pure and Applied Chemistry. Edited by *A. Varmavuori.* Pergamon Press, Oxford 1980. vii, 386 pp., bound, £ 44.50.—ISBN 0-08-023936-6

Reaction Rates of Isotopic Molecules. By *L. Melander* and *W. H. Saunders, Jr.* John Wiley & Sons, New York 1980. xiv, 331 pp., bound, £ 16.30.—ISBN 0-471-04396-6

Chemical Structure and Bonding. By *R. DeKock* and *H. Gray.* The Benjamin/Cummings Publishing Company, Menlo Park, Calif. 1980. xi, 491 pp., bound, $ 21.95.—ISBN 0-8053-2310-4

Katalytische Methoden in der Spurenanalyse. By *H. Müller, M. Otto,* and *G. Werner.* Verlag Chemie, Weinheim 1980. 168 pp., bound, DM 67.00.—ISBN 3-527-25851-5

Mengenberechnungen in der Chemie. Grundlagen und Praxis. By *W. Kullbach.* Verlag Chemie, Weinheim 1980. xiii, 474 pp., broch., DM 48.00.—ISBN 3-527-25869-8

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar,* **Translation Editors:** *A. J. Rackstraw and A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 10
October 1980
Pages 749–840

Pharmaceutical Chemistry Today—Changes, Problems, and Opportunities

By Horst König[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Dissatisfaction with empirical methods, high expectations of the public, poorly harmonized international regulations, and rising costs have induced pharmaceutical research to search for new approaches. As a consequence, the medicinal chemist's professional activity is in a state of change. His synthetic strategy is being increasingly influenced by the reasoning of molecular biology. Novel classes of biologically active compounds demand the development of new synthetic methods beyond the scope of modern preparative organic chemistry: enzymes and microorganisms, cell cultures, and genetic engineering are harnessed to supply highly complex structures. Major efforts are devoted to the development of reliable structure-activity relationships to rationalize his work. Thus the field of medicinal chemistry stretches from physical and physical organic chemistry far into the realm of biosciences, and the interdisciplinary character of this research is rapidly increasing. The author endeavors to convey an impression of this complex subject with the aid of selected examples.

1. Introduction: Is Pharmaceutical Research Still Worthwhile?

This question is frequently posed in a dual sense. On the one hand, it is often assumed that a sufficient number of drugs is already available and that new ones are not needed. On the other hand, cost analyses indicate that the development of a new drug has become extremely expensive. Only few products have the potential to recover the necessary investment of 50—150 million $ in a short period and thus to contribute quickly to the financing of new research projects[1].

However, this questioning of the usefulness of pharmaceutical research must be answered from both aspects in a clearly affirmative sense. Firstly, satisfactory therapy is available only for about a third of all ailments[2]. Widespread and dangerous diseases (cancer, virus infections, circulatory disorders, just to mention a few) will require great efforts to develop hopeful beginnings into reliable cures.

Secondly, products that initiate a therapeutic breakthrough are generally rewarded by economic success[*]. And finally, where else can chemistry solve important problems with such small consumption of costly energy and scarce raw materials.

[*] Prof. Dr. Horst König
Pharma-Sparte, BASF Aktiengesellschaft
D-6700 Ludwigshafen (Germany)

[*] New products for rare diseases are developed as a social and ethical obligation. Their costs must be carried by other drugs.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0749 $ 02.50/0

2. The Status Quo

The discovery of penicillin and the subsequent dramatic success of other antibiotics in the fifties heralded in an era of great optimism. Novel, highly active drugs were developed in rapid succession and the solution to most therapeutic problems appeared to be just around the corner. However, sudden disillusionment followed in the sixties. The widespread use of drugs logically had led to the more frequent observation of side effects. The miracle weapon of antibiotics was in danger of being blunted by the development of microbial resistance. Strict governmental regulations were called for by the public. As the detrimental consequences of introducing a new drug with unexpected severe side effects are much more obvious than the consequences of unduly blocking use of an effective drug for therapy, the requirements for testing and registration became enormous. For example, the documentation for a single new product in 1973 filled 45 volumes (1.5 tons of paper!) describing expensive biological experiments[3]. These quite often could only prove the exactness of the regulatory agency and the assiduity of the developing company but produced no new criteria.

Simultaneously, one was no longer satisfied with therapeutic success alone, but sought to clarify the biological action of drugs on a causal basis. Biological model conceptions have gained great importance for the medicinal chemist and guide his synthetic work wherever possible. "Rational drug design" circumscribes this effort to utilize our still scarce, but fortunately growing knowledge of molecular biology for the development of new drugs. Medicinal scientists try to orient their work on the molecular mechanisms of physiological and pathophysiological processes. Huge scientific gaps in many areas of medicine and biology still tend to frustrate this effort. Thus pharmaceutical research is passing through a difficult period where former guidelines prove unsatisfactory and new ones have to be established with the expenditure of great effort.

A promising new alley was opened by the discovery of novel classes of biological mediators. This research provides the medicinal chemist with new model substances. However, it has also demonstrated the complexity of biological signal systems and thus the difficulty of controlled therapeutic interference. Prostaglandins, for instance, or the hypothalamic peptides are frequently produced in minimal concentrations and in small defined areas[*] to elicit a specific physiological response. The same substance may trigger totally different responses in different tissues. Obviously, systemic therapy with such a substance must encounter problems of specificity.

3. Scope and Objectives of Current Pharmaceutical Research

From a chemical point of view the human organism is a highly complex arrangement of many, often specialized, molecules which cooperate in vital functions under the guidance of a well balanced system of electrophysiological and chemical signals. Disruption of the molecular network or a disturbance in the transmission of signals are experienced as an ailment. Thus pharmaceutical research looks for substances which can compensate for the disorder or, ideally, provide a causal cure. This latter, optimal treatment, however, is still rare in practice. Chemotherapy of infectious diseases is one of the most successful examples, because the extermination of the infective agent usually eliminates the disorder and reestablishes normal functions.

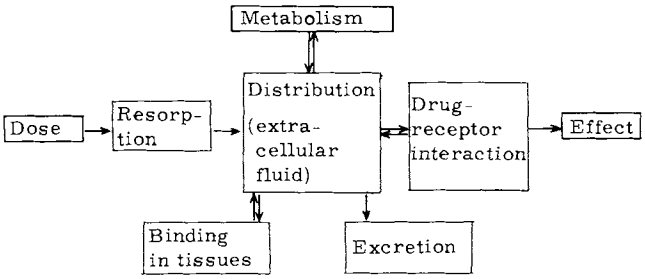


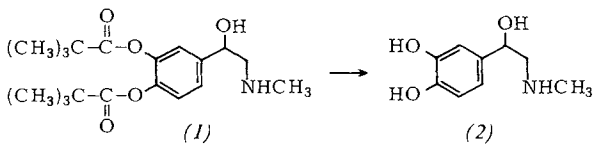
Fig. 1. Active substances and the human organism interact in many ways, the sum of all effects determines the practical value of a drug.

Figure 1 illustrates the various requirements of a drug: The desired therapeutic effect is usually accomplished by a specific binding of the active ingredient to defined structures of the target cell. These receptors are usually proteins or glycoproteins (in membranes or enzymes) and feed the cell information on its surroundings to regulate its activity. The molecules of the drug should enhance signals that have become too weak (agonist) or reduce excessive signals (antagonist). This modulation can only be precisely calibrated if a well defined number of drug molecules reach the target cells. This requirement poses a problem. Only in rare cases will it be possible to administer the drug directly to the inflicted area, as in the case of superficial wounds or infections. Usually the diseased organ or tissue is situated inside the body and systemic application of the drug is necessary to reach it *via* the blood stream. This is also true in the therapy of generalized infections where a sufficient concentration of therapeutic agent must be established in the majority of body cells. Resourceful formulation can help to ensure a sufficient resorption of the drug. For instance, an acid resistant coating may shield a drug that would be destroyed by gastric juices and allow its absorption in alkaline regions of the intestines. Slow-release formulations are designed to guarantee a steady supply of the agent over a prolonged period of time. Release from the formulation is defined as "pharmaceutical availability". After resorption into the blood-stream—for instance by passage through mucous membranes or directly by injection into veins—the drug's active ingredient will be distributed in the extracellular fluid. Binding in various tissues is to some extent determined by the lipophilicity of the substance and can establish depots (desired or otherwise).

Most substances can be chemically modified by the body's enzymes. If the products of these transformations are biologically inactive, this process mainly influences the lifetime of the drug. The same is true if the metabolite has the same type

[*] Detection and quantitative determination of unstable substances in picogram or nanogram quantities could only be accomplished by special analytical methods: immunoassays plus electrophoresis, isotope labeling, sensitive techniques of mass spectroscopy, *etc.*

of activity as the parent drug. If, however, metabolites with undesirable effects are formed, the usefulness of a drug is often destroyed. Finally, parent compound and degradation products must leave the body in a reasonable period of time. Quite often the first passage of a drug substance transported in the bloodstream through liver or lung will result in a decisive metabolic transformation (first pass effect). The chemist can save some drugs from this fate by masking sensitive functional groups, for example by ester or amide formation in the case of a carboxylic acid. The product, a prodrug, ideally should have no significant activity of its own but should release the active substance for instance by enzymatic hydrolysis after passage through the "threatening" organs. Prodrugs can also profit from their specific physicochemical properties (like greater lipophilicity than the parent compound) and thus ensure a different distribution. Furthermore, their toxicity may be reduced. For example, cytotoxic substances have been modified in such a way that they have little effect on normal cells but are reactivated by the different and faster metabolism in tumor cells.



(1) (2)

Fig. 2. Appropriate chemical "masking" of drugs yields prodrugs, which are reactivated by metabolic unmasking. For example, the dipivalate of epinephrine *(1)* is more active and has less side effects than epinephrine *(2)* itself in the topical treatment of glaucoma.

One important property of a drug is its bioavailability, *i. e.* the amount of active substance present after resorption. It is much more convenient for the patient to take a pill or receive an injection only once a day rather than at short time intervals. On the other hand, there must be a way of interrupting the treatment at short notice if advisable. Halflife times of 4—12 h are usually a reasonable compromise. Most important, a reliable and therapeutically efficient concentration of the drug at the target organ must be guaranteed between applications.

It is obvious that *in-vitro* test models, such as cell cultures, can provide only limited information with regard to resorption, distribution, metabolism, and excretion. *In-vivo* models are necessary to obtain these pharmacokinetic data and most pharmacodynamic parameters which describe the action of the drug on the organism. This is especially true for ailments with a systemic character, like hypertension.

4. Stages of Drug Development

The development of a new drug requires interdisciplinary cooperation of principally chemists, biologists, physicians, and pharmacists.

A simplified scheme of drug development is presented in Figure 3. The first stage is the synthesis of new substances with a promise of useful effects, or their isolation from natural materials, according to a research strategy. In a screening procedure those candidates are selected which possess the desired biological activity. The test models are designed to

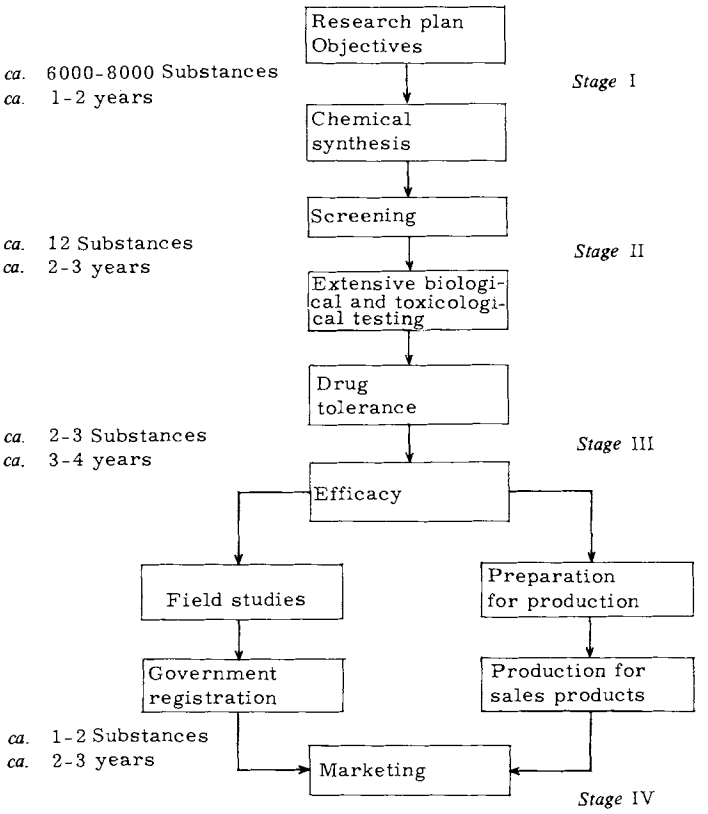


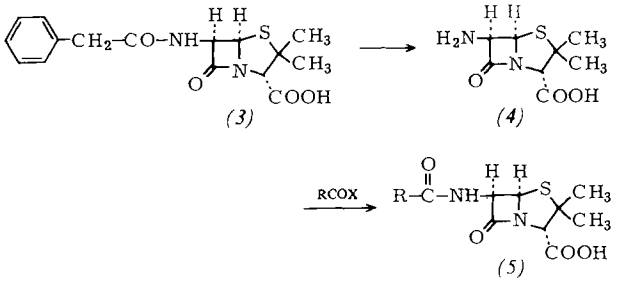
Fig. 3. Many professional disciplines cooperate in the development of a new drug which requires about 10 years of intensive work. Very few of the many substances tested are found sufficiently effective and safe for therapy. Stage IV comprises continued monitoring of therapeutic success and side effects.

simulate diseases and therapeutic processes as well as possible.

Subsequent thorough studies in pharmacology, biochemistry, and toxicology determine the risk/benefit ratio of the potential new drug. A substance may not be applied in human medicine without convincing evidence that the therapeutic benefit promises to outweigh any undesired side effect. A variety of toxicological studies are therefore carried out over prolonged periods of time and decide the fate of a test substance. Nevertheless, great care is exercised when a substance is finally studied in man, as no other species is completely comparable. A small dose is first checked with regard to tolerance in healthy volunteers. If no undesirable effects can be observed, the dose is slowly increased into the expected therapeutically effective range. Then the efficacy is tested in patients in comparison with established drugs or placebos (if warranted). Finally, field studies have to prove the reliability of the new drug in a great number of patients. These studies are also designed to reveal rare side effects which are encountered only in particularly predisposed individuals. Of course, the severity of the disease under study will influence the evaluation. A passing nausea may be tolerated for a lifesaving antibiotic while it could lead to rejection in the case of a sleep inducer. This stepwise development of a drug is regulated by detailed national laws[4]. To eliminate subjective factors in clinical trials for instance, double blind studies are prescribed where neither patient nor doctor know which trial group is receiving the experimental drug and which one the established drug.

The majority of test substances is eliminated during stages II and III. At present, only one out of approximately every 10000 new compounds is introduced into therapy after a trial period of, on average, 10 years. After the initial synthesis the chemist has to provide increasing amounts of test substance in a high and defined quality for the later stages of development. Finally, a technical process must be developed that guarantees high quality at reasonable costs.

Stereochemical uniformity often plays an important role. The separation of enantiomers or chiral synthesis is therefore of great interest in medicinal chemistry. The excellent specificity of enzymes is increasingly utilized in the synthesis of drugs: Penicillin-amidase, for instance, can be employed with great success to cleave Penicillin G *(3)*. The resulting 6-aminopenicillinic acid *(4)* is then routinely used as a synthon for semisynthetic penicillins *(5)* with superior therapeutic properties.



(3) *(4)* *(5)*

For many years, fermentation of molasses with yeast has been employed to provide active acetaldehyde and catalyze its stereospecific addition to benzaldehyde in a chiral production process of ephedrine[5].

Antibiotics are produced on a large scale and in excellent yields by fungal strains that have been developed by mutation and adaptation from wild strains which are not very effective.

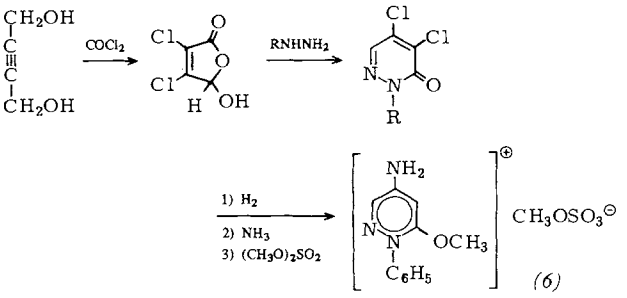
The synthesis of complicated structures like the glycoproteins of the interferon family with 166 amino acids requires the interplay of several enzymes. This can be achieved in cell cultures of fibroblasts for instance. As microorganisms in general can be fermented in simpler ways and reduplicate faster, human genes for hormones or other active substances have been spliced into bacterial genomes. Expression of these genes could be achieved by various techniques and offers a fascinating new approach for the production of very complicated chemical structures. The pharmaceutical industry therefore invests considerable research efforts in this spectacular but difficult field.

5. Synthesis in Medicinal Chemistry

At the very beginning of the development of a new drug the chemist has to select promising target structures (and a synthetic strategy to obtain them). Whenever possible he will try to utilize structure-activity considerations. In general, this means that he will start from a lead structure and try to improve its biological profile by molecular variations.

5.1. The Search for New Lead Structures

The problem consists in finding new structures that can serve as a starting point for variation. Chemical novelty can be a reasonable criterion if a well organized and broad pharmacological screening department cooperates closely with an effective and creative group of synthetic chemists. Chances are comparable with those in a lottery, with many blanks and few but substantial winners. Most substances will drop out in the screening process, but with some luck new classes of active compounds will be discovered. One example from BASF research are pyridazones. They are based on 2-butyne-1,4-diol, an important product of Reppe acetylene chemistry.

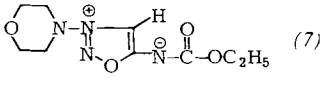


(6)

Its chlorination affords dichloromalealdehydic acid, a useful four-carbon synthon for heterocycles. Condensation with hydrazines, for instance, produces dichloropyridazones in excellent yields that can be further derivatized in many directions to provide dyestuffs or pesticides, for example. The pyridazones also appeared to be of interest in medicinal chemistry, though no structure activity relations were known to guide the molecular variation.

Thus, structural subgroups of 10—20 substances were synthesized and tested in a broad array of screening models. It soon became obvious that the 4-amino substitution established interesting biological activity. 4-Amino-6-methoxy-1-phenylpyridazinium salts in particular possess a pronounced antihypotensive effect. A thorough pharmacological analysis revealed that the stabilizing effect on blood pressure is due to a novel combination of inhibitory actions involving a specific monoaminoxidase and reuptake of norepinephrine into neuronal depots[6]. Thus the signal of the mediator norepinephrine on vascular tonus regains sufficient strength to produce a normal blood pressure. Furthermore, ameziniummetilsulfate *(6)* also displays good activity after oral application and is thus distinguished from other antihypotensive drugs. As all stages of development have been passed successfully, the product should be soon available for therapy.

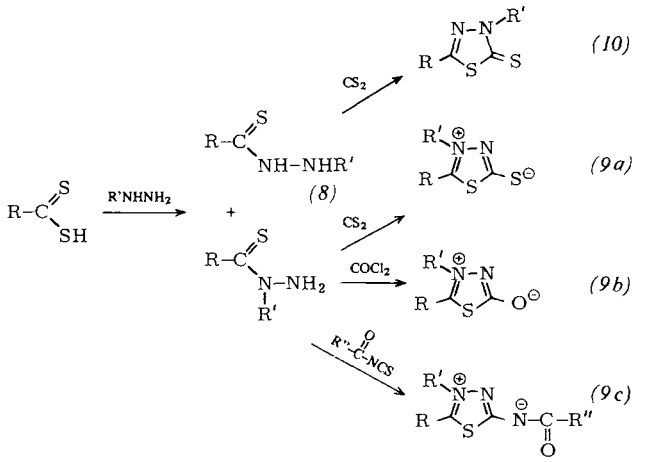
Mesoionic thiadiazolium compounds *(9)* provide a second example of a chemically motivated successful search for new classes of medicinally useful substances. To date very little is known about the pharmacological properties of mesoionic heterocycles. So far apparently only a single sydnone derivative morsydomin *(7)* has been introduced into therapy[7].



(7)

Our interest concentrated on five-membered heterocycles with sulfur and two nitrogen atoms, as the key intermediates *(8)* were readily available and the published methods for cyclization promised a wide variability[8].

The only major problem to solve was a rapid and definitive structural assignment of expected isomers. High energy photoelectron spectroscopy (ESCA)[9] in combination with ^{13}C-NMR was applied wherever ^{1}H-NMR, UV, or IR were not conclusive. The pharmacological test program produced no useful effects for compounds with exocyclic nitrogen *(9c)*



R = Aryl; R' = Alkyl, Aryl; R'' = Alkyl, Aryl

or oxygen *(9b)*, nor for the thiadiazolethiones *(10)*. The thiadiazolium sulfides *(9a)*, however, showed remarkable anticonvulsive activity. By systematic variation of the aromatic and aliphatic group, the effect could be improved considerably[10]. The outstanding substances of this research project raise considerable hopes of becoming new antiepileptic drugs.

It should not be overlooked that while new structures may implicate a genuine therapeutic advantage they also require especially careful preclinical studies, as there is no experience to be used as guidelines[11]. This is true for the mode of therapeutic action as well as for possible side effects. The thorough evaluation of risk-benefit ratios often slows down such projects.

5.2. Optimization of Lead Compounds

Chances of success are better calculable if a project can be based on some known structure-activity relationship. The objective of such work is to improve the therapeutic quality of lead compounds. Is such work useless and redundant as has been claimed by critics of the pharmaceutical industry? Nobody would be foolish enough to regard *Henry Ford*'s Tin Lizzy as the ultimate solution for a motor car. It is equally unrealistic to expect optimal therapeutic results from prototypes of drugs. The desired properties can be enhanced and undesired effects must be minimized. It is a legitimate and desirable goal in its own right if nothing more can be accomplished than a reduction in dosage[12]. The organism will then have to cope with less foreign material and the danger of serious side effects arising from rare individual metabolic anomalies will be diminished.

5.2.1. Natural Products as Lead Substances

Natural products are the most important source of lead substances (see Table 1). A number of alkaloids provide excellent examples for the successful entry of folk medicine into modern therapy.

The search for new lead substances from microorganisms has been extremely useful. The scientific era of antibiotics began with penicillin research and still produces new and highly effective drugs for the treatment of infectious diseases and also of cancer. The impressive role of antibiotics could not be stopped by the "instant success" experience that had caused physicians and patients to use antibiotics much too often and carelessly. The shocking observation of increasing resistance has caused a much more sophisticated and effective therapeutic use of antibiotics.

Research into mammalian natural products has provided a better understanding of normal and pathophysiological processes and their regulation. The important role of steroids as sexual hormones or regulators in inflammatory processes or of blood pressure has caused the development of many drugs as well as contraconceptives ("the pill"). Prostaglandins and peptide hormones may become equally useful in medicinal chemistry, as will be discussed a little later.

Table 1. Some examples of drugs derived from natural products.

Plants		*Animals*	
Quinine	Malaria	Steroids	Inflammation
Reserpine	Hypertension		Conception
Codeine	Cough	Peptide	Growth
Digitalis	Cardiac insufficiency	hormones	Diabetes
Microorganisms		*Marine organisms*	
Penicillin, Streptomycin, Adriamycin	Infectious diseases, Cancer	Algae, Fishes, Jellyfish	?
		Corals	Prostaglandins

At present a thorough search is going on for new lead substances from marine organisms. The underlying logic is that marine biotopes, with a high halogen ion concentration and—in deeper regions—high pressures may cause the formation of unusual structures. So far, the search has produced mostly halogenated derivatives of well-known structural classes and an impressive therapeutic product is still missing[13]. Some toxins (tetrodotoxin) from certain species of fish or from dinoflagellates (saxitoxin), however, are useful in pharmacological models as they selectively block the transport of Na^+ in nerve membranes. A peptide (53 amino acids) from a sea anemone, anthopleurine-A, influences the contractile force of cardiac muscle and has thus aroused scientific interest[14].

Usually, a natural product of pharmacological interest will first be isolated and characterized. If possible, a total synthesis will then be developed to ensure independence from natural sources, as they can vary widely in quantity and quality. This synthetic process is often designed to allow variations of the parent structure as the activity of natural products is often either too low or too unspecific to be useful as drugs. One typical example is provided by morphine alkaloids. Their analgesic activity is accompanied by side effects on respiration, the intestines, and most of all by their great addiction potential.

Many variations and simplifications of the morphine structure have proved that the analgesic power is obviously linked to a structural element that consists of a phenyl ring, a

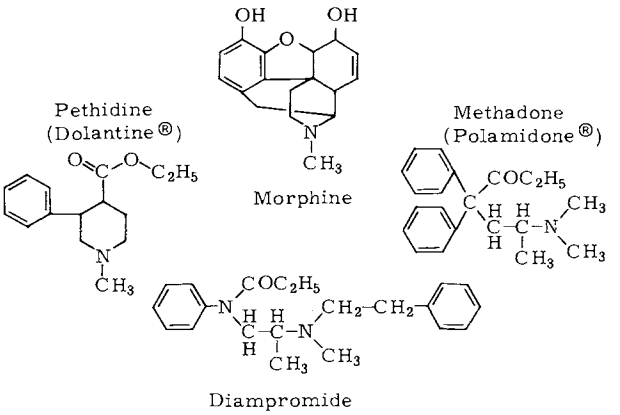
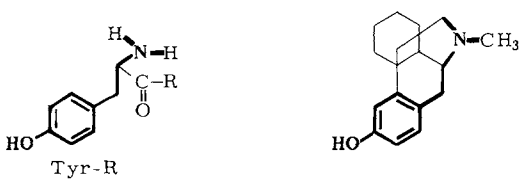


Fig. 4. Variations of the morphine structure retain the analgesic properties of the parent compound only if the structural element consisting of phenyl-$C_{quart.}$—C—C—NR_2 is not lost. At most the quarternary C-atom can be replaced by a tertiary nitrogen as in diampromide.

quaternary carbon atom (or tertiary nitrogen), a two-carbon chain, and a tertiary amine in that order with stereospecificity[15]. These structural requirements suggested receptors[16] but no natural mediators had been detected until very recently.

5.2.2. New Biological Mediators Serving as Lead Structures, Peptides

In 1975, however, a direct search for the natural mediators of the opiate receptors ended in a surprise[17]. Small peptides, a class of compounds very different from morphine alkaloids, turned out to function as the body's own analgesics. However, a N-terminal tyrosine molecule was found in these two pentapeptides, methionine-enkephalin *(11a)* and leucine-enkephalin *(11b)*[11]. It apparently plays an important role in opiate receptor affinity and Figure 5 shows clearly that the important substructure of morphine analogues mentioned above can be superimposed on this tyrosine and is obviously essential for binding to opiate receptors.



(11a), R = Gly-Gly-Phe-Met
(11b), R = Gly-Gly-Phe-Leu

(12)

Fig. 5. Comparison of enkephalins *(11)* with the morphine derivative levorphanol *(12)* clearly shows common structural features.

In the past decade or so, a number of other peptides have been discovered that consist of only a few amino acids and still are able to direct important and divergent bioprocesses. A picture of common features is emerging from this research. A number of different active peptides can apparently be derived from a single precursor peptide. Enzymes appear to cleave its chain at specific sites if a certain substructure is called for by regulatory mechanisms. It is not surprising that similar partial amino acid sequences are found in different peptide mediators[18].

Table 2. β-Lipotropine consists of a chain of 91 amino acids and contains the sequence of a number of peptide mediators. The terminal amino acids are indicated by their number in the β-lipotropine sequence and the usual symbols.

Peptide	Amino acid sequence
β-Lipotropine	1 37 47 58 61 65 76 77 79 91 NH_2-Glu-Ala-Met-Asp-Tyr···Met—Thr-Leu-Lys—Glu-OH
Methionine-enkephalin	61-65
α-Endorphine	61-76
γ-Endorphine	61-77
δ-Endorphine	61-79
β-Endorphine	61-91
β-MSH [a]	37-58
ACTH (4—10) [b]	47-53

[a] Melanocyte stimulating hormone (melanotropine). [b] Partial sequence (Met-Glu-His-Phe-Arg-Trp-Gly) of adrenocorticotropic hormone. Recent work suggests an ever bigger peptide (Big ACTH) as a common precursor of ACTH and β-lipotropine [19].

The same principle can be recognized in other examples: the antagonist of MSH, the inhibiting factor MIF, consists of a sequence of three amino acids that is part of the oxytocin structure *(13)* and is set free by enzymatic cleavage[20]. While oxytocin acts on the uterus and the mammary glands, MIF influences pigment formation and, interestingly, the low dopamine levels encountered in Parkinson's disease.

(13) Cys-Tyr-Ile-Glu-Asn-Cys-Pro-Leu-GlyNH$_2$
MIF

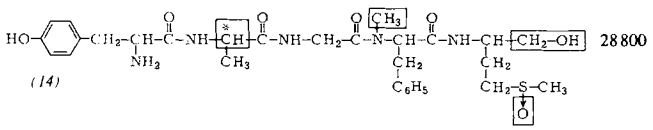
Some properties of these natural products are obviously a disadvantage for practical therapy: the biological signal is often regulated by short term variations of local concentrations of the mediator. The halflife of regulatory substances is therefore, in general, short. Furthermore, they are usually not stable towards digestive enzymes and thus cannot be administered orally. Finally, identical chemical substances are utilized as mediators in different organs or tissues and are there often involved in very different physiological processes[21]. The specificity of signals is then guaranteed by a localized biosynthesis of the mediator. This repeated occurrence may reflect evolutionary processes.

For the synthetic chemist it means a chance and a challenge. By alteration of the natural structure he can inhibit degradation by enzymes and obtain products with useful lifetimes for therapy. At the same time, structural variations may promote a more selective tissue distribution or better specificity in receptor binding. The same family of receptors apparently can have subgroups with small specific variations in structure. For the opiate receptor, for instance, a subgroup of μ-receptors has been found in the central nervous system

that has a higher affinity for morphine derivatives than the δ-receptor in the gut which shows a preference for the enkephalins. More subgroups are emerging from current research. A longer lifetime and better receptor binding can also mean better efficacy[*].

Again the enkephalins provide a good example of successful synthetic chemistry. The natural peptides *(11)* exhibit all effects that can be expected for a mediator of the opiate receptor: They are analgesics, act as antagonists to morphine narcotics; like the latter, they influence behavior and may therefore cause addiction. It was interesting to learn that enkephalin levels apparently rise under the influence of acupuncture. This old Chinese technique of eliminating pain sensations may thus have found a modern explanation. The pentapeptide Met-enkephalin has been systematically derivatized by exchanging three of the amino acids that are not essential for receptor binding for new structural elements[22] (Table 3).

Table 3. Chemical variation of the enkephalin structure accomplishes stabilization towards enzymatic degradation and enhances analgesic activity.

Structure	Analgesic activity [a]
Morphine → Tyr—Gly—Gly—Phe—Met	33
Tyr—[D-Ala]—Gly—Phe—Met	1
Tyr—[D-Ala]—Gly—Phe—Met-[ol]	100
Tyr—[D-Ala]—Gly—Phe—Met-[(o)]-[ol]	1600
Tyr—[D-Ala]—Gly—[MePhe]—Met-[(o)]-[ol]	9600
(14) 	28800

[a] In this model the substance is directly applied to certain regions of the brain.

Replacement of glycine by D-alanine resulted in a 100-fold increase of activity. Reduction of the *C*-terminal methionine to the primary alcohol and oxidation of its thioether to the sulfoxide gained another two powers of ten. Finally, a peptide bond was modified by *N*-methylation of phenylalanine. All variations together increased the analgesic power of *(14)* by 10^4. In connection with the recent progress of peptide synthesis similar results may be expected for other peptide mediators.

At present, the role of peptides in the regulation of blood pressure commands great interest[23]. For example, angiotensinogen, a globulin protein, is cleaved by the enzyme renin to give a decapeptide angiotensin I. This, in turn, is the precursor of angiotensin II, an octapeptide that acts as a vasoconstrictor and thus elevates blood pressure (Fig. 6)[24]. The converting enzyme, which splits off the C-terminal dipeptide histidylleucine from angiotensin I, can be blocked by the pentapeptide Pyr-Lys-Trp-Ala-Pro from snake venom as was shown by a research group at Squibb[25]. This results in an antihypertensive effect.

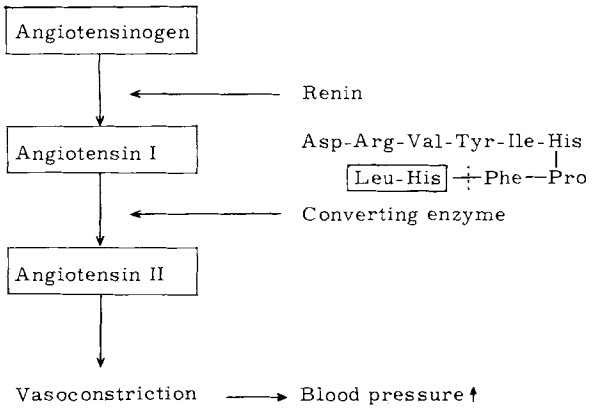
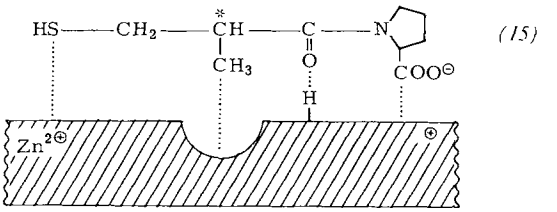


Fig. 6. The renin-angiotensin system of blood pressure regulation presents various possibilities of therapeutic interference. Antagonists of the angiotensins and enzyme inhibitors exhibit clinically useful properties.

Synthetic variations of the angiotensin structure also led to peptides that block the converting enzyme and thus lower blood pressure. Systematic slimming down of the lead structure ultimately afforded *N*-(3-mercapto-2-methylpropionyl)-L-proline *(15)* (SQ 14225, see Fig. 7) that obviously still fits excellently to the angiotensin converting enzyme[26]. *(15)* is active in man, even on oral administration. As Captopril® it has undergone extensive clinical testing and promises to become an antihypertensive of therapeutic value[27].



(15)

Fig. 7. Model concepts of receptor-substrate interactions served as guidelines in the development of simple molecules like *(15)* (SQ 14225) as inhibitors of angiotensin converting enzyme.

Very recently, evidence has been gathered in pharmacological and medical studies that these angiotensin-converting enzyme inhibitors may exert their hypotensive effect mainly by increasing levels of bradykinin[28], another peptide mediator. Certain prostaglandins[29] also appear to be involved in the effects of Captopril® on blood pressure. It is possible that once again a scientific hypothesis has led to progress by opening new research paths without being completely correct.

An important chapter of peptide research began with studies on release factors. They are formed in the hypothalamic region of the brain and reach the pituitary *via* specific channels. There they trigger or inhibit the release of pituitary hormones.

The signal cascade then includes the hormones from peripheral glands and these finally modulate physiological processes. The hypothalamic peptides are of great practical interest by virtue of their comparatively simple structures.

[*] The concept of receptor differentiation has been extremely successful in recent years. Drugs have been developed that influence various α- and β-receptors for epinephrine and norepinephrine (*e.g.* β-receptor blockers for cardiovascular therapy). A search for substances that selectively block the H_2-receptor of histamine has overcome early setbacks and resulted in a very successful drug (Tagamet®, SKF).

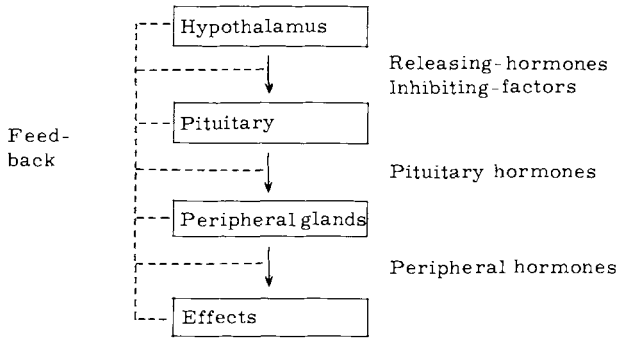


Fig. 8. Hypothalamic peptides, hormones from the pituitary and hormones of peripheral glands form a signal cascade with feedback mechanisms.

Thus human growth hormone (191 amino acids)[30] is released under the influence of a decapeptide[31]. The complementary inhibiting factor is somatostatin *(6)*[32], a sequence of 14 amino acids. Growth hormone itself is available either

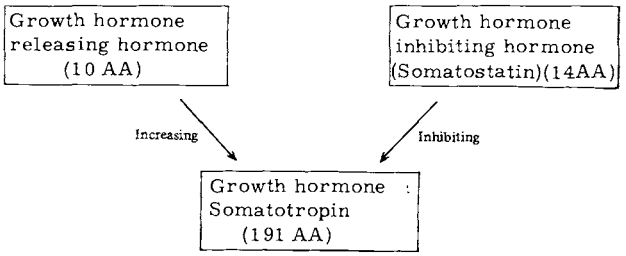
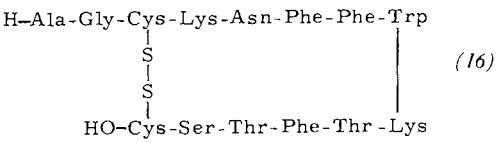


Fig. 9. The formation of pituitary hormones is modulated by release and inhibiting factors that consist of rather short peptide sequences, as shown for growth hormone (AA = amino acids).

by a multistep and difficult total synthesis[33] or *via* gene-manipulation by a biotechnical route[34]. Obviously, both its hypothalamic modulators present an economic and therapeutic alternative.



(16)

The state of the art in peptide chemistry and biology is illustrated well by somatostatin *(16)*. This cyclic disulfide *(16)* has been discovered in such divergent organs as brain and pancreas. As mentioned above, it inhibits the release of growth hormone. In addition, however, it also inhibits the secretion of insulin and its counterpart glucagon and is probably of great importance for the metabolism of glucose[35] and in diabetic disorders. Furthermore, somatostatin inhibits the secretion of gastric juices. Experience shows that such a variety of biological activities is a limiting factor for therapeutic application of a natural product[36]. Indeed, side effects were observed in most trials.

Somatostatin *(16)* was the first reported example of a human hormone that was produced by a microorganism and thus heralded a new era of gene technology. For the first time, a synthetic human gene had successfully been implanted into the genome of *E. coli* bacteria and expressed by a suitable operator[37]. Although somatostatin is also available by total synthesis[38], synthetic variations may be more important if they prove to be orally active and more specific than the parent compound[39].

Table 4. Peptides of quite different size and structure act as hormones or mediators in many organs of the human body.

Peptide		Number of amino acids
Hypothalamic releasing factors (release hormones)		
for luteinizing hormone	LRH	10
for follicle stimulating hormone	FRH	10
for thyreotropin	TRH	3
for growth hormone	GRH	10
Pancreatic hormones		
	insulin	51
	glucaton	29
	(somatostatin)	(14)
Pituitary hormones		
adrenocorticotropic hormone	ACTH	39
melanocyte stimulating hormone	MSH	13
	oxytocin	9
	vasopressin	9
Endorphins		>5
Enkephalins		5
Tissue hormones		
	bradykinin	9
	angiotensin II	8
	gastrin	17
	secretin	27
"Immune hormones"		
	factor thymique	
	serique	9
	thymosin α_1	28
	thymopoietin II	49
	fragment (32—36)	5

A selection of peptides that are currently under investigation in many laboratories is listed in Table 4. Our knowledge of tissue hormones and peptides involved in immunological processes is still very incomplete. There is sufficient evidence, however, that peptides participate in the process of expressing immune competence in B-cells and T-cells. As the entire immune system is very complicated, it may take some time before results from this type of peptide research can routinely be used in therapy. Selective stimulation of killer and helper cells would be of great importance for the treatment of cancer. Suppressor cell activation might help to control autoimmune diseases. Rheumatoid polyarthritis and some rare, but life-threatening diseases obviously involve immune defects of this kind (Fig. 10).

6. Molecular Biology in Drug Development: Prostaglandins

Extraordinarily intensive research activities were started when it became obvious that prostaglandins are formed almost ubiquitously in the human organism and participate in many physiological and pathophysiological processes. Many research teams[40] have contributed to our present knowledge about biogenesis, activity and metabolism of these short-lived substances (Table 5).

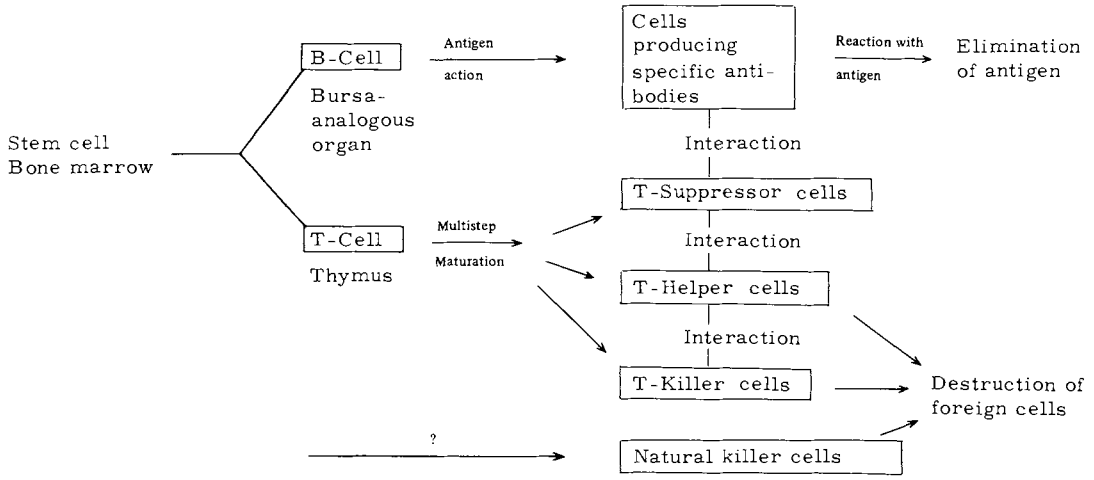


Fig. 10. Maturation of immune competent cells and their interactions are complex processes that are not yet completely understood. Here a highly simplified scheme is presented.

Table 5. Biological actions of prostaglandins.

Triggering:	Inflammation, pain
Regulating:	Neurotransmission in the vegetative peripheral nerve system, body temperature, birth, stomach secretion, bronchial resistance, function of blood platelets, microcirculation

It has been elucidated that polyunsaturated fatty acids, mainly arachidonic acid (Fig. 11), are enzymatically peroxidized to cyclic peroxides PGG_2 and PGH_2[41] that exhibit physiological activities in their own right but are rapidly transformed to give the so-called primary prostaglandins of the E, F, B, A, and D series[42].

As prostaglandins influence many important medicinal areas like blood pressure regulation, inflammatory processes, and pain a wealth of synthetic work was instigated. Brilliant syntheses made all natural prostaglandins available, despite their complex stereochemistry[43]. Structural variations were aimed at an increased specificity and at retardation of metabolic breakdown (Fig. 12). Nonetheless, the wide distribution and the diversity of physiological effects have so far proved a handicap for the therapeutic utilization of prostaglandins and their analogues.

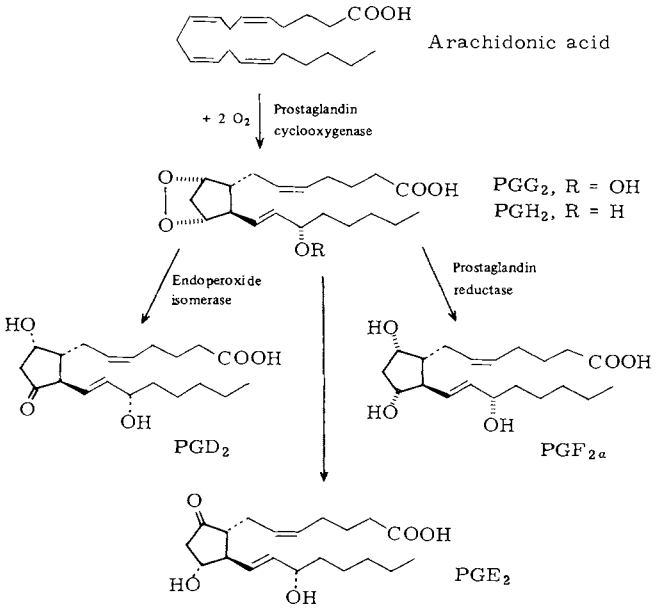


Fig. 11. Primary prostaglandins, *e.g.* PGD_2, PGE_2, $PGF_{2\alpha}$ are biogenetically formed *via* the "arachidonic acid cascade". They are not stored but are locally synthesized *de novo* and reach plasma or tissue levels in the order of ng/ml.

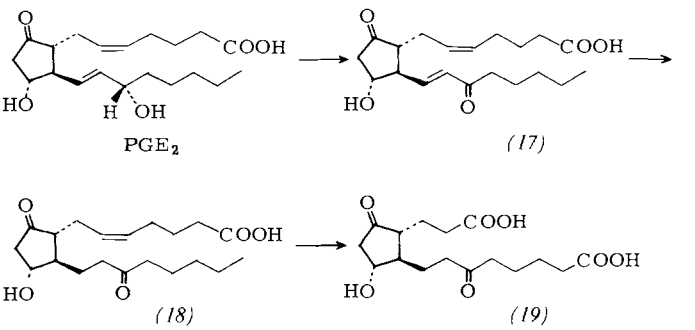


Fig. 12. In man, prostaglandins, *e.g.* PGE_2, are metabolized *via* oxidation to *(17)* by the enzyme 15-hydroxyprostaglandin-dehydrogenase and reduction of the double bond at C-13 to *(18)*. Once the keto group has been formed at C-15, all biological activity is lost. The half-lives of active prostaglandins range from seconds to a few minutes. Steric hindrance, for example by methyl groups at C-16, can retard the metabolic breakdown. β- and ω-oxidation transform *(18)* into *(19)*, the main metabolite in human urine.

In a period of initial resignation, fresh hopes were raised by the discovery of new very short-lived products of the arachidonic acid cascade. These substances are also formed from the endoperoxides and appear to play a major role in the regulation of blood pressure and function of blood platelets.

According to present knowledge, prostacyclin[44] is predominantly formed in the innermost endothelial lining of arteries and acts as a vasodilator and thus lowers blood pressure. At the same time it inhibits the adhesion of circulating platelets to the vessel wall and their aggregation. Under normal physiological conditions PGI_2 thus guarantees unhindered blood flow. On the other hand, TXA_2[45] is formed in platelets. It causes blood vessels to contract and platelets to aggregate. These functions acquire great importance if a vessel is injured. When blood flows through the lesion into the

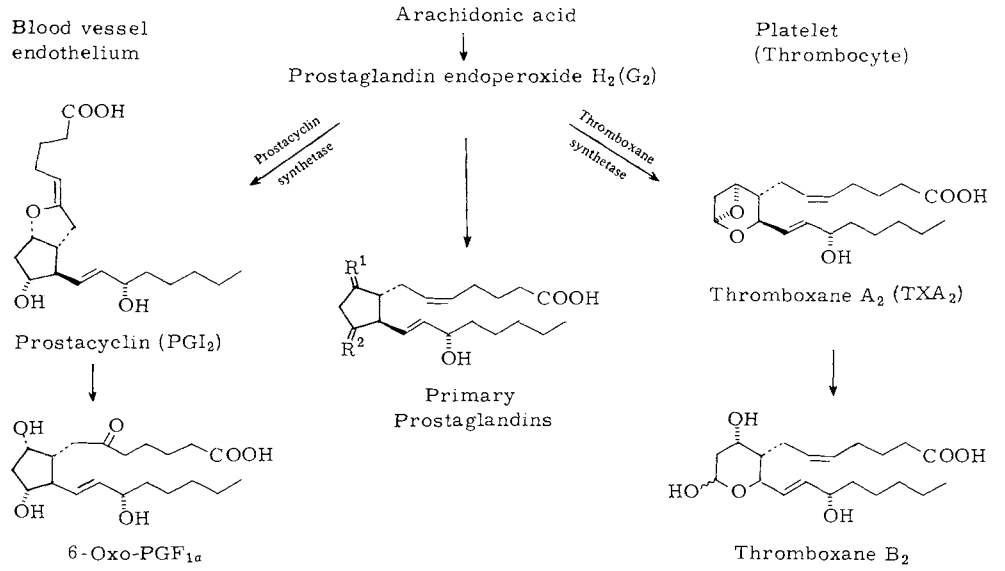


Fig. 13. In different locations—*i. e.* vessel wall and platelets—prostacyclin and thromboxane are formed from common precursors that are in turn derived from arachidonic acid. PGI_2 and TXA_2 have counteracting activities. They are rapidly degraded to inactive derivatives.

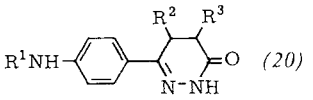
surrounding tissue, platelets contact the lower collageneous layers of the vessel. This contact triggers platelet aggregation. At the same time, local concentrations of prostacyclin have been lowered by destruction of the endothelial lining of the vessel. Thus the effects of thromboxane become predominant. The vessel contracts, platelets aggregate and thus the bleeding is stopped. Under the protective thrombus the vessel wall starts to regenerate.

In a number of cirulatory diseases the balance between prostacyclin and thromboxane A_2 is obviously disturbed. An increase in platelet aggregability has been observed in connection with arteriothrombotic disease and may be the result or even a causative factor of atheriosclerosis and infarctions[46]. Widely distributed risk factors like smoking, obesity, high blood pressure, diabetes make diseases of this type a frequent cause of premature invalidity or death. In consequence, major efforts are devoted to the search for structural analogues that act as agonists of PGI_2 or as antagonists of TXA_2[47]. Again prolongation of action is one of the important issues. This research effort has been encouraged by preliminary clinical results: Infusions of prostacyclin have caused a significant improvement of thrombotic disorders[48].

It is most interesting that substances with a very different structure possess biological activities which parallel those of prostacyclin. Substituted 6-aryl-4,5-dihydro-3(2*H*)-pyridazinones, especially derivatives bearing a *p*-aminophenyl or *p*-acylaminophenyl function *(20)*, were first investigated because of their excellent antihypertensive effects (Table 6).

This antihypertensive effect could be significantly increased by systematic variation of the basic structure and simultaneous biological testing. At the same time, an excellent inhibitory action on platelet aggregation was produced. Acetylsalicylic acid which is therapeutically used as inhibitor of prostaglandin endoperoxide synthetase, has been surpassed by more than four powers of ten.

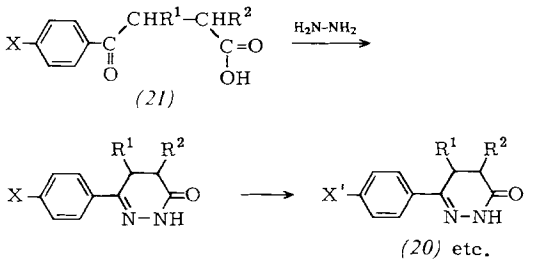
Table 6. Dihydropyridazinones *(20)* exert a pronounced inhibitory effect on platelet aggregation and lower the blood pressure by peripheral vasodilation. EC 50% = efficient concentration, which produces 50% of the measurable effect. ED 20% = efficient dose which produces 20% of the measurable effect.



(20)

Compound			Inhibition of platelet aggregation [a]			Antihypertensive action [b]	
			Collagen		ADP		
R^1	R^2	R^3	EC 50% [mg/ml]	RE	EC 50% [mg/ml]	ED 20% [mg/kg]	RE
H	H	H	14.75	33	46.44	0.180	1.89
CH_3CO	H	H	1.09	453	1.00	0.197	1.73
C_2H_5CO	H	H	0.74	667	0.64	0.060	5.67
CH_3CO	H	CH_3	6.31	11	46.40	15	0.02
$CH_3CHClCO$	CH_3	H	0.031	15900	0.099	0.0079	43.0
Acetylsalicylic acid			494	1.00	—	—	—
Dihydralazine			149	3.32	310	0.34	1.00

[a] Human platelets, *in vitro*, RE = relative efficiency, acetylsalicylic acid ≡ 1. [b] Rats, urethane narcosis, intraperitoneal application, RE = relative efficiency, dihydrazine ≡ 1.



(21)

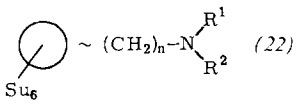
(20) etc.

Fig. 14. A great variety of biologically active substituted 6-aryldihydropyridazinones, *e.g. (20)*, can be obtained by cyclization of suitable γ-oxocarboxylic acids *(21)* with hydrazine and modification of the aromatic substituents.

Flexible synthetic pathways have been worked out for *(20)* and similar compounds (Fig. 14). They facilitate the search for compounds with either predominant antihypertensive or platelet aggregation inhibiting properties[49]. *In vitro* test models utilizing isolated thrombocytes[50] and the enzymes of the arachidonic acid cascade[45,51] are very useful for selecting these substances.

7. Structure-Activity Relationships in Synthetic Strategy

This last example showed once more the importance of structural variations of a new lead substance. Today, the enormous variety of preparative methods will allow the talented chemist to synthesize almost any substance he desires. However, economic considerations impose limitations. This can be illustrated by a simple calculation: The variation of a ring system *(22)* that is to be substituted at six positions by 50 different substituents (Su) and linked to a dialkylamine by a methylene chain of 1—10 units would require $50^6 \times 10 \times 30^2 = 140625 \times 10^9$ substances if 30 different alkyl substituents are to be considered.



(22)

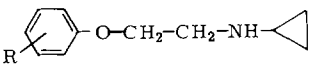
Obviously, costs of a few thousand dollars for the chemical synthesis and at least the same amount for a basic screening of one compound rule out such an approach. Great efforts are therefore devoted to methods that are able to limit the number of test compounds in a reasonable way. Many different methods[52] have been developed to establish quantitative structure-activity relationships[*].

So far, the relatively simple Hansch model and its variations have had the greatest success[53]. It is based on the plausible assumption that drugs have to pass lipophilic membranes and hydrophilic areas (for example, plasma) before reaching their receptor and that the binding to the receptor will also be influenced by hydrophobic interactions. In the Hansch model, biological activity is therefore correlated with the partition coefficient P (between H_2O and octanol) or the related factor π.

$$\log \frac{1}{BR} = k + a \log P + b (\log P)^2 + c\sigma + dE_s$$

BR = Biological activity (ED_{50} molar); k, a, b, c, d = constants; P = partition coefficient H_2O/octanol; σ = Hammett constant (electronic factor); E_s = Taft parameter (steric factor).

In addition, the Hammett constant can be considered as a measure of electronic factors and the Taft parameter as an indication of steric effects. If the structural variations are kept within rather narrow limits, Hansch analysis provides good predictions on the basis of even a small number of experimental data. An excellent example in point are the inhibitors of a monoaminooxidase[*] from the group of *N*-(phenoxyethyl)cyclopropylamines *(23)* (Fig. 15).



(23)

Experimentally determined equation:

$$\log(1/c) = 0.154\,\pi + 0.674\,E_s + 1.760\,\sigma + 4.226$$
$$r = 0.942,\ n = 16$$

Predictions:

R	calc.	observed
4-N=NC$_6$H$_5$	7.28	7.56
4-NH$_2$	4.57	4.40

Fig. 15. In the framework of well defined structural classes the Hansch model and its variations allow good predictions for structure activity relationships, specially for specific *in vitro* test models. c = concentration of test substance which produces a 50% inhibition of the enzyme monoamine oxidase. r = correlation coefficient, n = number of test substances.

The planning of a set of test compounds can profit greatly from use of the Craig diagram, which orders the functional groups common in medicinal chemistry by their contributions to the partition coefficient and to the Hammett parameter (Fig. 16).

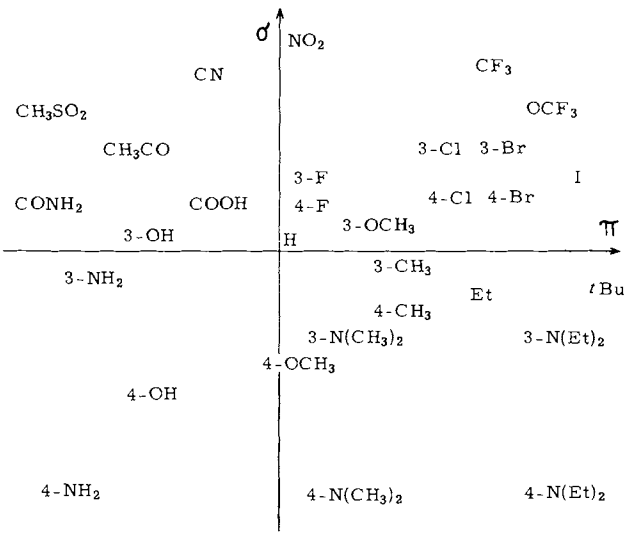


Fig. 16. The Craig diagram [54] facilitates selection of the most promising functional groups in the variation of aromatic substructures of drugs as it indicates the importance of π and σ parameters (see text).

[*] Hansch, Free-Wilson, discriminance, cluster analysis, pattern recognition, drug receptor mapping; quantum chemistry calculations.

[*] This enzyme degrades catecholamines such as epinephrin. MAO inhibitors have been clinically used as antidepressants.

One first selects a few examples from each quadrant formed by π and σ as coordinates. These compounds are synthesized and tested, and further synthetic work is then focused on substituents from that quadrant which produced the best test results.

The Topliss scheme[55] also assists in the systematic planning of test compounds by similar reasoning. For aromatic substructures, one synthesizes first the unsubstituted phenyl ring and then the *p*-chloro derivative. If the latter is more active this can either be attributed to a greater lipophilicity or an electron deficit in the aromatic ring. If a further increase in activity can be achieved with the 3,4-dichloro derivative, then lipophilicity is the more important factor. Logically, the dibromo or the iodo derivative are the next candidates for syntheses. If, however, the 3,4-dichloro derivative is less active than the *p*-chloro compound, 4-nitro substitution will tell if σ is the predominant factor. Corresponding considerations guide the synthetic work if the 4-chloro derivative is less active than or equiefficient with the unsubstituted phenyl derivative. The importance of quantitative structure activity relationships, such as the Hansch equation, lies mainly in selecting priorities for synthesis and in the assurance, that no reasonable compound in the area of the calculated optimum of biological activity has been overlooked. At this point, further improvement of activity can only be expected from a more profound variation of the lead structure. This, of course, then means that the equation used so far will no longer be valid and a new one will have to be developed.

A strategy for the rational development of new drugs could therefore be defined in the following way:

1) define a clear-cut goal;
2) select a lead substance based on biochemical considerations;
3) form a cooperative, multidisciplinary team;
4) apply relevant biological tests;
5) work out new lead substances by carefully designed variations;
6) check the significance of results and apply Hansch analysis, Topliss approach or Free-Wilson analysis to optimization wherever possible;
7) compare the results of structure activity analyses with the model ideas about the molecular mechanism of biological action;
8) utilize the refined model for future strategy of synthesis.

The application of these principles cannot guarantee success, but at least it improves the chances and reduces the dependance on serendipity in medicinal research.

8. Outlook

Until very recently, the organic chemist had little information about the reciprocal effects of molecules approaching each other and the detailed role of solvents and other components of a reaction medium. Frontier orbital calculations, and the study of membranes or other boundary surfaces, however, have increased our knowledge. The mutual influences between a bioactive substance and its receptor are much more complex, as biopolymers are flexible structures and intra- as well as extracellular body fluids have a complexity by far greater than most solvents used in organic chemistry.

Realistically, only a gradual reduction of effort can be expected in the search for new lead substances and their optimization to become useful drugs. For some time to come, therefore, the success of a medicinal chemist will depend on a combination of synthetic talent and versatility in the neighboring disciplines of biology and medicine. *Paul Ehrlich* was already aware of the importance of money, talent, patience, and good luck. Indeed, it often takes many years before a medicinal chemist knows with certainty whether his efforts were successful. He is compensated by the wide range of chemical methods and structures at his disposal. As the daily dose of most drugs is in the range of some milligrams to a few grams, even complex and therefore expensive substances can be acceptable. For life-saving drugs price considerations should be secondary in any case. This, of course, does not exclude great efforts to lower the costs of drug production. For instance, penicillins are available today at a fraction of the original costs.

The most important incentive for many medicinal researchers is the opportunity to alleviate the suffering of human beings. That this has been achieved to a considerable degree is well documented by the increase in life expectancy in civilized countries.

But much has still to be done to conquer further diseases. Speculation has no room in medicinal research. The danger of disappointment for the hopeful patient is too great. But some areas of interesting scientific progress may be mentioned. The intensive search for effective and well-tolerated drugs for the treatment of viral infections and/or malignant tumors may experience a breakthrough with the new results of interferon research. The clinical evaluation of these glycopeptides was made possible by recent progress in cell culture techniques. Methods of genetic engineering are also currently investigated to secure the supply of interferons should a routine therapy become feasible.

The study of trace elements[56] produces new insights as to their role in life processes and may trigger the development of new drugs.

The biological importance of fat soluble vitamins has been known for a long time; only recently, however, did we gain detailed information about their mode of action. Thus vitamin A and derivatives[57] apparently play an essential part in the differentiation of epithelial cells. They therefore offer new hopes for therapy and prevention of epithelial tumors (including cancer of the lung, the intestines, bladder, kidney, mamma, and skin)[57].

The transformation of such observations into the development of new drugs starts with the synthesis of substances that are more active, better tolerated and have a practical duration of action. Medicinal chemistry will therefore continue to be a challenge and an opportunity for talented and persevering chemists.

Received: June 18, 1980 [A 337 IE]
German version: Angew. Chem. 92, 802 (1980)

[1] *J. Thesing:* Industrielle Arzneimittelforschung, Medizinisch Pharmazeutische Studiengesellschaft e. V., Frankfurt/Main, 1977. From a 10-year survey of German companies. Similar, even higher costs have been reported from Anglosaxon countries.

[2] *E. Biekert:* Pharma-Dialog 54, Arzneimittelforschung 1978—Arbeit unter erschwerten Bedingungen. Issued by the Federal Association of the German Pharmaceutical Industry, Frankfurt/Main 1978.

[3] *J. F. Sadusk*, Pharm. Ind. *35*, 541 (1973). In 1973, for example, the Norwich Pharmacol Co. submitted 1.5 tons of documents to the FDA for the registration of "Dantrium".

[4] Gesetz zur Neuordnung des Arzneimittelrechts, vom 24. August 1976; Bundesgesetzblatt I p. 2445 (1976).

[5] *C. Neuberg, L. Liebermann*, Biochem. Z. *121*, 311 (1921).

[6] Contributions to the Fall Meeting of the Deutsche Pharmakologische Gesellschaft 1979, München; *D. Lenke, H. Gries, R. Kretzschmar:* Pharmacological Studies on the Mechanism of Action of Amezinium Metilsulfate (LU 1631), a New Compound with Sympathomimetic Action. *H.-D. Lehmann, J. Schuster, H. Giertz:* Hemodynamic Effects of a New Sympathomimetic: Amezinium Metilsulfate (LU 1631). *M. Traut:* Inhibition of Noradrenaline Uptake and of Monoamine Oxidase by Amezinium Metilsulfate (LU 1631). *K. W. Wilsmann:* Comparative Pharmacodynamic Studies in Healthy Volunteers on LU 1631—A New Type of Sympathomimetic Drug.

[7] *K. Masuda et al.*, Jap. Pat. 06265 (1970), Takeda; *K. Hashimoto, N. Taira, M. Hirata, M. Kokubun*, Arzneim.-Forsch. *21*, 1329 (1971); Corvaton®, Casella-Riedel.

[8] *R. Grashey, M. Baumann, W.-D. Lubos*, Tetrahedron Lett. *1968*, 5881; *W. D. Ollis, C. A. Ramsden*, Chem. Commun. *1971*, 1222; *J. Goerdeler*, Q. Rep. Sulfur Chem. *5*, 169 (1970).

[9] *P. Thieme, M. Patsch, H. König*, Justus Liebigs Ann. Chem. *764*, 94 (1972).

[10] *A. Amann, H. König, P. Thieme, H. Giertz, R. Kretzschmar*, DOS 2408288 (1974), BASF; Chem. Abstr. *83*, 193341g (1975).

[11] *G. Zbinden:* Wissenschaft und regulatorische Tendenzen in der Arzneimitteldiskussion. Symposium der Fachgruppe "Medizinische Chemie", GDCh General Meeting 1979, Berlin. Med.-Pharm. Studienges., Mainz 1980.

[12] *O. May*, Molekülvariationen; Basis für therapeutischen Fortschritt, Med.-Pharm. Studienges., Mainz 1980.

[13] *P. J. Scheuer:* Marine Natural Products, Chemical and Biological Perspectives, Academic Press, New York 1978.

[14] *J. de Barry, M. Fosset, M. Lazdunski*, Biochemistry *16*, 3850 (1977).

[15] *O. Schaumann*, Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmakol. *196*, 109 (1940); Pharmazie *4*, 364 (1949); Angew. Chem. *66*, 765 (1954).

[16] *C. B. Pert, S. H. Snyder*, Science *179*, 1011 (1973).

[17] *J. Hughes, T. W. Smith, H. W. Kosterlitz, L. A. Fothergil, B. A. Morgan, H. R. Morris*, Nature *258*, 577 (1975).

[18] *D. de Wied*, Life Sci. *20*, 195 (1977).

[19] *R. Mains, B. Eipper*, J. Biol. Chem. *74*, 4115 (1976); *R. Guillemin, T. Vargo, J. Rossier, S. Minick, N. Ling, C. Rivier, W. Vale, F. Bloom*, Science *197*, 1367 (1974); *R. Mains, B. A. Eipper, N. Ling*, Proc. Natl. Acad. Sci. USA *74*, 3014 (1977).

[20] *R. Walter, E. C. Griffiths, K. C. Hooper*, Brain Res. *60*, 449 (1973).

[21] Extremely sensitive and highly specific immuno-histochemical methods have allowed the localization of cells producing peptide hormones and transmitters as well as the corresponding channels of transport and receptors. *J. S. Hong et al.*, Brain Res. *134*, 383 (1977); *R. J. Miller et al.*, J. Biol. Chem. *253*, 531 (1978); *R. J. Miller, P. Cuatrecasas*, Naturwissenschaften *65*, 507 (1978).

[22] *D. Roemer, H. H. Buescher, R. C. Hill, J. Pless, W. Bauer, F. Cardinaux, A. Closse, D. Hansen, R. Huguenin*, Nature *268*, 547 (1977).

[23] *D. Regoli, W. K. Park, F. Rioux*, Pharmacol. Rev. *26*, 69 (1974); *L. Piesche, H. Hilse, E. Scheer*, Pharmazie *29*, 233 (1974).

[24] *L. T. Skeggs, J. R. Kahn, K. Lentz, N. P. Shumway*, J. Exp. Med. *106*, 439 (1957).

[25] *M. A. Ondetti, N. J. Williams, E. F. Sabo, J. Pluscec, E. R. Weaver, O. Kocy*, Biochemistry *10*, 4033 (1971).

[26] *M. A. Ondetti, B. Rubin, D. W. Cushman*, Science *196*, 441 (1977).

[27] *H. Gavras, H. R. Brunner, G. A. Turini et al.*, N. Engl. J. Med. *288*, 991 (1978).

[28] *R. Greenberg et al.*, Eur. J. Pharmacol. *57*, 287 (1979).

[29] *U. B. Olsen et al.*, Eur. J. Pharmacol. *54*, 229 (1979).

[30] *T. A. Bewley, J. S. Dixon, C. H. Li*, Int. J. Pept. Protein Res. *4*, 281 (1972); *H. D. Niall, M. L. Hogan, R. Sayer, I. Y. Rosenblum, F. C. Greenwood*, Proc. Natl. Acad. Sci. USA *68*, 866 (1971).

[31] *A. V. Schally, Y. Baba, R. M. G. Nair, C. D. Bennett*, J. Biol. Chem. *246*, 6647 (1971).

[32] *P. Brazeau, W. Vale, R. Burgus, N. Ling, M. Butcher, J. Rivier, R. Guillemin*, Science *179*, 77 (1973).

[33] *C. H. Li, D. Yamashiro*, J. Am. Chem. Soc. *92*, 7608 (1970); *A. Pecile, E. Muller:* Growth and Growth Hormone. Excerpta Medica, Amsterdam 1972.

[34] *D. V. Goeddel, H. L. Heyneker, T. Hozumit, R. Arentzen, K. Itakura, D. G. Yansura, M. J. Ross, G. Miozzari, R. Crea, P. H. Seeburg*, Nature *281*, 544 (1979).

[35] *D. Koerker, W. Ruch, E. Chidecel, J. Palmer, C. J. Goodner, J. Ensinck, C. C. Gale*, Science *184*, 482 (1974).

[36] *S. Efendic, T. Hokfelt, R. Luft*, Adv. Metab. Disord. *9*, 367 (1978); *M. Brown, W. Vale*, Biomedicine *28*, 93 (1978).

[37] *K. Itakura, T. Hirose, R. Crea, A. D. Riggs, H. L. Heyneker, F. Bolivar, H. W. Boyer*, Science *198*, 1056 (1977).

[38] *J. E. F. Rivier*, J. Am. Chem. Soc. *96*, 2986 (1974); *D. Sarantakis, W. A. McKinley*, Biochem. Biophys. Res. Commun. *54*, 234 (1973); *H. U. Immer, K. Sestanj, V. R. Nelson, M. Götz*, Helv. Chim. Acta *57*, 730 (1974).

[39] *D. F. Veber, R. Saperstein*, Annu. Rep. Med. Chem. *14*, 209 (1979).

[40] Surveys: *H. König*, Klin. Wochenschr. *53*, 1041 (1975); *P. C. Weber, W. Siess, B. Cherer, ibid. 57*, 425 (1979); *W. Bartmann*, Angew. Chem. *87*, 143 (1975); Angew. Chem. Int. Ed. Engl. *14*, 337 (1975).

[41] *M. Hamberg, J. Svensson, T. Wakabayashi, B. Samuelsson*, Proc. Natl. Acad. Sci. USA *71*, 345 (1974).

[42] *T. Miyamoto, S. Yamamoto, O. Hayaishi*, Proc. Natl. Acad. Sci. USA *71*, 3645 (1974); *N. Ogino, T. Miyamoto, S. Yamamoto, O. Hayaishi*, J. Biol. Chem. *252*, 890 (1977).

[43] For a well arranged survey see *J. S. Bindra, J. Bindra:* Prostaglandin Synthesis, Academic Press, New York 1977.

[44] *S. Moncada, R. Gryglewski, S. Bunting, J. R. Vane*, Nature (London) *263*, 663 (1976).

[45] *M. Hamberg, J. Svensson, S. Samuelsson*, Proc. Natl. Acad. Sci. USA *72*, 2994 (1975).

[46] *F. Gryglewski, R. Korbut, A. Ocetkiewicz*, Prostaglandins *15*, 637 (1978); *A. M. Lefer, M. L. Ogletree, J. B. Smith, M. J. Silver, K. C. Nicolaou, W. E. Barnette, G. P. Gasic*, Science *200*, 52 (1978); *M. T. Subbiah*, Mayo Clin. Proc. *53*, 60 (1978); *M. L. Ogletree et al.*, Europ. J. Pharmacol. *56*, 95 (1979).

[47] *K. C. Nicolaou, G. P. Gasic, W. E. Barnette*, Angew. Chem. *90*, 360 (1978).

[48] *A. Szczeklik, S. Skawinski, P. Gluszko, R. Nizankowski, J. Szczeklik, R. J. Gryglewski*, Lancet I, 1111 (1979).

[49] *R. Lebkücher, H. König, A. Amann*, DOS 2304977 (1973), BASF; Chem. Abstr. *81*, 136169s (1974); *R. Lebkücher, M. Thyes, H. König, H.-D. Lehmann, J. Gries, D. Lenke, J. Kunze*, DOS 2727481 (1977), BASF; Chem. Abstr. *90*, 137849m (1979).

[50] *H. J. Weiss*, N. Engl. J. Med. *298*, 1344 (1978); *C. Takeguchi, E. Kohno, C. J. Sih*, Biochemistry *10*, 2372 (1971); *N. Gilmore, J. R. Vane, J. H. Wyllie*, Nature *218*, 1135 (1968); *A. Eckenfels, J. R. Vane*, Br. J. Pharmacol. *45*, 451 (1972); *P. J. Piper, J. R. Vane*, Nature *223*, 29 (1969); *G. V. R. Born, ibid. 194*, 927 (1962); *G. V. R. Born, M. J. Cross*, J. Physiol. *170*, 397 (1964); *M. A. Packham, E. S. Warrior, M. F. Glynn, A. S. Senyi, J. F. Mustard*, J. Exp. Med. *126*, 171 (1967).

[51] *F. P. Nijkamp, S. Moncada, H. L. White, J. R. Vane*, Eur. J. Pharmacol. *44*, 179 (1977); *J. R. Vane*, Adv. Prostaglandin Thromboxane Res. *4*, 27 (1978); *E. F. Lüscher*, Agents Actions *8*, 282 (1978); *S. Moncada, R. Gryglewski, S. Bunting, J. R. Vane*, Nature *263*, 663 (1976); *P. Needleman, M. Minkes, A. Raz*, Science *193*, 163 (1976); *S. Moncada, R. Gryglewski, S. Buntin, J. R. Vane*, Prostaglandins *12*, 715 (1976).

[52] *Y. C. Martin:* Quantitative Drug Design. Marcel Dekker, New York 1978.

[53] *J. K. Seydel, K. J. Schaper*, Chemische Struktur und biologische Aktivität von Wirkstoffen, Methoden der QSWA, Verlag Chemie, Weinheim—New York (1979); *R. W. Fuller, M. M. Marsh, J. Mills*, J. Med. Chem. *11*, 397 (1968); *E. Kutter, C. Hansch*, J. Med. Chem. *12*, 647 (1969).

[54] *P. N. Craig*, J. Med Chem. *14*, 680 (1971).

[55] *J. G. Topliss*, J. Med. Chem. *15*, 1006 (1972).

[56] A recent symposium in Bielefeld, Germany, covered new aspects in this area.

[57] *H. Mayer, W. Bollag, R. Hanni, R. Ruegg*, Experientia *34*, 1105 (1978); *M. B. Sporn, N. M. Dunlop, D. L. Newton, J. M. Smith*, Fed. Proc. Fed. Am. Soc. Exp. Biol. *35*, 1332 (1976); *M. B. Sporn*, Nutr. Rev. *35*, 65 (1977); *R. Lotan, G. Neumann, D. Lotan*, Cancer Res. *40*, 1097 (1980).

The Synthesis of Unusual Organic Molecules from Azoalkanes

New synthetic methods (33)

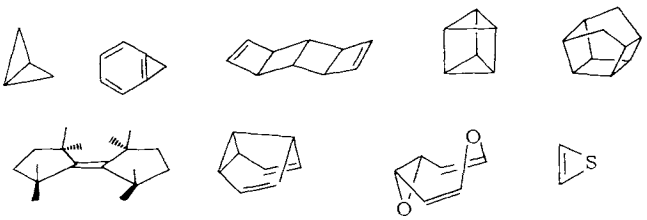
By Waldemar Adam and Ottorino De Lucchi[*]

Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday

The thermal or photochemical denitrogenation of azoalkanes constitutes an effective and convenient method for the preparation of unusual organic molecules, including highly ring-strained, sterically crowded, fluxional, antiaromatic and other interesting structures. The importance of this synthetic approach is that the azo linkage serves as a means of introducing the critical (usually last) bond in the complex target molecule. This article presents a cross-section of such elegant synthetic utilization of azoalkanes for fused-, bridged- and spiro-cyclization. Our coverage of the large body of literature has been directed by the complexity and novelty of the products. Azoalkanes are usually prepared *via* cycloaddition of azo dienophiles to appropriate substrates.

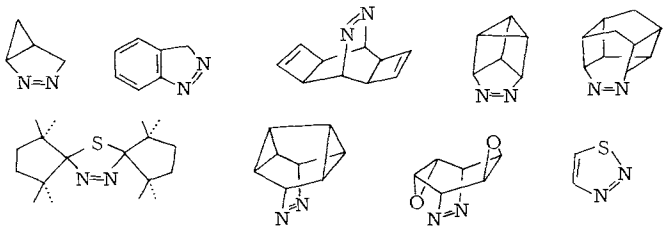
1. Introduction

Complex and unusual organic molecules such as the set of examples shown in Scheme 1, including ring strained, sterically crowded, fluctuating and antiaromatic structures, have captivated the organic chemist's curiosity and interest especially during the last two decades[1]. On the one hand, such molecules represent a formidable preparative challenge and allow us to sharpen and shape our synthetic tools; on the other hand they provide abundant opportunities for mechanistic and structural investigation and thereby permit us to enrich our knowledge of physical organic chemistry.



Scheme 1

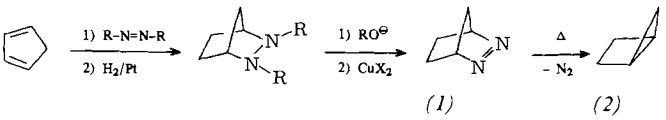
Although the illustrated set of unusual molecules displays great structural diversity, they share a common synthetic history. Specifically, the crucial step involved thermal and/or photochemical extrusion of molecular nitrogen from the corresponding azo compounds shown in Scheme 2. Clearly, the usefulness and convenience of this synthetic strategy cannot be overemphasized.



Scheme 2

[*] Prof. Dr. W. Adam (NIH Career Awardee, 1975—1980), Dr. O. De Lucchi
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931 (USA)
and Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

Criegee's elegant synthesis of bicyclo[2.1.0]pentane *(1)*[2] from the azoalkane *(2)* marks the beginning of this synthetic approach[3]. Not only was bicyclo[2.1.0]pentane *(1)* just about the most strained molecule that existed at the time,



(1) *(2)*

and thus provoked interest among the organic chemists to hunt for still more abused organic structures, but this sequence also laid down the essential *modus operandi* for the preparation of such unusual organic structures. During the last two decades, many interesting molecules have indeed been prepared *via* the elegant and convenient Criegee route.

In this article we report accomplishments and progress in this field. After surveying the various methods available for the preparation of azoalkanes[*], we shall illustrate the diversity of unusual molecules that can be prepared from the azoalkanes by thermal or photochemical extrusion of nitrogen. Complexity and novelty of the structures have dictated our choice of examples.

2. Synthesis of Azoalkanes

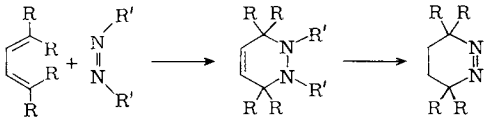
2.1. Cycloaddition of Azo Dienophiles

By far the most important method for the preparation of azoalkanes is Diels-Alder addition of azo dienophiles to appropriate diene substrates and subsequent oxidative hydrolysis of the resulting adduct (Scheme 3). In fact, the cycloaddition of azo dienophiles to 1,3-dienes marked the beginning of the famous Diels-Alder reaction[4]. The synthesis of 2,3-diazabicyclo[2.2.1]hept-2-ene *(2)* by *Criegee*[2] represents a specific application of this general synthetic pathway, which is of great importance in the present context.

The acyclic azodicarboxylates *(3a, b)* have often been employed as useful azo dienophiles[5]. However, the hydrolysis of the cycloadducts to the hydrazo compounds is frequently

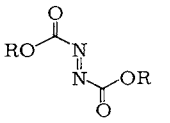
[*] The term "azoalkanes" is also taken to include unsaturated compounds.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0762 $ 02.50/0



Scheme 3

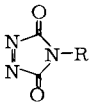
problematic, especially when sensitive functionalities are present. For this reason the more elaborate derivatives *(3c)*[6] and *(3d)*[7] were designed which permit cleavage under mild conditions. Recently, special techniques have been develop-



(3a), R = Me
(3b), R = Et
(3c), R = CH_2CH_2OTs
(3d), R = CH_2CCl_3

ed, *e.g.* with lithium methyl sulfide in hexamethylphosphoric triamide[8] and trimethylsilyl iodide or trimethylsilyl chloride and NaI[9], which facilitate cleavage of adducts derived from *(3a)* or *(3b)* under mild conditions.

More effective, and presently more widely used dienophiles are the 1,2,4-triazoline-3,5-diones (TAD) *(4)*. Particu-



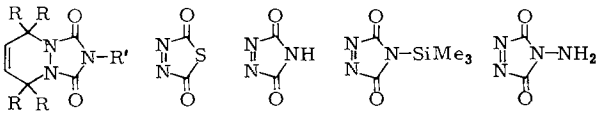
(4)
TAD

R = Et, *t*Bu, *n*Bu, *c*-C_6H_{11}, $PhCH_2$, *p*-MeC_6H_4, *p*-$NO_2C_6H_4$, *p*-ClC_6H_4, 3,4-$Cl_2C_6H_3$

R = Me (MTAD); R = Ph (PTAD)

larly popular are the *N*-phenyl (PTAD) and *N*-methyl (MTAD) derivatives[10]. An extensive mechanistic study[11] has revealed that the TAD derivatives *(4)* are among the most reactive dienophiles known. Furthermore, solvent and substituent effect show that the cycloaddition process is a typical concerted Diels-Alder reaction.

One of the serious disadvantages of the triazolinediones *(4)* is the difficulty of hydrolyzing the resulting urazoles *(5)*. The development of mild and selective hydrolytic methods for such urazole products will greatly widen the scope and synthetic potential of this excellent reagent. In order to cir-

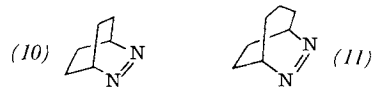


(5) *(6)* *(7)* *(8)* *(9)*

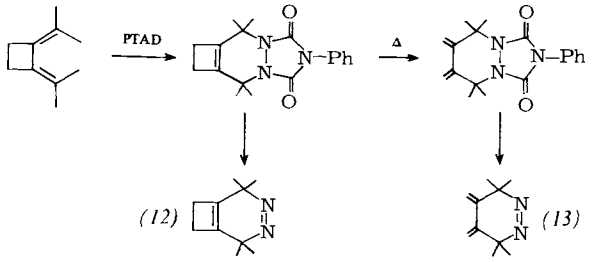
cumvent this problem, for example, the sulfur analogue *(6)* has been utilized as dienophile since the resulting cycloadduct can be hydrolyzed with great ease[12]. Unfortunately, *(6)* is rather unstable even under ambient conditions, and can only be employed for the most reactive Diels-Alder substrates. Also the parent triazolinedione *(7)*, formed *in situ* from its urazole, has been shown to undergo Diels-Alder reaction[13]. We feel that oxidative methods can be developed to transform the resulting unsubstituted urazoles *(5)*, R = H, into the corresponding azoalkanes. In the same vane, the *N*-silyl and *N*-amino derivatives *(8)* and *(9)*[14] might be useful, but no work has so far been reported along these lines.

2.1.1. Cyclic 1,3-Dienes

These remarks concerning the Diels-Alder reaction of azo dienophiles will now be illustrated by suitable examples. Let us first consider 1,3-dienes. By analogy with the preparation[2] of 2,3-diazabicyclo[2.2.1]hept-2-ene *(1)* from cyclopentadiene, 1,3-cyclohexadiene[15,16] and 1,3-cycloheptadiene[16] were converted into the corresponding azoalkanes *(10)* and *(11)*, respectively.

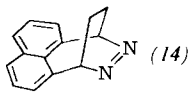


Interesting examples have been the preparation of azoalkanes *(12)* and *(13)*, obtained by the cycloaddition of PTAD with 1,2-diisopropylidenecyclobutane (dimethylallene dimer)[17]. Thus, hydrolysis and oxidation of the initial PTAD

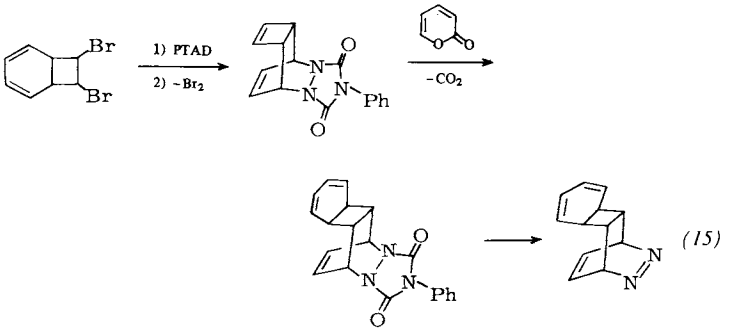


cycloadduct gave the very labile azoalkane *(12)*, while first thermal isomerization and subsequent hydrolysis and oxidation of the resulting urazole led to the considerably more stable azoalkane *(13)*.

The rather strained azoalkane *(14)* was prepared from pleiadiene by cycloaddition of ethyl azodicarboxylate, followed by hydrogenation, hydrolysis and oxidation[18].

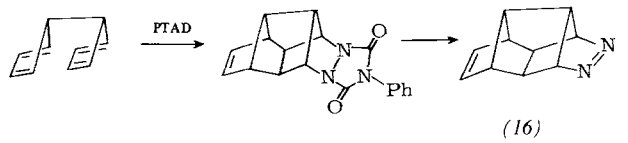


Among the more amazing applications are the preparation of the polycyclic azoalkanes *(15)* and *(16)*. The former commences with the cycloaddition of PTAD to the bicyclic dibromide[19]. The azoalkane *(16)* was prepared by PTAD cy-



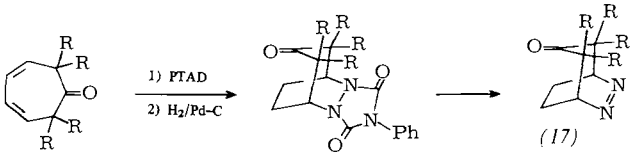
cloaddition to 1,1'-bicyclopentadienyl *via* the ingenious domino-Diels-Alder process[20].

The synthetic value of PTAD cycloaddition is clearly apparent. An unexpected example comes from our own work.



(16)

While 3,5-cycloheptadienones either isomerize or are unreactive towards the common dienophiles including azodicarboxylates, PTAD reacts smoothly to afford the corresponding urazoles, which are readily converted into their azo compounds *(17)*[21].

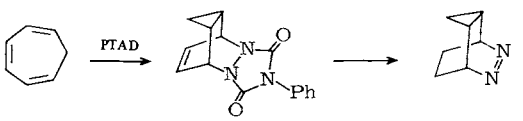


(17)

Numerous interesting PTAD cycloadditions have been performed which could be potentially useful for the preparation of exotic azoalkanes; however, the corresponding urazoles have not been converted into their respective azo compounds. Specific examples are the PTAD cycloadducts derived from dienic substrates[22a] such as divinylallene[22b], cyclopentadienone[23], isobenzofulvene[24], 1,2-dihydropyridines[25], phosphole sulfides[26], 2,3-dihydro-1,2-diazepines[27], 2,7-dihydrothiepin[28a], and homoheptafulvene[28b].

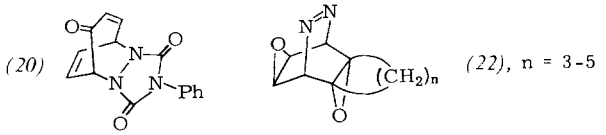
2.1.2. Cyclic Polyenes

One of the earliest cyclic polyenes to be employed was cycloheptatriene. Although ethyl azodicarboxylate[29] exclusively undergoes ene-reaction, PTAD[30] gives the norcaradiene adduct *(18)* in high yield. We have shown[31] that irre-



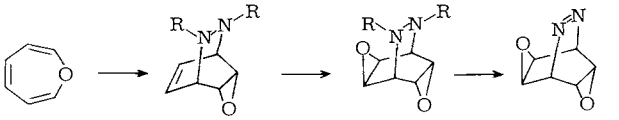
(18) (19)

spective of the electronic nature of the substituent at the 7-position, *i.e.* whether electron-withdrawing such as CO_2Me, CHO, CN, or Ph, or electron-donating such as MeO or Me, the exclusive product is the norcaradiene-type adduct *(18)*. Transformation of the urazole *(18)* into the azoalkane *(19)* has been accomplished in the usual way[15]. As expected, tropone gives the tropilidene-type PTAD adduct *(20)*[32a,b].



(20) (22), n = 3-5

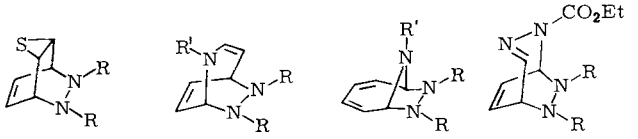
Among the hetero-analogues of cycloheptatriene, oxepin or benzene oxide has been converted into the bis(epoxy)azoalkane *(21c)*[33]. The difficult conversion of *(21b)* into *(21c)*, was accomplished with bis(trichloroethyl) azodicarboxylate as dienophile[7] which permits reductive cleavage under very mild conditions. The bridged azoalkanes *(22)*, $n=3$—5, have been prepared *via* a similar sequence[34]. Other unsaturated heterocycles forming adducts with azo dienophiles include thiepin [adduct *(23)*][35], azepine [adduct *(24)*][32], diazepine [adduct *(25)*][36], and heterocyclic polyenes *(26)*[37].



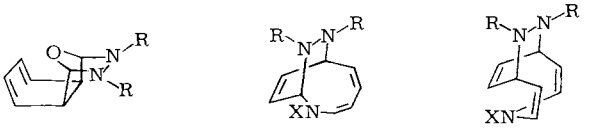
(21a) (21b) (21c)

R = $Cl_3CCH_2OC(=O)-$

Cyclooctatetraene has been a favored polyenic substrate for cycloaddition with azo dienophiles; for example, it is the



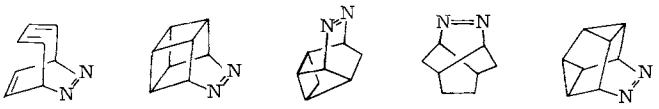
(23) (24a) (24b) (25)



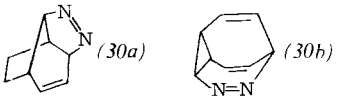
(26a) (26b) (26c)

X = $CONH_2$, COMe

precursor of azoalkanes *(27)*—*(30)*. Thus, early work[30,38] showed that PTAD leads to the [4.2.2.$0^{2,5}$]-product *(31a)*;

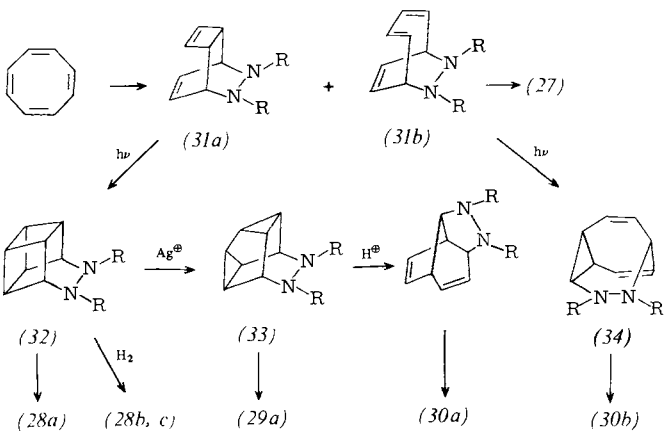


(27) (28a) (28b) (28c) (29a)



(30a) (30b)

however, on more careful examination[39], *(31b)* was also isolated and characterized. Photochemical isomerization gave the urazole *(34)* which was transformed into the azoalkane



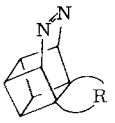
(31a) (31b) (27)

(32) (33) (34)

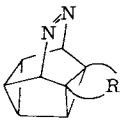
(28a) (28b, c) (29a) (30a) (30b)

(30b) (diazabullvalene)[39]. On the other hand, catalytic hydrogenation of the $Fe(CO)_3$-complex (protection of the diene moiety) of urazole *(31b)* and subsequent hydrolysis and oxidation afforded the azoalkane *(27)*[40a]. Furthermore, the $Fe(CO)_3$-complex of cyclobutadiene afforded the expected cycloadduct with ethyl azodicarboxylate, which was transformed into the useful azoalkane 2,3-diazabicyclo[2.2.0]hex-2-ene[40b].

Acetone-sensitized photocyclization of urazole *(31a)* produced *(32)* which was transformed into the interesting azoalkane *(28a)* (diazabasketene)[41]. However, silver ion-catalyzed rearrangement of the urazole *(32)* produced the snoutene derivative *(33)* which served as precursor to the azoalkane *(29a)* (diazasnoutene) and *(30)*[42]. Following this general synthesis, the structurally still more elaborate diazabasketene and diazasnoutene derivatives *(35)* and *(36)*, respec-



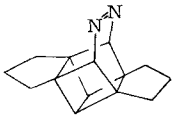
(35)



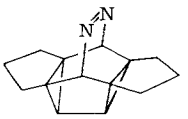
(36)

R = $-(CH_2)_n-$, (n = 3, 4, 5),
$-CH_2-CH=CH-CH_2-$,
$-CH_2-O-CH_2-$,
$-CH_2-NR-CH_2-$,
$-CH_2-SO_2-CH_2-$,
$-CH=CH-CH=CH-$

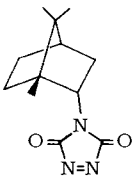
tively, have been prepared[43]. In fact, the doubly bridged diazabasketene *(37)* and diazasnoutene *(38)* could be synthesized in this way[44].



(37)

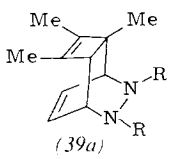


(38)

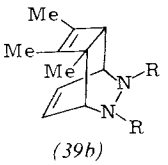


BTAD

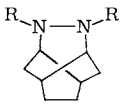
A potentially most valuable observation has been the very high degree of asymmetric induction when the optically pure (−)-4-(*endo*-2-bornyl)-1,2,4-triazoline-3,5-dione (BTAD) was allowed to cycloadd to cyclooctatetraene derivatives[45].



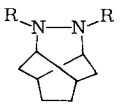
(39a)



(39b)

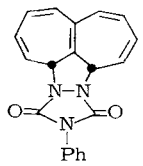


(39c)

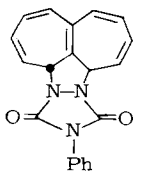


(39d)

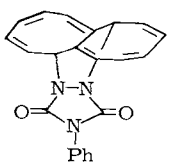
The optically pure urazoles *(39a, b)* could be isolated and converted into their labile azoalkanes in the usual way. No doubt, this ingenious application of the cycloaddition with azo dienophiles should be of great synthetic value and convenience.



(40a)



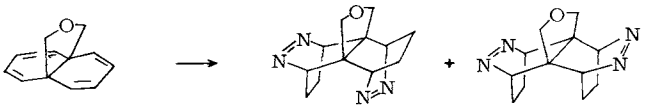
(40b)



(41)

Heptalene affords the isomeric PTAD adducts *(40a, b)*[46] while octalene gives the intriguing adduct *(41)*[47]. None of these urazoles has yet been transformed into the corresponding azoalkane.

Finally, bridged annulenes have also received some attention in terms of cycloaddition with PTAD. For example, the isomeric bis(azoalkanes) *(42a, b)* have been prepared *via* the

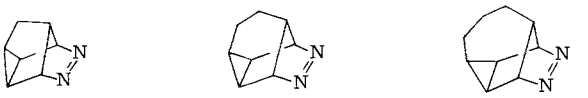


(42a) *(42b)*

PTAD route[48]. A number of other bridged annulenes have been shown to give similar PTAD adducts, but they have not been converted into the corresponding azo compounds[49].

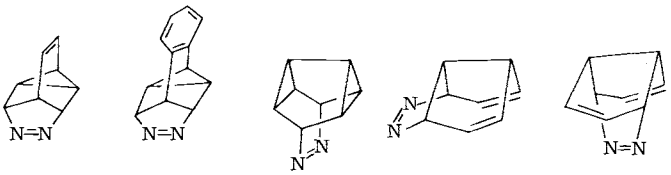
2.1.3. Cyclic 1,4-Dienes

The homo-Diels-Alder cycloaddition of azo dienophiles with 1,4-cyclodienes was first accomplished with bicyclo[2.2.1]heptadiene, affording the azoalkane *(43)* after the usual manipulations[30,50]. The congeners *(44)* and *(45)* were



(43) *(44)* *(45)*

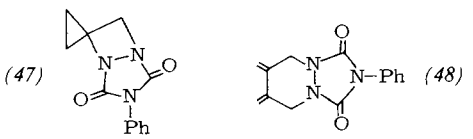
synthesized similarly[51]. Barrelene and benzobarrelene serve as precursors of azoalkanes *(46a, b)*[52]; semibullvalenes afford the exotic azoalkanes *(29)*[53].



(46a) *(46b)* *(29a)* *(29b)* *(29c)*

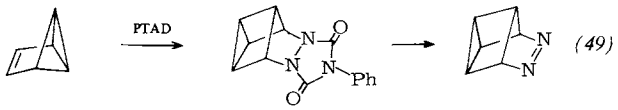
2.1.4. Strained Cycloalkenes

The ability of azo dienophiles, particularly TAD, to undergo [2+2]-cycloaddition with electron-rich olefins *via* dipolar intermediates is quite well established[54]. However, strained alkenes such as alkylidene- and alkenylidenecyclopropanes also give the urazoles *(47)*[55] and *(48)*[56], respectively.



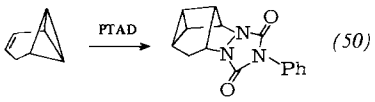
(47) *(48)*

A very clever application of such cycloaddition of PTAD has been the preparation of azoalkane *(49)* from benzval-



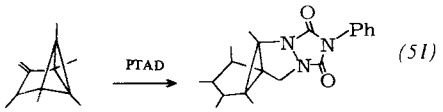
(49)

ene[57a]. Similarly, homobenzvalene has been converted into the urazole *(50)*[58] and isohomobenzvalene into urazole *(51)*



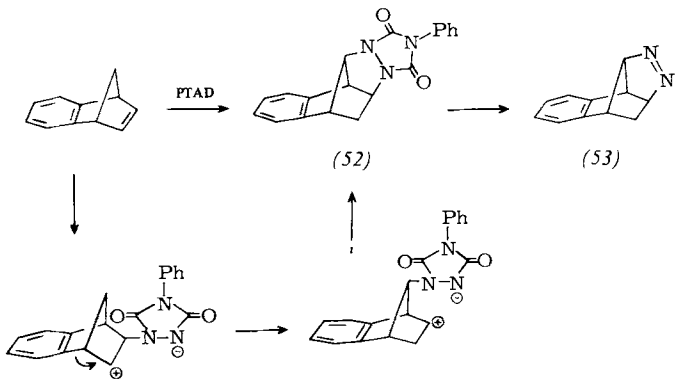
(50)

with PTAD[59]. Obviously some rather deep-seated rearrangements *via* dipolar intermediates are taking place in these intriguing cycloadditions.



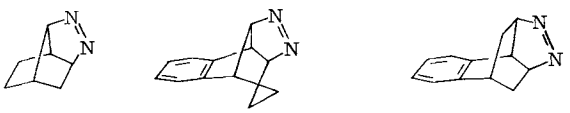
(51)

Along these lines, we have recently been able to demonstrate that benzonorbornadiene cycloadds with PTAD to give the interesting urazole *(52)* which has been converted into its azoalkane *(53)* in the usual way[60]. We rationalize that this fascinating reaction takes place *via* rearrangement of dipolar intermediates shown in Scheme 4. In a similar



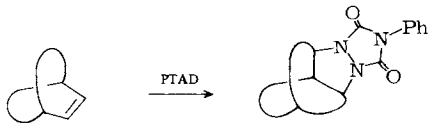
Scheme 4

manner the azoalkanes *(54)*—*(56)* could be prepared from norbornene, 7,7-dimethylenebenzonorbornadiene, and 6,7-benzobicyclo[3.2.1]nona-2,6-diene, respectively[60,61]. In fact,



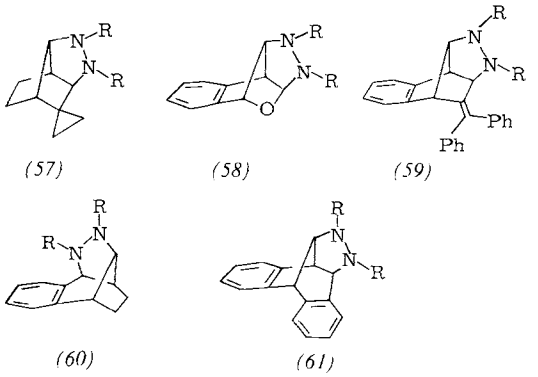
(54) *(55)* *(56)*

we could show that this dipolar addition to strained bicycloalkadienes is of general scope (5), allowing us to prepare the urazoles *(57)*—*(61)*[60–62]. However, bicyclo[2.2.2]octene



Scheme 5

did not react and the cyclopentadiene dimer gave exclusively ene-reaction.

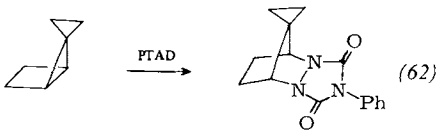


(57) *(58)* *(59)*

(60) *(61)*

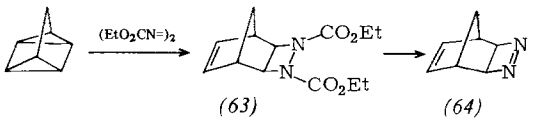
2.1.5. Compounds with Strained σ-Bonds

In view of the great reactivity of azo dienophiles, compounds with strained σ-bonds will undergo cycloaddition reactions. For example, 5,5-dimethylenebicyclo[2.1.0]pentane affords the urazole *(62)*[63]. Quadricyclane reacts with



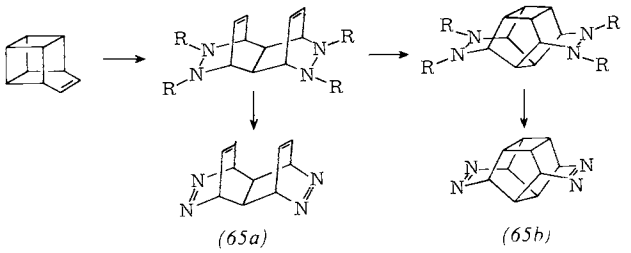
(62)

ethyl azodicarboxylate to give the unusual cycloadduct *(63)*, which has been converted into azoalkane *(64)*[64]. Finally,



(63) *(64)*

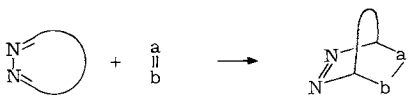
basketene is the precursor of the interesting bis(azoalkanes) *(65a, b)* formed on cycloaddition with ethyl azodicarboxylate[65].



(65a) *(65b)*

2.2. Cycloadditions to Cyclic 1,2-Diazadienes and Their Derivatives

This synthetic approach for the preparation of azoalkanes also utilizes the Diels-Alder reaction, but the azo linkage is created through the cycloheterodiene partner (Scheme 6).



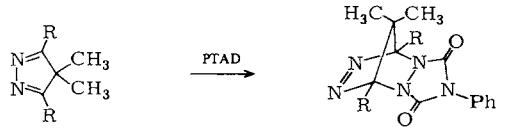
Scheme 6

Two heterodiene partners that have been employed for this purpose are the diazacyclopentadiene *(66)* and the tetrazine *(67)*[66].



(66) (67)

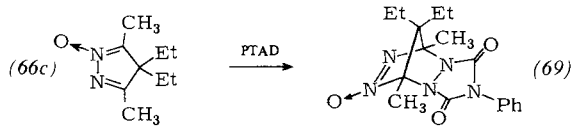
The preparation of the azoalkane *(68)* by addition of PTAD to *(66)* was one of the first examples of this synthetic



(66a), R = CH_3
(66b), R = Ph

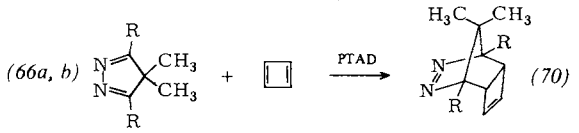
(68)

concept[67a-c]. Also the *N*-oxide derivative *(66c)* cycloadds PTAD to give the corresponding azoxy product *(69)*[67d].



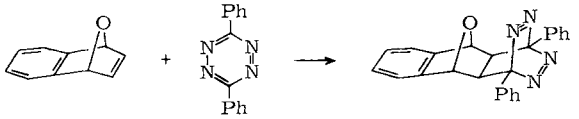
(66c) *(69)*

Furthermore, addition of cyclobutadiene to *(66)* affords the synthetically valuable azoalkane *(70)*[68].



(66a, b) *(70)*

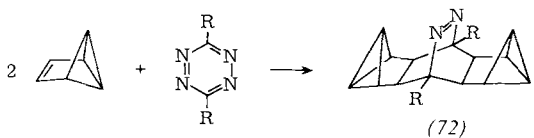
Some fascinating and elaborate azoalkanes have been prepared from tetrazines *(67)* as heterodienic cycloaddition partners. An early application was the synthesis of the bis(azoalkane) *(71)*[69]. A beautiful example is the double addition of benzvalene to *(67)* to afford the azoalkane *(72)*[70].



(67a) *(71)*

Similarly, the azoalkanes *(73)* and *(74)* are obtained by double addition of cyclobutadiene[71] or dimethylcyclopropene[72], respectively, to the tetrazine *(67)*.

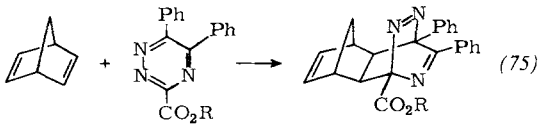
Related results are the preparation of azoalkane *(75)* by cycloaddition of bicyclo[2.2.1]heptadiene to a 1,2,4-triazine[73a]. Similar triazine cycloadditions have been reported recently with benzocyclopropene[73b] and cyclopropene[73c];



(67) *(72)*

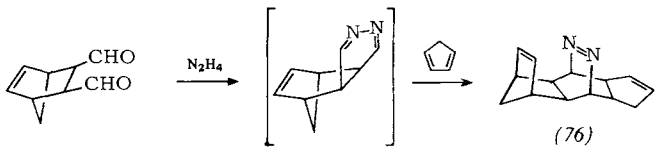


(73), R = Me, Ph, CO_2Me *(74)*



(75)

however the expected azoalkanes denitrogenate *in situ* to annulenes and azepines, respectively. Finally, the formation of azoalkane *(76)* in the reaction of the bicyclic dialdehyde with



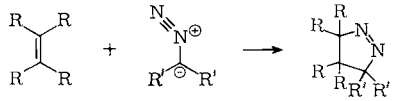
(76)

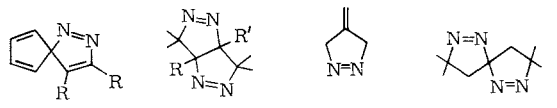
hydrazine presumably goes through the intermediary heteroiene[74]; the cyclopentadiene is produced *in situ* by retro-Diels-Alder of the heterodiene.

2.3. Cycloaddition with Diazoalkanes

A convenient and effective direct synthesis of cyclic azoalkanes by dipolar cycloaddition of diazoalkanes[75] is shown in its most generalized form in Scheme 7. To cite some interesting representative examples from the vast body of literature on this topic, acetylenes afford the azoalkanes *(77)*[76] and *(78)*[77] by single and double addition, respectively. Al-

Scheme 7





(77) *(78)* *(79)* *(80)*

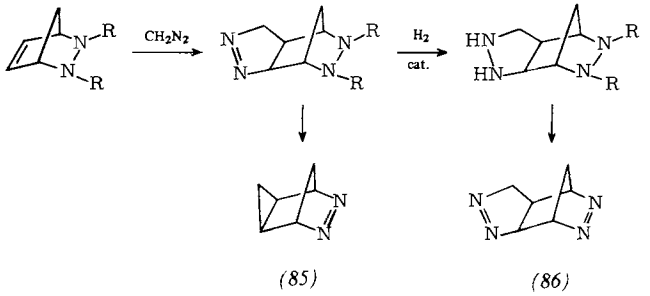


(81) *(82)* *(83)* *(84)*

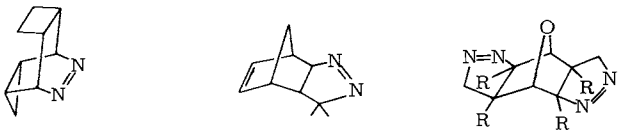
lene and diazomethane (and -propane) afford the azoalkane *(79)*[78] (and *(80)*[79]) again *via* the single and double addition of the diazoalkane. Butadienes lead to the azoalkanes *(81)* on reaction with 3-diazo-1-propene[80]. Cyclopropene[81], cyclobutene[82], and even cyclopentene[83] give the azoalkanes *(82)*, *(83)*, and *(84)*, respectively, with diazoalkanes.

The dipolar cycloaddition of diazoalkanes has also been applied successfully for the preparation of tricyclic and tetra-

cyclic azoalkanes. For example, the azoalkanes *(85)* and *(86)* have been prepared[84]. The azoalkanes *(87)*—*(89)* were prepared similarly by diazoalkane dipolar addition with 1,3,5-cyclooctatriene[85], with bicyclo[2.2.1]heptadiene[86], and 7-oxabicyclo[2.2.1]heptadiene[87].

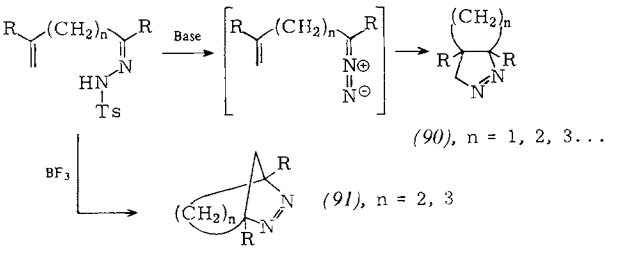


(85) *(86)*



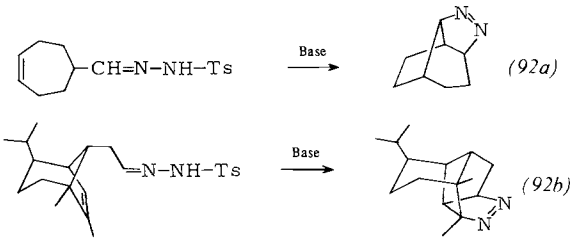
(87) *(88)* *(89)*

Interesting bicyclic azoalkanes are available through intramolecular diazoalkane cycloaddition. In these cases the diazo functionality is generated *in situ*, usually from the tosylhydrazone[88]. For example, bicyclo[*n*.3.0]-type azoalkanes *(90)* are prepared in this manner[89]. In this context it is of interest to mention that BF_3-catalyzed cyclization of such tosylhydrazones leads to the bicyclo[*n*.2.1]azoalkanes *(91)* instead[90]. Obviously the mechanism cannot involve a diazoalkane intermediate as in the base-catalyzed process. As more elaborate intramolecular cyclizations we cite the preparation of the azoalkanes *(92)*[91].



(90), n = 1, 2, 3...

(91), n = 2, 3

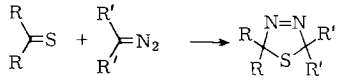


(92a)

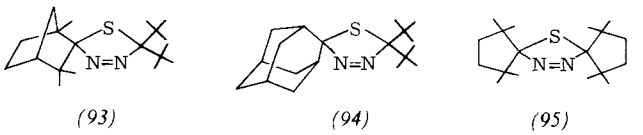
(92b)

Finally, it should be noted that diazoalkanes cycloadd to thioketones to generate the sulfur-containing azoalkanes

Scheme 8



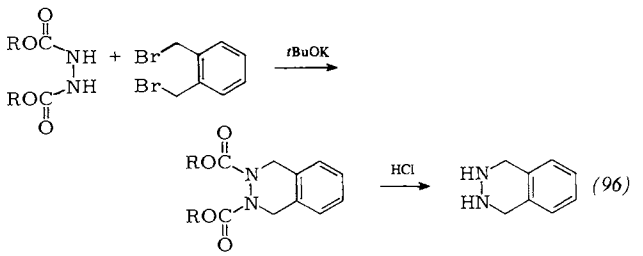
(Scheme 8). For example, the sterically hindered azoalkanes *(93)*[92], *(94)*[93], and *(95)*[94] have been prepared in this way.



(93) *(94)* *(95)*

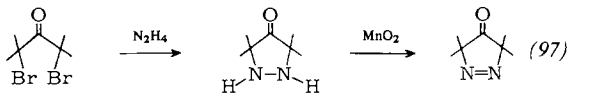
2.4. Cyclizations with Hydrazine and Derivatives

The 1,2-cycloalkylation of hydrazine and its derivatives constitutes a useful method for the preparation of hydrazo



(96)

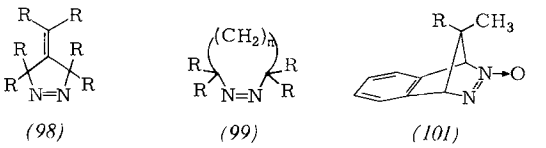
precursors to azoalkanes, as illustrated for the hydrazo compound *(96)*[95]. On the other hand, the interesting azoalkane



(97)

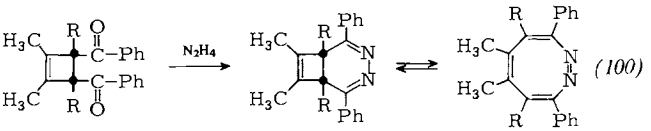
Scheme 9

(97) was prepared (Scheme 9) *via* the direct reaction of hydrazine and subsequent oxidation of the hydrazo product[96]. Derivatives of azoalkane *(98)* were prepared similarly, but



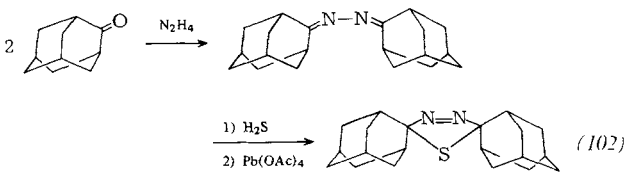
(98) *(99)* *(101)*

using ethyl hydrazodicarboxylate[97]. The sequence in Scheme 9 proved useful for the preparation of a number of azoalkanes *(99)*[98]. Diazocyclooctatetraene *(100)* was prepared



(100)

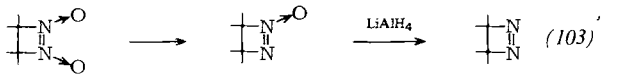
with hydrazine *via* elimination of water[99]. The azoxyalkanes *(101)* could be prepared from the corresponding 1,3-dibromoindans[100], and the azo compound *(102)* from adamantanone[101].



(102)

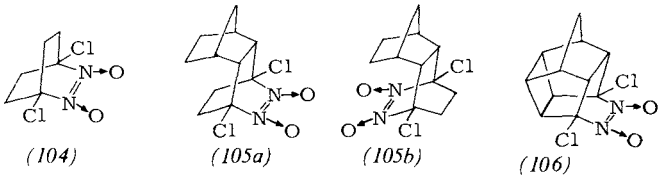
2.5. Miscellaneous Methods

We shall close this section with a potpourri of interesting preparations of azoalkanes which cannot be readily classified in any of the previous categories, but which are of synthetic potential. For example, the diazetine 1,2-dioxide[102] could be deoxygenated[103] to the diazetine *(103)*.



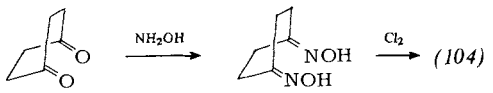
(103)

The fascinating azoalkane dioxides *(104)*[104], *(105)*, and *(106)*[105] have been prepared *via* the sequence illustrated for

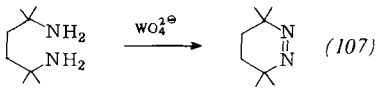


(104) *(105a)* *(105b)* *(106)*

(104). The latter has been reduced to its azoalkane. Thus, an effective method is at hand for further exploitation.

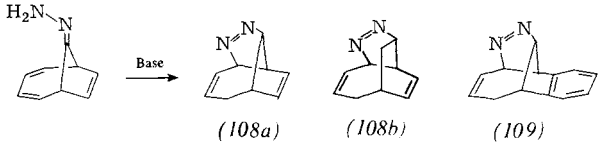


A convenient direct synthesis of azoalkane *(107)* (21% yield) is by tungstate oxidation of the corresponding diamine[104]. Clearly, this convenient transformation should be of



(107)

synthetic value, especially since it constitutes a convenient alternative for the iodine pentafluoride oxidative coupling of amines to form azoalkanes[106].



(108a) *(108b)* *(109)*

Of interest is the formation (75% yield) of the tricyclic azoalkane *(108a)*[107] and *(108b)* and the benzo-derivative *(109)*[108].

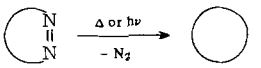
3. Denitrogenations of Azoalkanes

3.1. General Aspects

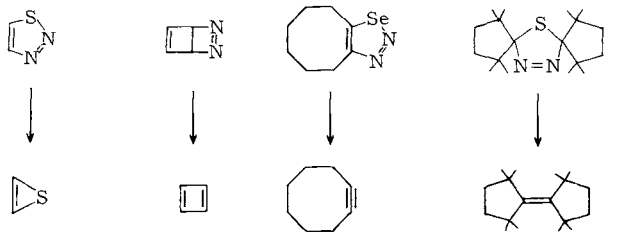
We are now ready to illustrate the usefulness and convenience of azoalkanes as precursors of unusual organic structures *via* thermal and photochemical denitrogenation. In view of the diverse repertory of synthetic methods that have been presented, it is assumed that the required azoalkanes can be made. Consequently, in this section we will not describe specifically the synthetic origin of the azoalkanes used.

Furthermore, the synthetic utilization of azoalkanes is so extensive that we are obliged to limit the scope of this article to cyclization reactions (Scheme 10). In other words, the very

Scheme 10



important applications for the introduction of double bonds, *e.g.* the preparation of antiaromatic thiirene[109] and cyclobutadiene[6], strained cyclooctyne[110,3a], or sterically congested bis(2,2,5,5-tetramethylcyclopentylidene)[94] (Scheme 11), will only be briefly considered. In fact, among the numerous cyclization reactions, we will be particularly concerned with bicyclizations leading to fused, bridged, and spiro structures (Scheme 12). The value of azoalkanes as synthons for unusual and complex structures will become quite apparent.



Scheme 11

Before taking up specific examples of azoalkane denitrogenations as a synthetic tool, we shall consider a number of practical aspects. For example, the range of activation energies for the pyrolytic extrusion of molecular nitrogen covers values as low as 15—20 kcal/mol to as high as 40—45 kcal/mol[3a]. This wide range of E_a values translates into decomposition temperatures as low as $-100\,^{\circ}C$ to as high as $+300\,^{\circ}C$. Many of the thermal denitrogenations are conducted in solutions of inert and thermally stable solvents. However, flash vacuum thermolysis (FVT) techniques are particularly convenient and have been used more and more frequently in recent years[3a,111].



Scheme 12 Fused Bridged Spiro-linked

Among the photochemical techniques either direct and/or sensitized photolysis have been used[3a,112]. From the spectral characteristics[113] of the *cis*-azoalkanes, which are of interest for our discussion, it is clear that the excitation process is $n_- \rightarrow \pi^*$ derived and lies in the 300—400 nm range. Although the $n_- \rightarrow \pi^*$ transition is much weaker (*ca.* 100-fold) than the $\pi \rightarrow \pi^*$ transition ($\varepsilon \approx 10^4$ to 10^5), the former is convenient for photoextrusion of nitrogen from azoalkanes. This

convenient long wavelength excitation is $n_- \rightarrow \pi^*$ in character and corresponds to the antisymmetric combination of the two nitrogen lone pair orbitals (Fig. 1). The corresponding $n_+ \rightarrow \pi^*$ excitation (from the symmetric combination) is at a considerably shorter wavelength and can fall below the $\pi \rightarrow \pi^*$ transition.

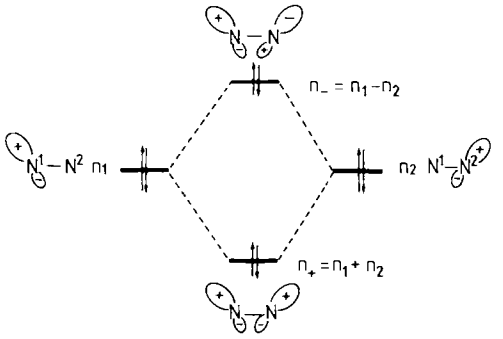


Fig. 1. Orbital diagram for azoalkanes.

The singlet states of the $n_- \rightarrow \pi^*$ transition have excitation energies E_S of *ca.* 70—90 kcal/mol and for the triplet states E_T is *ca.* 50—60 kcal/mol. Thus, triplet sensitization can be conveniently and effectively performed with the usual carbonyl sensitizers (acetone, benzophenone, benzil, *etc.*).

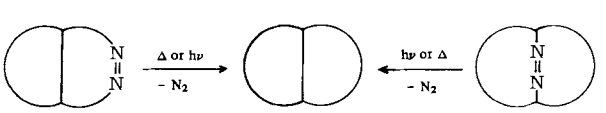
The quantum yields Φ for the photo-extrusion of nitrogen depend greatly on the structure of the azoalkane, ranging from as high as unity to essentially zero. In the latter case the azoalkane is termed a "reluctant" substrate for photodenitrogenation. For example, azoalkanes for which the —N=N— bond is contained in a five-membered ring photo-eliminate nitrogen efficiently (Φ *ca.* unity), while azoalkanes whose —N=N— bond is contained in a six-membered ring are reluctant (Φ *ca.* zero) towards photolysis.

The choice of thermal *vs.* photochemical activation depends on the structure of the particular azoalkane. This will now be illustrated by some representative examples, but our focus and emphasis will be on synthetic utility rather than mechanistic insight. In particular, we intend to demonstrate that the denitrogenation of azoalkanes is a viable route for fused, bridged, and spiro bicyclizations in organic synthesis.

3.2. Cyclizations to Give Fused Rings

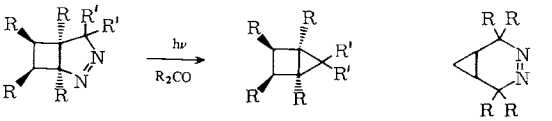
3.2.1. Bicyclic Structures

Cyclodenitrogenation from two structural types of azoalkanes, namely the fused and bridged azobicycloalkanes *(110)* and *(111)*, respectively, have been employed to construct



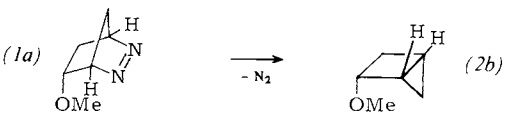
(110) *(111)*

fused-ring bicycloalkanes. In fact, the preparation of bicyclo[2.1.0]pentane *(2)* from 2,3-diazabicyclo[2.2.1]hept-2-ene *(1)* by *Criegee* and *Rimmelin*[2] demonstrated for the first time the viability and convenience of this synthetic concept for the construction of highly strained compounds[1c].



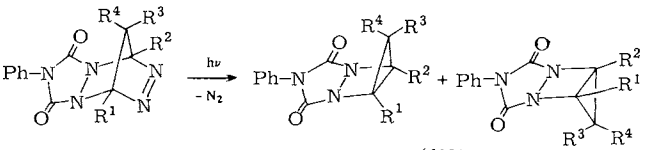
(83a) *(2a)* *(83b)*

The alternative route starting from a 2,3-diazobicyclo[3.2.0]hept-2-ene *(83a)* has been shown[82] to afford bicyclo[2.1.0]pentanes *(2a)* in high yield (50—100%) on photosensitized denitrogenation with triplet ketones. However, the isomeric 3,4-diazabicyclo[4.1.0]hept-3-ene *(83b)* eliminates nitrogen with great ease, leading to 1,4-dienes in a stereospecific concerted process[114] and such compounds are, therefore, not useful azo-synthons for bicyclization. While the stereochemistry at the bridgehead carbons in *(1)* is retained when the fused *(83a)*[115] serves as substrate[82], double inversion can predominate with the bridged [2.2.1]azoalkanes *(1a)* depending on the reaction conditions[116].



(1a) *(2b)*

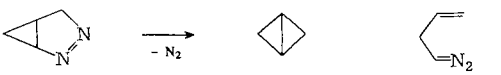
In a similar manner, the heterocyclic bicyclo[2.1.0]pentane *(112)* was prepared from the azo compounds *(68)*[66]. The in-



(68a), R = Me, $PhCH_2$, Ph *(112)*

termediacy of the 1,3-diradical precursor of these urazoles *(112)* was established by ESR, using matrix isolation techniques.

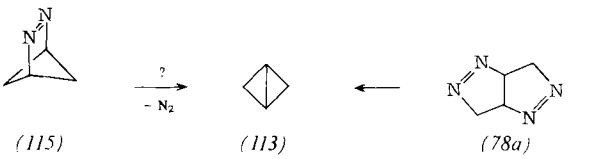
Substituted bicyclo[1.1.0]butanes *(113)*, the smallest and most strained fused bicycle, have been prepared by nitrogen extrusion from the fused 2,3-diazabicyclo[3.1.0]hex-2-enes *(82a)*[81a,116]. The yields of *(113)* are moderate (*ca.* 20—50%)



(82) *(113)* *(114)*

since the major products are isomeric 1,3-dienes. The mechanism of this denitrogenation is complex, since it has been shown that the diazoalkene *(114)*, generated by cycloreversion of *(82a)*, intervenes as precursor of the products[81,116,117].

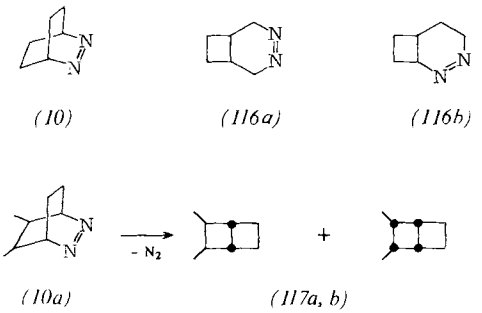
Use of the alternative route starting from the [2.1.1]azoalkane *(115)* seems not to have been reported. Presumably it is difficult to come by the highly strained *(115)*. However, double nitrogen extrusion from the fused bis(azoalkane) *(78)* takes place on heating or irradiation, affording the bicy-



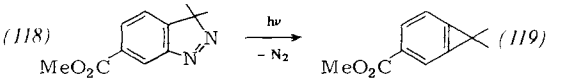
(115) *(113)* *(78a)*

clo[1.1.0]butane *(113)* in poor yields (15—20%)[77,118]. It was shown that nitrogen loss is stepwise, first leading to *(82)*. Again, diazoalkenes *(114)* are intermediates in this transformation and are the cause for the low yields of *(113)*.

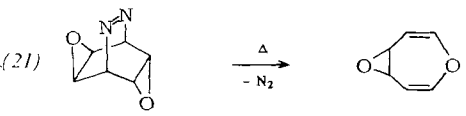
For the synthesis of bicyclo[2.2.0]hexanes *(117) via* denitrogenation, the [2.2.2]system *(10)* and the two [4.2.0]isomers *(116)* can serve as potential azo synthons. Thus, although the parent system *(10)* has been reported[15a] to give only 1,5-hexadienes, *i.e.* the acyclic product, the 5,6-dimethyl derivative *(10a)* afforded[119] the desired bicyclo[2.2.0]hexanes *(117)*. However, the [4.2.0]fused azoalkane *(116a)* gave exclusively[120] the 1,5-hexadienes *via* a stereospecific disrotatory cycloreversion process involving anchimeric assistance by cyclobutane. The isomer *(116b)* appears not to have been studied as a source of *(117)*.

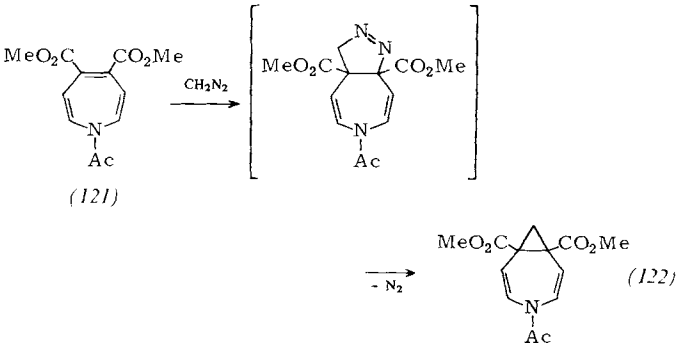


Fusion of a cyclopropane ring to an aryl moiety leads to highly strained compounds. For example, the benzopyrazole *(118)* photo-eliminates nitrogen to give *(119)*[121].



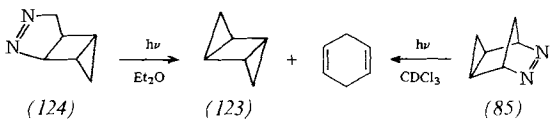
The bicyclo-fusion of heterocycles *via* azoalkanes has recently been accomplished, providing a convenient synthesis of *syn*-oxepin oxides *(120)*[33,122]. The bicyclo-fusion of a cyclopropane ring to a heterocycle is illustrated by *(121)*→*(122)*. Presumably an azoalkane formed as intermediate readily denitrogenates to yield the product *(122)*[123].





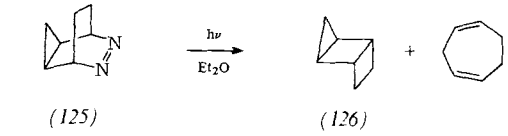
3.2.2. Polycyclic Compounds

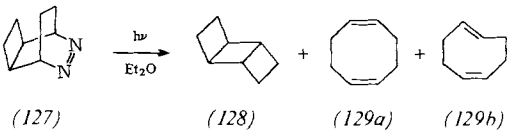
The smallest tricyclic system with fused rings that has been prepared by denitrogenation of azoalkanes is tricyclo[3.1.0.0^{2,4}]hexane *(123)*[84]. Thus, from the fused azotricycle *(124)* a *ca.* 10—15% yield of the *syn*-tricycle *(123)* was obtained along with minor amounts of the 1,4-cyclohexadiene.



Similarly, photolysis of the bridged azotricycle *(85)* gave a low yield (*ca.* 6%) of *(123)* and mostly (*ca.* 92%) 1,4-cyclohexadiene[124]. The latter was the exclusive product in the thermolysis of either *(85)* or *(124)*[84].

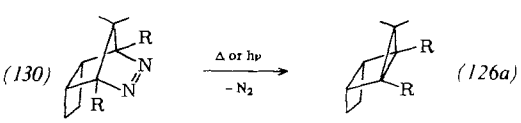
In analogous manner, thermolysis of the bridged azotricycle *(125)* gave only 1,4-cycloheptadiene[125], but photolytic denitrogenation[124] led to *ca.* 20% of the fused *anti*-tricycle *(126)* and 60% 1,4-cycloheptadiene. The fusion of three four-membered rings afforded the tricycle *(128)* from azoalkane *(127)*[124]. A more recent study showed[126] that in the photolysis as well as thermolysis the expected (1*Z*,5*E*)-1,5-cyclooctadiene *(129b)* is the major product, which thermally isomerizes to the *Z*,*Z*-isomer *(129a)*.



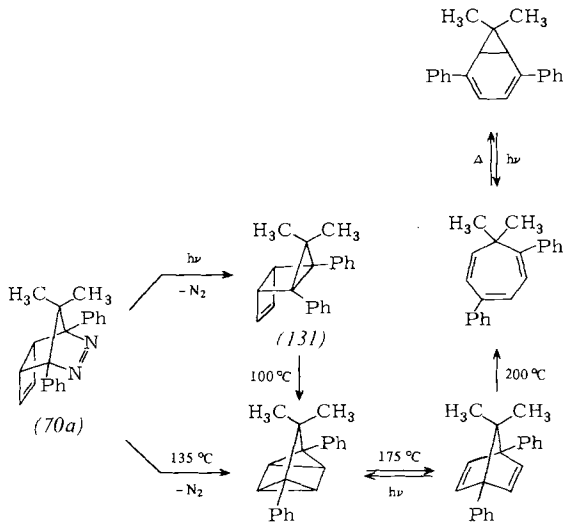


It is interesting to observe that in all three cases, *i.e.* tricycles *(123)*, *(126)*, and *(128)*, the rings are *anti* in the product, although in the azo precursors *(85)*, *(125)*, and *(127)* they were initially *syn* to the incipient cyclobutane bridge. This double inversion is apparently a general stereochemical course in the denitrogenation of such *syn*-azoalkanes. Furthermore, in this stereochemical arrangement of the reactants, denitrogenation is greatly enhanced through anchimeric assistance[15,51,84,127]. This concerted elimination affords the cyclic 1,4- or 1,5-diene as major product.

In contrast, when the azo-linkage and the cyclobutane ring are *syn* as in the bridged azo-tricycle *(130)*, the thermal (140 °C in $CHCl_3$) and photolytic nitrogen extrusions give essentially *quantitatively* the expected fused *anti*-tricycle *(126a)*[68a]. At higher temperatures (*ca.* 200 °C) *(130)* and/or *(126)* decompose into the corresponding ethylene and cyclo-

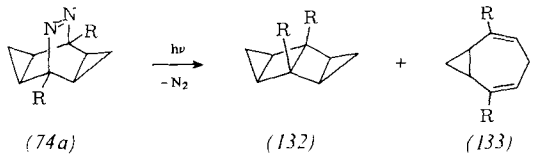


pentadiene. Similarly, the azoalkane *(70a)* photo-denitrogenates to give the fused tricycle *(131)* quantitatively[68b]; however, on thermolysis, the quadricyclane, norbornadiene, or

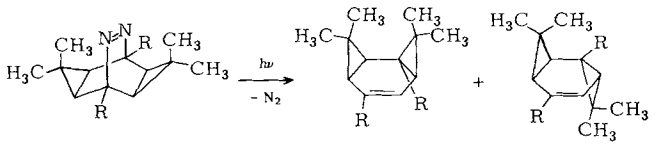


the cycloheptatriene valence isomers are produced, depending on the temperature. Other derivatives of type *(70)* lead to even more complicated product mixtures[68].

Four fused rings are present in the tetracycle *(132)* prepared from *(74a)*. Depending on the photolysis conditions,

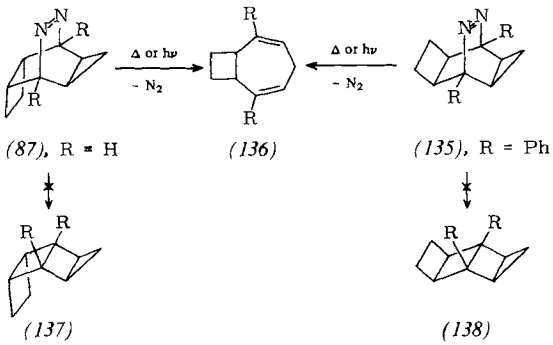


(132) is formed in high yield (90%), along with the homotropilidene *(133)*[72a,c]. However, when the cyclopropane rings are disubstituted as in *(74b)*, then for steric reasons the bishomobenzenes *(134)* are produced[72d].



(74b), R = CN, CO_2Me, CO_2H, COCl, $CONH_2$ *(134)*

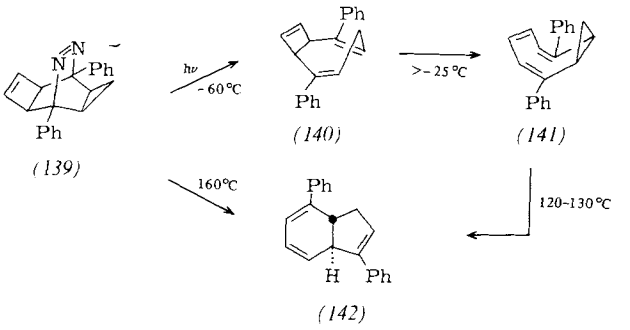
The isomeric azo compounds *(87)* and *(135)* on heating or irradiation afforded the bicyclodiene *(136)* rather than the expected tetracycles *(137)* and *(138)*, respectively[85,128]. The



(87), R = H *(136)* *(135)*, R = Ph

(137) *(138)*

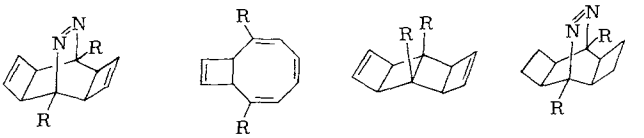
unsaturated analogue of *(135)*, *i.e.* azoalkane *(139)*, did also not furnish the corresponding tetracycle[128]. Instead, on photolysis at −60 °C the triene *(140)* was formed which above



(139) *(140)* *(141)* *(142)*

−25 °C valence-isomerized to *(141)*. The latter rearranged at 120—130 °C to the 3a,7a-dihydroindene *(142)*, the thermolysis product of azoalkane *(139)* at 160 °C.

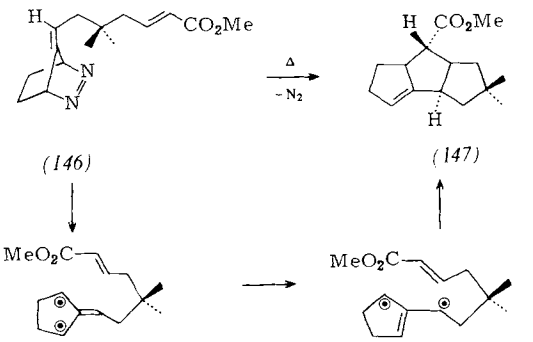
Thermal and photochemical denitrogenation of the azoalkane *(73)*, R = Ph[129], afforded complex product mixtures which can be rationalized *via* the intermediary bicycle *(143)*,



(73) *(143)* *(144)* *(145)*

R = Ph. However, a recent reinvestigation of *(73)*, R = Me, CO_2Me, Ph, confirmed that the tetracycle *(144)* is indeed produced[71]. The saturated analog *(145)* was reported[129] to give only the ring-opened product, *i.e.* the analogue of *(143)*.

A most ingenious fused tricyclization was executed recently *via* intramolecular trapping of a trimethylenemethane di-

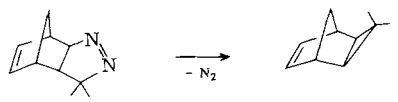


(146) *(147)*

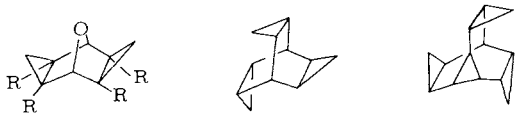
radical[130]. Thermal loss of N_2 leads to the diradical, which then undergoes regio- and stereoselective intramolecular cyclization to give the tricyclic product *(147)*.

3.2.3. Bridged Structures

The following examples concern cyclizations on substrates possessing bridged bicyclic skeletons. For example, denitrogenation of the azoalkane *(88)* leads to the tricycles *(148)*[86]. Quite analogously the complex polycyclic structures *(149)*, *(150)*, and *(151)* were prepared respectively from the azoalkanes derived from diazomethane addition to 7-oxabicyclo[2.2.1]hepta-2,5-diene[87] and homobarrelene and bullvalene[131].

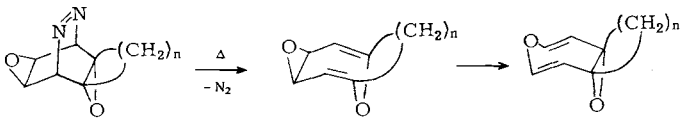


(88) (148)



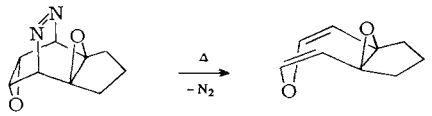
(149) (150) (151)

Finally, analogous to the preparation of *syn*-oxepin oxide *(120)*, the bridged oxepin oxides *(152)* and their valence isomers *(153)* have been prepared from azoalkanes *(22)*[34].



(22) (152) n = 3-5 (153)

For $n=3$, 4 the valence isomer *(152)* prevails, but for $n=5$ it is *(153)*. However, *(153)*, $n=3$, could be made from the isomeric azoalkane *(154)*. Clearly, a three-membered ring that is *anti* to the departing N_2 is essential to obtain a particular oxepin oxide[34].



(154) (153), n = 3

3.3. Cyclizations Foming Bridged Bicyclics

3.3.1. Cage Structures

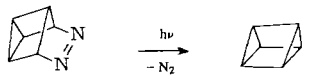
Quadricyclane *(155)*, synthesized *via* denitrogenation of the appropriate azoalkane, was one of the earliest target molecules in bridged bicyclization. First *Moriarty*[50b] reported that the caged azoalkane *(43)* gave a 35% yield of the quadricyclane *(155)* on thermolysis; however, *Allred* and *Johnson*[51]



(43) (155) (64)

showed that thermolysis of *(43)* did not afford quadricyclane *(155)*, but rather its valence isomer norbornadiene. These thermolysis results were recently[132] confirmed by *Turro et al.*; however, the quadricyclane was the major product. For example, triplet sensitized photolysis of *(43)* gave as much as 90% quadricyclane. It is of interest to mention in this context that the azoalkane *(64)* also served as an efficient source of quadricyclane. While in the thermolysis only *ca.* 5% of quadricyclane are produced[64], direct and triplet sensitized photolysis of *(64)* give a *ca.* 90% yield of this strained cage product[132].

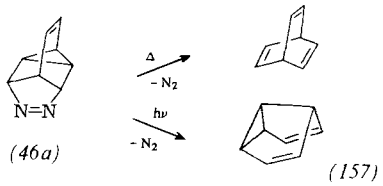
Another much studied and intriguing example is the synthesis of prismane *(156)* from the azo precursor *(49)*[57]. On heating at 130—150 °C, the caged azoalkane *(49)* quantitatively affords benzene instead of the desired prismane[133]. However, on singlet excitation in a nitrogen atmosphere *ca.* 10% of prismane was formed, accompanied by *ca.* 30% ben-



(49) (156)

zene, 45% Dewar benzene, and 3% benzvalene[57a,134]. The triplet sensitized process led to diazacyclooctatetraene, but these rearrangement processes of azoalkanes without denitrogenation are taken up in a later section.

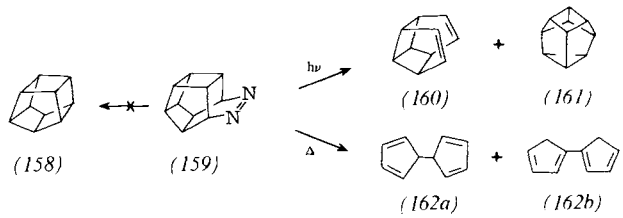
The caged azoalkane *(46a)* derived from barrelene did not produce the caged product, either on thermolysis or on photolysis[52]. Thus, on heating at 60—80 °C, *(46a)* smoothly lost N_2 to afford quantitatively barrelene, while triplet sensitized photolysis quantitatively afforded semibullvalene *(157)*, the



(46a) (157)

di-π-methane rearrangement product of barrelene. On direct photolysis of *(46a)* both barrelene (24%) and semibullvalene (73%) were formed along with cyclooctatetraene (3%). Analogous results were observed for the benzo- and naphtho-annelated derivatives.

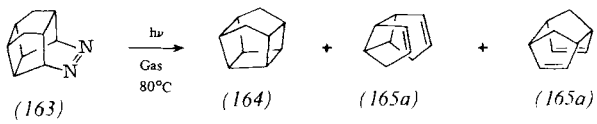
The synthesis of pentaprismane *(158)* was attempted by denitrogenation of the caged azoalkanes *(159)* and *(65a)*, but did not lead to this highly symmetrical and strained product. For example, on direct photolysis *(159)* gave the hydrocarbons *(160)* and *(161)* in 10% and 12% yields, respectively[135].



(158) (159) (160) (161) (162a) (162b)

Flash vacuum pyrolysis at 430 °C produced the isomeric dihydrofulvalenes *(162a, b)*. Similarly, the bis-azoalkane *(65a)* gave the dihydrofulvalene *(162a)*[65b].

On the other hand, *Turro et al.*[136] recently showed that the photo-reluctant azoalkane *(163)* gave the desired cage hydrocarbon *(164)* in 60% yield, together with the isomeric



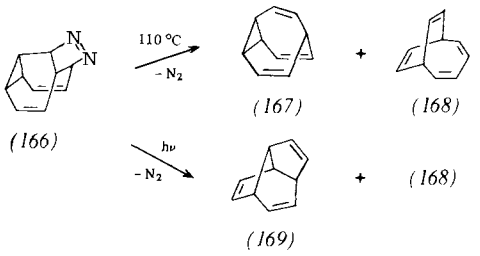
(163) (164) (165a) (165a)

cyclopentadiene dimers *(165a)* and *(165b)* in 22 and 5% yields, respectively. Clearly, the synthesis of caged hydrocarbons from suitable azo precursors *via* bridged bicyclization

on denitrogenation is a viable synthetic approach to such complex structures.

3.3.2. Fluxional Structures

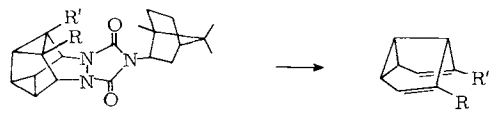
Bullvalene *(167)*, the best-known fluxional molecule, was prepared[137] *via* the azoalkane *(166)* by thermal extrusion of nitrogen. At 110 °C the bullvalene was formed in 46% yield



(166) *(167)* *(168)* *(168)* *(169)*

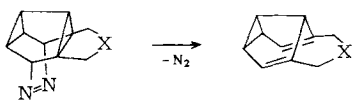
along with the bicyclic compound *(168)* (53% yield). However, on photolysis *(168)* and the tricyclic product *(169)* were formed instead of bullvalene.

Essentially simultaneously the elegant synthesis of semibullvalene *(157)* was accomplished *via* thermal denitrogenation of 9,10-diazasnoutene *(29a)* by *Askani*[42a], *Moriarty*[42b] and *Paquette*[42c]. A large number of 1(5)-, 2(4)-, and 3-substituted semibullvalenes *(157)* have been prepared in this way by *Paquette et al.*[42c] from the corresponding derivatives



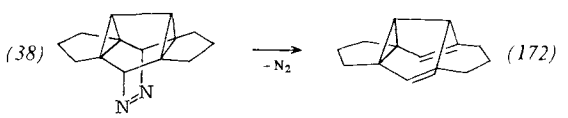
(170a), R = H; R' = CH_3
(170b), R = CH_3; R' = H

of *(29a)*[42d] with substituents such as CH_3, C_6H_5, CH_2OCH_3, CH_2OH, F, and CHO. Also, the absolute configuration and chiroptical properties of 2(4)-methylsemibullvalene were recently reported[43c]. Furthermore, a variety of fascinating 2,8-bridged semibullvalenes *(171)* could be synthesized from the corresponding bridged 9,10-diazasnoutenes *(36)* in this manner[43]. Particularly intriguing is the doubly bridged semibull-

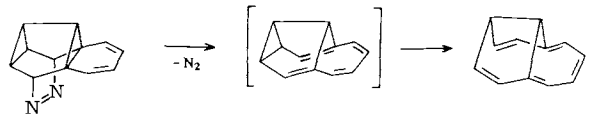


(36) *(171)*

valene *(172)*[44]. The semibullvalenes have been invaluable in providing essential information on the dynamics of such fluxional structures. For example, the fascinating 2,8-(1,3-



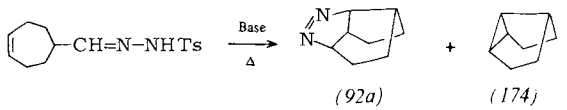
butadienylene)-bridged semibullvalene *(173)*, which was generated from the azoalkane *(36a)* on loss of nitrogen[138], exists exclusively as the bridged pentaene valence isomer *(173a)*.



(36a) *(173)* *(173a)*

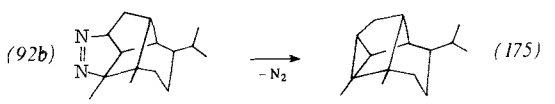
3.3.3. Miscellaneous Systems

To terminate this section, let us consider a number of azoalkane denitrogenations which lead to synthetically interesting molecules, but which cannot be classified as caged or fluctuating structures. Thus, the perhydro-semibullvalene *(174)* is formed in the base-induced decomposition from the tosylhydrazone, presumably *via* the azoalkane *(92a)*, which

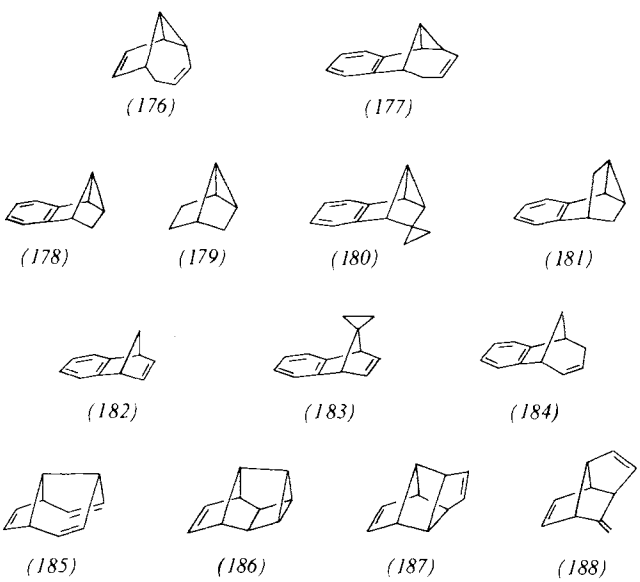


(92a) *(174)*

in turn results from intramolecular dipolar cycloaddition of the intermediary diazoalkane[91,42d]. Similarly, azoalkane *(92b)* afforded the tetracyclic product *(175)*[91b] on photo-de-



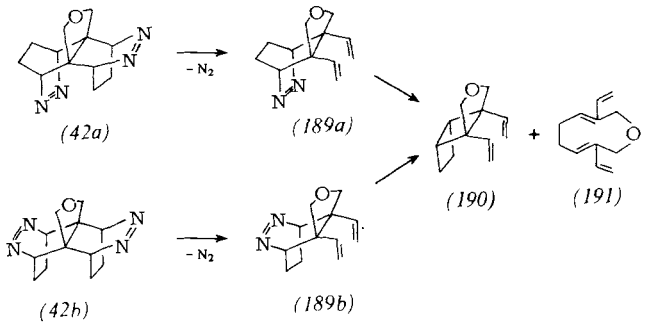
nitrogenation. Furthermore, the tricycloalkadiene *(176)* and its benzo-analogue *(177)* were obtained from the respective azoalkanes *(108)*[107] and *(109)*[108]. We have shown[139] that



(176) *(177)* *(178)* *(179)* *(180)* *(181)* *(182)* *(183)* *(184)* *(185)* *(186)* *(187)* *(188)*

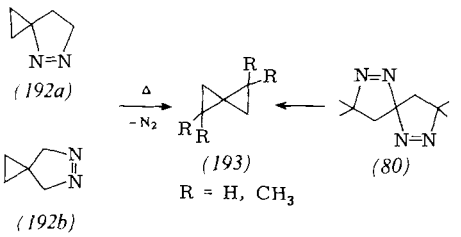
the azo compounds *(53)*—*(56)* afford the corresponding cyclopropanated products *(178)*—*(181)* on thermal and/or photochemical extrusion of molecular nitrogen. Of course, it should be recognized that these polycycloalkanes are, with the exception of *(179)*, the di-π-methane rearrangement products of the corresponding polycycloalkadienes *(182)*—*(184)*[140]. In fact, significant amounts (*ca.* 18—20%) of *(184)* are formed in the thermolysis and photolysis of *(56)*, providing valuable information on the mechanism of the di-π-methane rearrangement[139].

An amazing example is the photo-denitrogenation of the azoalkane *(16)* which gave the unusual products *(185)*—*(188)*[20]. Finally, the bis(azoalkanes) *(42a, b)* on short (20 min) irradiation led to the monoazoalkanes *(189a, b)*, respectively, and on long (3.5 h) irradiation the fully denitrogenated products *(190)* and *(191)*[48].

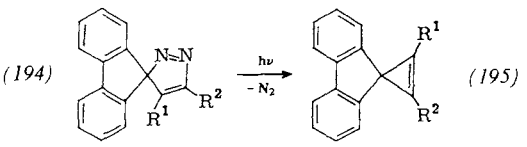


3.4. Cyclizations Forming Spiro Compounds

Two excellent recent reviews have been published on this topic, one on spiroalkanes in general[141] and the other on spiro-conjugated systems[142]. For this reason we will only mention an example of each for illustration. Thus, spiropentane *(193)* was prepared in two ways, by thermal and photolytic denitrogenation of (i) the isomeric spiroazoalkanes *(192a, b)*[143] and (ii) the bis(azoalkane) *(80)*[79]. In fact, the



monoazoalkane *(192a)* was an intermediate in the denitrogenation of *(80)*. Interestingly, photolysis with circularly polarized near-UV light caused *ca.* 5% asymmetric enrichment in the starting material on incomplete denitrogenation[79].



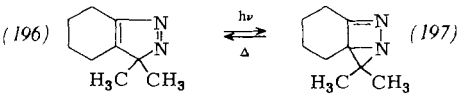
On the other hand, denitrogenation of azoalkane *(194)* gave the spiro-conjugated product *(195)*[144]. Many other examples of such highly strained molecules have been prepared in this way[142].

4. Transformations of Azoalkanes without Loss of Nitrogen

Azoalkanes do not always expel molecular nitrogen on thermal or photochemical activation. Instead, they can suffer rearrangements or retro-Diels-Alder reactions. Again we shall consider only those examples which may be of synthetic utility.

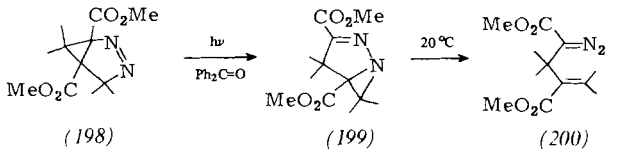
4.1. Rearrangements

An early example was observed by *Closs et al.*[145] in the photolysis of the fully alkylated 3*H*-pyrazoles *(196)*. Thus,

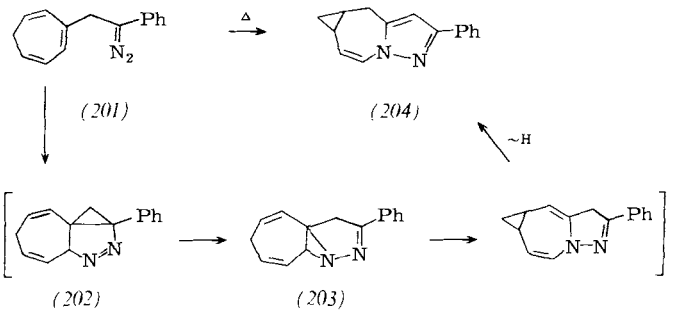


while photolysis of *(196)* at −60 °C in *n*-pentane gave the expected cyclopropene as major product on loss of nitrogen, photolysis of *(196)* at −60 °C in methanol gave exclusively the valence tautomer *(197)* on rearrangement. The 1,2-diazobicyclo[2.1.0]pent-2-ene skeleton *(197)* is unstable, and on warming to room temperature reverts to *(196)*.

A related example is the rearrangement of azoalkane *(198)* into the aziridine derivative *(199)* on benzophenone-sensitized photolysis[118b]. On standing at 20 °C, the thermally la-

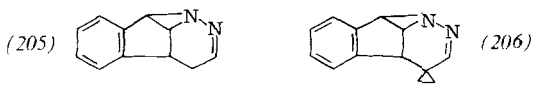


bile *(199)* retrocyclizes into the diazo derivative *(200)*. Analogously, the thermal transformation of the diazo compound *(201)* into *(204)* might involve the rearrangement of the in-



termediary azoalkane *(202)* into the aziridine derivative *(203)*, although a different pathway was preferred[146].

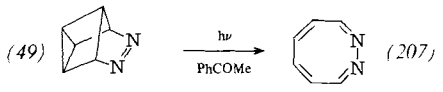
We recently observed similar rearrangements of the bridged azoalkanes *(53)* and *(55)*. While direct photolysis afforded the expected tricycloalkanes *(178)* and *(180)*, respectively, benzophenone-sensitized photolysis gave quantitatively the stable and isolable aziridines *(205)* and *(206)*, respectively[139]. It appears, therefore, that this type of azoal-



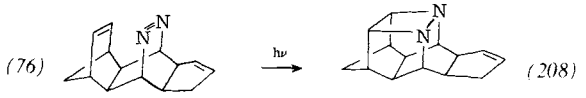
kane rearrangement may be general and of synthetic value since such aziridines would be difficult to prepare *via* classical methods.

An interesting and unexpected rearrangement was observed with the azoalkane *(49)* on attempted photo-denitrogenation. On direct photolysis, *(49)* afforded the expected prismane *(156)* in low yield[134a]. The major product, espe-

cially on acetophenone-sensitized photolysis (*ca.* 67%), however, was the 1,2-diazo-2,4,6,8-cyclooctatetraene *(207)*[134].

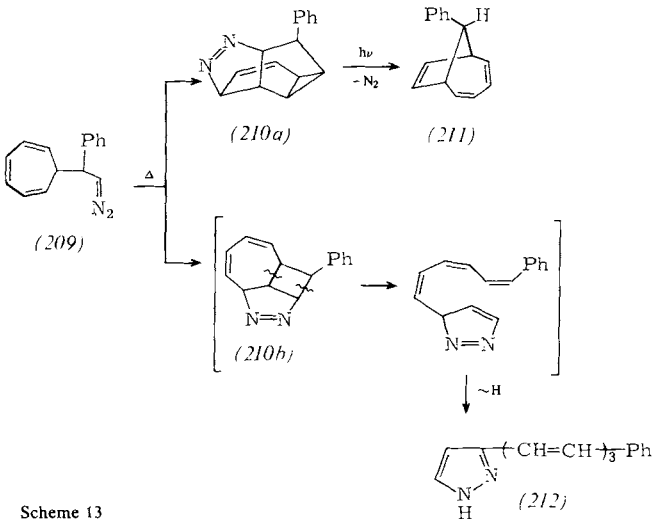


Also quite surprising was the intramolecular cycloaddition of the azo linkage to the juxtaposed C=C bond in the azoalkane *(76)* to give the caged product *(208)*[74]. This example appears to be unique!



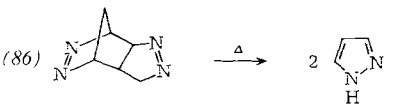
4.2. Cycloreversions

One of the earliest examples of interest is shown in Scheme 13[147]. The diazoalkane *(209)*, produced *via* thermal decomposition of its tosylhydrazone precursor, gave the azoalkane *(210a)* and the pyrazole *(212)* as products. The formation of the unexpected pyrazole *(212)* was rationalized in terms of the intermediary azoalkane *(210b)* *via* [2+2]-retrocyclization and 1,3-hydrogen shift. Azoalkane *(210a)* afforded the bicycloalkatriene *(211)* on photo-denitrogenation.

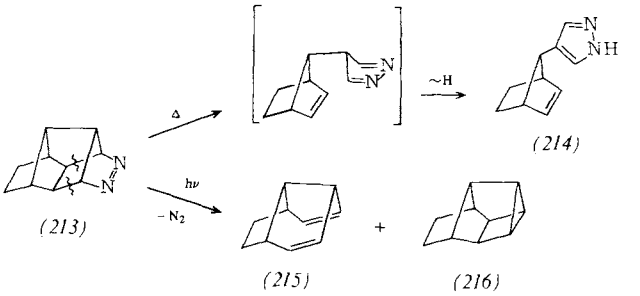


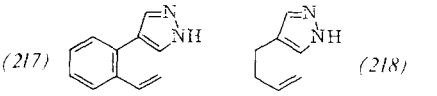
Scheme 13

Analogous to the thermal retrocyclization of the cyclopentadiene dimer, the bis(azoalkane) *(86)* decomposes into two moles of pyrazole. The intermediary 3*H*- and 4*H*-pyrazoles isomerize to the more stable 1*H*-tautomer[148].



A similar [4+2]-retrocyclization was observed by *Paquette et al.*[149a] on pyrolysis of azoalkane *(213)* at 370 °C, leading quantitatively to the pyrazole *(214)*. Again a 1,3-hydrogen shift gave the more stable tautomer. In contrast, photolysis of *(213)* afforded the hydrocarbons *(215)* and *(216)*[149b]. Finally, we recently observed[139] that the azoalkanes *(53)* and *(54)* undergo analogous [4+2]-retrocyclizations on flash vacuum pyrolysis at *ca.* 400 °C, leading quantitatively to the respective pyrazoles *(217)* and *(218)*.

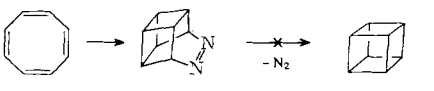




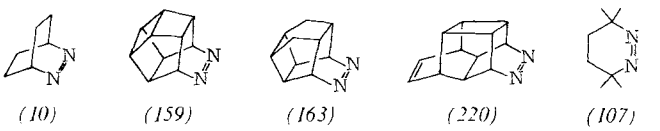
5. Reluctant Azoalkanes

The majority of azoalkanes lose molecular nitrogen on either thermal or photochemical excitation; only a few undergo transformations retaining the nitrogen. Both categories are, however, of synthetic utility and interest. Most frustrating is the third category of azoalkanes, namely the "reluctant" azoalkanes, which are essentially inert to denitrogenation, especially toward the photolytic variant. The term "reluctant" signifies that the quantum yields for denitrogenation are low (*ca.* 5% or less)[150]. Thus, an elegant synthetic sequence may falter at its last step, when attempts to introduce the last carbon-carbon bond by nitrogen extrusion are thwarted by the azoalkanes resistance to denitrogenation.

An early classical example is the attempt to prepare cubane *(219)* from cyclooctatetraene *via* diazabasketene *(28a)*.



Thus, prolonged photolysis afforded a low yield of cyclooctatetraene, while flash vacuum pyrolysis gave diazacyclooctatetraene[151]. Other "reluctant" azoalkanes are shown in Scheme 14[150].



Scheme 14

The interesting common structural feature of these "reluctant" azoalkanes is that the azo-linkage is part of a six-membered ring. 3,3,6,6-Tetramethyl-1,2-diazacyclohex-1-ene *(107)* is the simplest system possessing this structural feature and is itself a "reluctant" azoalkane[152].

Recently, much mechanistic work has been invested in order to gain an understanding of why such azoalkanes lose nitrogen reluctantly, in the hope of developing remedies when a synthetic sequence fails in the last critical step of denitrogenation. Some progress has been made along these lines. For example, denitrogenation of *(10)* was enhanced *ca.* 25-fold by introducing substituents which stabilize radical sites, such as cyano, vinyl, *etc.*, at the α-carbon to the azo linkage or by introducing strain into the ring containing the azo-linkage through cyclopropane ring-fusion[150]. Alternatively, vapor phase photolysis at elevated temperatures proved to be successful in denitrogenating *(163)*[136].

Clearly, the electronically excited "reluctant" azoalkane possesses an activation energy (*ca.* 2—10 kcal/mol) towards nitrogen elimination. Consequently, denitrogenation no longer takes place on the lowest energy path and photophysical or photochemical energy dissipation, *e.g.* fluorescence[136, 150] or *cis-trans* isomerization[152], respectively, can become competitive.

Recently[153] it was demonstrated that the reluctant azoalkanes *(10)*, *(28a)*, and *(107)* smoothly denitrogenate on irradiation at 185 nm. While *(10)* and *(107)* led to the expected hydrocarbons, *(28a)* afforded cyclooctatetraene in good yield. In the latter case it still needs to be established whether cubane is an intermediate. It was suggested that either n_+, π^* or π,π^* excitation of the reluctant azoalkane is responsible for the greatly enhanced photo-elimination[154]. However, more mechanistic work will be necessary in order to understand "reluctance" sufficiently to overcome this menacing problem in the synthesis of unusual organic molecules from azoalkanes.

We acknowledge generous financial support by the National Science Foundation (CHE-78-12621), National Institutes of Health (GM-00141-05 and RR-8102-07), and the Petroleum Research Fund (11022-ACI), administered by the American Chemical Society, for our own work in this area.

Received: February 1, 1980 [A 335 IE]
German version: Angew. Chem. *92*, 815 (1980)

[1] a) Houben-Weyl: Methoden der Organischen Chemie. Thieme, Stuttgart; b) see [1a], Vol. IV/3 and IV/4 (1971); Vol. IV/5a and IV/5b (1975); c) *J. F. Liebman, A. Greenberg*, Chem. Rev. *76*, 311 (1976).
[2] *R. Criegee, A. Rimmelin*, Chem. Ber. *90*, 414 (1957).
[3] a) *H. Meier, K.-P. Zeller*, Angew. Chem. *89*, 876 (1977); Angew. Chem. Int. Ed. Engl. *16*, 835 (1977); b) *S. Patai:* The Chemistry of the Hydrazo, Azo and Azoxy Groups. Vol. I and II. Wiley, London 1975. c) *V. Zanker* in [1a], Vol. IV/5a (1975), pp. 546 ff.; d) *W. Rundel* in [1a], Vol. IV/5b (1975), pp. 1131 ff.; e) *E. Müller* in [1a], Vol. X/2 (1967), pp. 127 ff.; f) *P. S. Engel*, Chem. Rev. *80*, 99 (1980).
[4] *O. Diels, J. H. Blom, W. Koll*, Justus Liebigs Ann. Chem. *443*, 242 (1925).
[5] *B. T. Gillis* in *J. Hamer:* 1,4-Cycloaddition Reactions in Heterocyclic Systems. Academic Press, New York 1967.
[6] *S. Masamune, N. Nakamura, J. Spadaro*, J. Am. Chem. Soc. *97*, 918 (1975).
[7] a) *D. Mackay, C. W. Pilger, L. L. Wong*, J. Org. Chem. *38*, 2043 (1973); b) *R. D. Little, G. L. Carroll, ibid. 44*, 4720 (1979).
[8] *R. D. Little, M. G. Venegas*, J. Org. Chem. *43*, 2921 (1978).
[9] a) *M. E. Jung, M. A. Lyster*, J. Chem. Soc. Chem. Commun. *1978*, 315; b) *T. Morita, Y. Okamoto, H. Sakurai, ibid. 1978*, 874.
[10] a) *R. C. Cookson, S. S. H. Gilani, I. D. R. Stevens*, Tetrahedron Lett. *1962*, 615; b) *J. C. Stickler, W. H. Pirkle*, J. Org. Chem. *31*, 3444 (1966); c) *R. C. Cookson, S. S. Gupte, I. D. R. Stevens, C. T. Watts*, Org. Syn. *51*, 121 (1971); d) *J. A. Moore, R. Muth, R. Sorace*, J. Org. Chem. *39*, 3799 (1974); e) *M. Lora-Tamayo*, Commentat. Pontif. Acad. Sci. *2*, 8 (1975); f) *G. Wamhoff, K. Wald*, Org. Prep. Proced. Int. *7*, 251 (1975).
[11] *M. E. Burrage, R. C. Cookson, S. S. Gupte, I. D. R. Stevens*, J. Chem. Soc. Perkin Trans. II *1975*, 1325.
[12] a) *E. J. Corey, B. B. Snider*, J. Org. Chem. *38*, 3632 (1973); b) *J. W. Mojé, P. Beak, ibid. 39*, 2951 (1974).
[13] a) *M. G. de Amezúa, M. Lora-Tamayo, J. L. Soto*, Tetrahedron Lett. *1970*, 2407; b) *J. E. Herweh, R. M. Fantazier, ibid. 1973*, 2101.
[14] a) *R. Stollé*, Chem. Ber. *45*, 273 (1912); b) *ibid. 46*, 260 (1913).
[15] a) *S. G. Cohen, R. Zand*, J. Am. Chem. Soc. *84*, 586 (1962); b) *E. L. Allred, J. C. Hinshaw*, Chem. Commun. *1969*, 1021; c) *M. Martin, W. R. Roth*, Chem. Ber. *102*, 811 (1969).
[16] *M. L. Heyman, J. P. Snyder*, Tetrahedron Lett. *1973*, 2859.
[17] *T. J. Levek, E. F. Kiefer*, J. Am. Chem. Soc. *98*, 1875 (1976).
[18] *R. M. Pagni, C. R. Watson, Jr.*, J. Am. Chem. Soc. *96*, 2291 (1974).
[19] a) *J. A. Berson, R. F. Davis*, J. Am. Chem. Soc. *94*, 3658 (1972); b) *R. Askani*, Chem. Ber. *102*, 3304 (1969).
[20] *M. J. Wyvratt, L. A. Paquette*, Tetrahedron Lett. *1974*, 2433.
[21] *W. Adam, I. Erden, O. Cox*, J. Org. Chem. *44*, 861 (1979).
[22] a) *R. Askani, M. Wieduwilt*, Tetrahedron Lett. *1979*, 925; b) *U. Moedlhammer, H. Hopf*, Angew. Chem. *87*, 492 (1975); Angew. Chem. Int. Ed. Engl. *14*, 501 (1975).
[23] *W. Ried, S.-H. Lim*, Justus Liebigs Ann. Chem. *1973*, 129.
[24] *P. L. Watson, R. N. Warrener*, Aust. J. Chem. *26*, 1725 (1973).
[25] *E. E. Knaus, F. M. Pasutto, C. S. Giam*, J. Heterocycl. Chem. *11*, 843 (1974).
[26] *Y. Kashman, O. Awerbouch*, Tetrahedron *31*, 53 (1975).
[27] *T. Tsuchiya, V. Snieckus*, Can. J. Chem. *53*, 519 (1975).
[28] a) *M. P. Schneider, M. Schnaithmann*, J. Am. Chem. Soc. *101*, 254 (1979); b) *M. Oda, N. Morita, T. Asao*, Tetrahedron Lett. *1980*, 471.
[29] *J. M. Cinnamon, K. Weiss*, J. Org. Chem. *26*, 2644 (1961).
[30] *R. C. Cookson, S. S. H. Gilani, I. D. R. Stevens*, J. Chem. Soc. *C 1967*, 1905.
[31] *W. Adam, M. Balci, B. Pietrzak*, J. Am. Chem. Soc. *101*, 6285 (1979).
[32] a) *T. Sasaki, K. Kanematsu, K. Hayakawa*, Chem. Commun. *1970*, 82; b) J. Chem. Soc. *C 1971*, 2142; c) *W. S. Murphy, J. P. McCarthy*, Chem. Commun. *1970*, 1129.
[33] a) *W. H. Rastetter*, J. Am. Chem. Soc. *98*, 6350 (1976); b) *D. D. Haas, W. H. Rastetter, ibid. 98*, 6353 (1976).
[34] *W. H. Rastetter, T. J. Richard*, J. Am. Chem. Soc. *101*, 3893 (1979).
[35] *E. Vogel, E. Schmidbauer, H. J. Altenbach*, Angew. Chem. *86*, 818 (1974); Angew. Chem. Int. Ed. Engl. *13*, 736 (1974).
[36] *G. Kiehl, J. Streith, G. Taurand*, Tetrahedron *30*, 2851 (1974).
[37] a) *A. G. Anastassiou, R. P. Cellura*, Chem. Commun. *1970*, 484; b) Tetrahedron Lett. *1970*, 911; c) *A. G. Anastassiou, R. P. Cellura, J. M. Spence, S. W. Eachus*, J. Chem. Soc. Chem. Commun. *1972*, 325.
[38] *G. Schröder:* Cyclooctatetraene. Verlag Chemie, Weinheim 1965, p. 51.
[39] a) *A. B. Evnin, R. D. Miller, G. R. Evanega*, Tetrahedron Lett. *1968*, 5863; b) *H. Isaksen, J. P. Snyder, ibid. 1977*, 889; c) *R. Askani, M. Wieduwilt*, Chem. Ber. *109*, 1887 (1976).
[40] a) *H. Olsen, J. P. Snyder*, J. Am. Chem. Soc. *100*, 285 (1978); b) *E. A. Wildi, B. K. Carpenter*, Tetrahedron Lett. *1978*, 2469.
[41] a) *D. G. Farnum, J. P. Snyder*, Tetrahedron Lett. *1965*, 3861; b) *R. J. Boyd, J.-C. G. Bünzli, J. P. Snyder*, J. Am. Chem. Soc. *98*, 2398 (1976); c) *H. Olsen, J. P. Snyder, ibid. 99*, 1524 (1977).
[42] a) *R. Askani*, Tetrahedron Lett. *1970*, 3349; b) *R. M. Moriarty, C.-L. Yeh, N. Ishibi*, J. Am. Chem. Soc. *93*, 3085 (1971); c) *L. A. Paquette, ibid. 92*, 5765 (1970); d) *R. Askani, I. Gurang, W. Schwertfeger*, Tetrahedron Lett. *1975*, 1315; e) *L. A. Paquette, D. R. James, G. H. Birnberg*, J. Am. Chem. Soc. *96*, 7454 (1974); f) *D. R. James, G. H. Birnberg, L. A. Paquette, ibid. 96*, 7465 (1974).
[43] a) *R. E. Wingard, Jr., R. K. Russell, L. A. Paquette*, J. Am. Chem. Soc. *96*, 7474 (1974); *R. K. Russell, R. E. Wingard, Jr., L. A. Paquette, ibid. 96*, 7483 (1974); b) *L. A. Paquette, R. K. Russell, R. L. Burson, ibid. 97*, 6124 (1975); c) *L. A. Paquette, R. F. Doehner, Jr., J. A. Jenkins, J. F. Blount*, J. Am. Chem. Soc. *102*, 1188 (1980).
[44] *E. Chamot, L. A. Paquette*, J. Org. Chem. *43*, 4527 (1978).
[45] a) *J. M. Gardlik, L. A. Paquette*, Tetrahedron Lett. *1979*, 3597; b) *J. A. Jenkins, R. F. Doehner, Jr., L. A. Paquette*, J. Am. Chem. Soc. *102*, 2131 (1980); c) *L. A. Paquette, R. F. Doehner, Jr., J. A. Jenkins, J. F. Blount, ibid. 102*, 1188 (1980); d) *R. Askani, W. Schwertfeger*, Chem. Ber. *110*, 3046 (1977).
[46] *L. A. Paquette, A. R. Browne, E. Chamot*, Angew. Chem. *91*, 581 (1979); Angew. Chem. Int. Ed. Engl. *18*, 546 (1979).
[47] *E. Vogel, H. V. Runzheimer, F. Hogrefe, B. Baasner, J. Lex*, Angew. Chem. *89*, 909 (1977); Angew. Chem. Int. Ed. Engl. *16*, 871 (1977).
[48] *M. Korat, D. Ginsburg*, Tetrahedron *29*, 2373 (1973).
[49] a) *R. Gleiter, D. Ginsburg*, Pure Appl. Chem. *51*, 1301 (1979); b) *P. Ashkenazi, J. Oliker, D. Ginsburg*, Tetrahedron *34*, 2171 (1978); c) *P. Ashkenazi, E. Vogel, D. Ginsburg, ibid. 34*, 2167 (1978); d) *J. Kalo, D. Ginsburg, ibid. 34*, 2155 (1978); e) *J. Kalo, D. Ginsburg, J. J. Bloomfield, ibid. 34*, 2153 (1978); f) *J. Kalo, E. Vogel, D. Ginsburg, ibid. 33*, 1183 (1977); g) *J. Kalo, D. Ginsburg, E. Vogel, ibid. 33*, 1177 (1977); h) *C. Amith, D. Ginsburg, ibid. 30*, 3415 (1974); i) *P. Ashkenazi, D. Ginsburg, E. Vogel, ibid. 33*, 1169 (1977); j) *D. Ginsburg*, Acc. Chem. Res. *7*, 286 (1974).

[50] a) *S. J. Cristol, E. L. Allred, D. L. Wetzel,* J. Org. Chem. *27*, 4058 (1962); b) *R. M. Moriarty, ibid. 28*, 2385 (1963); c) *B. T. Gillis, J. D. Hagarty, ibid. 32*, 330 (1967).

[51] *E. L. Allred, A. L. Johnson,* J. Am. Chem. Soc. *93*, 1300 (1971).

[52] *H. E. Zimmerman, R. J. Boettcher, N. E. Buehler, G. E. Keck, M. G. Steinmetz,* J. Am. Chem. Soc. *98*, 7680 (1976).

[53] a) *Y. C. Toong, W. T. Borden, A. Gold,* Tetrahedron Lett. *1975*, 1549; b) *R. Askani, R. Kirsten, B. Dugall, ibid. 1976*, 3891.

[54] a) *E. Koerner von Gustorf, D. V. White, B. H. Kim, J. Leitich,* J. Org. Chem. *35*, 1155 (1970); b) *R. W. Hoffmann,* Angew. Chem. *84*, 306 (1972); Angew. Chem. Int. Ed. Engl. *11*, 324 (1972); c) *R. B. Wagener, G. B. Butler,* J. Org. Chem. *38*, 3070 (1973); d) *J. H. Hall, M. Wojciechowska, ibid. 44*, 38 (1979).

[55] a) *D. J. Pasto, A. Chen,* J. Am. Chem. Soc. *93*, 2562 (1971); b) *D. J. Pasto, F. T. A. Chen,* Tetrahedron Lett. *1973*, 713; c) *D. J. Pasto, D. Wampfler, ibid. 1974*, 1933.

[56] a) *D. J. Pasto, J. K. Borchardt,* J. Am. Chem. Soc. *96*, 6220, 6937, 6944 (1974); b) *D. J. Pasto, ibid. 101*, 37 (1979).

[57] a) *T. J. Katz, N. Acton,* J. Am. Chem. Soc. *95*, 2738 (1973); b) *B. M. Trost, R. M. Cory, P. H. Scudder, H. B. Neubold, ibid. 95*, 7813 (1973).

[58] *A. R. Browne, L. A. Paquette,* J. Org. Chem. *43*, 4522 (1978).

[59] *H. Hogeveen, L. Zwart,* J. Org. Chem. *44*, 1365 (1979).

[60] *W. Adam, O. De Lucchi, I. Erden,* Angew. Chem. *91*, 512 (1979); Angew. Chem. Int. Ed. Engl. *18*, 468 (1979).

[61] a) *W. Adam, O. De Lucchi,* Tetrahedron Lett. *1979*, 4367; b) *W. Adam, O. De Lucchi, I. Erden,* J. Am. Chem. Soc. *102*, 4806 (1980).

[62] *T. Sasaki, K. Kanematsu, M. Uchide,* Tetrahedron Lett. *1971*, 4855.

[63] *W. R. Roth, M. Martin,* Tetrahedron Lett. *1967*, 4695.

[64] *N. Rieber, J. Alberts, J. A. Lipsky, D. M. Lemal,* J. Am. Chem. Soc. *91*, 5668 (1969).

[65] a) *K. W. Shen,* Chem. Commun. *1971*, 391; b) J. Am. Chem. Soc. *93*, 3064 (1971).

[66] *P. F. Wiley* in: The Chemistry of Heterocyclic Compounds. Vol. 33. Wiley, New York 1978, pp. 1073 ff.

[67] a) *A. B. Evnin, D. R. Arnold,* J. Am. Chem. Soc. *90*, 5330 (1968); b) *D. R. Arnold, A. B. Evnin, P. H. Kasai, ibid. 91*, 784 (1969); c) *A. B. Evnin, D. R. Arnold, L. A. Karnischky, E. Strom, ibid. 92*, 6218 (1970); d) *W. R. Dolbier, W. D. Lochle, W. M. Williams,* J. Chem. Soc. Chem. Commun. *1972*, 867.

[68] a) *L. A. Paquette, L. M. Leichter,* J. Am. Chem. Soc. *93*, 4922 (1971); b) *ibid. 93*, 5128 (1971); c) J. Org. Chem. *39*, 461 (1974).

[69] a) *R. A. Carboni, R. V. Lindsey,* J. Am. Chem. Soc. *81*, 4342 (1959); b) *J. Sauer,* Angew. Chem. *78*, 233 (1966); Angew. Chem. Int. Ed. Engl. *5*, 211 (1966).

[70] *M. Christl, H.-J. Lüddecke, A.-N. Neppel, G. Freitag,* Chem. Ber. *110*, 3745 (1977).

[71] *H. D. Martin, M. Hekman,* Tetrahedron Lett. *1978*, 1183.

[72] a) *H. D. Fühlhuber, G. Gousetis, T. Troll, J. Sauer,* Tetrahedron Lett. *1978*, 3903; b) *D. Dyllick-Brenzinger, J. F. M. Oth, H. D. Fühlhuber, G. Gousetis, T. Troll, J. Sauer, ibid. 1978*, 3907; c) *G. Gousetis, J. Sauer, ibid. 1979*, 1295; d) *H. D. Fühlhuber, G. Gousetis, J. Sauer, ibid. 1979*, 1299.

[73] a) *J. A. Elix, W. S. Wilson, R. N. Warrener,* Tetrahedron Lett. *1970*, 1837; b) *U. Göckel, U. Hartmannsgruber, A. Steigel, J. Sauer, ibid. 1980*, 595, 599; c) *L. M. Maddox, J. C. Martin, J. M. Muchowski, H. J. Lindner, ibid. 1980*, 7.

[74] *W. Berning, S. Hünig,* Angew. Chem. *89*, 825 (1977); Angew. Chem. Int. Ed. Engl. *16*, 777 (1977).

[75] a) *R. Huisgen,* Angew. Chem. *75*, 604 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565 (1963); b) *G. W. Cowell, A. Ledwith,* Q. Rev. Chem. Soc. *24*, 119 (1970); c) *A. Padwa,* Angew. Chem. *88*, 131 (1976); Angew. Chem. Int. Ed. Engl. *15*, 123 (1976); d) *D. Wendisch* in [1a], Vol. IV/3 (1971), pp. 42 ff.

[76] *E. Lüddecke, H. Rau, H. Dürr, H. Schmitz,* Tetrahedron *33*, 2677 (1977).

[77] a) *M. Franck-Neumann, D. Martina,* Tetrahedron Lett. *1975*, 1767; b) *M. Franck-Neumann, C. Dietrich-Buchecker, ibid. 1980*, 671.

[78] *R. J. Crawford, D. M. Cameron, H. Tokunaga,* Can. J. Chem. *52*, 4025 (1974).

[79] *M. Schneider, O. Schuster, H. Rau,* Chem. Ber. *110*, 2180 (1977).

[80] a) *R. J. Crawford, M. Ohno,* Can. J. Chem. *52*, 3134 (1974); b) *M. Schneider,* Angew. Chem. *87*, 717 (1975); Angew. Chem. Int. Ed. Engl. *14*, 707 (1975).

[81] a) *P. G. Gassman, W. T. Greenlee,* J. Am. Chem. Soc. *95*, 980 (1973); b) *M. Franck-Neumann, C. Buchecker,* Tetrahedron Lett. *1969*, 2659.

[82] a) *M. Franck-Neumann,* Tetrahedron Lett. *1968*, 2979; b) *D. H. White, P. B. Condit, R. G. Bergman,* J. Am. Chem. Soc. *94*, 1348 (1972); c) *R. A. Keppel, R. G. Bergman, ibid. 94*, 1350 (1972).

[83] *M. Schneider, I. Merz,* Tetrahedron Lett. *1974*, 1995.

[84] a) *E. L. Allred, J. C. Hinshaw,* J. Am. Chem. Soc. *90*, 6885 (1968); b) *E. L. Allred, J. C. Hinshaw, A. L. Johnson, ibid. 91*, 3382 (1969).

[85] *E. L. Allred, K. J. Voorhees,* J. Am. Chem. Soc. *95*, 620 (1973).

[86] *C. Dietrich-Buchecker, D. Martina, M. Franck-Neumann,* J. Chem. Res. *S 1978*, 78.

[87] *H. D. Martin,* Chem. Ber. *107*, 1403 (1974).

[88] *R. H. Shapiro,* Org. React. *23*, 405 (1976).

[89] *W. Kirmse, D. Grassmann,* Chem. Ber. *99*, 1746 (1966).

[90] a) *R. M. Wilson, J. W. Rekers,* J. Am. Chem. Soc. *101*, 4005 (1979); b) *R. M. Wilson, J. W. Rekers, A. B. Packard, R. C. Elder, ibid. 102*, 1633 (1980); c) *A. Padwa, H. Ku,* Tetrahedron Lett. *1979*, 4425; d) *ibid. 1980*, 1009.

[91] a) *M. Schwarz, A. Besold, E. R. Nelson,* J. Org. Chem. *30*, 2425 (1965); b) *E. Piers, P. W. Britton, R. J. Keziere, R. D. Smillie,* Can. J. Chem. *49*, 2623 (1971).

[92] *D. H. R. Barton, F. S. Guziec, Jr., I. Shahak,* J. Chem. Soc. Perkin Trans. I *1974*, 1794.

[93] *F. Cordt, R. M. Frank, D. Lenoir,* Tetrahedron Lett. *1979*, 505.

[94] *A. Krebs, W. Rüger,* Tetrahedron Lett. *1979*, 1305.

[95] a) *H. Stetter, H. Spangenberger,* Chem. Ber. *91*, 1982 (1958); b) *L. A. Carpino, J. Am. Chem. Soc. 85*, 2144 (1963); c) *E. Schmitz, R. Ohme,* Chem. Ber. *95*, 2012 (1962).

[96] *R. J. Crawford, H. Tokunaga,* Can. J. Chem. *52*, 4033 (1974).

[97] a) *R. J. Crawford, D. M. Cameron, H. Tokunaga,* Can. J. Chem. *52*, 4025 (1974); b) *R. J. Crawford, H. Tokunaga, L. M. H. C. Schrijver, T. C. Goddard, T. Nakashima, ibid. 56*, 992 (1978).

[98] *W. Duismann, C. Rüchardt,* Chem. Ber. *111*, 596 (1978).

[99] a) *G. Maier,* Chem. Ber. *99*, 1232 (1966); b) *G. Maier, F. Seidler, ibid. 99*, 1235 (1966); c) *G. Maier, U. Heep, M. Wiessler, M. Strasser, ibid. 102*, 1928 (1969).

[100] a) *W. R. Dolbier, Jr., K. Matsui, L. McCullagh, K. E. Anapolle,* J. Org. Chem. *44*, 2842 (1979); b) *W. R. Dolbier, Jr., K. E. Anapolle, L. McCullagh, K. Matsui, J. M. Riemann, D. Rolison, ibid. 44*, 2845 (1979).

[101] *A. P. Schaap, G. Faler,* J. Org. Chem. *38*, 3061 (1973).

[102] *P. Singh, D. G. B. Boocock, E. F. Ullman,* Tetrahedron Lett. *1971*, 3935.

[103] *F. D. Greene, K. E. Gilbert,* J. Org. Chem. *40*, 1409 (1975).

[104] *J. P. Snyder, M. L. Heyman, E. N. Suciu,* J. Org. Chem. *40*, 1395 (1975).

[105] *P. Singh,* J. Org. Chem. *40*, 1405 (1975).

[106] *S. F. Nelsen, P. D. Bartlett,* J. Am. Chem. Soc. *88*, 137 (1966).

[107] a) *T. V. Rajan Babu, D. C. Sanders, H. Shechter,* J. Am. Chem. Soc. *99*, 6449 (1977); b) *J. B. Press, H. Shechter,* J. Org. Chem. *40*, 2446 (1975).

[108] *M. Kato, T. Chikamoto, T. Miwa,* Bull. Chem. Soc. Jpn. *50*, 1082 (1977).

[109] a) *J. Font, M. Torres, H. E. Gunning, O. P. Strausz,* J. Org. Chem. *43*, 2487 (1978); b) *A. Krantz, J. Laureni,* J. Am. Chem. Soc. *99*, 4842 (1977).

[110] a) *H. Meier, J. Menzel,* Chem. Commun. *1971*, 1059; b) *I. Lalezari, A. Shafiee, M. Yalpani,* J. Heterocycl. Chem. *9*, 1411 (1972).

[111] *G. Seybold,* Angew. Chem. *89*, 377 (1977); Angew. Chem. Int. Ed. Engl. *16*, 365 (1977).

[112] a) *P. S. Engel, C. Steel,* Acc. Chem. Res. *6*, 275 (1973); b) *H. Dürr, B. Ruge,* Top. Curr. Chem. *66*, 53 (1976).

[113] *H. Rau,* Angew. Chem. *85*, 248 (1973); Angew. Chem. Int. Ed. Engl. *12*, 224 (1973).

[114] *J. A. Berson, S. S. Olin,* J. Am. Chem. Soc. *91*, 777 (1969).

[115] a) *E. L. Allred, R. L. Smith,* J. Am. Chem. Soc. *91*, 6766 (1969); b) *W. R. Roth, M. Martin,* Justus Liebigs Ann. Chem. *702*, 1 (1967).

[116] *M. Schneider, B. Csacsko,* Angew. Chem. *89*, 905 (1977); Angew. Chem. Int. Ed. Engl. *16*, 867 (1977).

[117] *D. F. Eaton, R. G. Bergman, G. S. Hammond,* J. Am. Chem. Soc. *94*, 1351 (1972).

[118] a) *M. Franck-Neumann,* Angew. Chem. *79*, 98 (1967); Angew. Chem. Int. Ed. Engl. *6*, 79 (1967); b) *M. Franck-Neumann, D. Martina, C. Dietrich-Buchecker,* Tetrahedron Lett. *1975*, 1763.

[119] *W. R. Roth, M. Martin,* Tetrahedron Lett. *1967*, 3865.

[120] *J. A. Berson, E. W. Petrillo, Jr., P. Bickart,* J. Am. Chem. Soc. *96*, 636 (1974).

[121] *R. Anet, F. A. L. Anet,* J. Am. Chem. Soc. *86*, 525 (1964).

[122] *W. H. Rastetter, T. J. Richard,* Tetrahedron Lett. *1978*, 2995, 2999.

[123] *H. Prinzbach, D. Stusche, R. Kitzing,* Angew. Chem. *82*, 393 (1970); Angew. Chem. Int. Ed. Engl. *9*, 377 (1970).

[124] a) *H. Tanida, S. Teratake, Y. Hata, M. Watanabe,* Tetrahedron Lett. *1969*, 5341, 5345; b) *H. Tanida, S. Teratake, ibid. 1970*, 4991.

[125] *M. Martin, W. R. Roth,* Chem. Ber. *102*, 811 (1969).

[126] *H. D. Martin, B. Heiser, M. Kunze,* Angew. Chem. *90*, 735 (1978); Angew. Chem. Int. Ed. Engl. *17*, 696 (1978).

[127] *J. P. Snyder, D. N. Harpp,* J. Am. Chem. Soc. *98*, 7821 (1976).

[128] a) *L. A. Paquette, M. J. Epstein,* J. Am. Chem. Soc. *93*, 5936 (1971); b) *ibid. 95*, 6717 (1973).

[129] *L. A. Paquette, M. R. Short, J. F. Kelly,* J. Am. Chem. Soc. *93*, 7179 (1971).

[130] *R. D. Little, G. W. Muller,* J. Am. Chem. Soc. *101*, 7129 (1979).

[131] *A. de Meijere, C. Weitemeyer,* Angew. Chem. *82*, 359 (1970); Angew. Chem. Int. Ed. Engl. *9*, 376 (1970).

[132] *N. J. Turro, W. R. Cherry, M. F. Mirbach, M. J. Mirbach,* J. Am. Chem. Soc. *99*, 7388 (1977).

[133] *B. M. Trost, R. M. Cory,* J. Am. Chem. Soc. *93*, 5573 (1971).

[134] a) *N. J. Turro, C. A. Renner, W. H. Waddell, T. J. Katz,* J. Am. Chem. Soc. *98*, 4320 (1976); b) *B. M. Trost, P. H. Scudder, R. M. Cory, N. J. Turro, V. Ramamurthy, T. J. Katz,* J. Org. Chem. *44*, 1264 (1979).

[135] *E. L. Allred, B. R. Beck,* Tetrahedron Lett. *1974*, 437.

[136] a) *N. J. Turro, K.-C. Liu, W. Cherry, J.-M. Liu, B. Jacobson,* Tetrahedron Lett. *1978*, 555; b) *H. Quast, A. Fuss, A. Heublein,* Angew. Chem. *92*, 55 (1980); Angew. Chem. Int. Ed. Engl. *19*, 49 (1980); c) *N. J. Turro, J.-M. Liu, H.-D. Martin, M. Kunze,* Tetrahedron Lett. *1980*, 1299.

[137] S. Masamune, H. Zenda, M. Wiesel, N. Nakatsuka, G. Bigam, J. Am. Chem. Soc. 90, 2727 (1968).
[138] L. A. Paquette, R. E. Wingard, Jr., R. K. Russell, J. Am. Chem. Soc. 94, 4739 (1972).
[139] a) W. Adam, N. Carballeira, O. De Lucchi, J. Am. Chem. Soc. 102, 2107 (1980); b) W. Adam, O. De Lucchi, ibid. 102, 2109 (1980); c) Angew. Chem., in press.
[140] S. S. Hixson, P. S. Mariano, H. E. Zimmerman, Chem. Rev. 73, 531 (1973).
[141] A. P. Krapcho, Synthesis 1978, 77.
[142] H. Dürr, R. Gleiter, Angew. Chem. 90, 591 (1978); Angew. Chem. Int. Ed. Engl. 17, 559 (1978).
[143] K. K.-w. Shen, R. G. Bergman, J. Am. Chem. Soc. 99, 1655 (1977).
[144] H. Dürr, W. Schmidt, R. Sergio, Justus Liebigs Ann. Chem. 1974, 1132.
[145] G. L. Closs, W. A. Böll, H. Heyn, V. Dev, J. Am. Chem. 90, 173 (1968).
[146] a) T. Miyashi, Y. Nishizawa, T. Sugiyama, T. Mukai, J. Am. Chem. Soc. 99, 6109 (1977); b) Y. Nishizawa, T. Miyashi, T. Mukai, ibid. 102, 1176 (1980).
[147] H. Tsuruta, K. Kurabayashi, T. Mukai, J. Am. Chem. Soc. 90, 7167 (1968).
[148] J. C. Hinshaw, E. L. Allred, Chem. Commun. 1969, 72.
[149] a) L. A. Paquette, M. J. Wyvratt, H. C. Berk, R. E. Moerch, J. Am. Chem. Soc. 100, 5845 (1978); b) L. A. Paquette, J. D. Kramer, P. B. Lavrik, M. J. Wyvratt, J. Org. Chem. 42, 503 (1977).
[150] P. S. Engel, C. J. Nalepa, R. A. Leckonby, W.-K. Chae, J. Am. Chem. Soc. 101, 6435 (1979).
[151] a) J. P. Snyder, Ph. D. Thesis, Cornell University, Ithaca 1965; Diss. Abstr. 26, 5728 (1966); b) D. W. McNeil, M. E. Kent, E. Hedaya, P. F. D'Angelo, P. O. Schissel, J. Am. Chem. Soc. 93, 3817 (1971).
[152] P. S. Engel, R. A. Hayes, I. Keifer, S. Szilagyi, J. W. Timberlake, J. Am. Chem. Soc. 100, 1876 (1978).
[153] W. Adam, F. Mazenod, J. Am. Chem. Soc., in press.
[154] M. B. Robin: Higher Excited States of Polyatomic Molecules. Vol. II. Academic Press, New York 1974, pp. 68ff.

Mechanistic Aspects of Diels-Alder Reactions: A Critical Survey

By Jürgen Sauer and Reiner Sustmann[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The question of concerted or consecutive bond formation arises in all types of cycloaddition reactions. Stereochemical investigations and studies of regiospecificity as well as intensive kinetic investigations with regard to substituent and solvent effects, and the dependence of the reaction on temperature and pressure permit in many cases mechanistic conclusions concerning the Diels-Alder reaction. Efforts towards a theoretical interpretation, *ab initio* and semiempirical calculations, the application of frontier molecular orbital theory (FMO) as well as thermochemical measurements permit a description of the energy hypersurface of these [4+2]-cycloadditions. An attempt is made here to draw a line of distinction between the mechanistic alternatives—one-step reaction *versus* two-step reaction—considering all experimental and theoretical criteria.

1. Introduction

On reading the first publication in the series "Synthesen in der hydroaromatischen Reihe" by *Otto Diels* and *Kurt Alder*[1], one anticipates there having been a door opened to virgin preparative territory:

"Bei der Ähnlichkeit im Verhalten der Azoester mit den Chinonen gegen Cyclopentadien und andere Kohlenwasserstoffe erschien es nicht ausgeschlossen, daß sich die Letzteren auch mit den Anhydriden der Malein-, Citracon- und Itaconsäure zu beständigen Verbindungen vereinigen würden. ... wir haben nun festgestellt, daß in der Tat Maleinsäureanhydrid, aber auch die freie Maleinsäure, ferner Citracon- und Itaconsäureanhydrid sich – meist schon bei gewöhnlicher Temperatur – glatt an Cyclopentadien und Butadien, aber auch an komplizierte Kohlenwasserstoffe mit einem System konjugierter Doppelbindungen, wie z. B. Cyclo-Hexadien oder Phellandren in der selben Weise wie Azoester und die Chinone anlagern. Die doppelte Bindung der genannten ungesättigten Anhydride oder Säuren öffnet sich, und es kommt in allen Fällen zu einer Angliederung der freien Valenzen in 1,4-Stellung an die betreffenden Kohlenwasserstoffe, wobei sich die neue Doppelbindung zwischen den Kohlenstoffatomen 2 und 3 bildet.

Die so entstehenden zahlreichen Produkte sind keineswegs "Molekülverbindungen", sondern festgefügt und stabil. Ein Teil von ihnen hat sich durch Überführung in altbekannte Stoffe identifizieren lassen"[**].

[*] Prof. Dr. J. Sauer
Institut für Organische Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)
Prof. Dr. R. Sustmann
Fachbereich Chemie der Universität
Universitätsstrasse 5, D-4300 Essen (Germany)

[**] "Since the behavior of azoesters and quinones towards cyclopentadiene and other kinds of hydrocarbons is similar, it seemed possible that the latter would also react with the anhydrides of maleic, citraconic and itaconic acid to give stable compounds ... we have now found that, in fact, not only maleic acid anhydride but also the free maleic acid and even citraconic acid and itaconic acid anhydride add—in most cases at normal temperatures, without any problem—to cyclopentadiene and butadiene in the same way as azoesters and quinones; moreover, they also add to more complex hydrocarbons having a system of conjugated double bonds, as for example cyclohexadiene or phellandrene. The double bond of the above mentioned unsaturated anhydrides or acids is broken, and in all cases the free valences in the 1,4 position link to the respective hydrocarbons, with the new double bond being formed between the carbon atoms 2 and 3. The various products thus generated are in no way "molecular complexes", but stable and definite compounds. Some of them could be identified by conversion into well-known products".

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0779 $ 02.50/0

In retrospect, the subsequent communications by these two authors, published in short succession, reveal that this memorable publication constitutes a milestone in organic chemistry, the hour of birth of cycloaddition reactions[2]. The [4+2]-cycloadditions[3], named after their discoverers, were later joined by [2+1]-, [2+2]-, [3+2]-cycloadditions (1,3-dipolar cycloadditions), and those leading to more extended ring systems.

Diels and Alder were already able to identify essential characteristics of the [4+2]-cycloaddition:

1. The addition reactions take a *stereospecific* course resulting in a *cis*-addition.
2. In the case of cyclic dienes the *endo principle* is often followed.
3. Unsymmetrically substituted reactants combine *regiospecifically* to give the cycloadduct.
4. With maleic acid anhydride, valued in those days as the most reactive test dienophile, electron releasing groups in the diene accelerate the reaction, while electron withdrawing groups in the diene retard it. Kinetic measurements[4-8] quantified the so-called *"Alder-rule"*, formulated by *Alder*.

A preparatively useful extension of the cycloaddition was provided by the discovery of its catalysis by Lewis-acids[9], which, with retention of stereospecificity, accelerates the rate of addition by several powers of ten. In the presence of Lewis-acids, *endo*-products and the normally favored regioisomers were formed even to a higher extent.

Concepts of the mechanisms of the Diels-Alder reaction were most strongly influenced by the Woodward-Hoffmann rules[10-13]. If in those days the experimental results were consistent with a simultaneous formation of both bonds, the selection rules of Woodward and Hoffmann appeared to apodictically exclude the two-step mechanism (see Scheme 1 in Section 3).

Theoretical predictions, *ab initio* calculations[14-18], approximation methods[19] and the FMO-theory[20-26] stimulated further detailed discussion of the mechanism of the cycloaddition and made it possible to give a more satisfactory interpretation of many phenomena, including *e.g.* relative sequences of reactivity and regiospecifity in the Diels-Alder reaction.

It is a legitimate aspiration of the chemist to incorporate as many experimental facts as possible into a uniform, mechanistic picture. Very often, however, and not only in the case of Diels-Alder reactions, one succumbed to the danger of trying to interpret all reactions of a given type in a uniform way. The controversial "here, one-step bond formation", "there, two-step reaction pathway with a biradical or zwitterionic intermediate", both with a claim to exclusivity, has proven to be more of a hindrance than a help in discussions on the mechanism of the Diels-Alder reaction.

Today, it would seem to be undisputable that many [4+2]-cycloadditions are best described in terms of a symmetry-allowed one-step mechanism. In principle, however, a two-step mechanism cannot be ignored. The experimental results suggest that the two-step mechanism is in most cases energetically more demanding; but in so far as simultaneous bond formation may be hindered, for example by steric or electronic effects, the two-step mechanism might be able to compete energetically.

An attempt is made to critically analyze all those mechanistic results which are relevant for a decision regarding these alternatives. In particular we shall make comparisons with [2+2]-cycloadditions[27,28] and [3+2]-cycloadditions[29-33]. On the basis of the selection rules of *Woodward* and *Hoffmann*, we have to expect biradical or zwitterionic intermediates in [2+2]-cycloadditions; in contrast, [3+2]-cycloadditions ought to take place by a one-step mechanism in the same way as the Diels-Alder reaction. Many reviews have been written which facilitate general access to cycloaddition reactions, and particularly to [4+2]-cycloadditions[3,4,10,11,13,20,28,34-42].

2. Attempted Theoretical Interpretations

The aim of a theoretical analysis of a reaction mechanism is to gain a detailed description of the energy hypersurface, which connects reactants with reaction products. However, owing to the complexity of the problem—the participation of N atoms implies $3N-6$ degrees of freedom of vibration on a hypersurface of the same dimension—all methods of interpretation are limited from the outset, on the one hand by the selection of simple model reactions and, on the other, by the approximations which are necessary in the case of selected theoretical procedures. Also solvent effects are generally not considered, because theoretical models are normally developed for isolated molecules in in the gas phase. The fact that these limitations can lead to a false interpretation of experimental results, has been demonstrated on a number of occasions in recent years, particularly with regard to vapor phase-acidity and basicity experiments[43].

Conclusions drawn from such investigations must always be examined carefully in the light of these approximations. *Herndon*[21] gives a survey of the results obtained up to the beginning of the seventies concerning cycloadditions.

2.1. MO-Methods

2.1.1. *Ab initio* and Semiempirical Calculations

As prototype of a cycloaddition, the Diels-Alder reaction has on several occasions been the subject of quantum chemical calculations of energy hypersurfaces. The increased efficiency of modern computers and the further development of theoretical methods has enabled more and more detailed investigations. Despite this progress, however, attention has been confined almost exclusively to the formation of cyclohexene from butadiene and ethylene and the corresponding reverse reaction. With these two reactants a [4+2]-cycloaddition could certainly be verified, but it is not the typical example.

Presently there are two contradictory mechanistic interpretations. *Ab initio* calculations[14,16] lead to a reaction profile with a symmetrical transition state without any intermediate (distance between the planes of the reactants about 2.2 Å[16]). Semiempirical calculations of *Basilevsky et al.*[44] are in agreement with this, whereas another approach, using SINDO[45] certainly indicates an unsymmetrical transition state, but no intermediate. Calculations according to MINDO/2[46] and MINDO/3[19] contradict these results in preferring an unsymmetrical, diradicaloid transition state and a biradical

as intermediate. The experimentally determined energy of activation of the reaction is approximately reproduced by all calculations. This is not the case, however, with older CNDO/2 calculations[47], where an energy minimization is not undertaken. This condition is best complied with in semiempirical calculations by *Dewar et al.*[46,19].

Arguments can be presented against all these investigations. May a method parametrized for ground states (MINDO) be applied to the exploration of transition state geometries? It is at least questionable. Is the quality of the *ab initio* methods really good enough to distinguish between a synchronous and a two-step reaction?[48] The delimitation of both reaction pathways explored by *Salem et al.*[16] is not sufficiently rigorous; it seems possible that an improvement of the *ab initio* methods will perhaps lead to a different result. A detailed discussion of these problems on the basis of the cycloaddition of fulminic acid with acetylene is to be found in ref. [18]. *Basilevski et al.*[44] as well as *Houk et al.*[17] attributed the tendency to unsymmetrical transition states in MINDO to the ZDO approximation. The neglect of overlap favors the unsymmetrical transition state. Thus indeed a reason for diverging behavior is realized, but the actual quality of theoretical calculations does not allow a definite statement about the "real" reaction course. Besides, this reaction path would refer only to one non-typical case of a Diels-Alder reaction. A study (MINDO/2 and MINDO/3) using 1-hydroxybutadiene and acrolein as reactants tries to remedy this shortcoming[49]. But a mechanistic decision is also not possible here, for the reasons already discussed.

Thus the *ab initio* and semiempirical calculations are hardly a decisive help in defining the mechanism.

2.1.2. Approximate Theoretical Models

Despite rapid development in the field of computer techniques, the interest attached to qualitative reactivity models has not waned. Initially, simple reactivity indices were in the foreground of discussions about reactivity problems[21,50], whereas the Woodward-Hoffmann-rules[10] represented the first attempt at obtaining information about energy hypersurfaces on the basis of non-numerical methods. The analysis of symmetry relations provides an indication of the course of pericyclic reactions[13,43,51,52]. Orbital-, configuration-, and state-correlation diagrams would infer that the suprafacial approach $[{}_{\pi}2_s + {}_{\pi}4_s]$ of diene and dienophile is, as a ground state reaction, symmetry allowed and consequently can be a synchronous reaction. For most of the known Diels-Alder additions this conclusion seems to be correct (see Section 5). The same conclusions were drawn from the theory of the aromatic or antiaromatic transition state[53,54]. Also other directions of approach—$[{}_{\pi}2_s + {}_{\pi}4_a]$, $[{}_{\pi}2_a + {}_{\pi}4_s]$ and $[{}_{\pi}2_a + {}_{\pi}4_a]$—can be analyzed by the rules of orbital symmetry. However, it seems that there is still no definite experimental proof of these types of reaction of dienophile and diene.

Excellent summaries of these ideas can be found in papers by *Woodward* and *Hoffmann*[10], by *Herndon*[21] (literature up to 1971) and by *Houk*[55] (who considers all contributions up to 1977).

2.1.3. Frontier Molecular Orbital (FMO) Method

The search for a simple as possible description of the reactivity and the regioselectivity in Diels-Alder reactions led to the application of frontier-orbital theory[20,56]. The restriction to the molecular orbitals of the reactants most important for the reactivity allowed the classification of Diels-Alder reactions into three types[23,57] (Fig. 1). This classification is based on an analysis of eq. (a), which describes mathematically the interaction of both pairs of frontier orbitals in the HMO model[20].

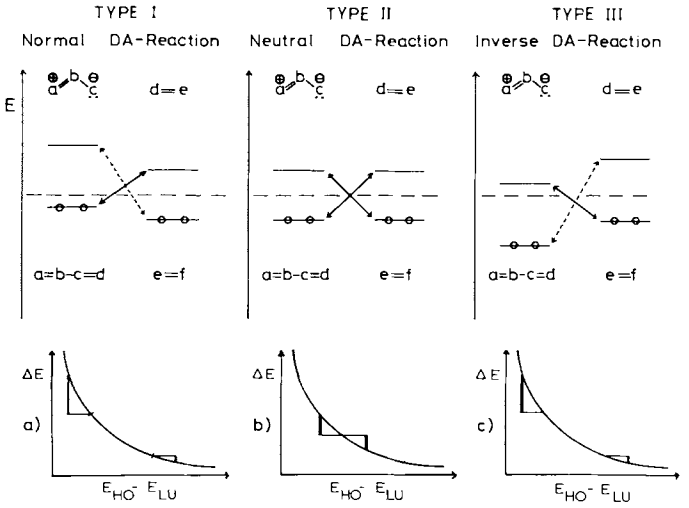
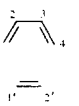


Fig. 1. Types of Diels-Alder (DA) reactions according to the frontier orbital (FMO) model. a)—c) see text.



$$\Delta E = \frac{(c_{1HO}\cdot c_{1'LU}\cdot \beta_{11'} + c_{4HO}\cdot c_{2'LU}\cdot \beta_{42'})^2}{E_{HO(diene)} - E_{LU(dienophile)}} + \frac{(c_{1LU}\cdot c_{1'HO}\cdot \beta_{11'} + c_{4LU}\cdot c_{2'LU}\cdot \beta_{42'})^2}{E_{HO(dienophile)} - E_{LU(diene)}} \quad \text{(a)}$$

Figure 2 illustrates more generally this relation for the interaction of two cycloaddition partners K and L[*] forming the adduct K—L. The following conclusions can be drawn from Figure 2:

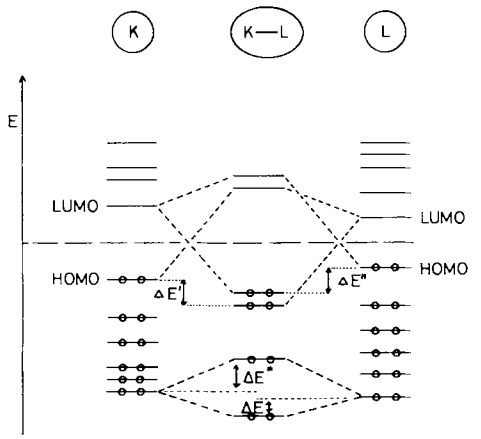


Fig. 2. MO-interaction diagram for two molecules K and L.

[*] The symbols K and L for the cycloaddition partners have been arbitrarily chosen.

1. *The interaction of occupied orbitals of K and L leads to a destabilization of the reaction complex.* The increase ΔE^* is larger than the decrease ΔE.
2. *Only the interaction of occupied orbitals of one reactant with vacant MO's of the other molecule leads to a stabilization of the system.*
3. *The extent of the interaction of two MO's is inversely proportional to their energy separation, i.e.* the more comparable the energies are, the greater is the interaction. The prerequisite for such an interaction is of course the same symmetry behavior of the molecular orbitals concerned.

These are basic statements of the qualitative perturbation theory; they do not only apply to cycloadditions[58-60] but are also fundamental for the orbital symmetry rules of *Woodward* and *Hoffmann*.

The classification of Diels-Alder reactions is to be seen in Figure 1.

As *Type I* we designate all those reactions whose $HOMO_{diene}$-$LUMO_{dienophile}$ separation is smaller than the second HOMO-LUMO separation. According to our above statements the $HOMO_{diene}$-$LUMO_{dienophile}$ separation is more important and dominates the reactivity.

For *Type II* both HOMO-LUMO separations are similar and therefore both must be considered.

Type III is just the converse of Type I. Here the $HOMO_{dienophile}$-$LUMO_{diene}$ separation governs the reactivity.

This classification makes it possible to describe the reactivity pattern of Diels-Alder reactions in a qualitative and, as we shall see later, also in a semiquantitative way; for application of this model, one has to know how substituents normally used in organic chemistry influence orbital energies. *Houk et al.*[61] have proposed a useful classification.

In a reaction of Type I with participation of a diene with a high lying HOMO, one expects that substituents which strengthen the dominant frontier orbital interaction increase the reactivity. For example, electron withdrawing substituents in the dienophile (Z-substituents according to *Houk*) or electron releasing substituents in the diene (X-substituents) are effective in this way. This situation is illustrated in Figure 1. The interaction energy is inversely proportional to the HOMO-LUMO separation. Suppose that a Z-substituent lowers the HOMO and LUMO of the dienophile by the same amount; one of the frontier orbital energy separations is enlarged, the other one is reduced. As a consequence of the inverse proportionality of stabilization and orbital separation the stabilization exceeds the destabilization, so that the overall-effect must be an acceleration of reaction. For Type I this is shown in a plot of ΔE against the HOMO-LUMO separation (Fig. 1a). The vertical lines indicate the extent of stabilization and destabilization, respectively, if the smaller HOMO-LUMO separation is shortened (left) by the same amount as the greater one (right) is lengthened. Type I represents the *normal Diels-Alder addition.*

The situation for Type II is demonstrated in Figure 1b. Both interactions are equally important. This diagram clearly illustrates the effect of a Z-substituent which decreases the HOMO and LUMO levels of a dienophile by the same amount. By strengthening one interaction the gain in stabilization is greater than the loss by weakening the other one, *i.e.* electron withdrawing substituents (Z-substituents) in the dienophile increase the reactivity. The same applies for electron releasing substituents (X-substituents), since the HOMO and LUMO will now be raised. The overall-result for Type II, which we have called a *neutral Diels-Alder reaction*[57] is: Any kind of substitution in the components effects an increase in the reactivity.

Type III is the converse of Type I (see Fig. 1c). The dominant interaction is increased by electron releasing substituents in the dienophile. This corresponds to the *Diels-Alder reaction with inverse electron demand.*

The equation for the frontier orbital interaction [eq. (a)] can be simplified to eq. (b)[23]. In doing so we assume that the value of the numerator in eq. (a) in discussing a reactivity series, *e.g.* the reaction of the same diene with several dienophiles, is constant to a first approximation. Thus, reactivity differences can be solely attributed to modifications of frontier orbital energies.

$$\Delta E = K\left[\frac{1}{E_{HO(diene)} - E_{LU(dienophile)}} + \frac{1}{E_{HO(dienophile)} - E_{LU(diene)}}\right] \quad (b)$$

As far as discussion of the Type I or Type III Diels-Alder reaction is concerned one can go one step further [eq. (c)] and restrict the discussion to the contribution of the dominant FMO-interaction. One should now expect an approximately linear correlation

$$\Delta E \approx \frac{1}{E_{HO} - E_{LU}} \quad (c)$$

between $1/(E_{HO} - E_{LU})$ and ΔE. The $\log k_2$-values of cycloaddition reactions represent an experimental measure of ΔE (see Section 5).

The numerator of eq. (a) contains information about the regiochemistry of the cycloadditions. This connection first mentioned by *Herndon et al.*[62] was later generalized[61,63]. Knowing the relative sizes of the eigenvector coefficients of the dominant HOMO-LUMO interaction, the favored orientation can be predicted. It is determined by the fact that those atoms of diene and dienophile unite which have the greatest and smallest coefficient, respectively, in the HOMO and LUMO. Generalized frontier orbital coefficients for dienes and olefins allow a simple mnemonic rationalization of orientation phenomena. Figure 3 depicts the generalized structures of frontier orbitals of dienes and dienophiles[22,56,61].

A perturbation theory, limited to frontier orbital interactions, can lead at best from a qualitative to a semiquantitative description of reaction patterns. There have been many attempts to extend the perturbational treatments[21]. *Klopman* and *Hudson*[64] developed an equation which enables description, not only of orbital interactions but also charge and steric effects. We undertook similar attempts on the basis of the ZDO approach[65,66]. These attempts were taken up by *Bachler* and *Mark*[67] and applied to specific Diels-Alder reactions[68]. *Salem*[69] enlisted similar considerations and applied them to the dimerization of acrolein[70]. Apart from the recognition that cycloadditions are not solely governed by frontier orbitals, the value of these efforts lies in the fact that specific examples, for instance the dimerization of acrolein[68] or the *endo*-addition of cyclopropene to cyclopentadiene[65], can be investigated more exactly. The interplay of

various factors, such as electronic, polar, and steric effects, can be estimated in this way. Though these numerical methods demand more exact assumptions about the structure of the reaction complex, they do not possess the simple applicability and elegance of the FMO-model.

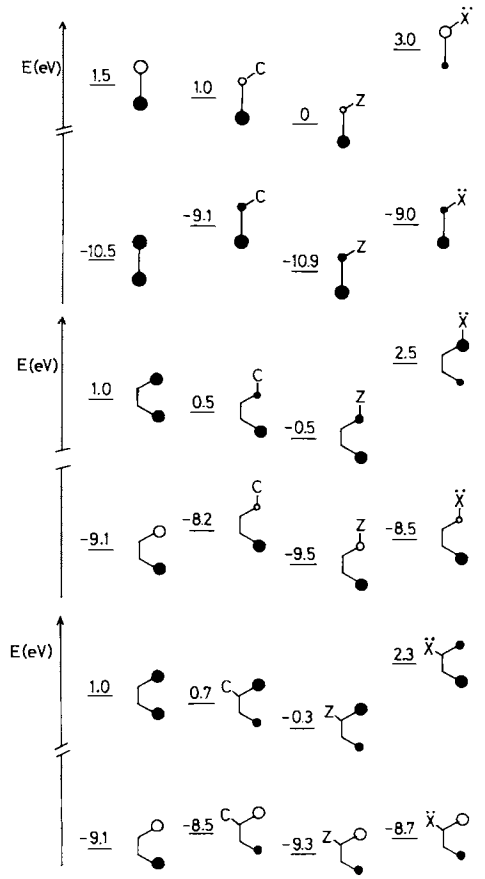


Fig. 3. Generalized frontier orbital energies and coefficients for monosubstituted alkenes (dienophiles) and dienes (C: $CH{=}CH_2$, Ph, *etc.*; Z: CHO, CN, *etc.*; X: alkyl, OR, NR_2, *etc.*).

The easier applicability of qualitative, theoretical concepts led to a further development of the ideas of *Woodward* and *Hoffmann*. *Halevi*[71] introduced the OCAMS method, which, as an orbital correlation procedure, does not lead to any fundamentally new conclusions for the Diels-Alder reaction. Interesting is the remark[72,73] that particularly the interaction of antisymmetric frontier orbitals should favor the concerted character of Diels-Alder additions. This concept would predict for the normal Diels-Alder addition a higher degree of synchronous character than for the cycloaddition with an inverse electron demand.

An exact description of the course of a cycloaddition demands an investigation of the energy hypersurface. The necessity of theoretical investigations of energy hypersurfaces was first demonstrated in the field of photochemical reactions[74,75], but in the meantime it has also proved to be a valuable extension to our theoretical interpretations of ground state reactions[75-77]. There have been several attempts to understand these problems in a quantitative manner[66,78-81]. These efforts are based essentially on the description of the reaction course as a linear combination of various electron configurations of the reaction complex [eq. (d)].

$$\Psi_{KL} = C_0\Psi_0 + \sum_{m(K)}^{occ.}\sum_{p(L)}^{unocc.} C_{m\to p}\cdot\Psi_{m\to p} + \sum_{p(L)}^{occ.}\sum_{m(K)}^{unocc.} C_{p\to m}\Psi_{p\to m} + \sum_{i(K)}^{occ.}\sum_{j(K)}^{unocc.} C_{i\to j}\Psi_{i\to j} + \sum_{r(L)}^{occ.}\sum_{s(L)}^{unocc.} C_{r\to s}\Psi_{r\to s} \quad (d)$$

Ψ_0 comprises only the molecular orbitals of the two cycloaddition partners K and L being occupied in the ground state. The second and third term of eq. (d) consist of contributions of electron configurations in which an electron has been transferred from K to L or L to K, the so called charge-transfer configurations. The last two terms of the linear combination include locally excited configurations. Each configuration in the equation is provided with a coefficient C, indicating the square of the weight of this configuration in the linear combination. This formalism can be evaluated and leads to formulas applicable for calculations[66,78].

Of great importance, is the fact that we can gain an understanding of the reaction course from the qualitative analysis of this formalism[77]. Figure 4 illustrates this by an example. For the sake of simplicity Ψ_{KL} is supposed to be a linear combination only of the ground state configuration and a charge-transfer configuration. The full lines show the energies of the configurations Ψ_0 and $\Psi_{K^+L^-}$ as a function of the separation R of the molecules K and L; these we can designate as a diabatic potential hypersurface[77]. Configuration interaction (CI) results in the adiabatic reaction course drawn with dotted lines. E_a is the activation energy of the reaction.

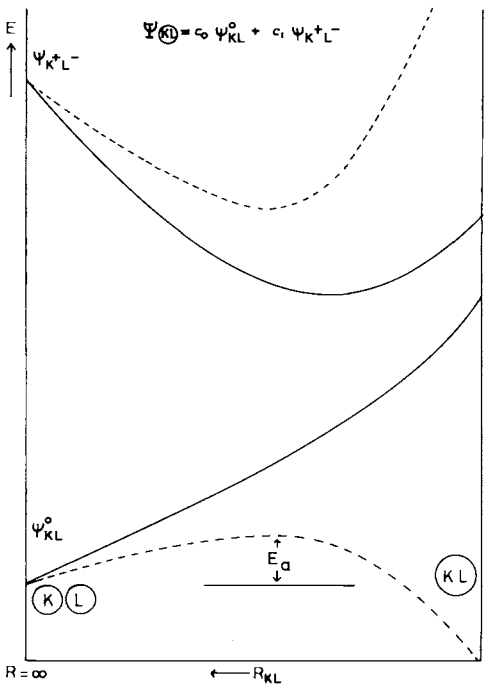


Fig. 4. Energies of the ground state configuration Ψ^0_{KL} and of a CT-configuration $\Psi_{K^+L^-}$ as a function of the separation R of K and L (full lines). Dotted lines: energy after configuration interaction (CI) between Ψ^0_{KL} and $\Psi_{K^+L^-}$

In the case of $R=\infty$, $\Psi_{K^+L^-}$ possesses a certain energy which must be on a higher level than Ψ^0_{KL}, because energy has had to be taken in order to transfer an electron from K to L. The complex $\Psi_{K^+L^-}$ is a radical ion-pair, whose energy content decreases with decreasing distance owing to the Coulomb-attraction; after passing through a minimum the ener-

gy increases again owing to steric interactions. The energy difference between Ψ^0_{KL} and $\Psi_{K^+L^-}$ corresponds to the charge-transfer excitation energy, which is thus a function of the separation of K and L. The dotted lines indicate that the mutual interaction of the two configurations leads to a stabilization and destabilization, respectively. Two states are arising; each of them contains, either in bonding or anti-bonding manner, a small amount of the other electron configuration. The size of E_a, that is the turning point of the lower, dotted curve depends on the energy separation between Ψ^0_{KL} and $\Psi_{K^+L^-}$. The smaller this is, the lower is E_a. At this point the relationship between FMO-model and CI-method becomes evident.

The FMO-model uses properties of the ground states of K and L for the discussion of the reactivity, which is identical with the assumption of an infinite separation of the reactants. In the extended model the contributions of the different configurations to the total energy are computed assuming a finite distance[79, 80]. Applications of these procedures to cycloadditions have already been described[66, 79, 81].

The chemist has already developed a feeling for orbitals and orbital correlation diagrams; it is essential that he now also gains a qualitative understanding of states and state correlation diagrams. Furthermore, apart from the aspect of correlation, an understanding of the energetics and the possibilities of influencing them must be fostered. Contributions to a qualitative understanding of energy hypersurfaces have recently been reported[82].

2.2. Thermochemical Analysis and Empirical Exploration of Hypersurfaces

After exact execution, the quantum-chemical scanning of an energy hypersurface supplies its precise shape. The pathway of lowest energy from starting compounds to end products defines the mechanism. The thermochemical analysis of reactants, intermediates, and end products offers another possibility of determining specific points of the hypersurface. With the aid of these distinct positions an approximate hypersurface can be constructed. Since the thermochemical increments for enthalpies of formation of isolated molecules are applicable in the vapor phase, only a comparison with experimental values obtained in the vapor phase is possible. This method was mainly developed by *Benson*[83].

In the meantime, there are many examples of such a treatment of Diels-Alder additions and retro-Diels-Alder reactions. The mechanistic alternative to the concerted reaction in the vapor phase is the reaction *via* a biradical. Thus, arguments focus on the question whether experimentally obtained activation parameters are in agreement with thermochemical data for a biradical mechanism. Table 1 lists Arrhenius parameters for Diels-Alder reactions in the vapor phase.

Whereas the data for the reaction of cyclopentadiene with acetylene and ethylene seem to be interpretable in the sense of a concerted process[83, 96, 97], and *Frey et al.* draw the same conclusions for the reaction of butadiene with ethylene[98], the reactions of cyclohexadiene with propene and with acrolein are interpreted as two-step processes[93–95]. Opinions about the dimerization of butadiene are varied[5, 84–86, 99]. Also the dimerization of *cis,cis*-1,4-dideuterio-1,3-butadiene—the stereochemistry of the adducts was investigated in this system—did not enable a definite decision[100]. For the dimerization of *trans,trans*-deuterio-1,3-pentadiene[101], however, the concerted character of the reaction seems to be the most plausible interpretation for the formation of the Diels-Alder adduct. This short discussion already shows the difficulties of this method, and the quotation of *Benson* seems appropriate at this juncture[83]: "Thermochemical analysis can be definitive in demonstrating the incompatibility of a biradical path with observed Arrhenius parameters, but it cannot prove the occurrence of a biradical path. It can only demonstrate the compatibility of kinetic parameters with thermochemical data".

A conclusion can be drawn from the existing investigations. The concerted reaction pathway and the biradical

Table 1. Arrhenius-parameters for Diels-Alder Reactions in the gas-phase.

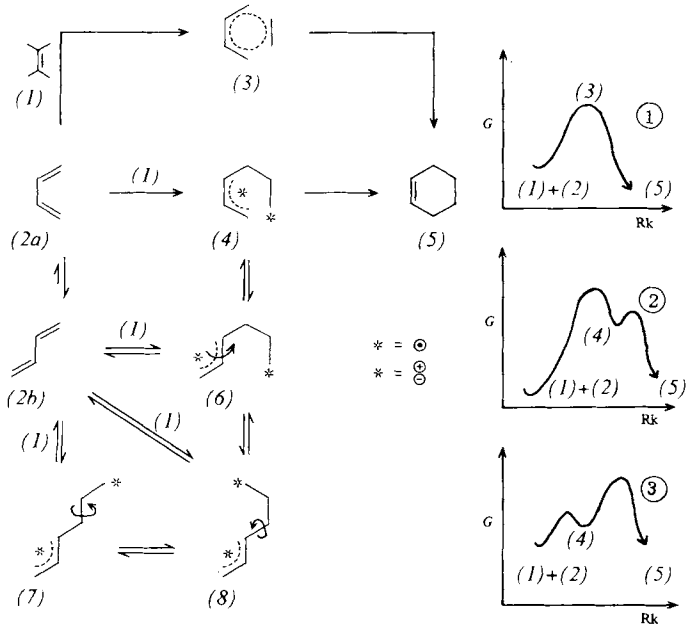
Diene	Dienophile	T [K]	log$A$ [l mol^{-1} s^{-1}]	E_A [kcal/mol]	Ref.
Butadiene	Ethylene	760—921	7.48	27.5	[84]
Butadiene	Butadiene	598—661	7.67	26.0	[85]
		446—660	6.95	23.7	[5]
		691—923	8.14	26.8	[84]
		464—557	6.95	24.5	[86]
Butadiene	Acrolein	428—605	6.16	19.7	[87]
Butadiene	Crotonaldehyde	515—573	5.95	22.0	[87]
Isoprene	Isoprene	559—664	8.95	29.5	[88]
1,3-Pentadiene	1,3-Pentadiene	552—652	7.54	26.0	[89]
2,3-Dimethylbutadiene	2,3-Dimethylbutadiene	582—673	7.16	25.3	[89]
Isoprene	Acrolein	492—606	6.07	18.7	[87]
Cyclopentadiene	Cyclopentadiene	393—433	4.93	14.9	[89]
		352—423	6.1	16.7	[90]
		405—455	6.8	16.9	[91]
1,3-Cyclohexadiene	1,3-Cyclohexadiene *(endo)*	471—639	6.08	24.3	[92]
	(exo)	471—639	5.97	25.1	[92]
Cyclopentadiene	Acrolein	351—483	6.18	15.2	[87]
1,3-Cyclohexadiene	Acrolein *(endo)*	486—571	5.65	19.5	[93]
	(exo)	486—571	5.51	20.6	[93]
1,3-Cyclohexadiene	Propene *(endo)*	512—638	5.74	26.1	[94]
	(exo)	512—638	6.66	30.1	[95]
Cyclopentadiene	Acetylene	525—656	7.51	24.2	[96]
Cyclopentadiene	Ethylene	521—570	7.59	23.7	[97]

mechanism in some of the cases examined—formal Diels-Alder reactions—are very similar energetically, so that a traversing of both kinds of reaction paths seems to be possible, depending on the structure of the reactants. It seems at least questionable whether all these reactions can be described by one and the same mechanism.

In connection with thermochemical procedures there are those which describe the energy hypersurface by means of empirical mathematical functions[102,103]. Starting from fixed points on the hypersurface, an attempt is made to establish the reaction coordinate by means of the experimentally obtained activation parameters. This results in determining the fraction of various "limiting mechanisms" in the true reaction course. As an empirical method this procedure seems attractive, but it is not very clear to what extent mechanistic conclusions are permitted. *Gajewski*[104] has recently analyzed the reaction of cyclopentadiene with cyanoethylenes in this way.

3. Stereospecificity of Diels-Alder Reactions

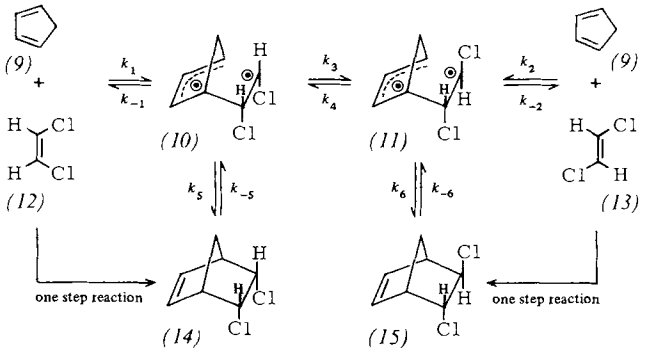
A simultaneous closure of the two new σ-bonds between diene and dienophile, with involvement of a transition state *(3)*, predicts a stereospecific reaction (Scheme 1, energy profile 1). A two-step mechanism with a zwitterionic or biradical intermediate *(4)* (Scheme 1), however, leads to a non-stereospecific reaction if rotations about single bonds in the intermediate *(4)* (Scheme 1) are faster than ring closure to the cycloadduct (energy profiles 2 and 3); if, on the other hand, rotations are slower than the very fast ring closure reaction, also a two-step reaction can take place stereospecifically. Thus a two-step reaction does not exclude *a priori* a stereospecific reaction.



Scheme 1.

Apart from the possibility of a reaction of the *s-cis* diene *(2a)*, Scheme 1 shows also the reaction of the *s-trans* diene *(2b)*. This reaction pathway cannot be excluded *a priori*, for most open-chain dienes exist mainly in the *s-trans* configuration. But, if cycloaddition of the *s-cis* form is 100 times faster and the *s-cis*→*s-trans* transformation occurs rapidly, this reaction pathway should not be realized. After attack of an olefin at the *s-trans* form the formation of a six-membered ring cannot take place in one step; biradicals or zwitterions must be the intermediates. To attain the conformation *(4)* favorable for ring closure, rotations about single bonds in *(7)* and *(8)*, and about an allylic bond in *(6)* have to take place. Whereas the first are energetically favorable, the latter have to surmount higher barriers. This however depends also on whether it is a radical[105] or an ionic allyl structure[106,107]. Since the rotation about the allylic bond in *(6)* needs more energy than rotation about single bonds in this molecule the [4+2]-addition *via* this route should be non-stereospecific.

The above statement is illustrated by the cycloaddition of the stereoisomeric 1,2-dichloroethylenes *(12)* and *(13)* to cyclopentadiene *(9)*[108] (Scheme 2). On starting from pure *cis*- and *trans*-dichloroethylene *(12)* and *(13)*, no stereochemically "false" [4+2]-adduct could be detected within the error



Scheme 2.

limit of gaschromatography (0.5%) at 180 °C; this observation is consistent with simultaneous bond formation. The presence of biradical intermediates *(10)* and *(11)*, respectively, not improbable energetically, is thus rather unlikely; k_3 and k_4 would have to be considerably smaller than k_5 and k_6.

Halogenated olefins take a special position with respect to cycloadditions to dienes; six-membered ring products as well as four-membered ring products are formed to various extents by way of biradical intermediates. In connection with the problem of one-step *versus* two-step formation of the six-membered ring product, the additions of *cis*- and *trans*-1,2-dichloro-1,2-difluoroethylene to *trans,trans*-2,4-hexadiene[109] are of great importance. It could be unequivocally demonstrated that the six-membered ring products, formed to 16.8% and 19.4%, respectively, were formed not only in a synchronous (85%) but also in a two-step process (15%) (see Scheme 14). Comparison of the partial loss of stereochemistry of the dienophile in the product with the corresponding results in the purely biradical cycloaddition of the same dienophiles to butadiene clearly shows that in these reactions the energy surfaces of both reaction pathways are comparable. In spite of the partial two-step reaction, the stereochemistry of the *trans,trans*-2,4-hexadiene is completely preserved in the adduct. This is an example for a reaction in which one rotation, namely about the C—$\overset{\ominus}{C}$ClF bond, is faster than the ring closure, and another rotation, about the

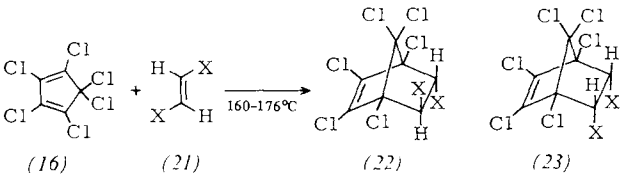
C—$\overset{\oplus}{C}$HCH $\cdot$CHCH$_3$ bond, is slower than the ring closure (see Scheme 14).

A perusal of the literature[3,4,36] shows, however, that only few Diels-Alder reactions have been investigated so precisely from the stereochemical standpoint. The proof of stereospecifity for many cycloadditions of this type refers to only 90–95%, which corresponds to the isolated yield of the pure product; however, this does not necessarily mean that the mother liquor contains the "wrong" stereoisomer, proving a two-step reaction. In any case more precise investigations of selected systems with improved analytical procedures would be desirable. With the above restriction, however, *the stereospecific [4+2]-cycloaddition in Diels-Alder reactions seems to be the rule,* as is proven by a plethora of examples.

When can one expect the two-step mechanism, and thus perhaps a non-stereospecific reaction? According to what has been mentioned in Section 2.1.3 the symmetry allowed suprafacial-suprafacial cycloaddition is fast if the separation $HOMO_{diene}$-$LUMO_{dienophile}$ or $LUMO_{diene}$-$HOMO_{dienophile}$ is small and the steric conditions allow a cisoid conformation of the diene and thus a smooth reaction in the 1,4-position.

Conversely, a large HOMO-LUMO separation as well as unfavorable steric factors slow down the rate of the synchronous reaction to such an extent that perhaps a slower two-step reaction becomes possible. Also substituents capable of stabilizing intermediates will favor the two-step mechanism; the small influence of solvents on the reaction rate in Diels-Alder reactions (Section 5.3) excludes completely zwitterionic intermediates. The examples, already described in the literature concerning non-stereospecific Diels-Alder additions seem to confirm these considerations. Similar arguments are given by *Houk*[55].

these results on the basis of biradical intermediates *(17)*⇌*(18)* would seem obvious. The geminal position of two bulky chlorine atoms in hexachlorocyclopentadiene *(16)* impede a synchronous [4+2]-cycloaddition; furthermore, the substitution by chlorine should increase the stabilization of the intermediates *(17)* and *(18)*. The steric factor mentioned here is also shown in the breakdown of the relation of reactivity and selectivity on going from 1,2,3,4-tetrachlorocyclopentadiene to hexachlorocyclopentadiene[111].

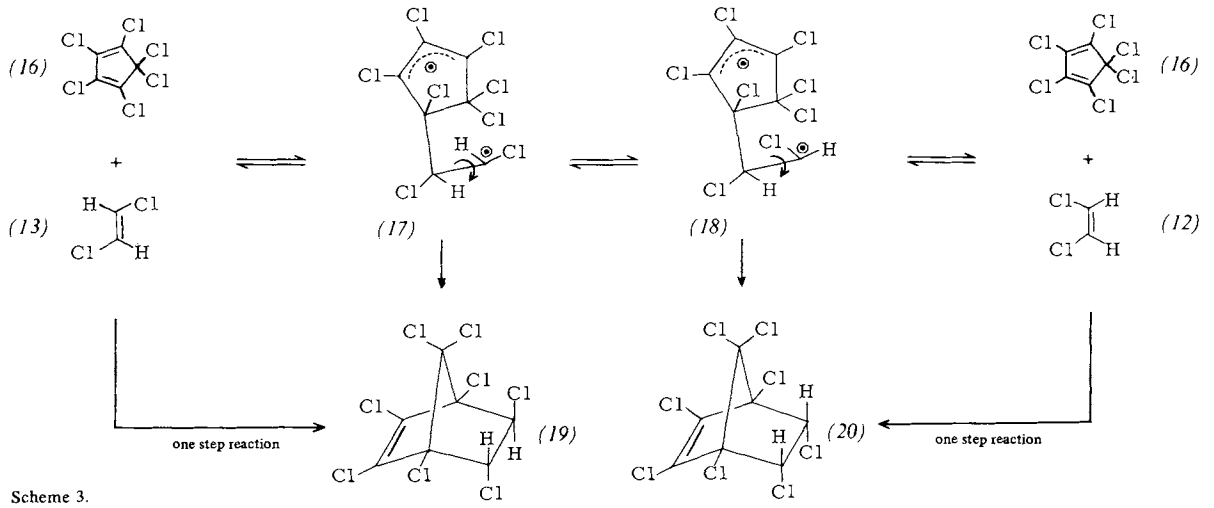


(16) *(21)* *(22)* *(23)*

Scheme 4.

(21), X=	*(22)* :	*(23)*
Cl [≡ *(13)*]	5 [≡ *(19)*] :	95 [≡ *(20)*]
CN	57 :	43
C_6H_5	71 :	29
CO_2CH_3	73 :	27
CH_3 [≡ *(30)*]	≈100 :	≈ 0

The non-stereospecific reaction of dichloroethylene as dienophile is not a singular example[110]; the values in the Table under Scheme 4 show the effect in a slightly reduced way for fumaronitrile, stilbene, and fumaric acid dimethyl ester; only *trans*-2-butene reacts in a stereospecific way. All dienophiles, except 2-butene, possess electron withdrawing substituents,

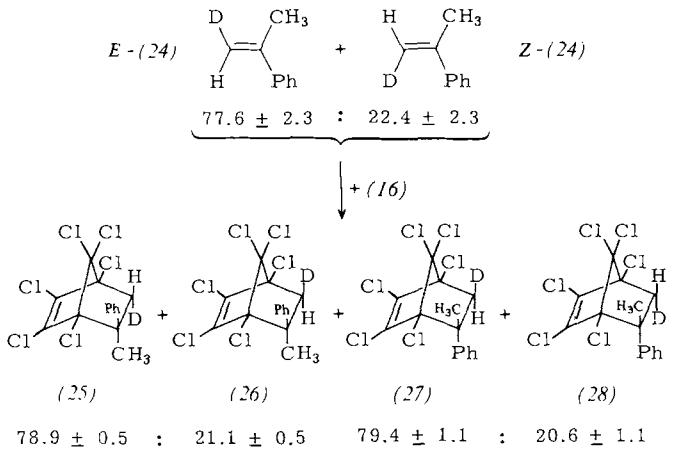


(16) *(13)* *(17)* *(18)* *(16)* *(12)* *(19)* *(20)*

Scheme 3.

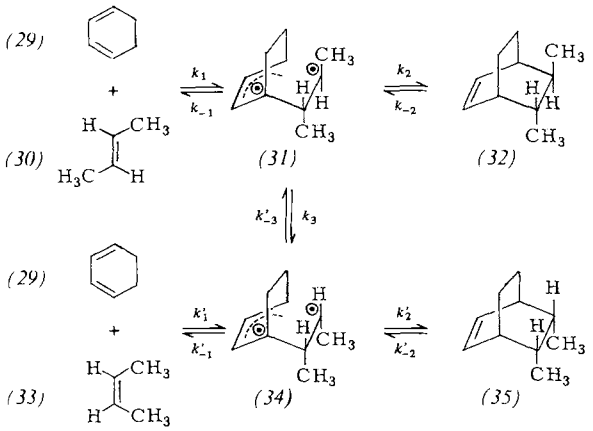
Mark[110] found that the kinetically controlled reaction of hexachlorocyclopentadiene *(16)* with *trans*-1,2-dichloroethylene *(13)* affords the [4+2]-adducts *(19)* and *(20)* in the ratio 5:95; recovered dichloroethylene contained 39% *cis*-isomer *(12)* (Scheme 3).

The Diels-Alder reaction of *(16)* and *(12)*, on the other hand, leads exclusively to *(20)* together with very small portions of the *cis-exo*-isomer; a *cis-trans* isomerization of unreacted dienophile *(12)* did not take place. An explanation of and in each case good radical stabilizers. It is difficult to make the above discussed steric effects responsible for the non-stereospecific reaction of fumaronitrile. An alternative explanation is provided by the assumption that combination of an electron deficient dienophile with an electron deficient diene (see Section 2.1.3) handicaps the one-step reaction as a result of the large HOMO-LUMO separation; moreover in this special case, steric factors as well as substituents favor a reaction *via* a biradical intermediate.



Scheme 5.

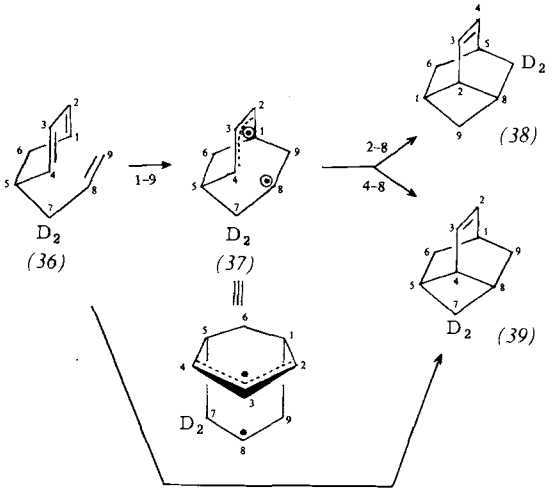
Interestingly, the cycloaddition of a mixture of 77.6 ± 2.3% *E*- and 22.4 ± 2.3% *Z*-β-deuterio-α-methylstyrene *(24)* with hexachlorocyclopentadiene *(16)* proceeds, within the limit of error, stereospecifically to the four products *(25)*—*(28)*[108, 112] (Scheme 5). Regarding the data of Scheme 3 we are not able to decide whether these results can be interpreted in favor of a simultaneous bond closure or whether the intermediates *(17)*/*(18)*, formed by analogy, close the ring faster than they interconvert by rotation (*(17)*⇌*(18)*).



Scheme 6.

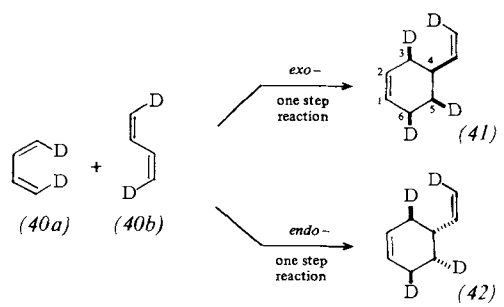
	(31)	(34)
Cycloreversion / Ring closure	$\frac{k_{-1}}{k_2} = \cong 220$	$\frac{k'_{-1}}{k'_2} \cong 25$
Cycloreversion / Rotation	$\frac{k_{-1}}{k_3} \cong 100$	$\frac{k'_{-1}}{k'_3} \cong 6.6$

Also the cycloaddition of *cis*- and *trans*-2-butene *(30)* and *(33)*, respectively, to 1,3-cyclohexadiene and the cycloreversion of the Diels-Alder adducts *(32)* and *(35)* seem to be partially non-stereospecific[113] (Scheme 6). The kinetically controlled cycloaddition was followed to 2% conversion, the cycloreversion to 6% conversion. In the authors' opinion the accurate gaschromatographic analysis supports the kinetic system of Scheme 6 with biradical intermediates *(31)* and *(34)*. Interestingly the reverse reaction of the intermediates to the educts is faster than the ring closure (see energy profile 3, Scheme 1) and likewise faster than rotations *(31)*⇌*(34)*. Also in the case of the reaction of 1,3-cyclohexadiene and 2-butene we are dealing with a system with large HOMO-LUMO separation favoring according to the above mentioned ideas a successful competition of a two-step mechanism with a symmetry allowed one-step cycloaddition; the high reaction temperature (327 °C) certainly also favors the two-step mechanism over the one-step addition with notoriously small $\Delta H^{\neq}$-values. The relatively easy reverse reaction of the intermediates *(31)* and *(34)* explains the *cis-trans*-isomerization of *(30)* and *(33)*, observed by the authors in the presence of 1,3-cyclohexadiene.



Scheme 7.

A large HOMO-LUMO separation does not guarantee a two-step mechanism, as is shown by interesting experiments by *Krantz*[114] (Scheme 7). The 5-allyl-1,3-cyclohexadiene *(36)* dideuteriated in position 7 yields exclusively the [4 + 2]-adduct *(39)* at 184 °C, corresponding to synchronous bond formation in position 1—9 and 4—8. A symmetrical, biradical intermediate *(37)* would lead to a 1:1 distribution of the D-labels [*(38)* + *(39)*]. Estimations of the rates indicate that the two-step mechanism at 184 °C is less favorable by about 4 kcal/mol. At higher temperatures a slight distribution of the labels can be observed, which, in the opinion of the author, must not be exclusively explained in terms of biradical intermediates.

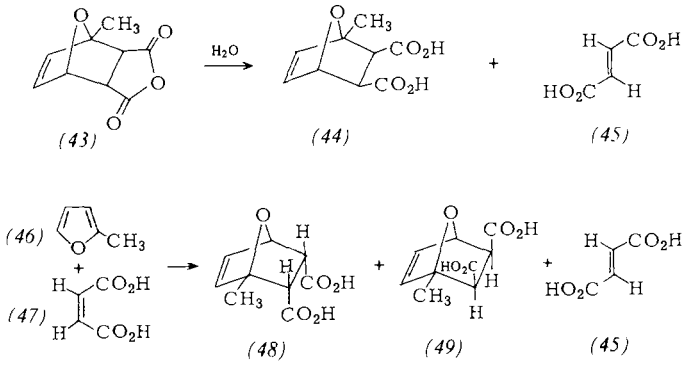


Scheme 8.

The mechanisms of dimerization of 1,3-dienes have been investigated intensively[99]. According to investigations by *Stephenson et al.*[100] the dimerization of the specifically deuteriated butadiene *(40)* does not lead exclusively to the products *(41)* and *(42)* (Scheme 8), corresponding to the one-step

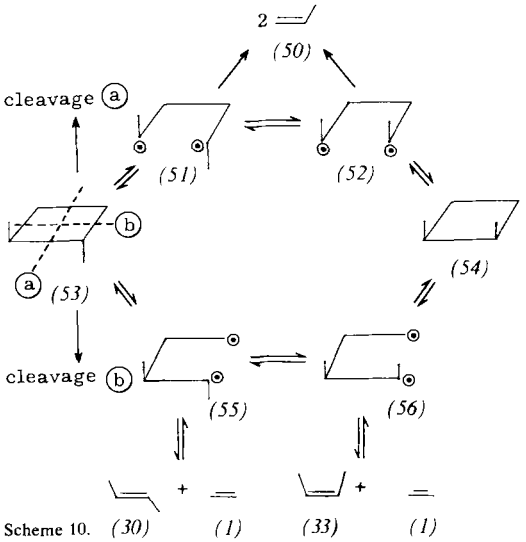
mechanism, but also to about 10% of a cycloadduct which has the vinyl group and the deuterium in positions 4 and 5 in *trans*-orientation. Although an explanation by way of a biradical intermediate is in principle possible, the authors discuss also a forbidden $[_{\pi}4_s + _{\pi}2_a]$ reaction. Even a seemingly slight structural variation of the diene, however, leads to a completely stereospecific reaction, as *Berson et al.* convincingly showed by means of *trans*-1-deuterio-1,3-pentadiene[115]. A dimerization with biradicals as intermediates is suggested for 1,3-diphenyl-substituted butadienes. An accelerating factor $>10^6$ compared with the dimerization of the unsubstituted butadiene is not compatible with a synchronous mechanism[116].

A final example of a non-stereospecific cycloaddition and cycloreversion is taken from the reactions of substituted furans (Scheme 9), whose reversible cycloadditions with maleic



Scheme 9.

anhydride and its derivatives are well known[117]. Thus, the cycloaddition of maleic acid to 2-methylfuran affords, besides the expected *endo*- and *exo*-adducts *(48)* and *(49)*, up to 17% fumaric acid *(45)*, which is also formed during the hydrolysis of the *exo*-maleic acid anhydride adduct *(43)*. In the analogous reactions of furan itself and its 2,5-dimethyl derivative, on the other hand, *no* fumaric acid is formed. The authors would explain this *cis-trans*-isomerization in terms of a reversible formation of a zwitterionic intermediate. The alternative explanation—by an isomerization as consequence

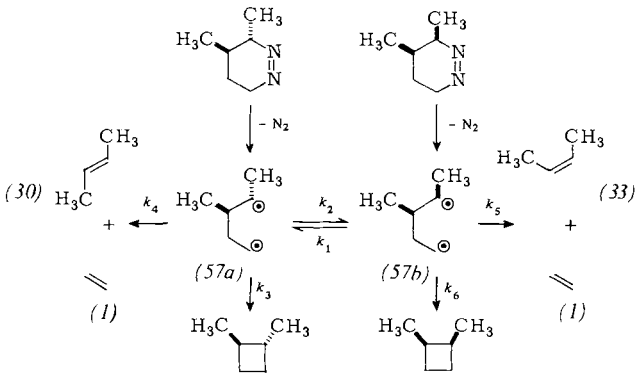


Scheme 10.

of a Michael-type addition in competition with the cycloaddition—can in our opinion not be ruled out, according to the experimental data.

Whereas in the case of the *symmetry allowed [4+2]-cycloadditions* the *stereospecific* reactions, as already mentioned, represent the *normal case,* and the above discussed *non-stereospecific* ones seem to be the exception, the non-stereospecific reaction in accordance with the Woodward-Hoffmann rules seems *to be the rule for [2+2]-cycloadditions.*

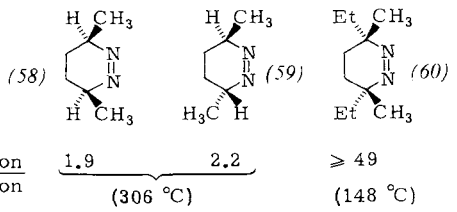
The cycloadditions of ethylene *(1)* to *cis*- and *trans*-2-butene *(33)* and *(30)*, respectively[118], as well as the cycloreversion reaction of the corresponding cyclobutane derivatives[119] have been intensively investigated in the vapor phase at 400 °C. The exact analysis of the kinetic data and product studies support Scheme 10; again rotations can compete in the biradical intermediates, not only with ring closure to the cycloadduct but also with the cleavage to the educts. The independent formation of the same biradical intermediates by thermolysis of cyclic azo compounds under the same conditions leads to the same mechanistic conclusions[120] (Scheme 11). The rate of rotation in the biradical



Scheme 11.

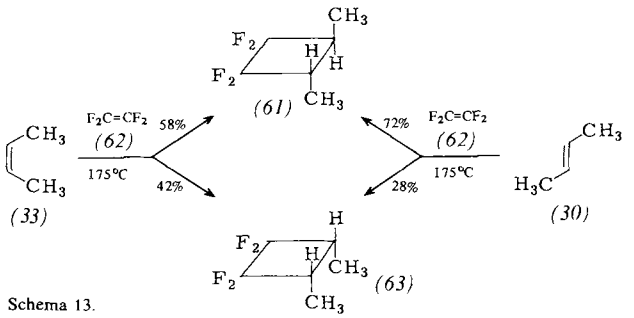
	(57a)	(57b)
Cleavage / Ring closure	$\frac{k_4}{k_3} = 1.4$	$\frac{k_5}{k_6} = 1.8$
Ring closure / Rotation	$\frac{k_3}{k_2} = 1.9$	$\frac{k_6}{k_1} = 0.7$

depends on its structure; progressive alkyl substitution of the radical centers hinders the rotation, as shown by the increase in the ratio retention/inversion for the formation of cyclobutane in the thermolysis of azo compounds *(58)*—*(60)*[120] (Scheme 12). The differing reaction temperatures, however, must be mentioned.



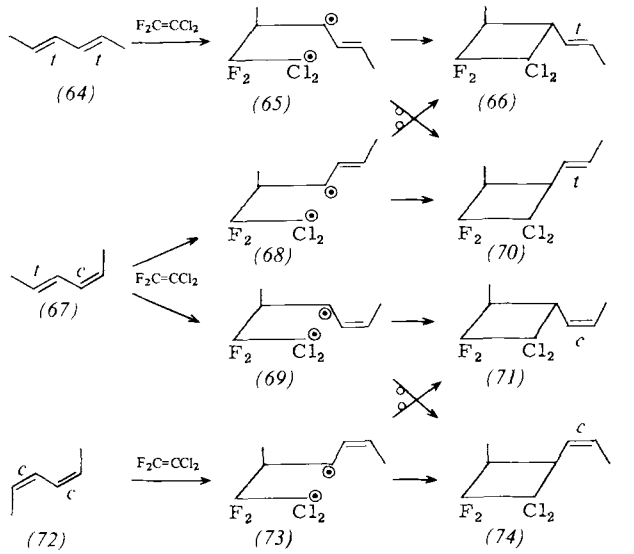
Schema 12

Also the cycloaddition of the isomeric 2-butenes *(30)* and *(33)* to tetrafluoroethylene *(62)*[121] is extremely non-stereospecific (Scheme 13).



Schema 13.

The already classical investigations by *Bartlett*[121,122] have considerably increased our knowledge about the mechanistic course of [2+2]-cycloadditions and also contributed indirectly to the mechanistic conceptions concerning the Diels-Alder reaction. 1,1-Dichloro-2,2-difluoroethylene ("1,1,2,2") reacts with the stereoisomeric 2,4-hexadienes *(64)*, *(67)* and *(72)* in a non-stereospecific way *via* intermediates *(65)*, *(68)*, *(69)* and *(73)* to give the cyclobutane derivatives *(66)*, *(70)*, *(71)* and *(74)*; rotations about single bonds successfully compete with ring closure reactions, the configuration of the allyl radical structure in the intermediates is preserved (Scheme 14)[123]. Kinetic measurements show only very small positive influences of solvents[122] on the reaction rate, consistent with a non-polar biradical intermediate. Competition experiments and a comparison of the relative rate constants so obtained



Schema 14.

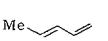
with rate constants of Diels-Alder reactions of the same dienes with maleic anhydride (MAA) and tetracyanoethylene (TCNE) reveal obvious differences[124]. This finding is taken as an argument against biradical intermediates in these special cases of [4+2]-cycloadditions, for similar substituent effects would be expected if analogous biradical intermediates did occur (Table 2).

In some cases *Bartlett et al.* observed with "1,1,2,2" and with the stereoisomeric 1,2-dichloro-1,2-difluoroethylenes ("1,2,1,2"), as well as with α-acyloxyacrylonitrile, competing [2+2]- and [4+2]-cycloadditions[125]. Are these two products formed by way of the same biradical intermediate? In all cases a definite decision is not possible; some facts may be cited. Thus substituents in the 2-position of the diene influence in the reaction with "1,1,2,2" the fraction of [4+2]-addition, which increases with the size of the substituent in the diene[126]; also in the Diels-Alder reaction of MAA, *Craig et al.*[127] noticed an increase in rate with increasing size of the 2-substituent. The reaction of cyclopentadiene with the stereoisomers of "1,2,1,2" affords the [2+2]-cycloadduct in a non-stereospecific reaction, whereas it gives the [4+2]-cycloadduct in a stereospecific fashion[121]; in this case a common biradical intermediate must be ruled out. α-Acetoxyacrylonitrile predominantly undergoes a stereospecific [4+2]-cycloaddition with the stereoisomeric 2,4-hexadienes, the fraction of [2+2]-addition is diminished to 0.4%; also in this case [4+2]- and [2+2]-cycloadditions seem to occur *via* different energy profiles.

Apart from biradical intermediates it is also possible to detect zwitterionic ones in [2+2]-cycloadditions[27,28,123]. A non-stereospecific reaction, a strong influence of solvent, and high ρ-values prove beyond doubt the zwitterionic intermediate, for example in the reaction of enol ethers with cyanoethylenes. The fact that the relative reaction rate of cyanoethylenes in [4+2]-cycloadditions can be excellently correlated by the HOMO-LUMO model[23] and that in the analogous [2+2]-cycloadditions this relation fails[128] proves the difference in mechanism (Table 3); the rate-differentiation of cyanoethylenes in the reaction with enol ethers is in complete agreement with the expected stabilization of the zwitterionic intermediate.

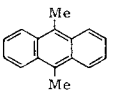
The competition between [2+2]- and [4+2]-cycloaddition of 1,1-disubstituted 1,3-dienes *(75)* as well as of *cis*-1-substituted 1,3-dienes often cited in the literature has recently been investigated by *Nishida et al.*[129]. Exact product analyses and kinetic studies, including the dependence of the reaction rate on solvents, are compatible with the mechanistic picture of Scheme 15. The kinetically controlled reaction furnishes, *via* the zwitterionic intermediate *(76)*, the thermodynamically unstable four-membered ring adduct *(77)*, which then trans-

Table 2. Relative rate-constants k_{rel} of different dienes for the [2+2]-cycloaddition with 1,1-dichloro-2,2-difluoroethylene and for the [4+2]-cycloaddition with maleic anhydride MAA and tetracyanoethylene TCNE [124, 125].

Dienophile \ Diene					
$Cl_2C{=}CF_2$ [a]	≡1.00 1.00	2.3 0.42	0.053 2.3	0.028 1.65	0.113
MAA [b]	≡1.00	2.25	very small	3.33	1350
$(NC)_2C{=}C(CN)_2$ [c]	≡1.00	44.5	0.00226	103	1970000

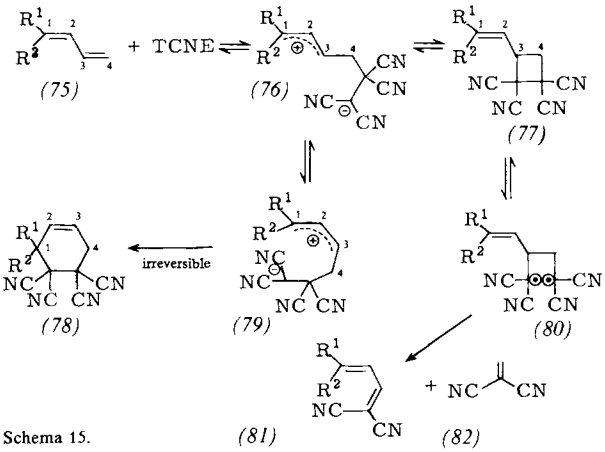
[a] 80 °C. [b] Dioxane, 30 °C. [c] Dioxane, 20 °C.

Table 3. Comparison of reactivity of [4+2]- and [2+2]-cycloadditions [23, 128].

Cyanoethylene	[4+2]-Cycloaddition $10^5 \times k_2$ [l mol^{-1} s^{-1}], 20 °C, dioxane		[2+2]-Cycloaddition $10^5 \times k_2$ [l mol^{-1} s^{-1}], 25 °C, benzene	
			$Me_2C{=}CH{-}OMe$	
	1.04	0.89	too slow	
	81	139	too slow	
	45000	127000	31.6	≈ 160 [a]
	480000	5900000	2.39	560 [b]
	43000000	13000000000	3.97	1450

[a] Ene reaction + subsequent [4+2]-cycloaddition. [b] Ene reaction + [2+2]-cycloaddition.

forms into the stable cyclohexene derivative *(78)* by way of *(76)* and *(79)*. The dipole *(76)* could be intercepted by thiophenol; an intramolecular course of the transformation *(77)*→*(78)* is secured. In so far as the [4+2]-adduct, as well as the [2+2]-product, is formed, the fraction of cyclobutane derivative increases with increasing amount of transoid diene-conformer. At high temperature (120 °C, cyclohexane) a cleavage, presumably *via* the diradical *(80)* to *(81)* and *(82)*, is observed.



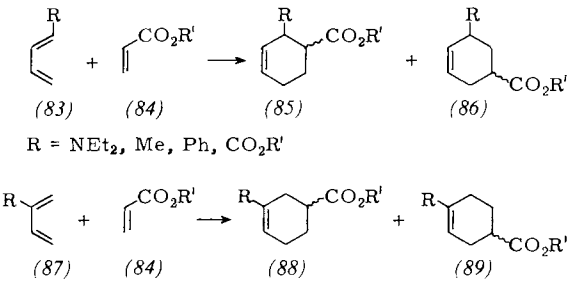
Schema 15.

These results support the concept of four-membered ring formation as consequence of an attack on the transoid diene, as already mentioned in the discussion of Scheme 1. The fact that dienophiles which are very active in normal Diels-Alder additions yield in the reaction with transoid fixed dienes vinyl-cyclobutane derivatives *via* a zwitterionic intermediate, has also been observed in other studies[121,130]. This also conforms with the above discussed halogenated olefins.

4. Regiospecificity of Diels-Alder Reactions

In the same way as the related 1,3-dipolar cycloadditions Diels-Alder additions show a strong preference for the formation of specific regioisomers[3,131,132]. For a long time, efforts have been made to interpret this finding by means of the combination of "electronic" and "steric" effects, however without finding a satisfactory solution. Only the application of simple perturbation theoretical considerations led to a breakthrough[61-63]. The present discussion is based on the generalized frontier orbitals of dienes and olefins by *Houk*[61].

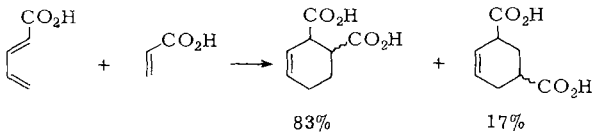
1-Substituted dienes, independently of the nature of the substituent (Scheme 16), preferably give the *"ortho"*-isomer *(85)* with electron-poor dienophiles like methyl acrylate or with phenyl substituted olefins. In contrast, 2-substituted dienes mainly afford the *"para"* isomer *(89)*, also independently of the substituent. All these reactions are $HOMO_{diene}$-$LUMO_{dienophile}$ controlled. By means of Figure 3 it is easily determined which isomer should preferably be formed: the HOMO of the diene has to be brought to an interaction with the LUMO of the dienophile in such a way that the larger and smaller coefficients, respectively, can lie side by side. Instead of considering all four eigenvector coefficients of the reacting C-atoms of HOMO and LUMO one can restrict the discussion to the larger ones[63].



Scheme 16.

The energies of the generalized frontier orbitals by *Houk* have been determined as average values of ionization potentials or electron affinities of appropriately substituted olefins and dienes. The eigenvector coefficients originate from calculations, mainly of the *ab initio* or CNDO/2 type. The eigenvector coefficients calculated according to the Hückel-method[63], conform with the other values, with the exception of electron-poor olefins (Z-substituted) and Z-substituted dienes. The structures of the frontier orbitals of *Epiotis*[133] correspond to those of *Anh et al.*[63]. *Anh et al.* and *Houk et*

al.[61] arrive at the same conclusions in spite of the discrepancy in the cases already mentioned, *e.g.* for the reaction of 2,4-pentadienoic acid with acrylic acid[134], since evaluation of the two HOMO-LUMO stabilizations in the Hückel-model leads to the same result as consideration of the stronger interaction based on the values of *Houk*.

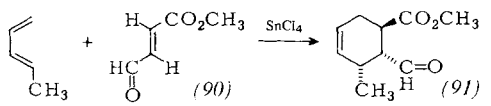


Epiotis[133], who deduced the preferred orientation solely from the size of the coefficients of the dominant HOMO-LUMO pair and relied upon Hückel-calculations, suggests that the discrepancy between theory and experiment in these cases demands a two-step reaction *via* a biradical. A detailed discussion of the results of various calculation methods for the determination of eigenvector coefficients can be found in ref.[135].

Which mechanistic conclusions enable interpretation of the regiochemistry by means of the FMO-model? Apart from the rare controversial examples, the accordance of FMO theory with experiment lends support for a multicentere mechanism. However, with respect to the different size of the eigenvector coefficients an unsymmetric transition state is suggested even during a simultaneous formation of the new bonds, as postulated by *Woodward* and *Katz*[136]. But this discussion cannot provide a mechanistic decision.

The generalized orbitals discussed by *Houk et al.*[61] are noteworthy, for they are easy to remember. On the other hand, in the case of multisubstitution of the diene or in the case of hetero multiple bonds their applicability is rather limited. Explicit HMO-calculations for a multitude of different dienes and dienophiles, even with hetero multiple bonds as for example in nitroso compounds[137], extend the range of applicability[63]. The qualitative agreement of theory and experiment in more than 100 examples emphasizes the usefulness of FMO-theory for the interpretation of regiochemistry.

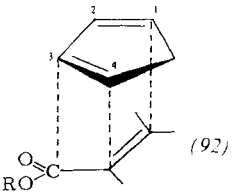
At this juncture it might also be pointed out that catalysis by Lewis acids can influence the regiochemistry of Diels-Alder reactions[138]. Thus the reaction of *(90)* with *trans*-1,3-pentadiene under non-catalytic conditions leads to a mixture of three adducts in the proportion 5:3:1. Addition of tin tetrachloride, however, effects exclusive formation of the main isomer *(91)*[139] also formed in the non-catalyzed reaction. The complexing of dienes and dienophiles by Lewis acids changes the energetic position and the structure of the frontier orbitals[140-142], and thus it affects the regiochemistry.



Apart from the relative magnitudes of the eigenvector coefficients of the dominant HOMO-LUMO interaction, secondary orbital interactions are cited as additional modifying factors for the regiochemistry[142-145]. They are supposed to enhance the orientation behavior indicated by primary interactions. The importance of such forces manipulating the regioselectivity is controversial[134].

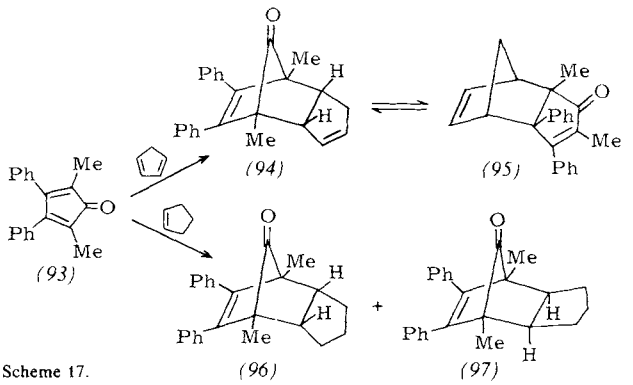
Besides the formation of *"ortho"* or *"para"* products in cycloadditions of unsymmetrical reactants, *Alder et al.* already observed the *preferred formation of endo-addition products*[146]. The experimental facts and attempts at their interpretation have been discussed on several occasions[3,37,131]. In this connection it was also pointed out that the energies determining the steric course of the addition are of the order of 0 to about 3 kcal/mol, corresponding to a 1:1 mixture and to a 100:1 preference for one isomer[3]. It is well known that the *endo/exo* ratios are both solvent[37,147] and temperature dependent[3,148]. The comparative interpretation of experimental data, very often obtained under different conditions, can only be effected very cautiously.

In recent years mainly secondary orbital interactions have been resorted to for such interpretations. This approach was initiated by *Woodward* and *Hoffmann*[149] and taken up by others[70,150,151]. For the normal Diels-Alder addition this



(92)

means that the $HOMO_{diene}$-$LUMO_{dienophile}$ interaction is not only limited to the reacting C-atoms but also includes interactions as are indicated in *(92)* between C-3 and the carboxyl C-atom. The importance of secondary orbital interactions follows from elegant experiments by *Houk*[152] who reacted 2,5-dimethyl-3,4-diphenylcyclopentadienone with cyclopentadiene and with cyclopentene (Scheme 17). Whereas the conjugated diene formed only the *endo*-adduct *(94)*, in the reaction of cyclopentene the two isomers *(96)* and *(97)* are produced in the ratio 1:1. *(94)* is in equilibrium with its rearrangement product *(95)* at higher temperatures.

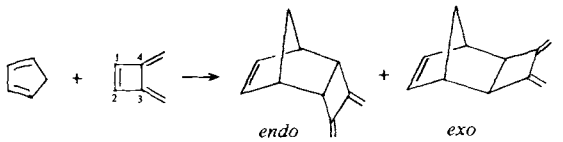


Scheme 17.

The Diels-Alder addition of 3,4-dimethylenecyclobutene with cyclopentadiene also points to the importance of secondary orbital interactions[153]. The smallness of the eigenvector coefficients in the 3- and 4-position of this triene is regarded as responsible for the fact that the reaction with cyclopentadiene results in a 1:1 mixture of *endo*- and *exo*-compounds.

The exclusive formation of *endo*-adducts in the reaction of cyclobutadienes[154-156] can be explained, on the other hand, by eigenvector coefficients which are increased in the 3- and

4-position. Therefore more intense secondary orbital interactions are possible.



The reaction of maleic acid anhydride with furan did not seem, for a long time, to corroborate the importance of secondary orbital interactions; first of all only the *exo*-product was isolated[157], but later on, however, it was found[158] that both *endo*- and *exo*-product are produced simultaneously and furthermore that the *endo*-adduct rearranged to the *exo*-product by reversible cleavage in the components. Recently, however, it has been shown[117] that the original *endo*-addition takes place 500 times faster than the *exo*-reaction. Thus it seems that secondary orbital interactions decide the regiochemistry also in the case of furan, since steric hindrance by the oxygen atom during *exo*-addition cannot be invoked.

The addition of cyclopentadiene to cyclopentene, resulting only in the *endo*-adduct[159], seems to underline the foremost importance of the CH_2-group of cyclopentadiene as an *endo* directing effect. This influence, which is only sterically justifiable, could perhaps be responsible for the fact that propene supplies mainly *endo*-adduct[160]. Cyclopropene[161] and cyclobutene do not make an exception in this series, as long as they are only substituted at the double bond[162]. But if one introduces substituents into the 3-position of cyclopropene[163-166] and into the 3- or 3- and 4-position of cyclobutene[162,167-169], the situation can change. Bulky substituents impair the formation of the *endo*-transition state such that the less favored *exo*-addition also gets a chance. The fact that the *endo*-addition of cyclopropene is due to steric hindrance in the *exo*-transition state, could be shown by SCF perturbation calculations[65].

The explanation of the orientation behavior in the reaction of cyclopentadiene with the dienophiles listed in Table 4 is controversial. A Japanese research group[170], on the one hand, concludes an attracting interaction between the methyl group of the dienophile and the π-system of the diene from the special position of the methacrylic acid derivatives, *i.e.* from the preferred *endo*-position of the methyl group in the adduct. On the other hand, it has been pointed out[171] that such a special behavior is not observed with 2,5-dimethyl-3,4-diphenylcyclopentadienone *(93)* as diene. It seems that the steric effect of the CH_2-group of cyclopentadiene is responsible for the preference of the *endo*-position of the methyl group. This fact is impressively confirmed by an analysis of the *endo/exo*-selectivity of these dienophiles by *Konovalov et al.*[172]; the *endo/exo*-selectivities found by the Russian group conform with those given in ref.[170]. In Figure 5, $\log k_x$ (k_x = *exo*-addition rate constant) is plotted against $\log k_n$ (k_n = *endo*-addition rate constant)[172]. One can see that the dienophiles of the acrylic acid and crotonic acid type lie on one regression line ($r = 0.997$), while those of the methacrylic acid type (5—8) occupy a special position. Common to all three types is the sequence of relative reactivities. A dotted straight line of gradient 1 is also drawn, which holds for $\log k_n = \log k_x$. It is very interesting that the deviation from the dotted line increases with increasing reactivity. This would point to the previously established higher selectivity at higher reactivity, interpretable by means of the FMO-model. It is important that the *endo/exo*-selectivity is not a phenomenon in itself but is coupled with the absolute reactivity of the dienophiles. The more reactive the dienophile, the greater the differences in the selectivity ought to be. The comparison of crotonic acid with acrylic acid derivatives is

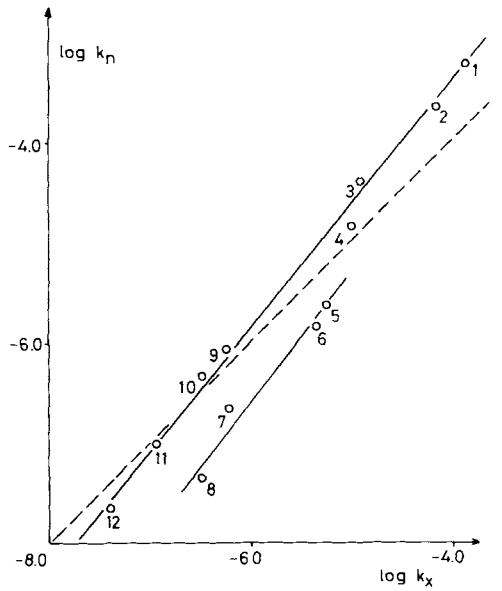


Fig. 5. Plot of $\log k_x$ against $\log k_n$ for the reaction of the dienophiles of Table 4 with cyclopentadiene.

Table 4. *endo/exo*-Ratios and activation parameters for the reaction of cyclopentadiene with α,β-unsaturated olefins [172] (see also Fig. 5).

No.	Olefin (Dienophile)	*endo/exo* 30 °C	$E_{a(endo)} - E_{A(exo)}$ [kcal/mol]	$E_{a(endo)}$ [kcal/mol]	$E_{a(exo)}$
1	$H_2C{=}CH{-}COOH$	4.36	−0.90	9.2	10.1
2	$H_2C{=}CH{-}CHO$	3.25	−0.60	12.1	12.7
3	$H_2C{=}CH{-}CO_2CH_3$	3.04	−0.60	12.6	13.2
4	$H_2C{=}CH{-}CN$	1.37	−0.20	13.2	13.4
5	$H_2C{=}C(CH_3)COOH$	0.440 [a]	+0.10	13.1	13.0
6	$H_2C{=}C(CH_3)CHO$	0.328 [a]	+0.60	14.6	14.0
7	$H_2C{=}C(CH_3)CO_2CH_3$	0.382 [a]	+0.90	16.1	15.2
8	$H_2C{=}C(CH_3)CN$	0.143 [a]	+1.2	17.2	16.0
9	$H_3C{-}HC{=}CH{-}COOH$	1.61 [a]	−0.70	13.3	14.0
10	$H_3C{-}HC{=}CH{-}CHO$	1.50 [a]	−0.80	15.8	16.6
11	$H_3C{-}HC{=}CH{-}CO_2CH_3$	0.91 [a]	−0.20	16.2	16.4
12	$H_3C{-}HC{=}CH{-}CN$	0.508 [a]	−0.80	15.2	16.0

[a] *endo/exo* referred to —COOH, —CHO, $-CO_2CH_3$, and —CN.

an indication in this direction. The exceptional position of methacrylic acid derivatives is also explained by the Russian authors in terms of the steric effect of the CH_2-group of the cyclopentadiene.

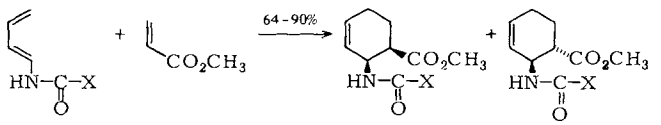
This explanation is confirmed by comparison of the reactivity of 2,3-dimethylbutadiene with the same dienophiles. But there exist arguments against this explanation by means of a steric effect[173], and there are also perturbation-theoretical objections[174].

Another regiochemical aspect of Diels-Alder reactions consists in the observation of *syn-anti*-addition of cyclopentadiene derivatives mono-substituted in the 5-position[175]. The selectivity in these reactions can be influenced by addition of Lewis-acids as catalysts[176]. *Anh*[177] interpreted the experiments by means of steric effects, van-der-Waals-London forces and by orbital interactions.

5. Kinetic Investigations

5.1. Influence of Diene and Dienophile Structure on the Reactivity

The preferred reaction of electron-rich dienes with electron-poor dienophiles with formation of six-membered carbocycles has represented the prototype of these cycloadditions since the original works of *Diels* and *Alder*. Various examples illustrate these facts[3,37,178]. The FMO-model provided a theoretical interpretation, by relating the high reactivity to the dominant influence of the $HOMO_{diene}$-$LUMO_{dienophile}$ separation[23,57]. Equation (c) describes this correlation in a quantitative way disclosing either a linear correlation of $1/(E_{HO(diene)} - E_{LU(dienophile)})$ with $\log k_2$—the latter as a measure of E_A—or a hyperbolic relation of $E_{HO(diene)} - E_{LU(dienophile)}$ with $\log k_2$. Of course in the case of a constant diene or dienophile in a reaction series it is also possible to consider only the orbital energy concerned in the substitution. A hyperbolic correlation was recognized for the reactions of substituted dienes with tetracyanoethylene and maleic anhydride[179]. That this kind of correlation becomes linear in a small section of the hyperbola is demonstrated by the reaction of 1-acylaminobutadienes with methyl acrylate[180].



X = CCl_3, OC_2H_5, OC_6H_5, SC_6H_5, -N⬡

Figure 6 shows the plot of $1/(E_{HO(diene)} - E_{LU(dienophile)})$ against $\log k_2$ for cycloadditions of cyclopentadiene and 9,10-dimethylanthracene, respectively, with cyano-substituted ethylenes[181]; kinetic data elaborated earlier by us[7].

Whereas Figure 6 is a good confirmation of the reactivity model, Figure 7, containing a plot of $\log k_2$ values against $1/(E_{HO(diene)} - E_{LU(dienophile)})$ for cycloadditions of substituted dienes with tetracyanoethylene, seems to contradict it[124]. An exact analysis of the rate data listed in Table 5 solves this problem.

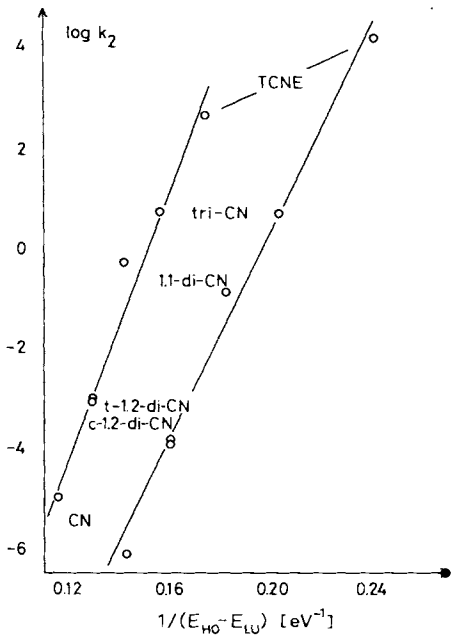


Fig. 6. Correlation of $\log k_2$ (20 °C) against $1/(E_{HO(diene)} - E_{LU(dienophile)})$ for the cycloaddition of cyclopentadiene (left curve) and 9,10-dimethylanthracene (right curve) to cyano-substituted ethylenes [181].

The reactivity in Diels-Alder reactions is not only controlled by orbital interactions but is also influenced by other effects, above all for example, by conformational effects in the diene. *Eisler* and *Wassermann*[182] have already drawn attention to the fact that the equilibrium of *s-cis*- to *s-trans*-diene influences the reaction rate. This holds true irrespective of whether the second conformation—being in equilibrium with the *s-trans*-diene in question—is a *cis*- or a *gauche*-conformation[183]. The dienes of Table 5 carry one or

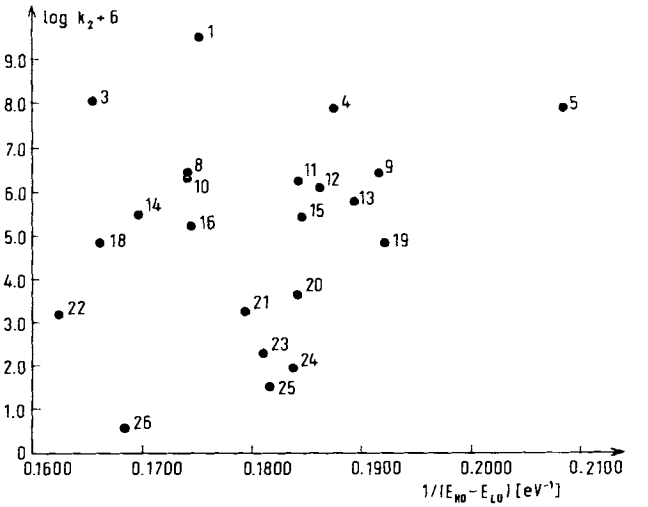


Fig. 7. Plot of $1/(E_{HO(diene)} - E_{LU(TCNE)})$ against $\log k_2$ for cycloadditions of substituted dienes to tetracyanoethylene (for numbering see Table 5).

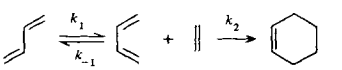


Table 5. Kinetic data for the reaction of substituted dienes with tetracyanoethylene [124] (TCNE) at 20 °C and maleic acid anhydride (MAA) at 30 °C.

No.	Diene	$\log k_2 + 6$ [a] TCNE	MAA
1	Cyclopentadiene	9.552	4.964
2	Alloocimene B	9.422	
3	1,2-Bis(methylene)cyclohexane	8.058	3.878
4	*trans*-1-Methoxybutadiene	7.935	2.925
5	*trans,trans*-1,4-Dimethoxybutadiene	7.925	
6	Hexamethylradialene (→monoadduct)	6.726	
7	Alloocimene A [b]	6.538	
8	2-Methoxybutadiene	6.471	
9	*trans,trans*-2,4-Hexadiene	6.449	
10	2,3-Dimethylbutadiene	6.386	2.526
11	*cis*-1-Methoxybutadiene	6.279	
12	1,3-Cyclohexadiene	6.137	2.120
13	*trans*-1-Phenylbutadiene	5.814	2.049
14	2-Phenylbutadiene	5.509	2.778
15	*trans*-1,3,5-Hexatriene	5.456	
16	*trans*-1,3-Pentadiene	5.243	2.356
17	Hexamethylradialene (→bisadduct)	5.146	
18	2-Methylbutadiene	4.882	2.187
19	*trans,trans*-1,4-Diphenylbutadiene	4.867	0.471
20	1,3-Cycloheptadiene	3.636	
21	4-Methyl-1,3-pentadiene [b]	3.262	
22	1,3-Butadiene	3.228	1.832
23	*cis,trans*-2,4-Hexadiene	2.305	
24	*cis*-1,3,5-Hexatriene	1.952	
25	*cis*-1-Phenylbutadiene [b]	1.502	
26	*cis*-1,3-Pentadiene	0.583	

[a] k-values in [l mol^{-1} s^{-1}]. [b] The k-values refer to the [4+2]- and [2+2]-cycloaddition.

more substituents in various positions of the molecule or are even cyclic. Hence the energy content of the *s-cis* form and its fraction in the equilibrium are greatly varied and therefore influence the rate. The very small reactivity of *cis*-1-substituted and 1,1-disubstituted dienes emphasizes this finding; for these dienes, however, the question is justified whether actually a *s-cis*-conformation can exist? Why should a [4+2]-cycloaddition not be possible based on a *gauche*-conformation? In connection with these conformational effects it is to be recognized, that as far as *cis*-1-substituted and 1,1-disubstituted dienes are concerned a [2+2]-cycloaddition takes place in competition with a [4+2]-cycloaddition (see Section 3). Figure 8 attempts to illustrate this relationship.

Normally the transition state of the [4+2]-addition is lower than that of the [2+2]-cycloaddition. The dotted lines show how the transition state changes if the *s-cis* form becomes energetically more unfavorable. It then may happen that it is higher or similar in energy to the transition state of the [2+2]-addition, as it originates from the *s-trans* form. [4+2]- and [2+2]-addition then take place in competition. This implies mechanistically that the four-membered ring formation does not result from the cisoid diene. This seems to be plausible because the transition state of the four-membered ring formation originating from the *s-cis* diene ought to be energetically higher by an amount which corresponds to the energy difference between *s-cis* form and *s-trans* diene and therefore should not be competitive.

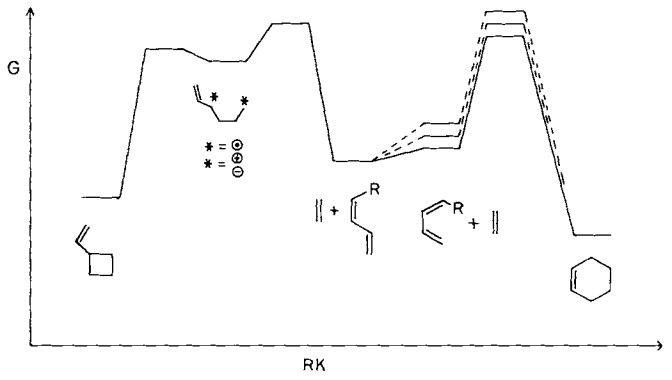


Fig. 8. Influence of the energy content of the *s-cis*-form of dienes on the ratio of a four-membered to six-membered ring formation, schematic (see text; R has been omitted from the products).

Is a mechanistic implication contained herein? Primarily not; however, a zwitterionic reaction path was definitely proved for the [2+2]-addition of a transoid fixed diene with TCNE by the kinetic investigations of *Huisgen* and *Ortega*[130]. Similar results were obtained in stereochemical investigations by *Bartlett* on [2+2]-cycloadditions which take place *via* biradicals[121]. *Stewart*'s observation[184] that the portion of four-membered ring product in the reaction of 4-methylpentadiene (1,1-dimethylbutadiene) with TCNE increases if the solvent polarity rises, indicates that the four-membered ring and the six-membered ring originate from two different path ways. The fact that cisoid fixed dienes in the reaction with TCNE do not produce any four-membered ring product points in the same direction.

The $\log k_2$-values of the reaction of cisoid fixed dienes with TCNE depend on the 1,4-distance in the diene[185,186]; they can be correlated linearly with this distance[186] (Fig. 9). Variation of the 1,4-distance by more than 1.0 Å leads to changes of several powers of ten in the reaction rate. The regression line is obtained by incorporating cyclopentadiene, the dotted line results when cyclopentadiene is omitted. The dotted line supports the fact that cyclopentadiene ought to react faster by virtue of its 1,4-distance. Obviously the CH_2-group is a handicap. The functional relationship of 1,4-distance and reaction rate can be a hint of a concerted cycloaddition. In the transition state, the *interaction with both centers*

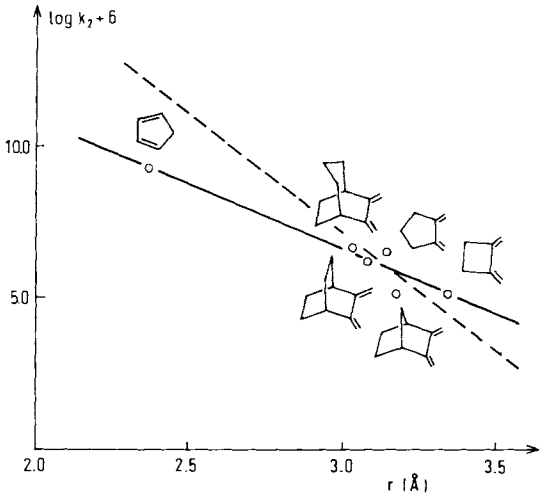


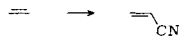
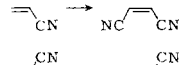
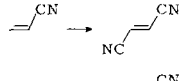
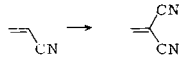
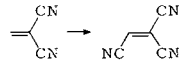
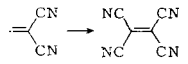
Fig. 9. Dependence of $\log k_2$-values on the 1,4-distance in dienes in the reaction with TCNE.

forming the new σ-bonds is important. This is in accordance with the FMO-model. This finding is only compatible with a two-step mechanism, if the ring closure of zwitterionic intermediate or a biradical is rate determining. However, experimental verifications of this possibility do not exist.

The kinetic data of Table 5 provide further support for the significance of the FMO-model. The higher reactivity of 1-substituted compared to the corresponding 2-substituted dienes results directly from the fact that the diene-HOMO has a greater eigenvector coefficient in the 1- than in the 2-position[57, 124].

Does the fact that the kinetic data for normal Diels-Alder reactions can be interpreted by the FMO-model, suggest the synchronous character of the cycloaddition? At least the example of cyano-substituted ethylenes shows that a cyano substituent influences the rate of a two-step four-membered ring cycloaddition[104] differently than in the Diels-Alder reactions: here one does not find a linear correlation between $\log k_2$ and the inverse HOMO-LUMO separation. *Huisgen et al.*[128] even see this different behavior as a new mechanistic possibility for differentiating between synchronous and multistep reactions.

Table 6. [4 + 2]-Cycloadditions of cyclopentadiene and 9,10-dimethylanthracene (20 °C, dioxane): influence of substituents on variation of the dienophile [7, 8, 97].

No.	Dienophile-Variation 1→2	k_2/k_1 for reaction with Cyclopentadiene	9,10-Dimethyl-anthracene
1		117000	—
2		88	147
3		78	156
4		44000	143000
5		10	46
6		≈950	100000

In the literature[19] kinetic data of the reaction of cyanoethylenes with dienes[7] were valued as proof for a biradical intermediate within the scope of a two-step mechanism. Table 6 contains the k_2-values, quoted as they are in ref. [7], in the form of rate ratios k_2/k_1 on successive introduction of nitrile functions into the dienophile. The k-value for the reaction of cyclopentadiene with ethylene was computed from data in ref. [97]. Without doubt, an unsymmetrical substitution of the dienophile (No. 1 and 4, Table 6) has the greatest influence on the ratio k_2/k_1 and seems to call for a biradical intermediate. However, the FMO-model supports the same effect as consequence of the reduction of the HOMO-LUMO separation and the modification of the eigenvector coefficients. A substitution of the second dienophilic C-atom (No. 2, 3, 5, and 6 in Table 6) is also linked to a rate increase; furthermore, in agreement with the FMO-model, the greater effect is observed for the more reactive diene. In the case of a biradical intermediate one should expect a decrease in the ratio k_2/k_1 due to loss of conjugation.

Table 5 contains $\log k_2$-values not only for the reaction of dienes with TCNE but also with maleic acid anhydride (MAA). Generally one finds, that the differences in reactivity for the dienes is smaller for MAA as dienophile than for TCNE. Similar results are obtained in the cycloaddition of substituted anthracenes with MAA[187] and TCNE[188]. Here, a higher selectivity at higher reactivity is reflected; it can be interpreted by the FMO-model[23]. Russian authors[189] arrived at the same conclusions for Diels-Alder reactions of acenes with *N*-arylmaleimides. This behavior deviates from normal reactivity-selectivity relationships (for a discussion see [190]).

Decreasing reactivity in normal Diels-Alder reactions as a consequence of the increasing orbital-energy separation $HOMO_{diene}$-$LUMO_{dienophile}$ signifies an increasing energy of the energy hypersurface. The contribution of the CT-configuration to the energy surface, which connects educts with products, diminishes. As a consequence it may be that alternatives on the potential energy surface become feasible and the original reaction path is prevented. Perhaps it is possible in this way to interpret the behavior of halogenated olefins, whose cycloadditions have been investigated by *Bartlett et al.* in a series of elegant studies[109, 121]. The promotion of the synchronous pathway by CT-interaction, as given for TCNE, does not exist anymore. However halogens, particularly the higher ones, have a marked ability to stabilize radical centers. Hence the direct, concerted route to the products is hindered, whereas the route *via* a biradical offers a favorable alternative. Unlike the findings in the reaction of TCNE with 1,1-disubstituted dienes[124, 129, 191], where the six-membered ring is formed without a zwitterionic intermediate, the results of the reaction of 1,1-dichloro-2,2-difluoroethylene with butadiene and 2,4-hexadienes[109] point to the six-membered rings arising at least partly by way of a biradical. The reaction coordinate might be similar to that in Figure 10.

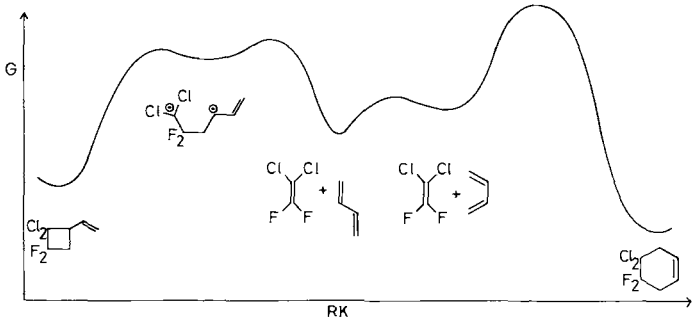


Fig. 10. Reaction coordinate for the reaction of 1,1-dichloro-2,2-difluoroethylene with butadiene.

The reactivity of dienophiles, and thus their selectivity, can often be enhanced by Lewis-acid catalysts. The numerous results collected by *Inukai* and *Kojima*[192] can be interpreted by means of the FMO-model[140, 141]. Complexing of the dienophiles with Lewis-acids has the effect of a strong electron withdrawing substituent, decreasing the LUMO level and thereby reinforcing the $HOMO_{diene}$-$LUMO_{dienophile}$ interaction.

5.2. Normal, Neutral, and Inverse Diels-Alder Reactions

As already mentioned in Section 2.1.3 (see also Fig. 1) one has, in principle, to expect three different types of cycloadditions according to FMO-theory:

Normal reactions (Type I) with $HOMO_{diene}$-$LUMO_{dienophile}$-control.

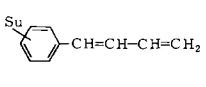
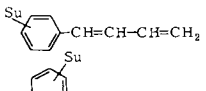
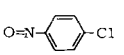
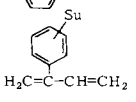
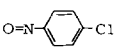
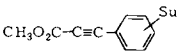
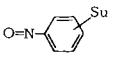
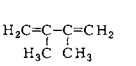
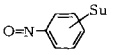
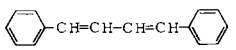
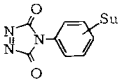
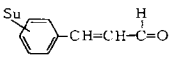
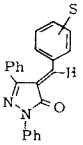
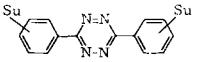
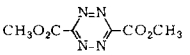
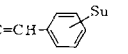
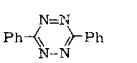
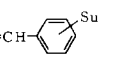
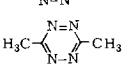
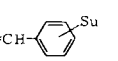
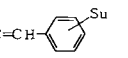
Neutral reactions (Type II), in which both HOMO-LUMO interactions must be considered; the characteristic of this reaction type is that not only the introduction of electron releasing substituents but also substitution by electron withdrawing groups in diene or dienophile leads to a rate acceleration.

Inverse reactions (Type III) with $LUMO_{diene}$-$HOMO_{dienophile}$-control.

In 1,3-dipolar cycloadditions kinetic experiments revealed examples for all three types of reaction[23]. What is the situation for Diels-Alder reactions?

Table 7 offers a selection of ρ-values for [4 + 2]-cycloadditions with CC-, NN-, and NO double- and CC-triple bonds as dienophiles. The sign of the ρ-values shows the systems 1.1—1.8 of Table 7 to be definitely *normal* Diels-Alder reac-

Table 7. Electronic substituent effects in [4 + 2]-cycloadditions: ρ values. As substituents (Su) *e.g.*, $N(CH_3)_2$, OCH_3, Cl, NO_2, CN were used.

	Diene	Dienophile	Solvent	T [°C]	ρ	Ref.
1.	*"Normal" Additions*					
1.1			Dioxane	25 35 45	−0.685 −0.621 −0.606	[197]
1.2			Benzene	15 25 35	−0.25 −0.24 −0.22	[198]
1.3			Benzene	24 34 44	−0.40 −0.36 −0.33	[199]
1.4			Tetrahydrofuran	~45	−1.79	[200]
1.5			Methylcyclohexane	176	+1.10	[201]
1.6			96% Ethanol	10	+2.57	[198]
1.7			CH_2Cl_2	2 25	+2.53 +2.50	[202]
1.8			Benzene	30	+0.58	[203]
	"Inverse" Additions					
2.1		CH_2=CH–O–C_8H_{17}	—	150	+0.71	[204]
2.2		CH_2=CH–$OCH(CH_3)_2$	Benzene	70	+0.84 [a] +0.83 [b]	[205]
2.3			Dioxane	30	+1.25	[206]
2.4			Dioxane	20	−1.07	[207]
2.5			Nitrobenzene	120	−0.59	[208]
2.6			Dioxane	100	−0.35	[208]
2.7			Dioxane	130	−0.28	[6]

[a] *endo*-Addition. [b] *exo*-Addition.

tions. In an analogous way the signs of the ρ-values for the systems 2.1—2.7 of Table 7 show the *inverse type of cycloaddition.* In the system 2.3 the $\log k$ values correlate in a linear way with the redox potentials of diaryltetrazines[206]. In so far as they have been investigated, the ρ-values decrease with increasing temperature. The absolute value of ρ is normally small and indicates only small partial charges in the rate determining transition state. Only for reactions of substituted nitrosoarenes (No. 1.6 and 1.7) is an unsymmetrical transition state with higher partial charges indicated. Likewise one can find a ρ-value exceeding the average in the cycloadditions of dehydrobenzene with substituted arenes (No. 1.4, Table 7); in this case the C-1-atom of the diene is directly substituted, whereas in the other examples of Table 7 the substituent is separated by a phenylene group from the diene system. In some cases, the Hammett-relation is only obeyed if σ^+ values are used. Other examples concerning the influence of substituents have been investigated particularly by *Konovalov et al.*[193].

What mechanistic importance do these ρ-values have? Transition states with higher partial charges, for example in solvolyses[194] or in electrophilic aromatic substitutions, show ρ-values below -3 to -4. Thus, nitration of benzene derivatives exhibits a ρ-value of -6.53. Also the [2+2]-cycloadditions of cyanoethylenes *via* zwitterionic intermediates show very high negative ρ-values[27]; for instance *Bartlett* found for the [2+2]-cycloaddition of substituted styrenes to TCNE on evaluation according to the Yukawa-Tsuno-equation, a ρ-value of -7.1 ± 0.5 (25 °C). The small ρ-values of the Diels-Alder reactions investigated so far thus exclude a two-step reaction *via* a zwitterionic intermediate. The FMO-model also makes it possible to interpret the existence of ρ-values not equal to zero in concerted cycloadditions[195,196].

From *Konovalov*'s research group stem the first examples of *Type II Diels-Alder reactions,* which could recently be confirmed by *Kanematsu et al.*[209]. Table 8 contains some typical examples. In the case of tetrachloro- and tetrabromo-*o*-ben-

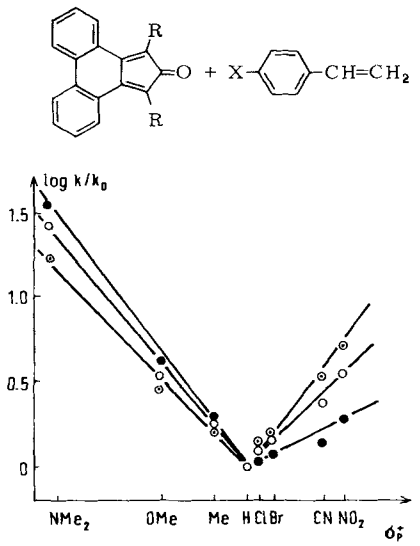
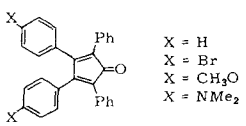
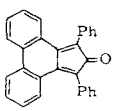
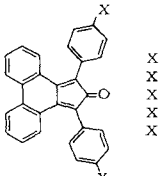


Fig. 11. Relationships between $\log k/k_0$ and σ_p^+ for [4+2]-cycloadditions of substituted phenacyclones and substituted styrenes (34.1 °C, in chlorobenzene) [209]. ○ R = H, ⊙ R = OCH_3, ● R = Cl; X, see abscissa.

Table 8. [4+2]-Cycloadditions with substituted styrenes $H_2C{=}CH{-}C_6H_4R$. Values for $10^5 \times k_2$ [l mol^{-1} s^{-1}].

No.	Diene (conditions) R =	*p*-NO_2	*m*-NO_2	*p*-Br	*p*-Cl	H	*m*-CH_3	*p*-CH_3O	*p*-NMe_2	Ref.
1	Tetrachloro-*o*-benzoquinone ($ClCH_2CH_2Cl$, 30 °C)	7950	2880	—	35.4	64.6	145	970	—	[210]
2	Tetrabromo-*o*-benzoquinone ($ClCH_2CH_2Cl$, 30 °C)	13800	4900	—	69.2	100	250	1660	—	[210]
3	6,13-Dichloropentacene (Toluene, 50 °C)	45.5	32	17.6	—	12.5	—	19.2	44.6	[211]
4	 X = H	8.80	7.90	—	7.80	7.30	—	10.2	33.8	[212]
	X = Br	7.80	8.50	—	9.50	18.8	—	19.5	102	
	$X = CH_3O$	8.30	6.20	—	4.45	4.46	—	5.25	17.6	
	$X = NMe_2$	8.60	4.80	—	3.10	1.55	—	2.00	3.70	
	(Toluene, 60 °C)									
5	 [a] $HC{\equiv}C{-}C_6H_4R$	1330	—	350	334	149	251	614	—	[213]
	(Toluene, 60 °C)									
6	 $X = NO_2$	612	452	815	—	940	—	4710	71000	[214]
	X = Cl	1170	700	870	—	600	—	1850	11200	
	X = H	1820	790	750	—	440	—	1240	74800	
	$X = CH_3$	2200	1120	945	—	410	—	1330	4550	
	$X = CH_3O$	2320	930	740	—	460		1200	5480	
	(Toluene, 40 °C)									

[a] Reaction with $HC{\equiv}C{-}C_6H_4R$.

zoquinone as O=C—C=O-diene the minimum reaction rate is found for *p*-chlorostyrene, compared to styrene itself for the other dienes. It is interesting that in the cyclopentadienone series as well as in other systems a transition from Type II to Type I is possible by introduction of appropriate electron withdrawing substituents into the diene in accordance with theoretical predictions. Whereas pentacene represents Type I (normal Diels-Alder reaction[193]), two chlorine atoms in positions 6 and 13 of the molecule modify the reaction to Type II (neutral Diels-Alder reaction). The plot of $\log k_2$ *versus* E_{HOMO} of the dienophile displays for the reaction with phenacyclone a U-shaped curve as expected for Type II[209]. Figure 11 shows the data collected by *Kanematsu*[209]. The rate-data for substituted styrenes result in a linear Hammett-plot with a minimum for R = H only if σ^+ values are used; the ρ-values change sign. One finds for $\sigma_p^+ < 0$ that the *p*-chloro-substituted diene reacts fastest whereas for $\sigma_p^+ > 0$ the *p*-methoxy-derivative shows the lowest reactivity (Fig. 11).

5.3. Solvent Effects

Investigation of the dependence of reaction rates on solvents enable conclusions to be drawn about changes in the polarity on going from educt to transition state; an increase in the reaction rate with increasing solvent polarity proves, for example, that the transition state is more polar than the ground state. In the case of [4 + 2]-cycloadditions also the influence of solvents has been studied intensively in connection with systematic kinetic investigations. Tables 9—16 show a selection of kinetic data. They contain a variation of the diene and dienophile components corresponding to many powers of ten in the absolute reaction rate. Besides the *k*-values corresponding to $\Delta G^{\neq}$ a splitting of the $\Delta G^{\neq}$ term into $E_A/\log A$ or $\Delta H^{\neq}/\Delta S^{\neq}$ can be found in some cases.

Table 9. Solvent influence on the dimerization of cyclopentadiene. Values for $10^7 \times k_2$ [l mol^{-1} s^{-1}] at 20 °C [4].

Solvent	$10^7 \times k_2$	E_a [kcal/mol]	log*A*
C_2H_5OH	19	16.4	6.4
$C_6H_5—NO_2$	13	15.1	5.5
CH_3CO_2H	10	14.7	5.0
Paraffin oil	9.8	17.4	7.1
Dioxane	9.4	17.3	6.8
CS_2	9.3	16.9	6.2
CCl_4	7.9	17.1	6.7
C_6H_6	6.6	16.4	6.1
Cyclopentadiene	5.6	16.2	5.8

Table 10. Solvent influence on the [4 + 2]-cycloaddition of fumaronitrile with 9,10-dimethylanthracene. $10^3 \times k_2$ [l mol^{-1} s^{-1}] at 85 °C [3].

Solvent	$10^3 \times k_2$	Solvent	$10^3 \times k_2$
$HCBr_3$	~21	CH_3CN	9.0
$HCCl_3$	22	Pyridine	7.9
CH_3CO_2H	20	Dioxane	6.5
CH_3OH	~19	CH_3SOCH_3	6.5
C_2H_5OH	16	$HCON(CH_3)_2$	4.2
CCl_4	15	$N(C_2H_5)_3$	~4
CH_2Cl_2	14	CH_3COCH_3	3.9
$ClCH_2CH_2Cl$	14	$CH_3OCH_2CH_2OCH_3$	2.8
CH_3NO_2	12		

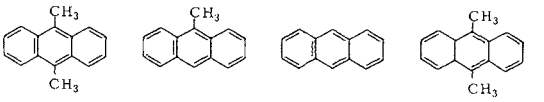
Table 11. Solvent influence on the [4 + 2]-cycloaddition of tetracyanoethylene with anthracene. Values for $10^2 \times k_2$ [l mol^{-1} s^{-1}] [215, 216].

Solvent	$10^2 \times k_2$	$\Delta H^{\neq}$ (±0.5 kcal/mol)	$\Delta S^{\neq}$ (±2.0 cal K^{-1} mol^{-1})
$CHCl_3$	628	4.2	−49
$ClCH_2CH_2Cl$	469	6.4	−42
o-Dichlorobenzene	465	4.5	−47
C_6H_5Cl	286	7.5	−36
Sulfolane	274	6.0	−42
CH_3CN	271	7.3	−37
Propylene carbonate	194	7.1	−38
C_6H_6	50	9.2	−30
$CH_3CO_2CH_3$	45.7	7.5	−35
Cyclohexanone	26	9.7	−29

Table 12. Solvent dependence of the [4 + 2]-cycloaddition of maleic anhydride with isoprene. $k_{rel.}$ values at 30.3 °C [217]; for comparison: dielectric constants (DC).

Solvent	DC	$k_{rel.}$
o-Dichlorobenzene	7.5	13.3
Nitrobenzene	36	10.5
Benzonitrile	26	6.84
Nitromethane	39	6.63
m-Dichlorobenzene	5.0	6.59
Chlorobenzene	5.6	5.03
Anisole	4.3	5.03
Benzene	2.3	3.49
Isopropyl ether	4.3	≡1.00

Table 13. Solvent influence on the [4 + 2]-cycloaddition of dicyanoethylenes with substituted anthracenes. Values for $10^4 \times k_2$ [l mol^{-1} s^{-1}] at 20 °C [218].



Solvent	+ 	+	+	+ 
CH_2Cl_2	4850	679	7.08	3.80
CH_3CN	3800	689	6.83	2.73
C_6H_5CN	3330	—	—	—
$C_6H_5CH_3$	1800	255	—	—
Dioxane	1270	192	2.55	1.40

Table 14. Solvent influence on the [4 + 2]-cycloaddition of 4-phenyl-1,2,4-triazolindione with anthracene. Values for $10^4 \times k_2$ [l mol^{-1} s^{-1}] at 25 °C [203, 216].

Solvent	$10^4 \times k_2$	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [cal K^{-1} mol^{-1}]
$CHCl_3$	50900	5.6	−37
$ClCH_2CH_2Cl$	15500	6.7	−35
C_6H_5Cl	10100	7.6	−33
C_6H_6	5200	8.4	−32
	6700 [a]	9.3 [a]	−28.7 [a]
$C_6H_5CH_3$	3300	10.3	−26
CH_3CN	3200	9.2	−30
C_6H_5CN	2900	10.0	−28
o-Xylene	2100	11.0	−25
Dioxane	1300	10.5	−28
	1310 [a]	10.5 [a]	−28.0 [a]
$CH_3CO_2C_2H_5$	830	11.6	−25
	830 [a]	11.6 [a]	−25.4 [a]
Tetrahydrofuran	280	12.0	−25

[a] At 30 °C.

Table 15. Solvent influence on the [4 + 2]-cycloaddition of nitrosobenzene with 1,3-cyclohexadiene. Values for $10^2 \times k_2$ [l mol^{-1} s^{-1}] at 25 °C [219].

Solvent	$10^2 \times k_2$
C_2H_5OH	1.16
CH_2Cl_2	1.07
$CHCl_3$	1.11
C_6H_6	1.00
CCl_4	1.04

Table 16. Solvent influence on the [4+2]-cycloaddition of styrene with hexachlorocyclopentadiene (85 °C) and 3,6-diphenyl-1,2,4,5-tetrazine (90 °C). Values for $10^5 \times k_2$ [l mol^{-1} s^{-1}] [218].

Solvent	Hexachlorocyclopentadiene $10^5 \times k_2$	3,6-Diphenyl-1,2,4,5-tetrazine $10^5 \times k_2$
$HCON(CH_3)_2$	11.1	106
$C_6H_5NO_2$	10.2	106
$C_6H_5CO_2C_2H_5$	9.5	78
Dioxane	6.8	49
$C_6H_5CH_3$	6.6	44

The following conclusions can be drawn from the data of Tables 9—16:

1. In general the influence of the solvent on the reaction rate—independently of the systems investigated—is relatively small and even if greater polarity changes are covered it is rarely above a factor of 10. Only in the reactions of TCNE (Table 11) and 4-phenyl-1,2,4-triazolinedione (Table 14) is the acceleration factor greater.
2. The nature of the dienophile (CC-, NN-, and NO-dienophiles) has just as little influence on the solvent dependence as that of the diene. Unsymmetrical educts (Table 13) certainly reveal an increase in the absolute reaction rate, for example in the reaction of 1,1-dicyanoethylene with anthracene, 9-methylanthracene and 9,10-dimethylanthracene; the solvent influence on the k_2-values however is comparatively small in all the systems of Table 13.
3. As far as investigations are available, [4+2]-cycloadditions seem to occur as fast in the vapor phase as in nonpolar solvents. Table 17 lists values for the dimerization of cyclopentadiene and butadiene[37].

Table 17. Solvent influence on the dimerization of 1,3-cyclopentadiene (20 °C) and 1,3-butadiene (82 °C) (cf. also Table 9) [37].

	1,3-Cyclopentadiene $10^7 \times k_2$ [l mol^{-1} s^{-1}]	1,3-Butadiene $10^9 \times k_2$ [l mol^{-1} s^{-1}]
Gas phase	5.3	24
Liquid phase	4.1—5.0	21

4. The same small solvent dependence is also observed in both normal (see Tables 6—15) as well as inverse Diels-Alder reactions (Table 16).

A plausible interpretation of the influence of the solvent, particularly in combination with the remaining mechanistic criteria, is provided by the synchronous bond formation in the [4+2]-cycloaddition step; this, however, proceeds with the formation of partial charges in the transition state which show up in the ρ-values (see Section 5.2), and also in the solvent effects. Zwitterionic intermediates, however, are definitely excluded by the small solvent dependence of the k-values; in analogous kinetic studies on [2+2]-cycloadditions proceeding *via* zwitterionic intermediates[27,28] acceleration effects of several powers of ten are observed if the polarity of the solvent is increased. Biradical intermediates cannot be excluded completely by means of the solvent influence on the reaction rate. Interestingly the solvent influence in the reaction of TCNE with anthracene is completely analogous[215] to that of the reaction of the same dienophile with bicyclo[2.2.1]heptadiene (symmetry allowed [2+2+2]-cycloaddition with simultaneous bond formation)—a further indication of the same reaction mechanism, *i.e.* a simultaneous bond formation in the Diels-Alder reaction.

Thermochemical investigations by *Haberfield* and *Ray*[220] and by *Konovalov et al.*[216] present an interesting aspect; they measured the enthalpies of solvation for educts and products of a series of systems already studied kinetically[187,221]. Some energy diagrams resulting from these thermochemical data and the kinetic data (see Fig. 12) show that reasons for the difference in enthalpy between ground state and transition state on changing the solvent may be quite different for different systems. Thus TCNE and *N*-aryltriazolinediones show very strong CT-interactions, particularly with aromatic solvents, which strongly modify the reactivity of these dienophiles[216]. Undoubtedly a new mechanistic discussion of solvent effects on the reaction rate must take into consideration these aspects. Entropy effects which are likewise able to affect the k-values are, of course, not taken care of in these considerations; the examples investigated in Figure 12 show differences in the $\Delta S^{\neq}$-values of up to 6—8 entropy units.

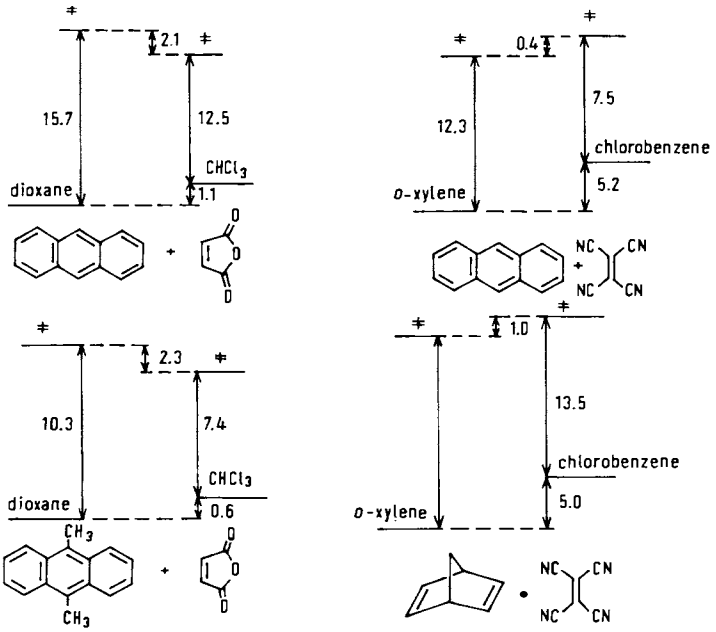


Fig. 12. Relative enthalpies [kcal/mol] of the educts and transition states of some cycloadditions in various solvents [220].

5.4. Activation Parameters

According to *Arrhenius* the temperature dependence of the rate constants discloses the values of the activation energy E_A and the frequency factor $\log A$, and according to *Eyring* it discloses the analogous quantities activation enthalpy $\Delta H^{\neq}$ and activation entropy $\Delta S^{\neq}$. Whereas the mechanistic interpretation of E_A and $\Delta H^{\neq}$ values, which are generally small for Diels-Alder reactions, is rather difficult, the quantities $\log A$ and $\Delta S^{\neq}$ offer criteria for a mechanistic discussion. In Table 18 representative values of the activation entropy $\Delta S^{\neq}$ for a total of 16 different systems are listed with approxi-

Table 18. Activation entropies ΔS^{+} for Diels-Alder reactions.

	Diene	Dienophile	Solvent	ΔS^{+} [cal K^{-1} mol^{-1}]	Ref.
1	Cyclopentadiene	17 Dienophiles	Dioxane	−38 to −29	[7]
		Cyclopentadiene	9 solvents	−38 to −28	[4]
2	9,10-Dimethylanthracene	16 Dienophiles	Dioxane	−41 to −33	[7]
3	12 subst. Anthracenes	Maleic anhydride	Dioxane	−36 to −31	[187]
4	7 Dienes	Maleic anhydride	Dioxane	−42 to −33	[124]
5	8 Dienes	Tetracyanoethylene	Dioxane	−42 to −30	[124]
6	Anthracene	Tetracyanoethylene	14 solvents	−49 to −30	[215]
7	Anthracene, tetracene	N-Arylmaleimide	Toluene	−29 to −22	[224]
8	6,13-Dichloropentacene	H_2C=CH—Aryl	Toluene	−36 to −33	[211]
9	Pentacene	H_2C=CH-Aryl	Toluene	−33 to −27	[193]
10	1,3-Diphenylisobenzofuran	H_2C=CH-Aryl	Toluene	−35 to −30	[193]
11	Cyclopentadienone derivatives	H_2C=CH-Aryl	Toluene	−39 to −28	[212—214, 225]
		HC≡C-Aryl			
		CH_3O_2C—C≡C-Aryl	C_6H_5—C_6H_{11}		
12	2,3-Dimethylbutadiene	*m*-Chloro- and methyl-nitrosobenzene	CH_2Cl_2	−33	[202]
13	1- and 2-Phenylbutadiene	*p*-Chloronitrosobenzene	Benzene	−39 to −31	[198]
14	Anthracene, 1,4-Diphenylbutadiene	4-Alkyl- and 4-Aryl-1,2,4-triazolinedione	3 solvents	−35 to −22	[203, 216]
15	3,6-disubstituted 1,2,4,5-tetrazines (R = Alkyl, Aryl, CO_2CH_3)	8 Dienophiles	Dioxane, nitrobenzene	−35 to −42	[207, 208]
16	Hexachlorocyclopentadiene	4 Dienophiles	Dioxane	−40 to −34	[6]
17	Tetrachloro- and tetrabromo-*o*-benzoquinone	H_2C=CH-Aryl		−38 to −31	[210]

mately 150 individual examples. The reaction rates of the systems studied differ by many powers of ten; as dienophiles, systems with CC-double and triple-bonds as well as hetero-multiple bonds were employed; the structure of the dienes was also extensively varied. Furthermore there are ΔS^{+} values for reactions in very different solvents.

The following conclusions can be drawn from Table 18:

1. The ΔS^{+} values are largely independent of the absolute reaction rate. Modifications of the reaction rate are normally reflected in the energy term E_A (or ΔH^{+}).
2. Structural factors in the diene and dienophile do not substantially influence the ΔS^{+} values.
3. The solvent has only little influence on the rate constants (see Section 5.3) and on the ΔS^{+} values. The dimerization of cyclopentadiene in the vapor phase and in solution shows comparable log A and ΔS^{+} values. The same conclusion follows from Table 1, which lists comparable log A values for a larger number of reactions in the gas phase. In discussing these values and comparing them with those in Table 18 the difference in temperature, in part considerable, must be taken into account.
4. The absolute values for ΔS^{+} are in the range of about −40 to −30 entropy units. This means that on going from the ground state to the transition state an extensive restriction of degrees of freedom must be considered. A highly ordered transition state, required by the simultaneous bound formation in [4 + 2]-cycloadditions, is consistent with these data. Zwitterionic intermediates as explanation are excluded by the generally very small influence of solvent and substituents on the reaction rate. A biradical intermediate for these Diels-Alder reactions would certainly be in accordance with substituent- and solvent-effects, but would be opposed in most cases to the stereochemical results; the biradical intermediate could be preserved only if in all cases a fast cleavage of the intermediate to the educts and a rate determining ring closure to the Diels-Alder adduct is postulated. Under this assumption also very negative ΔS^{+} values for a two-step reaction involving a biradical intermediate are expected.

Unfortunately the present experimental material concerning the ΔS^{+} values for [2 + 2]-cycloadditions is not very extensive. In [2 + 2]-cycloadditions of ketenes to enol ethers the reaction rate shows a strong dependence on the solvent; highly negative ΔS^{+} values are expected which, however, do not constitute evidence against simultaneous bond formation in [4 + 2]-cycloadditions. The dimerizations of tetrafluoroethylene, trifluoroethylene, as well as the mixed [2 + 2]-cycloaddition between tetrafluoroethylene and trifluorochloroethylene which were investigated in the vapor phase show ΔS^{+} values between −26.5 to −29.2[222]. Whether these few examples possessing on the average less negative ΔS^{+} values than [4 + 2]-cycloadditions, can be taken as a proof of a different mechanism, remains to be seen.

Obviously the greatest portion of the ΔS^{+} value has to be ascribed to the formation of one bond (abolition of translational degrees of freedom) whereas the prevention of a rotation, as required for a one-step reaction in the transition state, contributes only to a small extent. Thus one can find an overlapping area for the ΔS^{+} values of one-step [4 + 2]-cycloadditions of the Diels-Alder type and of two-step [2 + 2]-cycloadditions. Recently *Berson et al.* referred to this aspect in connection with the study of the cycloaddition of singlet- and triplet-trimethylene biradicals[223]. It is certainly necessary to explore some further systems in the field of [2 + 2]-cycloadditions with regard to the ΔS^{+} values; in these studies also [4 + 2]-cycloadditions should be included which were shown to react in a non-stereospecific way.

5.5. Pressure Dependence of the Cycloaddition: Activation Volumes[41]

During the last 10—15 years the industrially well developed high-pressure technique found more and more access to organic chemical laboratories. Reactions which involve a decrease in volume (for example cycloadditions as prototypes for bimolecular reactions) profit from a rise in pressure, *i.e.*

the reaction rate (k-value) increases. In accordance with the theory of *Eyring* one can determine the activation parameter ΔV^{+} (difference of volume between transition state and ground state) from the pressure dependence of the k-value:

$$\left(\frac{\partial \ln k}{\partial \ln p}\right)_T = -\frac{\Delta V^{+}}{RT}$$

The absolute values of ΔV^{+} and their signs as well as a comparison with the values ΔV of the decrease in volume for the overall reaction permit important mechanistic conclusions; a different extent of bond formation, specific solvent influences and other factors are reflected for example in ΔV^{+}. For the closure of one bond one has to expect a value for ΔV^{+} of about 10—15 [cm³/mol], provided that there is no electrostriction in non-polar solvents.

Earlier measurements by *Walling*'s group[226] seemed to demand a two-step mechanism for [4+2]-cycloadditions. ΔV^{+} was found to be only half as large as the total volume decrease ΔV (Table 19). These values, however, had to be revised[227,228]. The improvement of the experimental technique—nowadays the ΔV^{+} values are reliable to ± 1 [cm³/mol]—has made these activation parameters an important mechanistic criterion.

Table 19. Early ΔV^{+} values for Diels-Alder reactions.

	Reaction	ΔV^{+} [cm³/mol]	ΔV [cm³/mol]	Ref.
1.	Isoprene dimerization	−24.3	−45.5	[226a]
2.	Cyclopentadiene dimerization	−22.3	−32.2	[226a]
3.	2,3-Dimethylbutadiene + Butyl acrylate	−22.6	−42.2	[226b]

Table 20 presents a selection of ΔV^{+} and ΔV values for various systems with partly very different reactivities; solvent effects were investigated in a number of cases. Several characteristics can be gathered from the ΔV^{+} values:

1. The ΔV^{+} values are generally very large for [4+2]-cycloadditions and exceed the order of magnitude expected for the closure of *one* bond in non-polar solvents.
2. In some cases when maleic acid anhydride is the dienophile, ΔV^{+} exceeds (No. 1—4) the value of ΔV considerably. One can therefore conclude that the transition state requires a smaller volume than the reaction products. In the literature this phenomenon, particularly observed in the case of maleic acid anhydride, is attributed to the strong *endo* orientation, as postulated for the transition state of a one-step [4+2]-cycloaddition[3]. Normally, ΔV^{+} is only slightly larger or smaller than ΔV (No. 6—9).
3. Solvent influences on the reaction rate of [4+2]-cycloadditions are normally small compared with corresponding influences on [2+2]-cycloadditions with zwitterionic intermediates[27,28] (see Section 5.3); also in system No. 2, ΔV^{+} responds only insignificantly to a variation in solvent. In contrast $\Delta\Delta V^{+}$ is larger for the more polar system No. 4 with distinctly discernible electrostriction. Here one has to expect a more polar transition state; in the analogous reaction with 2-methoxybutadiene the electrostriction of $\Delta\Delta V^{+} = 6$—7 is significantly smaller.
4. For the $AlCl_3$-catalyzed reaction of acrylic acid butyl ester with 2,3-dimethylbutadiene one finds $\Delta V^{+} = -26$ and $\Delta V = -29$ [cm³/mol] (non-catalyzed reaction: $\Delta V^{+} = -28$, $\Delta V = -32$) cm³/mol[234]). Thus the ΔV^{+} values for catalyzed and non-catalyzed reaction differ only negligibly.

What mechanistic conclusions can be drawn? Obviously in [4+2]-cycloadditions we have a highly ordered transition state, very similar to the products with regard to space requirements. This is consistent with a *simultaneous* formation of *both* bonds in the transition state. If one wants to save the concept of a two-step bond formation for the examples of Table 20, this is only possible by supposing that the second step is rate determining in all cases; only then can one expect ΔV^{+} values of similar order of magnitude. The fact may be recalled here that such an assumption can hardly be reconciled with the small solvent influence on the reaction rate and the results of stereochemical investigations.

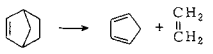
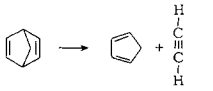
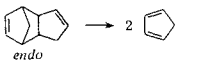
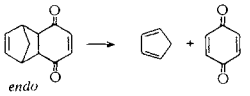
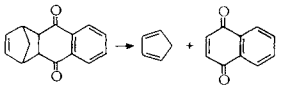
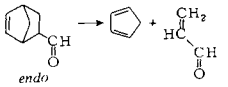
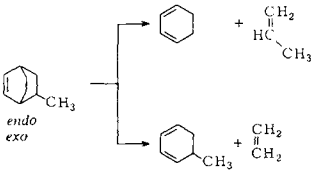
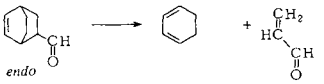
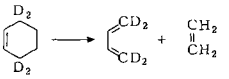
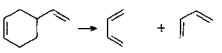
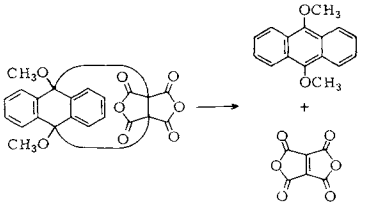
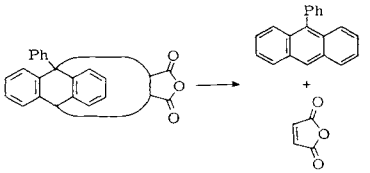
Stewart[235] studied the product spectrum and the pressure dependence of the dimerization of 2-chlorobutadiene to products of the formal [2+2]-, [4+2]- and [4+4]-cycloaddi-

Table 20. ΔV^{+} and ΔV values for different Diels-Alder reactions.

No.	Reaction	Solvent	T [°C]	ΔV^{+} [cm³/mol]	ΔV[cm³/mol]	Ref.
1	Maleic anhydride + 1,3-Pentadiene	$ClCH_2CH_2Cl$	35	−44.7	−33.3	[229]
2	Maleic anhydride + 2-Methylbutadiene	CH_3NO_2	35	−32.5	−30.7	[230]
		$ClCH_2CH_2Cl$	35	−37.0	−35.5	
		CH_3CO_2Et	35	−37.4	−36.8	
		CH_3CN	35	−37.5	−34.5	
		n-C_4H_9Cl	35	−38.0		
		i-Pr_2O	35	−38.5	−38.3	
		$(CH_3)_2CO$	35	−39.0	−35.9	
		$(CH_3)_2CO_3$	35	−39.3		
3	Maleic anhydride + 2-Chlorobutadiene	CH_3CN	65	−41.6	−36.9	[229]
4	Maleic anhydride + 1-Methoxybutadiene	CH_3CN	35	−32.0	−32.4	[231]
		CH_3NO_2	35	−43.0	−28.2	
		$ClCH_2CH_2Cl$	35	−43.7	−30.4	
		n-C_4H_9Cl	35	−45.4	−35.5	
		$(CH_3)_2CO_3$	35	−53.6	−32.2	
5	Maleic anhydride + 1,3-Cyclohexadiene	CH_2Cl_2	35	−39.6	−30.3	[232]
6	Acrylonitrile + 2-Methylbutadiene	n-C_4H_9Br	21	−33.1	−37.0	[233]
7	Methyl acrylate + 2-Methylbutadiene	n-C_4H_9Br	21	−30.8	−36.9	[233]
8	Methyl vinyl ketone + 2-Methylbutadiene	n-C_4H_9Br	21	−36.9	−37.1	[233]
9	Dimethyl acetylenedicarboxylate + Cyclopentadiene	CH_3CO_2Et	10	−30.2	−33.9	[232]

tion. The pressure dependence of the product distribution led him to the conclusion that in this case two different mechanisms are competing; the two-step [2+2]-reaction, probably involving a biradical intermediate ($\Delta V^{+} \approx -22$ [cm^3/mol]), and the one-step [4+2]-cycloaddition to cyclohexene derivatives ($\Delta V^{+} = -29$ to -31 [cm^3/mol]). For [2+2]-cycloadditions with zwitterionic intermediates[27,28] one also finds very negative ΔV^{+} values of about -30 to -40 [cm^3/mol]. This, however, can be explained by the strong electrostriction in the transition state which manifests itself also in a strong solvent dependence of the reaction rate[236].

Table 21. Values of activation entropy ΔS^{+} for Retro-Diels-Alder reactions.

No.	System	Conditions	ΔS^{+}	Ref.
	Cyclopentadiene adducts			
1		Gas phase, 257—297 °C	+ 3.7	[97]
2		Gas phase, 311—357 °C	+ 5.7	[96]
3	 *endo*	Paraffin, 145—175 °C Gas phase, 152—211 °C	− 2 − 2	[241] [242]
4	 *endo*	Benzene, 55—79 °C	− 3	[241]
5		Benzene, 49—79 °C	− 3.5	[243]
6	 *endo*	Gas phase, 192—242 °C	− 5	[87]
	Cyclohexadiene adducts			
7	 *endo*	Gas phase, 335-406 °C	+ 3.1 [a] + 2.4 [a]	[95]
8	*exo*	Gas phase, 335—406 °C	+ 5.4 [b] + 7.0 [b]	[95]
9	 *endo*	Gas phase, 213—298 °C	− 2.1	[93]
	Butadiene adducts			
10		Gas phase, 477—525 °C	+ 5.9	[244—246]
11		Gas phase, 630—780 °C	+ 7	[244]
	Anthracene adducts			
12		Dioxane, 30—50 °C	+ 11	[247]
13		*o*-Dichlorobenzene, 132—175 °C	+ 5.1	[248]

[a] *endo*-Educt; upper value: products 1,3-cyclohexadiene + propene; lower value: products 5-methyl-1,3-cyclohexadiene + ethylene. [b] *exo*-Educt; upper value: products 1,3-cyclohexadiene + propene; lower value: 5-methyl-1,3-cyclohexadiene + ethylene.

6. Retro-Diels-Alder Reactions

In the [4+2]-cycloaddition step two π bonds are transformed into two σ bonds. On the basis of bond energies one expects for Diels-Alder additions highly exothermic reactions in the order of $\Delta H = 30$–40 kcal/mol. Thermochemical measurements[237–240] confirm this. Depending on the structure of educts and products, ΔH values of 15—40 kcal/mol are found for the reactions with TCNE and MAA. Thus, for a cycloreversion one has to expect relatively high ΔH^{+} values, signalizing high reaction temperatures.

Retro-Diels-Alder reactions were used mainly from a preparative point of view for syntheses of new compounds or of molecules which are difficult to obtain by conventional procedures[35]. Mechanistic studies, however, are less frequent. The criterion of stereospecificity can only be applied in a limited way in Retro-Diels-Alder reactions, since either the Diels-Alder adducts themselves or the *cis-trans*-isomeric dienophiles, originating from the cycloreversion, isomerize under the drastic reaction conditions. In Section 3 reference has already been made to the cleavage of the adducts of 1,3-cyclohexadiene and *cis*- or *trans*-2-butene, which according to the literature[113] is partly non-stereospecific. The isotope effects investigated in Retro-Diels-Alder reactions will not be discussed here, for no new mechanistic findings have been published in the literature since the last review[3,4,36].

The literature contains a number of kinetic studies of [4+2]-cycloreversions. A selection of data, particularly with respect to the magnitude of the ΔS^{+} value, is presented in Table 21. In all cycloreversions performed in the gas phase a homogeneous reaction was secured.

The ΔS^{+} values of Table 21 are relatively uniform and allow some mechanistic conclusions:

1. The magnitude of ΔS^{+} is not influenced systematically by the fact that the reaction takes place either in solution or in the gas phase. Here too, as in the studies of the cycloaddition itself (see Section 5.3), it is evident that the rate determining transition states are just as polar as the ground states; at best small partial charges can occur.
2. The ΔS^{+} values normally cover a range of about -5 to $+6$ entropy units. One can conclude from this that there are no important modifications of rotational or vibrational degrees of freedom in the transition state. From the "entropy viewpoint" the transition state of the cycloreversion is comparable to the product, as expected for simultaneous bond formation in the addition step or for bond cleavage in the reversion step. A sandwich structure for the transition state is discussed in the literature.
3. Remarkably the ΔS^{+} values for those cyclopentadiene adducts (No. 3—6) which are formed in a relatively strong *endo*-mode are nearly always negative. The analogous picture for the ΔV^{+} values (Section 5.5) increases the credibility of this interpretation; there too, particularly negative ΔV^{+} values were found in those cases partly exceeding the total volume decrease ΔV of the reaction.

Are the present mechanistic criteria adequate for a decision between one-step or two-step reaction? Does one have to expect more positive ΔS^{+} values for a two-step cleavage *via* a 1,6-biradical? The literature does not yet offer definitive help for this decision. The kinetically well studied cycloreversion of *cis*- and *trans*-1,2-dimethylcyclobutane *(54)* and *(53)*, respectively[118], which involves a biradical intermediate provides an example (see also Scheme 10); the ΔS^{+} values determined by the authors (temperature range 390—430 °C) for the [2+2]-cycloreversions, which are marked in Scheme 10 as ⓐ and ⓑ are on the average between 8.5 to 9.1

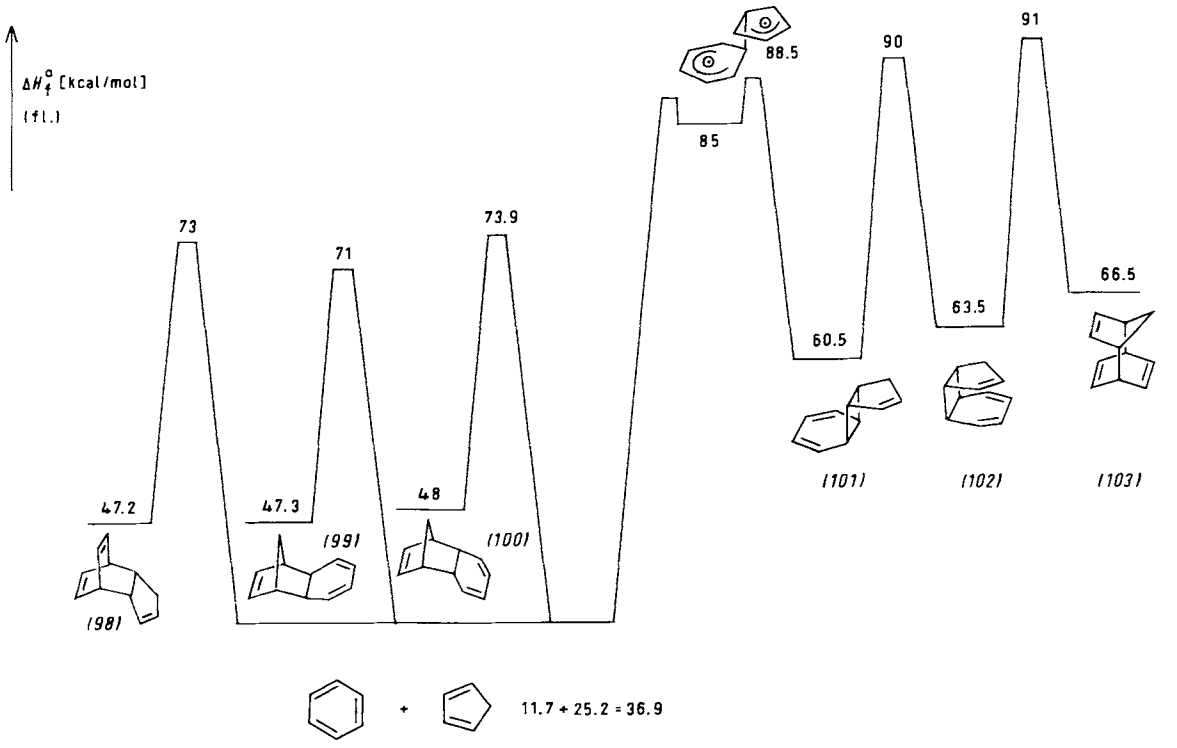
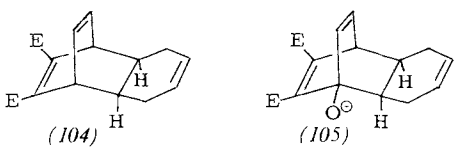
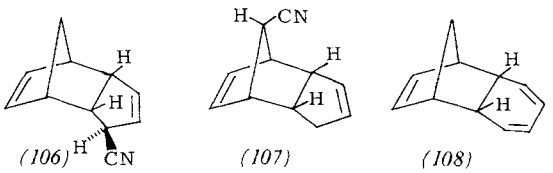


Fig. 13. Energy diagram of the cycloreversion of benzene-cyclopentadiene adducts *(98)*—*(103)*.

entropy units. Thus they are on the higher side of the data of Table 21 and slightly exceed the average; with caution they are used as an argument for simultaneous bond formation in the [4+2]-cycloaddition. As for the cycloaddition step (see Section 5.4) there obviously exists an overlapping area for ΔS^{+} values of [2+2]- and [4+2]-cycloreversion.

Kinetic and thermochemical data of *Grimme et al.*[249] allow interesting mechanistic conclusions for a number of [2+2]-, [4+2]- and [4+4]-cycloadducts of benzene and cyclopentadiene (see Fig. 13). The educts *(98)—(100)*, in which a symmetry allowed, *simultaneous* bond cleavage takes place pass transition states which energetically lie maximally 36 kcal/mol above the reaction products benzene and cyclopentadiene; in contrast the transition states for the cleavage of the [2+2]- and [4+4]-cycloadducts *(101)—(103)*, which should have a biradical as intermediate, lie more than 15 kcal/mol higher. For the [4+2]-cycloreversions explored by *Grimme* a simultaneous bond cleavage seems to be the simplest interpretation. It should be mentioned that this conclusion can not be applied uncritically to all Retro-Diels-Alder reactions. As already pointed out in Section 4 one has to expect that for systems with a large HOMO-LUMO separation under certain conditions the two-step reaction *via* a biradical intermediate will become compatible; in these cases one evidently has to assume for the cycloreversion a two-step mechanism in accordance with the principle of microscopic reversibility.





Recently, *Grimme et al.*[250] found an interesting acceleration effect in the decomposition of anionic Diels-Alder adducts. For example ΔG^{+} for the cycloreversion is lowered by about 9 kcal/mol in proceeding from *(104)* to *(105)*. Also the cleavage of *(106)* and *(107)* in presence of bases (formation of anions) occurs significantly faster than that of *(108)*.

In both cases the transition state takes advantage of the stability of the products (phenolate ion and cyclopentadienide ion, respectively). These results, too, are in agreement with simultaneous bond cleavage in the cycloreversion step.

7. Conclusion and Outlook

It is certainly justified to finally ask whether a reaction like the Diels-Alder cycloaddition, which was discovered more than 50 years ago, is still of general interest. The several hundred original publications appearing regularly each year on this topic give a positive answer. The preparative potential of these [4+2]-cycloadditions has not been exhausted yet. The almost unlimited possibility to vary the diene- and dienophile-components provides in many cases the simplest access to cyclohexene- and 1,4-cyclohexadiene derivatives; the possibility of using *cyclic* compounds, heterodienes and heterodienophiles opens up access in "one pot syntheses" to monocyclic, bicyclic and polycyclic carbocycles and heterocycles. The high preparative value of [4+2]-cycloadditions follows—not only from the mostly very high yields—but also from the stereospecific and generally regiospecific course of the reaction; the catalysis by Lewis acids reinforces stereo- and regiospecificity, so that often nearly exclusively one reaction product is formed. The recent systematic studies of *intramolecular* Diels-Alder reactions[40,251] provided a new impact.

The preparative exploitation of a reaction optimally succeeds if the reaction mechanism is known in detail. This review has revealed that considerable progress has been made during the last 10—15 years in the mechanistic area. In particular the FMO-model has provided the experimental chemist with a distinct and relatively simple aid for selecting his educt from the viewpoint of optimum reactivity and regiospecificity. The HOMO-LUMO model will increasingly permit semi-quantitative estimations when electron affinities and ionization potentials or redox potentials are known. Last but not least it would seem most important to be able to define clearly the factors which are responsible for a one-step orbital symmetry-allowed [4+2]-cycloaddition or for a two-step reaction involving an intermediate.

Many thanks go to all our collaborators cited individually in this article for their interest and valuable cooperation. We are indebted to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, as well as many other individual companies who have generously supported this work.

Received: July 30, 1980 [A 336 IE]
German version: Angew. Chem. *92*, 773 (1980)

[1] *O. Diels, K. Alder*, Justus Liebigs Ann. Chem. *460*, 98 (1928).
[2] For a definition of cycloadditions see *R. Huisgen*, Angew. Chem. *80*, 329 (1968); Angew. Chem. Int. Ed. Engl. *7*, 321 (1968).
[3] Access to the relevant literature can be found in *J. Sauer*, Angew. Chem. *78*, 233 (1966); *79*, 76 (1967); Angew. Chem. Int. Ed. Engl. *5*, 211 (1966); *6*, 16 (1967).
[4] *A. Wassermann:* Diels-Alder Reactions. Elsevier, New York 1965.
[5] *G. B. Kistiakowsky, W. W. Ransom*, J. Chem. Phys. *7*, 725 (1939) and earlier publications.
[6] *J. Sauer, H. Wiest*, Angew. Chem. *74*, 353 (1962); Angew. Chem. Int. Ed. Engl. *1*, 269 (1962).
[7] *J. Sauer, H. Wiest, A. Mielert*, Chem. Ber. *97*, 3183 (1964).
[8] *J. Sauer, D. Lang, H. Wiest*, Chem. Ber. *97*, 3208 (1964).
[9] *P. Yates, P. Eaton*, J. Am. Chem. Soc. *82*, 4436 (1960).
[10] *R. B. Woodward, R. Hoffmann:* The conservation of orbital symmetry. Verlag Chemie, Weinheim 1970; Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[11] *R. Hoffmann, R. B. Woodward*, Acc. Chem. Res. *1*, 17 (1968).
[12] Orbital Symmetry Papers, ACS Reprint Collections 1974.
[13] *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions. Vol. I and II. Academic Press, New York 1977.
[14] *Ab initio* calculations for various cycloadditions see [14—18]; *L. A. Burke, G. Leroy, M. Sana*, Theor. Chim. Acta *40*, 313 (1975); *L. A. Burke, G. Leroy, ibid. 44*, 219 (1977).
[15] *D. Poppinger*, J. Am. Chem. Soc. *97*, 7486 (1975).
[16] *R. F. Townshend, G. Ramunni, G. Segal, W. J. Hehre, L. Salem*, J. Am. Chem. Soc. *98*, 2190 (1976).
[17] *P. Caramella, K. N. Houk, L. N. Domelsmith*, J. Am. Chem. Soc. 99, 4511 (1977).

[18] *A. Komornicki, J. D. Goddard, H. F. Schaefer III,* J. Am. Chem. Soc. *102*, 1763 (1980).
[19] For earlier references see: *M. J. S. Dewar, S. Olivella, H. S. Rzepa,* J. Am. Chem. Soc. *100*, 5650 (1978).
[20] *K. Fukui,* Fortschr. Chem. Forsch. *15*, 1 (1970); Acc. Chem. Res. *4*, 57 (1971).
[21] *W. C. Herndon,* Chem. Rev. *72*, 157 (1972).
[22] *K. N. Houk,* Acc. Chem. Res. *8*, 361 (1975).
[23] *R. Sustmann,* Pure Appl. Chem. *40*, 569 (1974).
[24] *K. Fukui:* Theory of Orientation and Stereoselection, in: Reactivity and Structure Concepts in Organic Chemistry. Vol. 2. Springer, Berlin 1975.
[25] *N. D. Epiotis:* Theory of Organic Reactions, in: Reactivity and Structure Concepts in Organic Chemistry. Vol. 5. Springer, Berlin 1978.
[26] *N. T. Anh, E. Canadell, O. Eisenstein,* Tetrahedron *34*, 2283 (1978).
[27] *R. Huisgen,* Acc. Chem. Res. *10*, 117 (1977).
[28] *R. Huisgen,* Acc. Chem. Res. *10*, 199 (1977).
[29] Alternative mechanistic discussions for [3 + 2]-cycloadditions see [29—33]; *R. Huisgen,* J. Org. Chem. *41*, 403 (1976).
[30] *R. Huisgen,* J. Org. Chem. *33*, 2291 (1968).
[31] *R. A. Firestone,* Tetrahedron *33*, 3009 (1977).
[32] *R. A. Firestone,* J. Org. Chem. *37*, 2181 (1972).
[33] *R. A. Firestone,* J. Org. Chem. *33*, 2285 (1968).
[34] *J. Hamer:* 1,4-Cycloaddition Reactions. Academic Press, New York 1967.
[35] Retro-Diels-Alder Reactions: *H. Kwart, K. King,* Chem. Rev. *68*, 415 (1968); *J. L. Ripoll, A. Rouessac, F. Rouessac,* Tetrahedron *34*, 19 (1978).
[36] *H. Wollweber:* Diels-Alder-Reaktion. Thieme, Stuttgart 1972.
[37] *P. Beltrame,* Addition of Unsaturated Compounds to Each Other, in Comprehensive Chemical Kinetics *9*, 87 (1973).
[38] *C. K. Bradsher,* Cationic Polar Cycloaddition, in Adv. Heterocycl. Chem. *16*, 289 (1974).
[39] *G. Desimoni, G. Tacconi,* Chem. Rev. *75*, 651 (1975).
[40] *W. Oppolzer,* Angew. Chem. *89*, 10 (1977); Angew. Chem. Int. Ed. Engl. *16*, 10 (1977).
[41] Pressure-dependence: *T. Asano, W. J. le Noble,* Chem. Rev. *78*, 407 (1978); *J. R. McCabe, C. A. Eckert,* Acc. Chem. Res. *7*, 251 (1974); cf. *G. Jenner,* Angew. Chem. *87*, 186 (1975); Angew. Chem. Int. Ed. Engl. *14*, 137 (1975); *W. J. le Noble, H. Kelm,* Angew. Chem., in press.
[42] *S. M. Weinreb, J. I. Levin,* Heterocycles *12*, 949 (1979).
[43] See *e.g. T. H. Lowry, K. E. Schueller-Richardson:* Mechanism and Theory in Organic Chemistry. Harper & Row, New York 1976.
[44] *M. V. Basilevsky, A. G. Shamov, V. A. Tikhomirov,* J. Am. Chem. Soc. *99*, 1369 (1977).
[45] *K. Jug, H.-W. Krüger,* Theor. Chim. Acta *52*, 19 (1979).
[46] *M. J. S. Dewar, A. C. Griffin, S. Kirschner,* J. Am. Chem. Soc. *96*, 6225 (1974).
[47] *O. Kikuchi,* Tetrahedron *27*, 2791 (1971).
[48] For a critical evaluation of different theoretical procedures see: *W. Kutzelnigg,* Pure Appl. Chem. *49*, 981 (1977).
[49] *A. Oliva, J. I. Fernandez-Alonso, J. Bertran,* Tetrahedron *34*, 2029 (1978).
[50] *K. Fukui, T. Yonezawa, H. Shingu,* J. Chem. Phys. *20*, 722 (1952).
[51] *N. T. Anh:* Die Woodward-Hoffmann-Regeln und ihre Anwendung. Verlag Chemie, Weinheim 1972.
[52] *R. E. Lehr, A. P. Marchand:* Orbital Symmetry. Academic Press, New York 1972.
[53] *M. J. S. Dewar,* Angew. Chem. *83*, 859 (1971); Angew. Chem. Int. Ed. Engl. *10*, 761 (1971).
[54] *H. E. Zimmerman,* Acc. Chem. Res. *4*, 272 (1971); see also *H. E. Zimmerman* in [13], Vol. I.
[55] *K. N. Houk* in [13], Vol. II.
[56] *I. Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, New York 1976; see also *K.-L. Mok, M. J. Nye,* J. Chem. Soc. Perkin Trans. I *1975*, 1810.
[57] *R. Sustmann,* Tetrahedron Lett. *1971*, 2717.
[58] *M. J. S. Dewar, R. C. Dougherty:* The PMO-Theory of Organic Chemistry. Plenum Press, New York 1975.
[59] *W. L. Jorgensen, L. Salem:* Orbitale organischer Moleküle. Verlag Chemie, Weinheim 1974.
[60] *R. F. Hudson,* Angew. Chem. *85*, 63 (1973); Angew. Chem. Int. Ed. Engl. *12*, 36 (1973).
[61] *K. N. Houk,* J. Am. Chem. Soc. *95*, 4092 (1973); *K. N. Houk, J. Sims, C. R. Watts, L. J. Lushus, ibid. 95*, 7301 (1973).
[62] *J. Feuer, W. C. Herndon, L. H. Hall,* Tetrahedron *24*, 2575 (1968).
[63] *O. Eisenstein, J. M. Lefour, N. T. Anh,* Chem. Commun. *1971*, 969; *O. Eisenstein, J. M. Lefour, N. T. Anh, R. F. Hudson,* Tetrahedron *33*, 523 (1977).
[64] *G. Klopman, R. F. Hudson,* Theor. Chim. Acta *8*, 165 (1967); *G. Klopman,* J. Am. Chem. Soc. *90*, 223 (1968).
[65] *R. Sustmann, G. Binsch,* Mol. Phys. *20*, 1, 9 (1970).
[66] *R. Sustmann, A. Ansmann, F. Vahrenholt,* J. Am. Chem. Soc. *94*, 8099 (1972).
[67] *V. Bachler, F. Mark,* Theor. Chim. Acta *43*, 121 (1976).
[68] *V. Bachler, F. Mark,* Tetrahedron *33*, 2857 (1977).
[69] *L. Salem,* J. Am. Chem. Soc. *90*, 543 (1968).
[70] *L. Salem,* J. Am. Chem. Soc. *90*, 553 (1968).
[71] *E. A. Halevi,* Angew. Chem. *88*, 664 (1976); Angew. Chem. Int. Ed. Engl. *15*, 593 (1976).
[72] *H. Fujimoto, S. Inagaki, K. Fukui,* J. Am. Chem. Soc. *98*, 2670 (1976).
[73] *H. Fujimoto, T. Sugiyama,* J. Am. Chem. Soc. *99*, 15 (1977).
[74] *W. Th. A. M. van der Lugt, L. J. Oosterhoff,* J. Am. Chem. Soc. *91*, 6042 (1969).
[75] *J. Michl,* Top. Curr. Chem. *46*, 1 (1974).
[76] *N. D. Epiotis,* Angew. Chem. *86*, 825 (1974); Angew. Chem. Int. Ed. Engl. *13*, 751 (1974).
[77] *N. D. Epiotis, S. Shaik,* J. Am. Chem. Soc. *100*, 1, 9 (1978).
[78] *K. Fukui, H. Fujimoto,* Bull. Soc. Chim. Jpn. *41*, 1989 (1968).
[79] *T. Minato, S. Yamabe, S. Inagaki, H. Fujimoto, K. Fukui,* Bull. Soc. Chim. Jpn. *47*, 1619 (1974).
[80] *R. Sustmann, F. Vahrenholt,* Theor. Chim. Acta *29*, 305 (1973).
[81] *R. Sustmann, E. Wenning, R. Huisgen,* Tetrahedron Lett. *1977*, 877.
[82] *H. Metiu, J. Ross, G. M. Whitesides,* Angew. Chem. *91*, 363 (1979); Angew. Chem. Int. Ed. Engl. *18*, 377 (1979).
[83] *S. W. Benson:* Thermochemical Kinetics. 2nd Edit. Wiley, New York 1978.
[84] *D. Rowley, H. Steiner,* Disc. Faraday Soc. *10*, 198 (1951).
[85] *W. E. Vaughan,* J. Am. Chem. Soc. *54*, 3863 (1932).
[86] *G. Huybrechts, L. Luyckx, Th. Vandenboom, B. van Mele,* Int. J. Chem. Kinet. *9*, 283 (1977).
[87] *G. B. Kistiakowsky, J. R. Lacher,* J. Am. Chem. Soc. *58*, 123 (1936).
[88] *W. E. Vaughan,* J. Am. Chem. Soc. *55*, 4109 (1933).
[89] *J. B. Harkness, G. B. Kistiakowsky, W. H. Mears,* J. Chem. Phys. *5*, 682 (1937).
[90] *G. A. Benford, A. Wassermann,* J. Chem. Soc. *1939*, 362.
[91] *G. R. Schultze,* Oel, Kohle, Erdoel, Teer *14*, 113 (1938).
[92] *G. R. De Mare, G. Huybrechts, M. Toth, P. Goldfinger,* Trans. Faraday Soc. *67*, 1397 (1971).
[93] *G. Huybrechts, G. Paternoster, P. Baetens,* Int. J. Chem. Kinet. *8*, 641 (1976).
[94] *G. Debande, G. Huybrechts,* Int. J. Chem. Kinet. *6*, 545 (1974).
[95] *G. Huybrechts, G. Ngoy,* Int. J. Chem. Kinet. *7*, 775 (1975).
[96] *R. Walsh, J. M. Wells,* Int. J. Chem. Kinet. *7*, 319 (1975).
[97] *R. Walsh, J. M. Wells,* J. Chem. Soc. Perkin Trans. II *1976*, 52.
[98] *H. M. Frey, R. Pottinger,* J. Chem. Soc. Faraday Trans. I *74*, 1827 (1978).
[99] *W. v. E. Doering, M. Franck-Neumann, D. Hasselmann, R. L. Kaye,* J. Am. Chem. Soc. *94*, 3833 (1972).
[100] *L. M. Stephenson, R. V. Gemmer, S. Current,* J. Am. Chem. Soc. *97*, 5909 (1975).
[101] *J. A. Berson, R. Malherbe,* J. Am. Chem. Soc. *97*, 5910 (1975).
[102] *W. J. le Noble, A. R. Miller, S. D. Hamann,* J. Org. Chem. *42*, 338 (1977).
[103] *J. E. Critchlow,* J. Chem. Soc. Faraday Trans. I *68*, 1774 (1972).
[104] *J. J. Gajewski,* J. Am. Chem. Soc. *101*, 4393 (1979).
[105] *R. Sustmann, D. Brandes,* Chem. Ber. *109*, 354 (1976); *R. Sustmann, H. Trill, D. Brandes, ibid. 110*, 245 (1977); *R. Sustmann, H. Trill, F. Vahrenholt, D. Brandes, ibid. 110*, 255 (1977).
[106] a) *J. M. Bollinger, J. M. Brinich, G. A. Olah,* J. Am. Chem. Soc. *92*, 4025 (1970); b) *G. A. Olah, J. M. Bollinger, ibid. 90*, 6085 (1968); c) *P. v. R. Schleyer, T. M. Su, M. Saunders, J. C. Rosenfeld, ibid. 91*, 5174 (1969); d) *N. C. Deno, R. C. Haddon, E. N. Nowak, ibid. 92*, 6691 (1970).
[107] *T. B. Thompson, W. T. Ford,* J. Am. Chem. Soc. *101*, 5459 (1979); see also *S. W. Staley* in [13], Vol. II.
[108] *J. B. Lambert, J. D. Roberts,* Tetrahedron Lett. *1965*, 1457. Both the noncatalyzed as well as the $AlCl_3$-catalyzed [4 + 2]-cycloadditions of dimethyl maleate and fumarate also proceed stereospecifically within the limit of error (99.99 %) of GC analysis: *B. Prantl, J. Sauer,* unpublished.
[109] *P. D. Bartlett, J. J.-B. Mallet,* J. Am. Chem. Soc. *98*, 143 (1976).
[110] *V. Mark,* J. Org. Chem. *39*, 3179, 3181 (1974).
[111] *K. Seguchi, A. Sera, K. Maruyama,* Bull. Chem. Soc. Jpn. *49*, 3558 (1979).
[112] *J. B. Lambert, C. D. McLaughlin, V. Mark,* Tetrahedron *32*, 2075 (1976).
[113] *G. Huybrechts, V. van Mele,* Int. J. Chem. Kinet. *10*, 1183 (1978).
[114] *A. Krantz,* J. Am. Chem. Soc. *94*, 4020 (1972).
[115] *J. A. Berson, P. B. Dervan, R. Malherbe, J. A. Jenkins,* J. Am. Chem. Soc. *98*, 5937 (1976); *J. A. Berson, R. Malherbe, ibid. 97*, 5910 (1975).
[116] *J. Mulzer,* Universität München, private communication; Habilitationsarbeit, Universität München 1979.
[117] The complete energy profile was obtained by kinetic measurements: *M. W. Lee, W. C. Herndon,* J. Org. Chem. *43*, 518 (1978).
[118] *H. R. Gerberich, W. D. Walters,* J. Am. Chem. Soc. *83*, 3935, 4884 (1961).
[119] *G. Scacchi, R. Richard, M. H. Back,* Int. J. Chem. Kinet. *9*, 513 (1977); *G. Scacchi, M. H. Back, ibid. 9*, 525 (1977).
[120] *P. B. Dervan, T. Uyehara,* J. Am. Chem. Soc. *98*, 1262 (1976); relative rates of rotation, cleavage, and ring closure for the 1,4-diradical dideuteriotetramethylene: *P. B. Dervan, D. S. Santilli,* J. Am. Chem. Soc. *102*, 3863 (1980).
[121] *P. D. Bartlett,* Q. Rev. Chem. Soc. *24*, 473 (1970).

[122] *L. K. Montgomery, K. Schueller, P. D. Bartlett*, J. Am. Chem. Soc. *86*, 622 (1964).

[123] *P. D. Bartlett, L. K. Montgomery*, J. Am. Chem. Soc. *86*, 628 (1964).

[124] *C. Rücker, D. Lang, J. Sauer, H. Friege, R. Sustmann*, Chem. Ber. *113*, 1663 (1980).

[125] *P. D. Bartlett, G. E. H. Wallbillich, A. S. Wingrove, J. S. Swenton, L. K. Montgomery, B. D. Kramer*, J. Am. Chem. Soc. *90*, 2049 (1968); for the temperature dependence in the case of butadiene: *J. S. Swenton, P. D. Bartlett, ibid. 90*, 2056 (1968).

[126] *R. Wheland, P. D. Bartlett*, J. Am. Chem. Soc. *92*, 3822 (1970).

[127] *D. Craig, J. J. Shipman, R. B. Fowler*, J. Am. Chem. Soc. *83*, 2885 (1961).

[128] *R. Huisgen, R. Schug*, J. Am. Chem. Soc. *98*, 7819 (1976).

[129] *F. Kataoka, N. Shimizu, S. Nishida*, J. Am. Chem. Soc. *102*, 711 (1980).

[130] *R. Huisgen, J. P. Ortega*, Tetrahedron Lett. *1978*, 3975.

[131] *J. G. Martin, R. K. Hill*, Chem. Rev. *61*, 537 (1961).

[132] *Yu. A. Titov*, Russ. Chem. Rev. *31*, 267 (1962).

[133] *N. D. Epiotis*, J. Am. Chem. Soc. *95*, 5624 (1973).

[134] *I. Fleming, J. P. Michael, L. E. Overman, G. F. Taylor*, Tetrahedron Lett. *1978*, 1313.

[135] *C. Minot, N. T. Anh*, Tetrahedron *33*, 533 (1977).

[136] *R. B. Woodward, T. J. Katz*, Tetrahedron *5*, 70 (1959).

[137] *R. Häussinger, G. Kresze*, Tetrahedron *34*, 689 (1978); *G. Kresze, A. Mavromatis, ibid. 34*, 697 (1978); see also *G. Kresze, J. Firl*, Fortschr. Chem. Forsch. *11*, 245 (1969).

[138] *Z. Stojanac, R. A. Dickinson, N. Stojanac, R. J. Woznow, Z. Valenta*, Can. J. Chem. *53*, 616 (1975); *B. M. Trost, J. Ippen, W. C. Vladuchik*, J. Am. Chem. Soc. *99*, 8116 (1977); *H.-J. Liu, E. N. C. Browne*, Can. J. Chem. *57*, 377 (1979).

[139] *M. Kakushima, J. Espinosa, Z. Valenta*, Can. J. Chem. *54*, 3304 (1976).

[140] *N. T. Anh, J. Seyden-Penne*, Tetrahedron *29*, 3259 (1973).

[141] *K. N. Houk, R. W. Strozier*, J. Am. Chem. Soc. *95*, 4094 (1973).

[142] *P. V. Alston, R. M. Ottenbrite*, J. Org. Chem. *40*, 1111 (1975).

[143] *P. V. Alston, R. M. Ottenbrite, D. D. Shillady*, J. Org. Chem. *38*, 4075 (1973).

[144] *P. V. Alston, R. M. Ottenbrite, T. Cohen*, J. Org. Chem. *43*, 1864 (1978).

[145] *T. Cohen, R. J. Ruffner, D. W. Shull, W. M. Daniewski, R. M. Ottenbrite, P. V. Alston*, J. Org. Chem. *43*, 4052 (1978).

[146] *K. Alder, G. Stein*, Angew. Chem. *50*, 510 (1937).

[147] *J. A. Berson, Z. Hamlet, W. A. Mueller*, J. Am. Chem. Soc. *84*, 297 (1962).

[148] *J. R. Lindsay Smith, R. O. C. Norman, M. R. Stillings*, Tetrahedron *34*, 1381 (1978).

[149] *R. Hoffmann, R. B. Woodward*, J. Am. Chem. Soc. *87*, 4388 (1965).

[150] *W. C. Herndon, L. H. Hall*, Theor. Chim. Acta *7*, 4 (1967).

[151] *M. J. S. Dewar*, Tetrahedron Suppl. *8*, 75 (1967).

[152] *K. N. Houk*, Tetrahedron Lett. *1970*, 2621.

[153] *H.-D. Martin, R. Iden, H. J. Schiwek*, Tetrahedron Lett. *1978*, 3337.

[154] *M. P. Cava, M. J. Mitchell*, J. Am. Chem. Soc. *81*, 5409 (1959).

[155] *H. E. Simmons*, J. Am. Chem. Soc. *83*, 1657 (1961).

[156] *L. Watts, J. D. Fitzpatrick, R. Pettit*, J. Am. Chem. Soc. *88*, 623 (1965).

[157] *R. B. Woodward, H. Baer*, J. Am. Chem. Soc. *70*, 1161 (1948).

[158] *F. A. L. Anet*, Tetrahedron Lett. *1962*, 1219.

[159] *S. J. Cristol, W. K. Seifert, S. B. Soloway*, J. Am. Chem. Soc. *82*, 2351 (1960).

[160] *N. A. Belikova, V. G. Berezkin, F. A. Palté*, J. Gen. Chem. USSR *32*, 2896 (1962).

[161] *K. B. Wiberg, W. J. Bartley*, J. Am. Chem. Soc. *82*, 6375 (1960).

[162] *D. Bellus, K. von Bredow, H. Sauter, C. D. Weis*, Helv. Chim. Acta *56*, 3004 (1973).

[163] *D. C. F. Law, S. W. Tobey*, J. Am. Chem. Soc. *90*, 2376 (1968).

[164] *P. B. Sargent*, J. Am. Chem. Soc. *91*, 3061 (1969).

[165] *H. Monti, M. Bertrand*, Tetrahedron Lett. *1970*, 2587.

[166] *H. Monti, M. Bertrand*, Tetrahedron Lett. *1970*, 2591.

[167] *D. W. Jones, J. Chem. Soc. Chem. Commun. 1975*, 199.

[168] *D. W. Jones, G. Kneen*, J. Chem. Soc. Chem. Commun. *1973*, 420.

[169] *C. M. Anderson, I. W. McCay, R. N. Warrener*, Tetrahedron Lett. *1970*, 2735.

[170] *Y. Kobuke, T. Fueno, J. Furukawa*, J. Am. Chem. Soc. *92*, 6548 (1970).

[171] *K. N. Houk, L. J. Luskus*, J. Am. Chem. Soc. *93*, 4606 (1971).

[172] *A. I. Konovalov, G. I. Kamasheva, M. P. Loskutow*, J. Org. Chem. USSR *9*, 2064 (1973).

[173] *Y. Kobuke, T. Sugimoto, J. Furukawa, T. Fueno*, J. Am. Chem. Soc. *94*, 3633 (1972).

[174] *T. Sugimoto, Y. Kobuke, J. Furukawa, T. Fueno*, Tetrahedron Lett. *1976*, 1587.

[175] *K. L. Williamson, Y. F. L. Hsu, R. Lacko, C. H. Youn*, J. Am. Chem. Soc. *91*, 6129 (1969).

[176] *K. L. Williamson, Y. F. L. Hsu*, J. Am. Chem. Soc. *92*, 7385 (1970).

[177] *N. T. Anh*, Tetrahedron *29*, 3227 (1973).

[178] *S. Seltzer*, Adv. Alicyclic Chem. *2*, 1 (1968).

[179] *R. Sustmann, R. Schubert*, Angew. Chem. *84*, 888 (1972); Angew. Chem. Int. Ed. Engl. *11*, 840 (1972).

[180] *L. E. Overman, G. F. Taylor, K. N. Houk, L. N. Domelsmith*, J. Am. Chem. Soc. *100*, 3182 (1978).

[181] *K. N. Houk, L. L. Munchhausen*, J. Am. Chem. Soc. *98*, 937 (1976).

[182] *B. Eisler, A. Wassermann*, J. Chem. Soc. *1953*, 979.

[183] *C. W. Bock, P. George, M. Trachtman, M. Zanger*, J. Chem. Soc. Perkin Trans. II *1979*, 26.

[184] *C. A. Stewart*, J. Am. Chem. Soc. *84*, 117 (1962).

[185] *H. D. Scharf, H. Plum, J. Fleischhauer, W. Schleker*, Chem. Ber. *112*, 862 (1979).

[186] *R. Sustmann, M. Böhm, J. Sauer*, Chem. Ber. *112*, 883 (1979).

[187] *A. Mielert, Ch. Braig, J. Sauer, J. Martelli, R. Sustmann*, Justus Liebigs Ann. Chem. *1980*, 954.

[188] *V. D. Kiselev, A. I. Konovalov, E. A. Veisman, A. N. Ustyugov*, J. Org. Chem. USSR *14*, 118 (1978).

[189] *Ya. D. Samuilov, L. F. Uryadova, B. N. Solomonov, A. I. Konovalov*, J. Org. Chem. USSR *11*, 1931 (1975).

[190] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).

[191] *N. Shimizu, S. Nishida*, J. Chem. Soc. Chem. Commun. *1978*, 931.

[192] *T. Inukai, T. Kojima*, J. Org. Chem. *36*, 924 (1971), and references cited therein.

[193] *Normal* Diels-Alder additions: *A. I. Konovalov, B. N. Solomonov*, J. Org. Chem. USSR *11*, 2178 (1975); isobenzofurans + substituted styrenes: *Ya. D. Samuilov, A. I. Konovalov, L. F. Uryadova, ibid. 10*, 1945 (1974); pentacene + substituted styrenes; [189]: anthracene or tetracene + substituted *N*-phenylmaleimides. *Inverse* Diels-Alder additions: *Ya. D. Samuilov, L. F. Uryadova, A. I. Konovalov, ibid. 12*, 811 (1976): substituted indanocyclones + substituted styrenes.

[194] *Y. Okamoto, H. C. Brown*, J. Am. Chem. Soc. *79*, 1913 (1957).

[195] *R. Sustmann*, Tetrahedron Lett. *1974*, 963.

[196] *O. Henri-Rousseau, F. Texier*, J. Chem. Educ. *55*, 437 (1978).

[197] *E. J. De Witt, C. T. Lester, G. A. Ropp*, J. Am. Chem. Soc. *78*, 2101 (1956).

[198] *G. Kresze, J. Firl, H. Zimmer, U. Wollnik*, Tetrahedron *20*, 1605 (1964).

[199] *G. Kresze, O. Korpiun*, Tetrahedron *22*, 2493 (1966).

[200] *I. Tabushi, H. Yamada, Z. Yoshida, R. Oda*, Bull. Chem. Soc. Jpn. *50*, 285 (1977).

[201] *I. Benghiat, E. I. Becker*, J. Org. Chem. *23*, 885 (1958).

[202] *M. Ahmad, J. Hamer*, J. Org. Chem. *31*, 2829 (1966).

[203] *M. E. Burrage, R. C. Cookson, S. S. Gupte, I. D. R. Stevens*, J. Chem. Soc. Perkin Trans. II *1975*, 1325.

[204] *M. Mizuta, Y. Ishii*, Kogyo Kagaku Zasshi *66*, 1442 (1963); Chem. Abstr. *60*, 11880 (1964).

[205] *G. Desimoni, A. Gamba, M. Monticelli, M. Nicola, G. Tacconi*, J. Am. Chem. Soc. *98*, 2947 (1976).

[206] *H. Appler, J. Sauer*, unpublished results; *H. Appler*, thesis, Universität Regensburg 1980.

[207] *D. Stepanow, J. Sauer*, unpublished results.

[208] *D. Lang, J. Sauer*, unpublished results; *D. Lang*, Dissertation, Universität München 1963.

[209] *M. Yasuda, K. Harano, K. Kanematsu*, J. Org. Chem. *45*, 659 (1980).

[210] *A. I. Konovalov, B. N. Solomonov, O. Y. Chertov*, J. Org. Chem. USSR *11*, 113 (1975).

[211] *A. I. Konovalov, Ya. D. Samuilov, L. F. Uryadova, E. A. Berdnikov*, J. Org. Chem. USSR *12*, 636 (1976).

[212] *A. I. Konovalov, B. N. Solomonov, O. Yu. Chertov*, J. Org. Chem. USSR *11*, 103 (1975).

[213] *A. I. Konovalov, Ya. D. Samuilov, L. F. Slepova, V. A. Breus*, J. Org. Chem. USSR *9*, 2539 (1973). The reactions of tetracyclone with substituted phenylacetylenes also belong to Type II.

[214] *A. I. Konovalov, L. F. Uryadova, Ya. D. Samuilov*, J. Org. Chem. USSR *12*, 2519 (1976).

[215] *P. Brown, R. C. Cookson*, Tetrahedron *21*, 1977 (1965).

[216] *A. I. Konovalov, J. P. Breus, I. A. Sharagin, V. D. Kiselev*, J. Org. Chem. USSR *15*, 315 (1979).

[217] *M. J. S. Dewar, R. S. Pyron*, J. Am. Chem. Soc. *92*, 3098 (1970).

[218] *J. Sauer, A. Mielert*, unpublished results.

[219] *M. Ahmad, J. Hamer*, J. Org. Chem. *31*, 2831 (1966).

[220] *P. Haberfield, A. K. Ray*, J. Org. Chem. *37*, 3093 (1972).

[221] *L. J. Andrews, R. M. Keefer*, J. Am. Chem. Soc. *77*, 6284 (1955).

[222] *J. R. Lacher, G. W. Tompkin, J. D. Park*, J. Am. Chem. Soc. *74*, 1693 (1952); *B. Atkinson, A. B. Trenwith*, J. Chem. Soc. *1953*, 2082; J. Chem. Phys. *20*, 764 (1952).

[223] *C. D. Duncan, L. R. Corwin, J. H. Davis, J. A. Berson*, J. Am. Chem. Soc. *102*, 2350 (1980); *M. S. Platz, J. A. Berson, ibid. 102*, 2358 (1980).

[224] *Ya. D. Samuilov, L. F. Uryadova, B. N. Solomonov, A. I. Konovalov*, J. Org. Chem. USSR *11*, 1931 (1975).

[225] *D. N. Matthews, E. I. Becker*, J. Org. Chem. *31*, 1135 (1966).

[226] a) *C. Walling, J. Peisach*, J. Am. Chem. Soc. *80*, 5819 (1958); b) *C. Walling, H. J. Schugar, ibid. 85*, 607 (1963); c) *B. Raistrick, R. H. Sapiro, D. M. Newitt*, J. Chem. Soc. *1939*, 1770.

[227] *S. W. Benson, J. A. Berson*, J. Am. Chem. Soc. *84*, 152 (1962).

[228] a) *M. G. Gonikberg, L. F. Vereshagin*, Zh. Fiz. Khim. *23*, 1447 (1949); b) *M. G. Gonikberg, ibid. 34*, 106 (1960).

[229] J. R. McCabe, C. A. Eckert, Ind. Eng. Chem. Fundam. 13, 168 (1974).
[230] R. A. Grieger, C. A. Eckert, Trans. Faraday Soc. 66, 2579 (1970).
[231] R. A. Grieger, C. A. Eckert, Ind. Eng. Chem. Fundam. 10, 369 (1971).
[232] R. A. Grieger, C. A. Eckert, J. Am. Chem. Soc. 92, 2918, 7149 (1970).
[233] C. Brun, G. Jenner, Tetrahedron 28, 3113 (1972).
[234] B. E. Poling, C. A. Eckert, Ind. Eng. Chem. Fundam. 11, 451 (1972).
[235] a) C. A. Stewart, J. Am. Chem. Soc. 93, 4815 (1971); b) 94, 635 (1972).
[236] A very detailed study of the pressure-dependence of [2+2]-cycloadditions including CT phenomena has been carried out by J. von Jouanne, H. Kelm, R. Huisgen, J. Am. Chem. Soc. 101, 151 (1979).
[237] F. E. Rogers, J. Phys. Chem. 75, 1734 (1971); 76, 106 (1972); F. E. Rogers, S. W. Quan, ibid. 77, 828 (1973).
[238] K. J. Breslauer, D. S. Kabakoff, J. Org. Chem. 39, 721 (1974).
[239] H. D. Fühlhuber, A. Miedaner, J. Sauer, R. Sustmann, unpublished results; A. Miedaner, Diplomarbeit, Universität Regensburg 1978.
[240] V. D. Kiselev, A. I. Konovalov, E. A. Veisman, A. N. Ustyugov, J. Org. Chem. USSR 14, 118 (1978).
[241] B. S. Khambata, A. Wassermann, J. Chem. Soc. 1939, 375.
[242] W. C. Herndon, C. R. Grayson, J. M. Manion, J. Org. Chem. 32, 526 (1967).
[243] A. Wassermann, Trans. Faraday Soc. 34, 128 (1938), and references cited therein.
[244] M. Uchiyama, T. Tomioka, A. Amano, J. Phys. Chem. 68, 1878 (1964).
[245] W. Tsang, J. Chem. Phys. 42, 1805 (1965).
[246] D. C. Tardy, R. Ireton, A. S. Gordon, J. Am. Chem. Soc. 101, 1508 (1979): The cleavage described for the tetradeuteriated compound is the main reaction (>95%); in addition there is also D_2-, HD-, and H_2-elimination as competing reaction.
[247] J. Sauer, B. Schröder, R. Wiemer, Chem. Ber. 100, 306 (1967).
[248] J. A. Berson, W. A. Mueller, J. Am. Chem. Soc. 83, 4940 (1961).
[249] W. Grimme, H. G. Köser, Angew. Chem. 92, 307 (1980); Angew. Chem. Int. Ed. Engl. 19, 307 (1980) and earlier work; W. Grimme, private communication.
[250] W. Neukam, W. Grimme, Tetrahedron Lett. 1978, 2201; O. Papies, W. Grimme, ibid. 1980, 2799.
[251] G. Brieger, J. N. Bennett, Chem. Rev. 80, 63 (1980).

COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Diagonal Interaction in the Four-Membered Ring. Experimental Demonstration of a Dominating Circumannular Conjugation: 5,6-Dimethylenebicyclo[2.1.1]hexane[**]

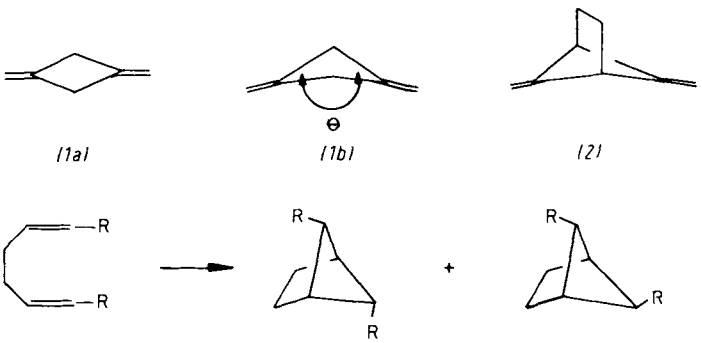
By *Hans-Dieter Martin, Mirjana Eckert-Maksić,* and *Bernhard Mayer*[*]

Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday

Diagonal interaction in the four-membered ring, with its chemical[1] and spectroscopic[2] consequences, is one of the most interesting transannular relationships. From UV and PE spectroscopic investigations, *Vala* and *Klessinger* (cf. [2]) concluded the involvement of a considerable amount of through-bond coupling (circumannular conjugation) in 1,3-di-π-substituted cyclobutanes. We report here on an experimental determination of the orbital sequence in planar 1,3-dimethylenecyclobutane *(1a)* using the reference compounds *(2)*, *(10)*[3], and *(12)*, with a procedure proposed by *Heilbronner*[4] being used in the case of *(10)*.

The splitting of the first two ionization potentials of *(1a)*[2] cannot be independent of the dihedral angle θ. A diminution of θ, as in *(1b)*, however, has different consequences depending on whether the sequence S > A (circumannular) or A > S (transannular) in *(1a)* predominates. In the former case a diminution in the splitting is to be expected, in the second case an increase (Fig. 1, columns a—d). The PE spectroscopic investigation of *(2)*, whose dihedral angle in the model is 130°, can answer this question.

(3) is photochemically cyclized to a mixture (35:65) of *(4a)* and *(4b)*[5]. Hydrolysis ($KOH/CH_3OH/H_2O$) and reaction



(3), R = $COOCH_3$ (4a)–(9a) (4b)–(9b)

(4), R = $COOCH_3$; (5), R = COOH; (6), R = COCl; (7), R = $CON(CH_3)_2$;

(8), R = $CH_2N(CH_3)_2$; (9), R = $CH_2\overset{\oplus}{N}(CH_3)_2$

[*] Prof. Dr. H.-D. Martin, Dipl.-Chem. B. Mayer
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)
Dr. M. Eckert-Maksić,
present address: Organisch-chemisches Institut der Universität
Heidelberg (Germany)

[**] Small Rings, Part 37. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Prof. Dr. R. Gleiter for use of the PE spectrometer.—Part 36: H.-D. Martin, C. Heller, B. Mayer, H.-D. Beckhaus, Chem. Ber. 113, 2589 (1980).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0807 $ 02.50/0

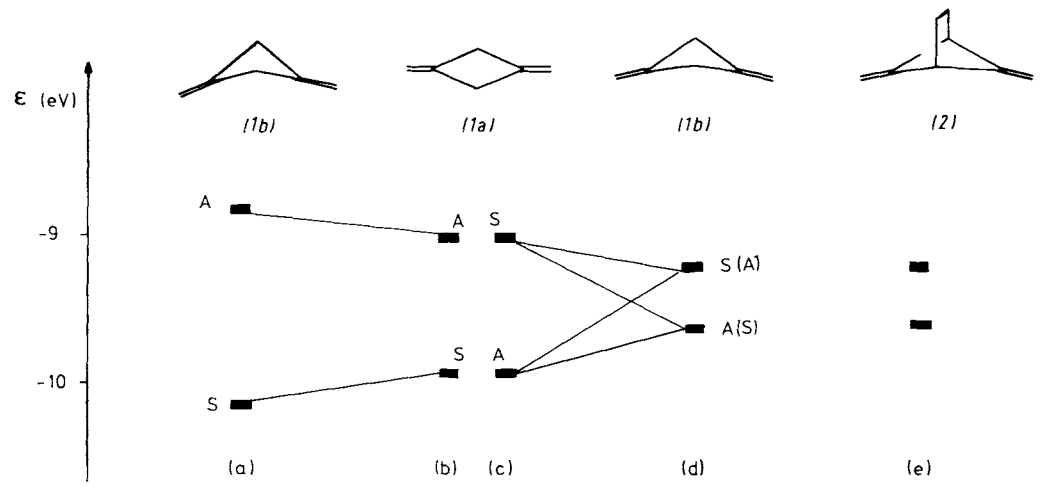


Fig. 1. Orbital correlation diagram. (a)—(e), see text.

with thionyl chloride affords—*via* carboxylic acids *(5a)/(5b)*, which are separable by fractional crystallization—the acid chlorides *(6a)/(6b)* (1:3). Reaction with dimethylamine (ether, 0 °C) furnishes *(7a)/(7b)*, from which ($LiAlH_4$, tetrahydrofuran) the gas-chromatographically separable amines *(8a)* and *(8b)* are obtained. Oxidation (30% H_2O_2, CH_3OH, room temperature) leads to the hydrated amine oxides *(9a)/(9b)*, which are dehydrated at 120 °C/12 torr, and at 180 °C/12 torr give the diene *(2)* (yield 40—55%). Table 1 contains ^{1}H-NMR data. The first two ionization potentials of *(2)* ($IP_{1,v}=9.25$, $IP_{2,v}=9.65$ eV, Fig. 1, column e) show that only the sequence S > A in *(1a)* (column c) is consistent with the experimental findings (column e). This experiment alone provides no information about the sequence in *(2)*.

In Figure 2 the same sequence S > A for *(1a)* (column e) leads *via* the experimental result for *(11)*[6] (column f) to a prediction of the orbital sequence in *(10)* (column g), which is in excellent agreement with the observed ionization potentials of *(10)* (column i) [$IP_{1,v}(\pi_S)=8.50$, $IP_{2,v}(\pi_A)=9.75$, $IP_{3,v}(\sigma)=11.00$, $IP_{4,v}(\pi_S)=11.40$ eV]. The assumption A > S for *(1a)* (column d), on the other hand, leads to a contradiction (columns b and c). Finally comparison of *(10)* with 3-

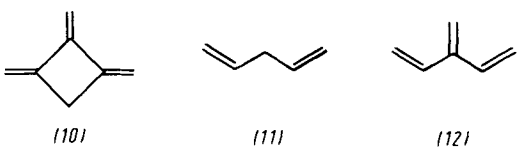


Table 1. ^{1}H-chemical shifts.

Cpd.	Solvent	CH_2(2,3)	CH(1,4)	$CH^{5(6)}_{exo}$	$CH^{6(5)}_{endo}$	CH_3—N	CH_2—N
(2),	CCl_4	1.65 (bs)	3.03 (m)	4.33 (bs), =CH_2			
(5a),	D_2O	1.70 (m)	2.90—3.10 (m)	2.55 (m)	—		
(5b),	D_2O	1.70 (m)	2.90—3.10 (m)	3.25 (m)	2.25 (s)		
(6a),	$CDCl_3$	2.20—2.30 (m)	3.65 (m)	3.10 (m)	—		
(6b),	$CDCl_3$	2.20—2.30 (m)	3.65 (m)	3.90 (m)	3.00 (s)		
(7a),	$CDCl_3$	1.70 (m)	≈2.90 (m)	2.30 (m)	—	2.85, 3.00 (s)	
(7b),	$CDCl_3$	1.57—2.00 (AA'BB')	≈2.98 (m)	3.05 (m)	2.17 (s)	2.87, 2.96, 3.00	
(8a),	$CDCl_3$	1.50 (m)	1.90—2.43 (m)	1.33—1.83 (m)	—	2.18	1.90—2.43 (m)
(8b),	$CDCl_3$	1.58 (m)	1.87—2.67 (m)	1.23—1.80 (m)		2.20	1.87—2.67 (m)

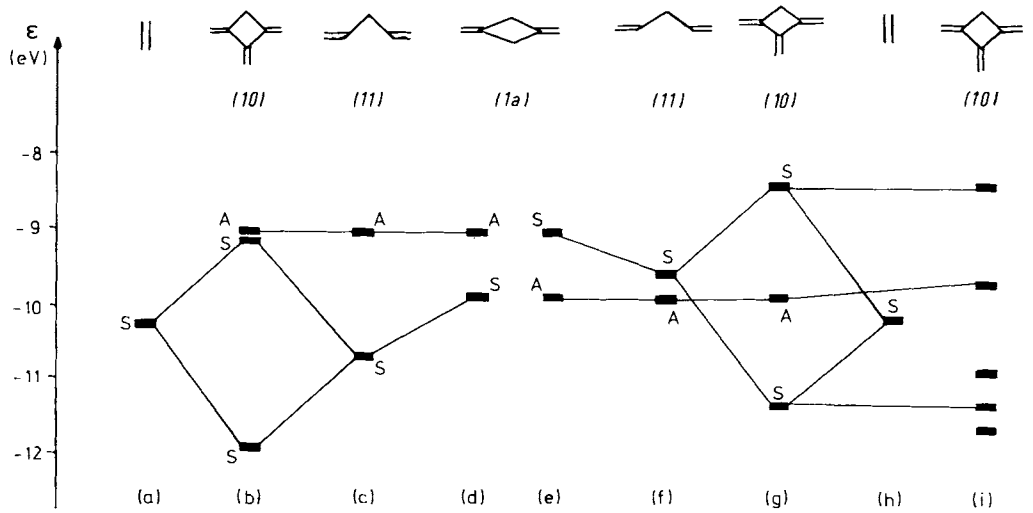


Fig. 2. Orbital correlation diagram. (a)—(i), see text.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0808 $ 02.50/0

methylene-1,4-pentadiene *(12)*[7] [$IP_{1,v}(\pi_s) = 8.80$, $IP_{2,v}(\pi_A) = 9.95$ eV] shows that the sequence derived for *(10)* in Figures 1 and 2 is in very good agreement with that of the structurally related triene *(12)*. All three reference compounds *(2)*, *(10)*, and *(12)* demonstrate that in *(1a)* the circumannular through-bond conjugation (sequence S > A) dominates over the transannular through-space interaction (sequence A > S)[8].

Received: March 18, 1980 [Z 569 IE]
German version: Angew. Chem. 92, 833 (1980)

CAS Registry numbers:
(2), 74965-17-6; *(3)*, 4756-84-7; *(4a)*, 32426-61-2; *(4b)*, 32426-60-1; *(5a)*, 74965-18-7; *(5b)*, 74985-45-8; *(6a)*, 74965-19-8; *(6b)*, 74985-46-9; *(7a)*, 74965-20-1; *(7b)*, 74985-47-0; *(8a)*, 74965-21-2; *(8b)*, 74985-48-1; *(9a)*, 74965-22-3; *(9b)*, 74985-49-2

[1] *M. Horner, S. Hünig*, J. Am. Chem. Soc. *99*, 6120 (1977); *J. Harnisch, G. Szeimies*, Tetrahedron Lett. *1978*, 247; *S. Mazur, A. H. Schröder, M. Weiss*, J. Chem. Soc. Chem. Commun. *1977*, 262; *M. Dagonneau, P. Metzner, J. Vialle*, Tetrahedron Lett. *1973*, 3675.

[2] *P. Hemmersbach, M. Klessinger, P. Bruckmann*, J. Am. Chem. Soc. *100*, 6344 (1978); *J. M. Behan, R. A. W. Johnstone, J. J. Worman, T. P. Fehlner*, J. Mol. Struct. *40*, 151 (1977); *R. Spafford, J. Baiardo, J. Wrobel, M. Vala*, J. Am. Chem. Soc. *98*, 5217, 5225 (1976); *M. Simonetta, S. Carra*, Tetrahedron Lett. *1965*, 913; *J. J. Wormann, E. A. Schmidt, E. S. Olson, R. D. Schultz*, Spectrochim. Acta *A 32*, 1415 (1976).

[3] *H.-D. Martin, B. Mayer*, Tetrahedron Lett. *1979*, 2351.

[4] *E. Heilbronner*, Isr. J. Chem. *10*, 143 (1972); *E. Heilbronner, H.-D. Martin*, Helv. Chim. Acta *55*, 1490 (1972).

[5] *J. R. Scheffer, R. A. Wostradowski*, J. Org. Chem. *37*, 4317 (1972).

[6] *J. C. Bünzli, A. J. Burak, D. C. Frost*, Tetrahedron *29*, 3735 (1973).

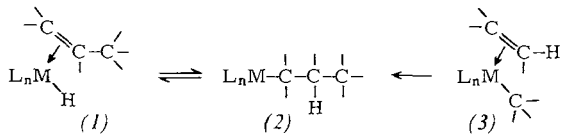
[7] Synthesis of *(12)*: 1,2,3-propanetricarboxylic acid is converted *via* the trichloride, tris(dimethylamide), and tris(dimethylamine) into the corresponding quaternary ammonium hydroxide, which is then thermolyzed at 180 °C/12 torr. Synthesis by ester pyrolysis: *W. Bailey*, J. Am. Chem. Soc. *77*, 1133 (1955).

[8] The reference compounds *(10)* and *(12)* also enable a satisfactory construction of the PE spectrum of [4]-radialene according to the LCBO method; see *T. Bally, U. Buser, E. Haselbach*, Helv. Chim. Acta *61*, 38 (1978).

Olefin-Insertion into Cobalt(d^8) Complexes—Structure of Ethylene(phenyl)tris(trimethylphosphane)cobalt[**]

By *Hans-Friedrich Klein, Reinhard Hammer, Joachim Gross*, and *Ulrich Schubert*[*]

The formal insertion of olefins into transition metal-hydrogen or -carbon bonds is a cardinal problem of organometallic chemistry and the principal feature of important industrial processes[1].



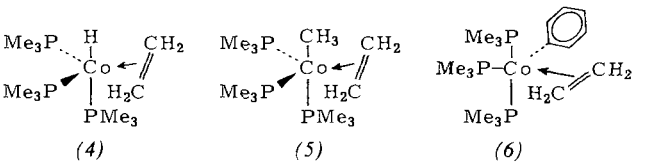
(1) *(2)* *(3)*

While the σ-π rearrangement *(1)*⇌*(2)*, a reversible β-elimination, is relatively well established[2], there is only little experimental evidence supporting the practically irreversible insertion *(3)*→*(2)*[3].

As potential insertion precursors, we have prepared the three pentacoordinated cobalt(I) complexes *(4)*—*(6)*, which contain a Co—H or Co—C bond in the *cis* position to the equatorially bound ethylene ligand.

[*] Prof. Dr. H.-F. Klein, Dr. R. Hammer, Dipl.-Chem. J. Gross, Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



(4) *(5)* *(6)*

The new olefincobalt complexes were synthesized from known compounds[4] according to eqs. (a) and (b); propene or cyclopentene can also be used, instead of ethylene.

$$K[Co(C_2H_4)(PMe_3)_3] \xrightarrow[-\,CH_3OK]{+\,CH_3OH} CoH(C_2H_4)(PMe_3)_3 \quad (a)$$

(4), 60%

$$CoCl(PMe_3)_3 + LiR \xrightarrow[-\,LiCl]{+\,C_2H_4} CoR(C_2H_4)(PMe_3)_3 \quad (b)$$

(5), R = CH_3, 63%
(6), R = C_6H_5, 55%

The diamagnetic ethylenecobalt(I) complexes *(4)*—*(6)* were crystallized from pentane solutions. The complexes gave correct elemental analyses. The crystals can be stored under Ar at 20 °C, but rapidly decompose on exposure to air.

(4) forms greenish yellow leaflets, which sublime with decomposition at 35–40 °C/0.1 mbar and are stable up to 95 °C under 1 bar Ar. The brownish-yellow crystals of *(5)* sublime at 60—65 °C/0.1 mbar, likewise with decomposition; m.p. 115—117 °C (dec.). *(6)* was obtained as well-formed orange-yellow crystals, dec. > 99 °C.

The dynamic ^1H- and ^{31}P-NMR spectra of *(4)*—*(6)* evidence anisochronic ^{31}P nuclei (2:1) for the ground state, and thus indirectly the *cis* relationship of anionic ligands and ethylene. An axial position of the hydride ligand in *(4)* cannot be deduced from the spectra; the structure *(4)* was formulated in analogy to the structure of the methyl compound *(5)*. A comparison of the NMR data of *(5)* with those of $CoCH_{3(ax)}(PMe_3)_4$[4c] indicates an axial position for the CH_3 ligand, consistent with a theoretical postulate[2c,5].

All three complexes behave differently in solution. On using CH_3OD for the synthesis of *(4)* according to eq. (a), IR spectroscopy reveals a nearly random distribution of the deuterium over five positions of the product: four sites in ethylene (ν_{CD} 2100 cm^{-1}) and one at the cobalt (ν_{CoH} 1850 cm^{-1}). Solvent-free 1-pentene is catalytically isomerized by *(4)* (0.5 mol-%, 20 °C, 48 h) to 2-pentene (*cis*:*trans* = 9:1)[6], thus demonstrating σ-π rearrangement in the 18-electron compound *(4)* (Scheme 1).

$$L_3CoH(CH_2{=}CH_2) \rightleftharpoons L_3Co{-}CH_2{-}CH_3$$
(4)

$$L_3CoR(CH_2{=}CH_2) \rightleftharpoons L_3Co{-}CH_2{-}CH_2R \rightleftharpoons L_3CoH(CH_2{=}CHR)$$
(5), *(6)*

Scheme 1. L = PMe_3; R = CH_3, C_6H_5.

In contrast, a thermal isomerization into the complex of type *(4)* (Scheme 1) in the sense of an insertion-β-elimination reaction sequence[7] is not observed in the case of *(5)*; 1-pentene is not isomerized by *(5)*.

$$(6) \rightarrow Co(C_2H_4)(PMe_3)_3 + 1/2\,C_6H_5{-}C_6H_5$$
(7)

On warming, ethylene-saturated solutions of *(6)* (*e.g.* in toluene, 1 bar C_2H_4, 50 °C, 8 h) furnish biphenyl and paramagnetic ethylenetris(trimethylphosphane)cobalt(0) *(7)*[4a] in quantitative yield. Styrene and hydridocobalt complexes, as by-products of an insertion reaction (Scheme 1), were not detected.

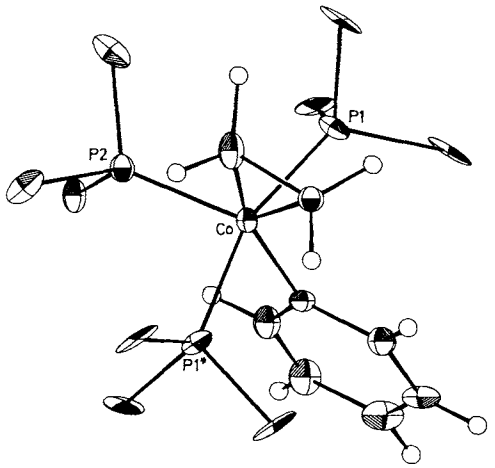


Fig. 1. ORTEP diagram of the molecule *(6)* in the crystal. The hydrogen atoms have been omitted for sake of clarity. Co—P1 219.2(3), Co—P2 221.5(2), Co—C(Ph) 199.9(6), Co—C(Eth) 204.0(7), 205.6(7), C—C(Eth) 143(1) pm. P2—Co—C(Ph) 111.7(2), P2—Co—Eth 110.4(2), C(Ph)—Co—Eth 137.9(2), P1—Co—P1* 160.26(8), P1—Co—P2 97.91(7), P1—Co—C(Ph) 81.6(2), P1—Co—Eth 92.6(2). Eth = center of the C=C bond in the ethylene ligand. *(6)* crystallizes orthorhombically, $a = 1342(1)$, $b = 1301(4)$, $c = 2423(4)$ pm; $V = 4230$ pm^3; ϱ(calc.) = 1.23 g/cm^3; space group Cmca; $Mo_{K\alpha}$ radiation, ($\lambda = 71.069$ pm, graphite monochromator); 1800 independent reflections ($2° \leq 2\theta \leq 50°$). $R_1 = 0.041$, $R_2 = 0.046$ for 1169 structure factors with $F_0 \geq 3.92\sigma(F_0)$.

The X-ray structure analysis of *(6)*, however, revealed that the configuration is favorable for the insertion step, at least in the solid state (Fig. 1). The complex has crystallographic C_s-symmetry with coplanar arrangement of all C-atoms of phenyl and ethyl ligands and of the vector of the Co—P2 bond in the mirror plane. Thus, a reaction path is available which involves minimal rearrangement of the participating atomic centers. The reason for insertion not taking place lies either in the unfavorable orbital symmetries[2c] or unknown thermodynamic quantities. The complex *(6)* is markedly distorted from a trigonal pyramidal coordination (P1 and P1* axial) in the direction of a square pyramidal coordination with P2 in the axial position. This distortion could be caused by the strong steric interaction between ethyl- and phenyl-ligand, which results from their coplanarity.

Procedure

(6): A 0.90 M solution (1.62 ml) of LiC_6H_5 in ether is pipetted into a suspension of $CoCl(PMe_3)_3$[4c] (470 mg, 1.46 mmol) in ether (20 ml) at −78 °C under 1 bar ethylene. The stirred mixture is warmed to 20 °C and stirring continued for a further 1 h. The volatile components are removed in a vacuum and the brown residue is extracted twice with 10 ml pentane. On slowly cooling over dry-ice, orange-yellow crystals of *(6)* separate out; yield 310 mg (55%).

Received: February 13, 1980 [Z 570 IE]
German version: Angew. Chem. *92*, 835 (1980)

CAS Registry numbers:
(4), 68830-26-2; *(5)*, 73557-04-7; *(6)*, 74965-07-41; $CoCl(PMe_3)_3$ 53432-06-7

[1] a) *G. Henrici-Olivé, S. Olive:* Coordination and Catalysis. Verlag Chemie, Weinheim 1977, p. 122f.; b) *J. L. Davidson*, Inorg. React. Mech. *5*, 346 (1977); c) *F. Calderazzo*, Angew. Chem. *89*, 305 (1977); Angew. Chem. Int. Ed. Engl. *16*, 299 (1977); d) cf. also *H.-F. Klein, ibid. 92*, 362 (1980) and *19*, 362 (1980).

[2] a) *M. Tsutsui, A. Courtney*, Adv. Organomet. Chem. *16*, 241 (1977); b) *B. Gorewit, M. Tsutsui*, Adv. Catal. *27*, 227 (1978); c) *D. L. Thorn, R. Hoffmann*, J. Am. Chem. Soc. *100*, 2079 (1978).

[3] *E. R. Evitt, R. G. Bergman*, J. Am. Chem. Soc. *101*, 3973 (1979); *K. J. Ivin, J. J. Rooney, C. D. Stewart, M. L. H. Green, R. Mahtab*, J. Chem. Soc. Chem. Commun. *1978*, 604; *M. L. H. Green, R. Mahtab*, J. Chem. Soc. Dalton Trans. *1979*, 262.

[4] a) *H.-F. Klein, R. Hammer, J. Wenninger, J. Gross* in *B. Pullman:* Catalysis in Chemistry and Biochemistry. D. Reidel, Amsterdam 1979, p. 285; b) *H.-F. Klein, H. H. Karsch*, Inorg. Chem. *14*, 473 (1975); c) Chem. Ber. *108*, 944 (1975).

[5] *J. K. Burdett*, Adv. Inorg. Chem. Radiochem. *21*, 113 (1978).

[6] *R. Hammer*, Dissertation, Technische Universität München 1977.

[7] The expected hydrido(propene)cobalt complex could previously only be obtained analogously to *(4)*, according to eq. (a) [6]. One of the thermolysis products of *(5)* (60 °C, toluene, 1 bar C_2H_4) is $(Me_3P)_2Co(PMe_2)(CH_2PMe_2)Co(PMe_3)_2$ [8].

[8] *H.-F. Klein, J. Wenninger, U. Schubert*, Z. Naturforsch. *B 34*, 1391 (1979).

The Nitrile Function of Tetracyanoethylene as Dienophile in Diels-Alder Reactions[**]

By *Klaus Burger* and *Herbert Goth*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Cycloaddition reactions to tetracyanoethylene (TCNE) proceed with high site selectivity at the CC double bond[1]. Examples of [3 + 2]-cycloaddition reactions, in which one of the nitrile groups functions as reaction partner, are rare[2], and no examples of Diels-Alder reactions have, to our knowledge, been reported[3].

We have found that the 1-thia-3-aza-1,3-pentadienes *(2)*[4], accessible by electrocyclic ring opening from 2,2-bis(trifluoromethyl)-2*H*-1,3-thiazete derivatives *(1)*, react with TCNE already at 120 °C (bath temperature). A [1:1]-adduct can be isolated from the product mixture in 50—60% yield (Table 1).

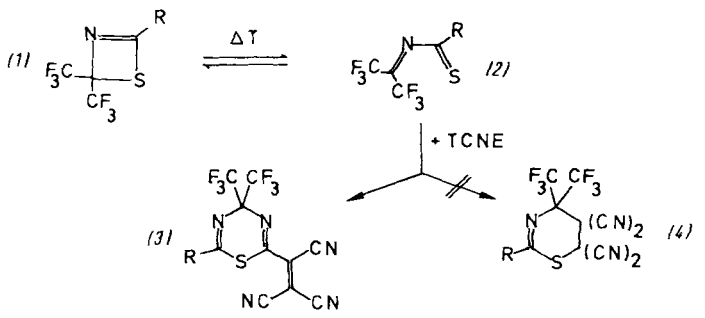
Table 1. Yields, melting points, and IR data of compounds *(3)*.

(3)	R	Yield [%]	M.p. [°C]	IR [cm^{-1}] (KBr)
a	C_6H_5	60	162—163	2233, 1658, 1578
b	*p*-$CH_3C_6H_4$	55	158—160	2232, 1657, 1607
c	*p*-ClC_6H_4	53	140—141	2233, 1660, 1642, 1584

The color of the products, an IR absorption at 1655—1660 cm^{-1}, and a singlet representing six fluorine atoms at $\delta = -2.1$ in the ^{19}F-NMR spectrum[5] indicate reaction of one of the nitrile functions. The mass spectrometric fragmentation pattern, which reveals the electron-impact induced retro-Diels-Alder processes[6] $[M - RCN]^{\oplus}_{\odot}$ and $[M - TCNE]^{\oplus}_{\odot}$ of comparable intensity and intense lines for the fragmentation ions $[(CN)_2C{=}C(CN)C{\equiv}S]^{\oplus}$ and $[RC{\equiv}S]^{\oplus}$, confirms the constitution of a 4*H*-1,3,5-thiadiazine *(3)*. The possible conversion into a symmetric [2:1]-adduct on subsequent heating in the presence of *(1)* is also consistent with structure *(3)*. The [2:1]-adducts are present in minor amounts in the crude products of the reaction of *(1)* with TCNE, even on using twice the amount of *(1)*. Compounds of type *(2)* with oxygen instead of sulfur do not react with TCNE under comparable reaction conditions.

[*] Prof. Dr. K. Burger, Dr. H. Goth
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.



Procedure

A mixture of *(1)*[4] (10 mmol) and TCNE (1.28 g, 10 mmol) in anhydrous xylene (25 ml) is heated to 120 °C—130 °C (bath temperature) for 48 h under an atmosphere of N_2. After removal of the solvent by distillation *in vacuo*, the 4,4-bis(trifluoromethyl)-4*H*-1,3,5-thiadiazines *(3)* are obtained from the crystalline product mixture by fractional digestion with ligroin (fraction 90—110 °C).

Received: December 17, 1979 [Z 571 IE]
German version: Angew. Chem. 92, 836 (1980)

CAS Registry numbers:
(1a), 57014-95-6; *(1b)*, 57014-96-7; *(1c)*, 57014-98-9; *(3a)*, 75067-03-7; *(3b)*, 75067-04-8; *(3c)*, 75067-05-9; TCNE, 670-54-2

[1] *W. J. Middleton, R. E. Heckert, E. L. Little, C. G. Krespan*, J. Am. Chem. Soc. *80*, 2783 (1958); *D. N. Dhar*, Chem. Rev. *67*, 611 (1967).
[2] *R. M. Scribener, G. N. Sausen, W. W. Prichard*, J. Org. Chem. *25*, 1440 (1960); *J. E. Franz, R. K. Howe, H. K. Pearl, ibid. 41*, 620 (1976); *K. Burger, H. Schickaneder, M. Pinzel*, Justus Liebigs Ann. Chem. *1976*, 30.
[3] *H. C. Berk, J. E. Franz*, J. Org. Chem. *44*, 2395 (1979).
[4] *K. Burger, R. Ottlinger, J. Albanbauer*, Chem. Ber. *110*, 2114 (1977).
[5] Recordings: Jeol C 60 HL, 56.45 MHz; solvent: tetrahydrofuran; external standard: trifluoroacetic acid.
[6] a) *S. Meyerson, J. D. McCollum, P. N. Rylander*, J. Am. Chem. Soc. *83*, 1401 (1961); b) *K. Biemann*, Angew. Chem. *74*, 102 (1962); Angew. Chem. Int. Ed. Engl. *1*, 98 (1962); c) *H. Budzikiewicz, J. I. Brauman, C. Djerassi*, Tetrahedron *21*, 1855 (1965).

^{13}C-NMR Study of Protonated Thioketones in Superacidic Media: Significance of Mercaptocarbenium Ion Contributions[**]

By *George A. Olah, Tadashi Nakajima*, and *G. K. Surya Prakash*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In general, thioketones have been studied less thoroughly than the parent ketones[1], and only very few ^{13}C-NMR spectroscopic studies of the thiocarbonyl group have been reported[2,3].

We now wish to report the ^{13}C-NMR spectroscopic study of a series of thioketones *(1)*[2,4] and their protonation under superacidic conditions[5]. The chemical shifts obtained are tabulated in Table 1, along with those of their carbonyl analogues *(3)* and *(4)*. For comparison, we have also obtained ^{13}C chemical shifts of the hindered selenoketones *(5e)* and *(5g)*[6].

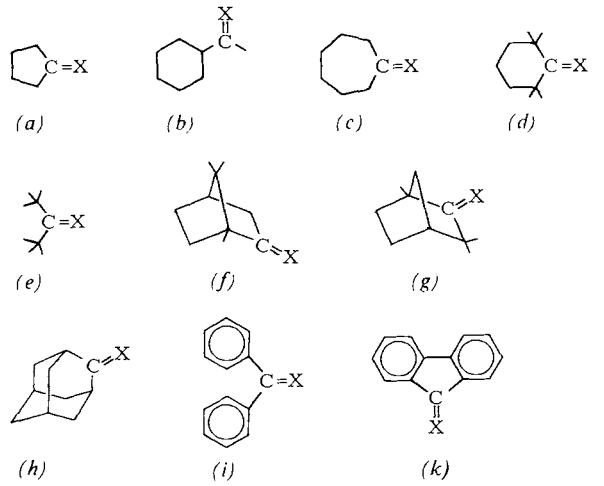
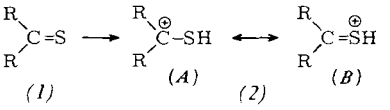


Table 1. ^{13}C-NMR data [a] of thioketones *(1)*, ketones *(3)*, selenoketones *(5)*, as well as thioketones *(2)* and ketones *(4)*.

Cpd. \ C=X	*(1)* C=S [b]	*(2)* C=S$^{\oplus}$H [c]	*(3)* C=O [b]	*(4)* C=O$^{\oplus}$H [c]	*(5)* C=Se [b]
(a)		285.0	215.5	260.5	
(b)	262.7	279.3	212.7	249.4	
(c)	261.4	282.7	205.8	253.4	
(d)	279.8	300.4	222.3	263.1	
(e)	279.8	298.5	216.0	259.4	291.4
(f)	273.2 [d]	284.4	216.7	253.8	
(g)	281.8	291.2	224.4	257.2	291.7
(h)	272.5	286.0	219.9	257.2	
(i)	240.1	228.0	195.2	211.9	
(k)	229.5	217.0	195.0	205.5	

[a] δ values tetramethylsilane external. [b] In $CDCl_3$ at room temperature. [c] In $FSO_3H:SbF_5/SO_2ClF$ or FSO_3H/SO_2ClF at −70 °C. [d] Cf. [3a].

In general, the thiocarbonyl carbon of *(1)* is deshielded by 35—63 ppm, compared to the analogous carbonyl carbon in *(3)* (this is valid for aromatic and aliphatic systems). The magnitude of the deshielding of the C=S$^{\oplus}$H atoms relative to the C=S atoms in *(1)* decreases dramatically in the case of protonated thioketones *(2)*. In fact, a shielding effect of *ca.* 12 ppm is observed for protonated aromatic thiocarbonyl carbons *(2i)* and *(2k)* relative to their neutral precursors *(1i)* and *(1k)*. This effect can be rationalized only by considering a significant mercaptocarbenium ion *(A)* contribution to the protonated thioketone structure, the resultant change in bond order causes a decrease in the deshielding effect. The shielding observed in the case of protonated aromatic thioketones *(2)* is due to the extensive charge delocalization[7] into the aromatic ring through the mercaptocarbenium ion form. In contrast, the contribution of hydroxycarbenium ion forms in related protonated ketones *(4)* is small[8].



[*] Prof. Dr. G. A. Olah, Dr. T. Nakajima, Dr. G. K. S. Prakash
Hydrocarbon Research Institute and Department of Chemistry
University of Southern California, University Park
Los Angeles, California 90007 (USA)

[**] Stable Carbocations, Part 227. Support of our work by the National Science Foundation is gratefully acknowledged. *G. A. O.* thanks the Alexander von Humboldt foundation for a senior U. S. Scientist Award which facilitated part of this work and Professor *P. v. R. Schleyer* for his hospitality and stimulating discussions.— For Part 226: *G. A. Olah, M. I. Watkins*, Proc. Natl. Acad. Sci. USA *77*, 703 (1960).

Attempted correlation of the ^{13}C chemical shifts of the corresponding thiocarbonyl carbons with those of carbonyl carbons shows only a very poor fit, demonstrating the importance of steric effects on the functionality. However, excellent correlations have been reported earlier in the case of relatively unhindered thioureas and thiocyanates, *etc.*[3b,c].

The strong deshielding of the thiocarbonyl carbon relative to the carbonyl carbon is rather interesting, considering the relative dipole moments of C=S and C=O bonds and relative electronegativities of sulfur and oxygen[9]. It has been argued that contributions to the paramagnetic term (σp) are responsible for such behavior[3]. The paramagnetic term σp is inversely proportional to the mean excitation energy (ΔE), and ΔE is considerably smaller for the >C=S bond than the >C=O bond. The above concept is also supported by the fact that thioketones *(1)* are more strongly colored, and $n\rightarrow\pi^*$ transitions occur at higher wavelengths than for ketones *(3)*[3]. However, π-electron densities[3c] obtained by simple Hückel molecular orbital calculations did not reproduce the ^{13}C chemical shift trend in thioureas.

This kind of deshielding effect appears to be even more pronounced in seleno ketones *(5)*. In fact, the ^{13}C chemical shifts of di-*tert*-butyl selenoketone *(5e)* and selenofenchone *(5g)* represent the most deshielded carbon shifts ever observed in neutral molecules. All our attempts to protonate selenocarbonyls under a variety of superacidic conditions failed, however, and resulted only in polymeric materials.

Thioketones containing α-hydrogen atoms tend to exist in their thioenolic form[1]; hence, it was necessary to obtain the spectra of cyclohexyl methyl thioketone *(1b)* and cycloheptanethione *(1c)* immediately after their synthesis. We were unable to record the chemical shift of cyclopentanethione *(1a)*, as it enolized rather rapidly. Protonation of such thioenols, however, also leads to protonated thioketones.

Received: April 22, 1980 [Z 572a IE]
German version: Angew. Chem. *92*, 837 (1980)

CAS Registry numbers:
(1b), 6007-67-6; *(1c)*, 75031-88-8; *(1d)*, 63702-84-1; *(1e)*, 54396-69-9; *(1f)*, 7519-74-6; *(1g)*, 875-06-9; *(1h)*, 23695-65-0; *(1i)*, 1450-31-3; *(1k)*, 830-72-8; *(2a)*, 75031-89-9; *(2b)*, 75031-90-2; *(2c)*, 75031-91-3; *(2d)*, 75031-92-4; *(2e)*, 75031-93-5; *(2f)*, 75031-94-6; *(2g)*, 75031-95-7; *(2h)*, 75031-96-8; *(2i)*, 75031-97-9; *(2k)*, 75031-98-0; *(3a)*, 120-92-3; *(3b)*, 823-76-7; *(3c)*, 502-42-1; *(3d)*, 1195-93-3; *(3e)*, 815-24-7; *(3f)*, 76-22-2; *(3g)*, 1195-79-5; *(3h)*, 700-58-3; *(3i)*, 119-61-9; *(3k)*, 486-25-9; *(4a)*, 64725-64-0; *(4b)*, 75031-99-1; *(4c)*, 75032-00-7; *(4d)*, 75032-01-8; *(4e)*, 18639-87-7; *(4f)*, 75032-02-9; *(4g)*, 75032-03-0; *(4h)*, 75032-04-1; *(4i)*, 25721-22-6; *(4k)*, 25721-28-2; *(5e)*, 56956-23-1; *(5g)*, 61849-83-0

[1] *R. Mayer, J. Morgenstern, J. Fabian*, Angew. Chem. *76*, 157 (1964); Angew. Chem. Int. Ed. Engl. *3*, 277 (1964).
[2] a) *J. B. Stothers:* Carbon-13 NMR Spectroscopy. Academic Press, New York 1972; b) *G. C. Levy, G. L. Nelson:* Carbon-13 Nuclear Magnetic Resonance for Organic Chemists. Wiley-Interscience, New York 1972; c) *E. Breitmaier, W. Voelter:* Carbon-13 NMR Spectroscopy. Verlag Chemie, Weinheim 1974.
[3] a) *P. V. Demarco, D. Doddrell, E. Wenkert*, Chem. Commun. *1969*, 1418; b) *H. O. Kalinowski, H. Kessler*, Angew. Chem. *86*, 43 (1974); Angew. Chem. Int. Ed. Engl. *13*, 90 (1974); c) Org. Magn. Reson. *6*, 305 (1974).
[4] a) *A. Ohno, K. Nakamura, Y. Nakazima, S. Oka*, Bull. Chem. Soc. Jpn. *48*, 2403 (1975); b) *C. P. Klages, J. Voss*, J. Chem. Res. *1977*, 1828.
[5] All thioketones were fully protonated in $FSO_3H:SbF_5/SO_2ClF$; the thiol protons gave ^1H-NMR signals at $\delta\approx 6.5$—7.0.
[6] *T. G. Beck, D. H. R. Barton, M. R. Britten-Kelly, F. Guziec, Jr.*, J. Chem. Soc. Perkin Trans. I, 2079 (1976).
[7] The chemical shifts of *ortho* and *para* carbons in *(2i)* and *(2k)* were observed around $\delta = 145$ and 138, respectively; *i.e.*, they are significantly deshielded relative to those of the thioketones *(1i)* and *(1k)*.
[8] *G. Liang*, Ph. D. Dissertation, Case Western Reserve University 1973.
[9] *M. Karplus, T. P. Das*, J. Chem. Phys. *34*, 1683 (1961).

Thiobenzoyl Cations[**]

By *George A. Olah, G. K. Surya Prakash,* and *Tadashi Nakajima*[*]

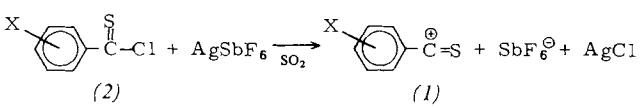
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In contrast to extensive chemical and spectroscopic investigations[1] on acyl cations, thioacyl cations have so far remained practically unexplored although they were postulated as intermediates in the Friedel-Crafts reactions of thiobenzoyl and thioamidoyl chlorides, *O*-aryl chloro(thioformates) and *S*-alkyl and *S*-aryl chloro(thioformates) with benzene[2]. The only synthesis of thioacyl cation was reported by *Lindner* and *Karmann*[3] in 1968, who prepared the thiobenzoyl hexafluoroantimonate from the reaction of thiobenzoyl chloride and silver hexafluoroantimonate in SO_2 solution. Although no conclusive spectral data were obtained for the thiobenzoyl cation *(1a)*, the structure was indicated by the CS vibrational stretching in its IR spectrum at 1332 cm^{-1} (shifted considerably from that of its precursor thiobenzoyl chloride *(2a)* at 1250 cm^{-1}), by conductivity measurements and its ability to thiobenzoylate benzene to the corresponding thiobenzophenone. *Lindner* and *Karmann*[3] also stated "the $[C_6H_5CS]^{\oplus}$ cation can thus be said to exist mainly in two mesomeric limiting forms, which have approximately equal importance so that the mean bond order for G—S is 2.5."



In continuation of our study of acyl cations we now wish to report the preparation and ^{13}C-NMR characterization of the parent *(1a)* and a series of substituted thiobenzoyl cations *(1b)*—*(1g)*. Attempts[4] to generate thioacyl cations *via* cleavage of protonated alkyl and aryl dithioesters and dithioacids under a variety of superacidic conditions were unsuccessful. Some of the protonated dithioacids were found to be stable up to 100 °C in the superacidic media[4a].

Although thiobenzoyl chlorides are well characterized in the literature[5], the corresponding aliphatic counterparts are still unknown, except for perfluorinated analogues. Hence our research effort was directed to the generation of thiobenzoyl cations *(1)* from the readily available[5] thiobenzoyl chlorides. Experiments carried out to generate the thiobenzoyl cation *(1a)* by ionizing thiobenzoyl chloride either in $FSO_3H:SbF_5/SO_2$ or SbF_5/SO_2 solution were unsuccessful and resulted in a complex mixture (according to ^{13}C-NMR spectra). Application of the metathetic silver salt method[1] of preparation of acylium salts, also utilized by *Lindner* and *Karmann*[4], turned out to be of general utility for generating thiobenzoyl cations. The thiobenzoyl chloride *(2)*[5b] was treated with a tenth molar excess of freshly prepared silver hexafluoroantimonate in SO_2 solution at −78 °C. Warming the solution to −20 °C effected precipitation of silver chloride and led to a burgundy colored solution.



(2) *(1)*

[*] Prof. Dr. G. A. Olah, Dr. T. Nakajima, Dr. G. K. S. Prakash
Hydrocarbon Research Institute
University of Southern California, University Park
Los Angeles, California 90007 (USA)

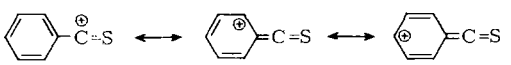
[**] Stable Carbocations, Part 229. Support of this work by the National Institutes of Health and National Science Foundation is gratefully acknowledged.—Part 228: *G. A. Olah, G. K. S. Prakash, A. L. Berrier, G. Liang*, Nouveau J. Chim., in press.

Table 1. ^{13}C-NMR chemical shifts [a] of substituted thiobenzoyl cations *(1)* in SO_2 at −65 °C.

Cation	X	$-\overset{\oplus}{C}=S$	C-1	C-2	C-3	C-4	C-5	C-6	Others
(1b)	4-OCH_3	198.3	103.1	146.6	119.1	173.8	119.1	146.6	CH_3 = 58.7
(1c)	4-CH_3	198.3	109.6	143.3	133.1	161.70	133.1	142.3	CH_3 = 24.8
(1d)	2-CH_3	197.2	113.4	158.5	133.4	145.4	129.4	143.5	CH_3 = 21.8
(1a)	H	195.5	113.1	143.3	131.8	145.3	131.8	143.3	
(1e)	4-Cl	195.1	111.6	144.0	132.7	153.2	132.7	144.0	
(1f)	4-F	195.5	109.8	147.8 *J*(C—C—C—F) = 13.7 Hz	121.0 *J*(C—C—F) = 22.4 Hz	173.2 *J*(C—F) = 279.3 Hz	121.0 *J*(C—C—F) = 22.4 Hz	147.8 *J*(C—C—C—F) = 13.7 Hz	
(1g)	4-CF_3	191.8	115.9	143.7	127.8	161.6 *J*(C—C—F) = 37.0 Hz	127.8	143.7	CF_3 = 122.2 *J*(C—F) = 271.0 Hz

[a] δ values, TMS as external standard.

The 20 MHz ^{13}C-NMR spectrum of the solution of *(1a)* was distinctly different from that of thiobenzoyl chloride *(2a)*[6]. In the spectrum the thiocarbonyl peak of *(1a)* was observed at δ 195.5, about 6.5 ppm more shielded relative to that in the chloride *(2a)*[5b]. This observation, together with the remarkable upfield shift of C-1 [$\approx$30 ppm relative to *(2)*] as well as substantial deshielding of C-2,6 and C-4, clearly proves the formation of thiobenzoyl cation *(1a)* with considerable delocalization of positive charge into the aryl ring through thioketene-like resonance forms. Comparing the observed chemical shifts to those of the benzoyl cation[1] shows similarities between the species, but the carbonyl carbon and C-1 are shielded by 51 and 25 ppm in *(1a)*. The deshielding of the thiocarbonyl carbon relative to the carbonyl carbon is readily rationalized by contributions from paramagnetic terms[7] as well as by the lack of contribution of the sulfonium type form ($C_6H_5C\equiv\overset{\oplus}{S}$) in the thiobenzoyl cation *(1a)*.



(1a)

We also prepared a series of thiobenzoyl cations *(1b)*—*(1g)* with both electron releasing and electron withdrawing substituents on the aryl ring. Their ^{13}C-NMR data are summarized in Table 1. The chemical shift of the thiocarbonyl carbon ranges from δ 198.3 for *(1b)* and *(1c)* to δ 191.8 for *(1g)* (a range of 7.5 ppm). A larger spread of 12 ppm is observed for the shift of C-1. However, it is apparent[8] that there is no linear correlation of thiocarbonyl carbon chemical shifts with the σ^+ substituent parameters of the substituent on the aryl ring. Even in the case of *para*-fluoro and *para*-chloro substituents [*(1f)* and *(1e)*], there is significant stabilization of the positive charge through back donation of the halogen atoms *via para*-quinonoid forms in accordance with the significance of thioketene-like forms.

Our present ^{13}C-NMR spectroscopic study constitutes the first structural characterization of thiobenzoyl cations under long-lived stable ion conditions. The study shows that contribution of thioketene-like resonance forms to the thiobenzoyl cation structure is significant, whereas, in contrast to benzoyl cations, the sulfonium ion type involvement is negligible.

Received: April 22, 1980 [Z 572b IE]
German version: Angew. Chem. 92, 838 (1980)

CAS Registry numbers:
(1a), 45582-58-9; *(1b)*, 75031-82-2; *(1c)*, 75031-83-3; *(1d)*, 75031-84-4; *(1e)*, 75031-85-5; *(1f)*, 75031-86-6; *(1g)*, 75031-87-7

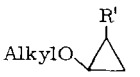
[1] *G. A. Olah, A. Germain, A. M. White* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Vol. 5. Wiley-Interscience, New York 1976, pp. 2049 ff.
[2] *H. Viola, S. Scheithauer, R. Mayer*, Chem. Ber. *101*, 3517 (1968).
[3] *E. Lindner, H. G. Karmann*, Angew. Chem. *80*, 567 (1968); Angew. Chem. Int. Ed. Engl. *7*, 548 (1968).
[4] a) *G. A. Olah, A. T. Ku*, J. Org. Chem. *35*, 331 (1970); b) *G. A. Olah, A. T. Ku, A. M. White, ibid. 34*, 1827 (1969).
[5] a) *K. T. Potts, C. Sapino* in *S. Patai:* The Chemistry of Acyl Halides. Wiley-Interscience, New York 1952, pp. 350 ff.; b) *R. Mayer, S. Scheithauer*, Chem. Ber. *98*, 1418 (1965).
[6] Thiobenzoyl chloride *(2a)*, ^{13}C-NMR ($CDCl_3$): δ = 202.3 (C=S), 142.8 (C-1), 132.7 (C-2,6), 132.4 (C-4), 130.5 (C-3,5).
[7] a) *P. V. Demarco, D. Doddrell, E. Wenkert*, Chem. Commun. *1969*, 1418; b) *H. O. Kalinowski, H. Kessler*, Angew. Chem. *86*, 43 (1974); Angew. Chem. Int. Ed. Engl. *13*, 90 (1974); c) Org. Magn. Reson. *6*, 305 (1974); d) *G. A. Olah, T. Nakajima, G. K. S. Prakash*, Angew. Chem. *92*, 837 (1980); Angew. Chem. Int. Ed. Engl. *19*, 811 (1980).
[8] Considering the similarities of ^{13}C chemical shifts of thiocarbonyl carbon with a wide variety of substituted cations *(1)*.

Donor-Acceptor Substituted Cyclopropanes: Synthesis and Ring Opening to 1,4-Dicarbonyl Compounds[**]

By *Hans-Ulrich Reissig* and *Elisabeth Hirsch*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Cyclopropanes are playing an increasingly important role in the synthesis of carbon skeletal structures[1]. A survey of the utility of "oxycyclopropanes" *(1)* and *(2)* has recently been published[2]. The donor-acceptor substituted cyclopropanes *(2)*, which are obtained from diazocarbonyl compounds and alkylenol ethers, and which, as masked 1,4-dicarbonyl compounds, are valuable precursors for the synthesis of cyclopentane, furan, and lactone systems, would appear to be especially versatile.



(1), R' = Alkyl, H
(2), R' = $CO_2C_2H_5$, COAlkyl

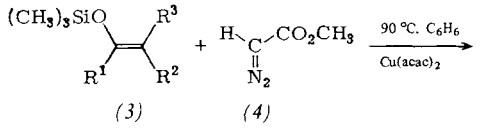
However, the scope of application of *(2)* is limited by the following disadvantages: 1. The alkylenol ethers required for synthesis of *(2)* are frequently only obtained under drastic conditions (usually acetal pyrolysis at 160—200 °C) and without regioselectivity; 2. the yield of *(2)* is only about 50%; 3. the ring-opening must be performed in strong acid medium (1 M or conc. hydrochloric acid).

Silylenol ethers *(3)*, on the other hand, are often regioselectively accessible by comparatively mild methods[3]. We obtained the siloxy-substituted cyclopropanes in good, synthetically useful yields by copper salt-catalyzed cyclopropanation of *(3)* with methyl diazoacetate *(4)* (Table 1)[4]. The

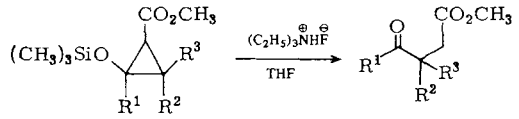
[*] Dr. H.-U. Reissig, E. Hirsch
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

small amounts of dimers formed from methoxycarbonylcarbene—dimethyl fumarate and maleate—could easily be removed by filtration through aluminum oxide.



(3) (4)



(5) (6)

Table 1. Synthesized methyl siloxycyclopropanecarboxylates *(5)* and methyl 4-oxoalkanoates *(6b)*.

	R¹	R²	R³	Yield [%] [b]	*(5)* [a] B.p. [°C/torr] [c]	*(6)* Yield [%] [b]
a	*t*-C₄H₉	H	H	87	65/0.1	83
b	H	CH₃	CH₃	66	80/20	89
c	H	—(CH₂)₄—		58	80/0.05	80
d	H	—(CH₂)₅—		75	100/0.05	93
e	—(CH₂)₃—		H	71	70/0.01	80
f	—(CH₂)₄—		H	75	90/0.01	83
g	—(CH₂)₅—		H	76	100/0.01	78
h	—(CH₂)₄—		OSi(CH₃)₃	55	100/0.01	67 [d] R³ = OH

[a] *cis/trans* Mixture. [b] Yields isolated after bulb-to-bulb distillation; all the new compounds gave satisfactory elemental analyses and characteristic spectra. [c] Bath temperature. [d] Yields of crude product (NMR spectroscopically pure).

The removal of the trimethylsilyl group with ring opening of the cyclopropane to give the 1,4-dicarbonyl compounds *(6)* could be achieved smoothly with fluoride ions[5] under essentially neutral conditions. *(6)* is most conveniently liberated by the readily accessible triethylammonium fluoride[6]. This gentle method (1 h, 25 °C, tetrahydrofuran) also enables straightforward synthesis of the aldehyde esters *(6b—d)* and of the alcohol *(6h)*.

Procedure

(5): A solution of methyl diazoacetate *(4)* (1.28 g, 12.8 mmol) in anhydrous benzene (50 ml) is added dropwise in 3 h to a suspension of copper(II) pentanedionate in *(3a)* (2.00 g, 11.6 mmol) kept at 90 °C. After cooling and removal of solvent the residue is dissolved in pentane and filtered through 35 g aluminum oxide (neutral, activity grade III). On evaporation of the eluate there remains 2.58 g (91%) *(5a)* as a colorless, NMR spectroscopically pure oil. Bulb-to-bulb distillation at 65 °C/0.1 torr furnishes 2.47 g (87%) of analytically pure *(5a)*.

Received: March 24, 1980 [Z 573 IE]
German version: Angew. Chem. *92*, 839 (1980)

CAS Registry numbers:
(3a), 17510-46-2; *(3b)*, 6651-34-9; *(3c)*, 60484-91-5; *(3d)*, 53282-55-6; *(3e)*, 19980-43-9; *(3f)*, 6651-36-1; *(3g)*, 22081-48-7; *(3h)*, 6838-67-1; *(4)*, 6832-16-2; *cis-(5a)*, 75032-05-2; *trans-(5a)*, 75032-06-3; *cis-(5b)*, 75032-07-4; *trans-(5b)*, 75032-08-5; *cis-(5c)*, 75032-09-6; *trans-(5c)*, 75032-10-9; *cis-(5d)*, 75045-86-2; *trans-(5d)*, 75032-11-0; *cis-(5e)*, 75032-12-1; *trans-(5e)*, 75081-68-4; *cis-(5f)*, 75032-13-2; *trans-(5f)*, 75081-69-5; *cis-(5g)*, 75032-14-3; *trans-(5g)*, 75081-70-8; *cis-(5h)*, 75032-15-4; *trans-(5h)*, 75081-71-9; *(6a)*, 34553-32-7; *(6b)*, 52398-45-5; *(6c)*, 75032-16-5; *(6d)*, 75032-17-6; *(6e)*, 4934-95-6; *(6f)*, 13672-64-5; *(6g)*, 75032-18-7; *(6h)*, 75032-19-8; *(6h)*, (R³ = OH), 75032-20-1

[1] Review: *R. V. Stevens*, Acc. Chem. Res. *10*, 193 (1977); *S. Danishefsky*, *ibid. 12*, 66 (1979); *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979), and references cited therein.
[2] *E. Wenkert*, Acc. Chem. Res. *13*, 27 (1980).
[3] *G. Stork*, *P. F. Hudrlik*, J. Am. Chem. Soc. *90*, 4462, 4464 (1967); *H. O. House*, *L. J. Czuba*, *M. Gall*, *H. D. Olmsted*, J. Org. Chem. *34*, 2324 (1969); for new methods see *R. D. Miller*, *D. R. McKean*, Synthesis *1979*, 730; *G. A. Olah*, *B. G. B. Gupta*, *S. C. Narang*, *R. Malhotra*, J. Org. Chem. *44*, 4272 (1979), and references cited therein.
[4] The reactions of *(3a)* and *(3f)* with ethyl diazoacetate did not afford the cyclopropanes, but directly the corresponding γ-keto esters: *R. LeGoaller*, *J.-L. Pierre*, C. R. Acad. Sci. *C 276*, 193 (1973); the publication does not contain any experimental details.
[5] First synthetic utilization of the high affinity of the fluoride ion towards silicon: *E. J. Corey*, *A. Venkateswarlu*, J. Am. Chem. Soc. *94*, 6190 (1972).
[6] *S. Hünig*, *G. Wehner*, Synthesis *1975*, 180.

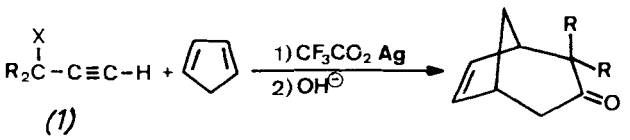
Competing [3+4]- and [2+4]-Cycloadditions of Allenyl Cations[**]

By *Herbert Mayr* and *Inge K. Halberstadt*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The number of synthetic applications of cationic cycloadditions is steadily increasing. Whereas [3+4]-cycloadditions[1] of allyl cations are already one of the most widely used synthetic approaches to seven-membered carbocycles[2], the first [2+2]-cycloaddition of a solvolytically generated vinyl cation to cyclohexene has only just been accomplished[3]. The acid catalyzed cyclodimerization of acetylenes and allenes to give cyclobutanes also proceeds *via* vinyl cations[4].

We recently demonstrated the formation of [3.2.1]bicyclic compounds by treatment of propargyl halides *(1)* and cyclopentadiene with equimolar amounts of silver trifluoroacetate; this reaction was rationalized in terms of [3+4]-cycloadditions of intermediate allenyl cations[5].



(1)

R = H, CH_3

We now report that trisubstituted allenyl cations can be generated more easily from propargyl halides *(3)* and catalytic amounts of zinc chloride; the type of cycloaddition depends upon the nature of the substituents.

Vinyl halides *(2a, b)* and *(4c—h)* were obtained in 20—65% yield from propargyl halides *(3a—h)* and cyclopentadiene (molar ratio 1:1—2) at −30 to −50 °C in the presence of zinc chloride-ether, a complex soluble in dichloromethane (Table 1). Apart from higher-molecular-weight compounds, the only side products observed were enynes *(9)* and *(10)* arising from hydrogen chloride elimination from *(3e)* and *(3h)*. Spontaneous increase of temperature could not be avoided when the reactions were carried out under heterogeneous conditions (suspension of zinc chloride in dichloromethane) and only traces of the addition products could be isolated.

The bicyclooctadienes *(2)* have ^{1}H- and ^{13}C-NMR spectra similar to 3-chloro-4,4-dimethyl-bicyclo[3.2.1]octa-2,6-

[*] Dr. H. Mayr, I. K. Halberstadt
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[**] Presented at the 1st European Symposium on Organic Chemistry, Cologne, August 1979. This work was supported by the Deutsche Forschungsgemeinschaft.

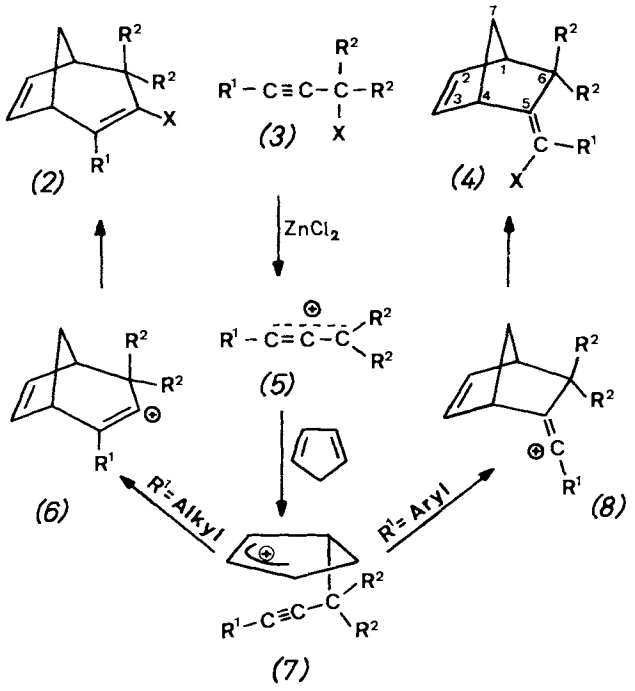
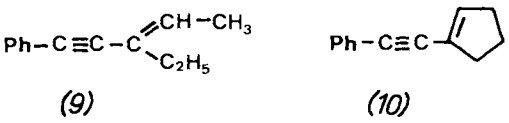


Table 1. Addition products *(2)* and *(4)* of propargyl halides *(3)* to cyclopentadiene [a].

	R^1	R^2		Yield [%] *(2)*	Yield [%] *(4)*	B.p. [°C/torr] [b] M.p. [°C]
a	CH_3	CH_3	Cl	36	—	37/0.05
b	C_2H_5	CH_3	Cl	28	—	90—95/15
c	C_6H_5	CH_3	Cl	—	65	79—80
d	C_6H_5	CH_3	Br	—	24	81.5—82.5
e [c]	C_6H_5	C_2H_5	Cl	—	35	110—115/0.02
f	*p*-$MeOC_6H_4$	CH_3	Cl	—	38	74—75.5
g	*p*-BrC_6H_4	CH_3	Cl	—	40	101—102
h [d]	C_6H_5	[e]	Cl	—	20	77—78.5

[a] Reaction products confirmed by IR, NMR, MS, and CH analyses. [b] Bath temperature. [c] Side product: 4% *(9)*. [d] Side product: 7% *(10)*. [e] $-R^2-R^2- = -(CH_2)_4-$.

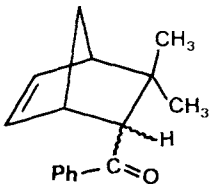
diene[5]. Whereas the two bridgehead protons of both *(2a)* and *(2b)* show similar chemical shifts ($\delta = 2.48$—2.63), H-4 is considerably more deshielded than H-1 in the norbornenes *(4)* (Table 2). The significant upfield shift of one methyl



(9) *(10)*

group in the 5-(α-halobenzylidene)-6,6-dimethylnorbornenes *(4)* indicates the presence of the (*E*)-isomers; steric interactions prevent a coplanar arrangement of the phenyl group with the exocyclic double bond so that one methyl group moves into the positive shielding zone of the benzene ring[6]. Reaction of *(4c)* with silver trifluoroacetate in boiling ether and alkaline work-up affords *exo*- and *endo*-*(11)* with a carbonyl band at 1670 cm^{-1}.

We propose that the propargyl halides *(3)* initially dissociate under the influence of zinc chloride to give the allenyl cations *(5)*. Cyclopentadiene then attacks the sp^2 carbon of *(5)*, forming the cyclopentenyl cation *(7)* which cyclizes to the vinyl cations *(6)* or *(8)*. A concerted mechanism with unequal extent of bond formation in the transition state is also conceivable. Addition of a halide ion gives the vinyl chlo-



(11)

Table 2. ^{1}H-NMR chemical shifts (δ values) of the benzylidenenorbornenes *(4)* in CCl_4.

	H-1	H-2, H-3	H-4	H-7a	H-7b	6-CH_3
(4c) [a]	2.41	6.27	3.89	1.55	1.85	0.68, 1.09
(4d)	2.47	6.25	3.83	1.53	1.90	0.66, 1.09
(4e)	2.85	6.24	3.87	masked		—
(4f)	2.41	6.23	≈3.80	1.54	1.86	0.69, 1.11
(4g) [a]	2.41	6.20	3.81	1.53	1.82	0.67, 1.08
(4h)	2.53	6.23	3.87	masked		—

[a] In $CDCl_3$.

rides *(2)* and *(4)*; *(8)* is selectively attacked from the sterically less hindered side, resulting in the exclusive formation of *(E)-(4)*.

According to force-field calculations, bicyclo[3.2.1]octa-2,6-diene [type *(2)*] is 9 kcal/mol more stable than the isomeric 5-methylene-2-norbornene [type *(4)*][7]. This energy difference is responsible for the formation of the cyclic vinyl cation *(6)* when R^1 = alkyl even though the ideal geometry of the vinyl cation fragment cannot be achieved[8]. In contrast, an aryl group R^1 directly attached to the cationic center stabilizes *(8)* to such an extent that the higher strain energy of the norbornene is overcompensated.—The formation of *(4)* cannot be due to isomerization of *(3)* to haloallenes which then might undergo Diels-Alder reaction with cyclopentadiene: non-activated allenes do not react with 1,3-dienes at low temperatures[9]. Furthermore, 3-chloro-3-methyl-1-butyne does not undergo zinc chloride-catalyzed reaction with cyclopentadiene but yields 1-chloro-3-methyl-1,2-butadiene, which is stable under these conditions.

Procedure

$ZnCl_2$ (1.2 g) was dissolved in ether (1.5 ml), diluted with CH_2Cl_2 (30 ml), and cooled to −40 °C. A solution of *(3f)* (5.2 g, 25.0 mmol) and cyclopentadiene (1.65 g, 25.0 mmol) in CH_2Cl_2 (20 ml) was added dropwise with stirring. After 1 h (−40 °C) the catalyst was washed out with conc. aqueous ammonia and the organic phase was dried over $CaCl_2$. Filtration over silica gel (10 g) afforded *(4f)* (2.62 g, 38%) as NMR-pure oil which crystallized from a solution in light petroleum on scratching (colorless prisms).

Received: February 29, 1980 [Z 575 IE]
German version: Angew. Chem. *92*, 840 (1980)

CAS Registry numbers:
(2a), 75111-02-3; *(2b)*, 75111-03-4; *(3a)*, 999-79-1; *(3b)*, 17553-39-8; *(3c)*, 3355-29-1; *(3d)*, 75111-04-5; *(3e)*, 75111-05-6; *(3f)*, 75111-06-7; *(3g)*, 75111-07-8; *(3h)*, 75111-08-9; *(E)-(4c)*, 75111-09-0; *(E)-(4d)*, 75111-10-3; *(E)-(4e)*, 75111-11-4; *(E)-(4f)*, 75111-12-5; *(E)-(4g)*, 75111-13-6; *(E)-(4h)*, 75111-14-7; *(9)*, 75111-15-8; *(10)*, 55110-61-7; endo-*(11)*, 75111-16-9; exo-*(11)*, 75111-17-0; cyclopentadiene, 542-92-7

[1] Ring size classification according to *Huisgen: R. Huisgen*, Angew. Chem. *80*, 329 (1968); Angew. Chem. Int. Ed. Engl. *7*, 321 (1968).
[2] *H. M. R. Hoffmann*, Angew. Chem. *85*, 877 (1973); Angew. Chem. Int. Ed. Engl. *12*, 819 (1973); *D. I. Rawson, B. K. Carpenter, H. M. R. Hoffmann*, J. Am. Chem. Soc. *101*, 1786 (1979), and references cited therein.
[3] *G. Hammen, M. Hanack*, Angew. Chem. *91*, 649 (1979); Angew. Chem. Int. Ed. Engl. *18*, 614 (1979).
[4] *K. Griesbaum*, Angew. Chem. *81*, 966 (1969); Angew. Chem. Int. Ed. Engl. *8*, 933 (1969) and later publications.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1010-0815 $ 02.50/0*

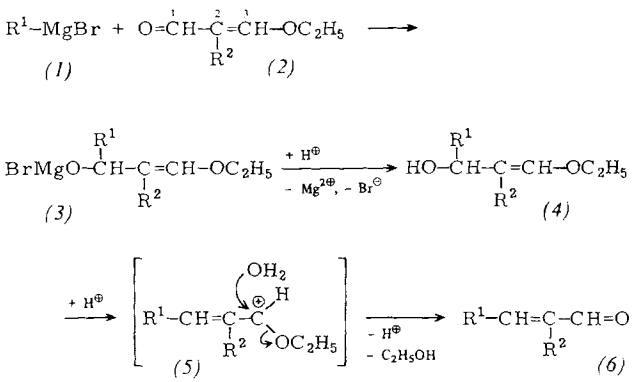
[5] *H. Mayr, B. Grubmüller*, Angew. Chem. *90*, 129 (1978); Angew. Chem. Int. Ed. Engl. *17*, 130 (1978).
[6] The (*E*)-configuration also follows from the chemical shift of H-4, as demonstrated by comparison of similar (*E*)- and (*Z*)-isomers: *H. Mayr*, unpublished.
[7] Calculated according to *N. L. Allinger*, MMI Molecular Mechanics, QCPE Program No. 318. Indiana University, Bloomington, Indiana 1975. We thank *D. Wilhelm* performing the calculations.
[8] *W. D. Pfeifer, C. A. Bahn, P. v. R. Schleyer, S. Bocher, C. E. Harding, K. Hummel, M. Hanack, P. J. Stang*, J. Am. Chem. Soc. *93*, 1513 (1971); *E. Lamparter, M. Hanack*, Chem. Ber. *105*, 3789 (1972).
[9] *H. Pledger, Jr.*, J. Org. Chem. *25*, 278 (1960).

Oxopropenylation of Grignard Compounds with 3-Ethoxyacroleins[**]

By *Klaus Rustemeier* and *Eberhard Breitmaier*[*]

Dedicated to Professor Rudolf Tschesche on the occasion of his 75th birthday

3-Ethoxyacroleins *(2)* are versatile C_3 building blocks, especially in heterocyclizations[1]. We have now found that they are suitable in a general way for the introduction of the oxopropenyl moiety. For this purpose they are allowed to react with an alkyl, aryl, or heteroarylmagnesium bromide *(1)*; after work-up in acid solution one obtains the corresponding α,β-unsaturated aldehydes *(6)* in yields between *ca.* 30 and 60% (Table 1). Comparable reactions with enols[2a], with enol ethers[2b], and with open-chain enamino aldehydes[2c] have already been described.



That the oxopropenylation proceeds *via* the alcohol *(4)* is supported by the isolation of the intermediates *(4x)* and *(4y)* (R^1 = 2-pyridyl, R^2 = methyl or ethyl), which are stabilized by an intramolecular hydrogen bond. The hydrolysis of the alcohol *(4)* to the aldehyde *(6)* on heating in 2 N sulfuric acid is almost quantitative. The alcohol *(4)* can also be detected NMR spectroscopically in the product mixture obtained on gentle hydrolysis of other Grignard reagents *(3)* (*e.g.* in ice-cold ammonium chloride solution).



The compounds *(6)* synthesized were identified by elemental analysis, ^{1}H- and ^{13}C-NMR spectroscopy, and by mass spectrometry. Compounds *(6)* are found to exist in the *E*-form, though the isopropyl-substituted compounds, in particular, contain small amounts of the *Z*-form (NMR data).

Procedure

(1): 2 g of magnesium turnings are covered with 20 ml of the solvent quoted in Table 1. 0.055 mol of the bromide is then added dropwise, such that the solution constantly boils. After addition of the total amount of bromide the solution is boiled under reflux for a further 30 min and then allowed to cool.

(6): The solution of *(1)* is added dropwise with stirring to an ice-cooled solution of *(2)* (0.05 mol) in diethyl ether (100 ml). The mixture is stirred for 2 h at room temperature, cooled with ice and then treated dropwise in the cold with

Table 1. 3-Alkyl-, 3-aryl-, and 3-heteroarylacroleins *(6)*; physical data and yields. *(1)* is generated with stoichiometric amounts of R^1Br.

(6)	Solvent [a]	R^1	R^2	B.p. [°C/torr]	M.p. [°C] (solvent)	Yield [%] [b]	Ref.
a	Et_2O	Phenyl	Me	64—65/0.5		52	[3]
b			Et	62—64/0.1		45	[4]
c			*i*Pr	77—78/0.2		49	[5]
d			*n*Pr	79/0.5		49	[4]
e	THF/Et_2O	*p*-Methoxyphenyl	Me	101—102/0.1		42	[6]
f			Et	102—104/0.1		40	[6]
g			*i*Pr	114—115/0.2		42	
h			*n*Pr	110—115/0.05		39	
i	THF/Et_2O	*p*-Biphenylyl	Me	140—145/0.05	79 (*n*-hexane)	56	
j			Et	145—150/0.05	78 (ligroin)	53	
k			*i*Pr	150—160/0.05	75—78 (ligroin)	55	
l			*n*Pr	160—170/0.1		45	
m	THF/Et_2O	2-Thienyl	Me	92—93/0.2		40	
n			Et	84—85/0.1		49	
o			*i*Pr	92—94/0.2		39	
p			*n*Pr	85/0.05		48	
q	THF/Et_2O	α-Naphthyl [c]	Me	120—121/0.07	52—58 (ligroin)	52	
r			Et	124—128/0.05	44—51 (ligroin)	42	
s	THF	Styryl	Me	108—110/0.05	58 (MeOH/H_2O)	28	[7]
t	Et_2O	*n*-Butyl	Me	64—65/15		56	[8]
u		*n*-Pentyl	Me	84—85/15		39	[9]
v		*n*-Hexyl	Me	98—100/15		41	[10]
w		*n*-Octyl	Me	124/15		50	
x	THF	2-Pyridyl	Me	70—72/0.2	39	50	
y			Et	71—73/0.2	Oil	54	

[a] Solvent in the Grignard reaction. THF/Et_2O: tetrahydrofuran: diethyl ether 3:2. [b] Referred to initial amount of *(2)*. Yields referred to *(2)* consumed are on average 20% higher. [c] The commercial α-naphthyl bromide used in the reaction contained about 20% of the β-isomer.

[*] Prof. Dr. E. Breitmaier, Dipl.-Chem. K. Rustemeier
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

1 N sulfuric acid (60 ml). The organic phase is washed with saturated sodium hydrogen carbonate and dried over magnesium sulfate. After removal of solvent *in vacuo* the residue is distilled and the distillate redistilled or recrystallized.

(1), R^1 = 2-pyridyl: A small amount of ethyl bromide is added to 5 g magnesium turnings in 20 ml tetrahydrofuran. As soon as reaction commences a solution of 5 g ethyl bromide and 16 g 2-bromopyridine in 100 ml tetrahydrofuran is added dropwise such that the mixture just boils. After completion of addition the mixture is heated for a further 2 h under reflux and then allowed to cool.

(4x, y): A solution of *(1)*, R^1 = 2-pyridyl, is added dropwise to an ice-cold solution of *(2)* (0.15 mol) in diethyl ether (150 ml) and the mixture is stirred at room temperature for 2 h. The ice-cold product mixture is then hydrolyzed with 100 ml 2 N sulfuric acid. The organic phase is separated off and washed twice with a little 2 N sulfuric acid. The combined acid extracts are rended alkaline with ammonia and extracted with ether. After removal of ether from the extract the residue is distilled and finally recrystallized. The almost colorless tabular crystals of *(4x)* and *(4y)* are stable for long periods only when stored in a refrigerator; b.p. 98 °C/0.05 torr and 100—105 °C/0.40 torr, m.p. 51 °C and 42 °C, yield 50 and 54%, respectively.

(6x, y): *(4x, y)* is dissolved in 2 N sulfuric acid and heated to 50 °C with stirring for 2 h. After addition of aqueous ammonia until alkaline and subsequent extraction with ether, *(6x)* and *(6y)* can be isolated almost quantitatively. Crystalline *(6x)* is stable for some time at room temperature, while *(6y)* solidifies only when stored in the refrigerator, and rapidly decomposes on heating.

Received: March 4, 1980 [Z 576 IE]
German version: Angew. Chem. 92, 841 (1980)

CAS Registry numbers:
(1) (R' = Ph), 108-86-1; *(1)* (R' = *p*-methoxyphenyl), 104-92-7; *(1)* (R' = *p*-biphenylyl), 92-66-0; *(1)* (R' = thienyl, 1003-09-4; *(1)* (R' = α-naphthyl), 90-11-9; *(1)* (R' = styryl), 103-64-0; *(1)* (R' = *n*-butyl), 109-65-9; *(1)* (R' = *n*-pentyl), 110-53-2; *(1)* (R' = *n*-hexyl), 111-25-1; *(1)*, (R' = *n*-octyl), 111-83-1; *(1)* (R' = 2-pyridyl), 109-04-6; *(2)* (R^2 = Me), 42588-57-8; *(2)* (R^2 = Et), 30989-75-4; *(2)* (R^2 = *i*-Pr), 30989-77-6; *(2)* (R^2 = *n*-Pr), 21037-71-8; *(E)-(6a)*, 15174-47-7; *(E)-(6b)*, 1755-45-9; *(E)-(6c)*, 75101-96-1; *(Z)-(6c)*, 75101-97-2; *(E)-(6d)*, 75101-98-3; *(E)-(6e)*, 75101-99-4; *(E)-(6f)*, 75102-00-0; *(E)-(6g)*, 75102-01-1; *(Z)-(6g)*, 75102-02-2; *(E)-(6h)*, 75102-03-3; *(E)-(6i)*, 75102-04-4; *(E)-(6j)*, 75102-05-5; *(E)-(6k)*, 75102-06-6; *(Z)-(6k)*, 75102-07-7; *(E)-(6l)*, 75102-08-8; *(E)-(6m)*, 63283-77-2; *(E)-(6n)*, 75102-09-9; *(E)-(6o)*, 75102-10-2; *(Z)-(6o)*, 75102-11-3; *(E)-(6p)*, 75102-12-4; *(E)-(6q)*, 75102-13-5; *(E)-(6r)*, 75102-14-6; *(E)-(6s)*, 75102-15-7; *(E)-(6t)*, 56161-68-3; *(E)-(6u)*, 49576-57-0; *(E)-(6v)*, 69625-48-5; *(E)-(6w)*, 75102-16-8; *(E)-(6x)*, 75102-17-9; *(E)-(6y)*, 75102-18-0

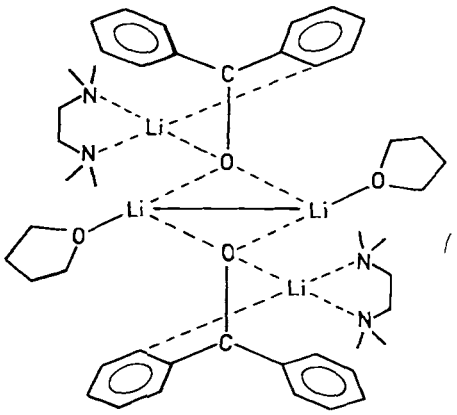
[1] Cf. *e.g. G. Mühmel, E. Breitmaier*, Angew. Chem. *90*, 818 (1978); Angew. Chem. Int. Ed. Engl. *17*, 772 (1978).
[2] a) *A. S. Dreiding, S. N. Nickel*, J. Am. Chem. Soc. *76*, 3965 (1964); b) *G. P. Mueller, C. B. Honaker, ibid. 73*, 2377 (1951); *S. D. Gupte, S. V. Sunthankar*, J. Org. Chem. *24*, 1334 (1959); c) *C. Jutz*, Chem. Ber. *91*, 1867 (1958).
[3] *V. Miller, Kinkelin*, Ber. Dtsch. Chem. Ges. *19*, 526 (1886).
[4] *P. Shoruigin, V. Isogulyantz, E. Smolyaninova, K. Bogacheva, S. Skoblinskaya*, J. Russ. Phys.-Chem. Soc. *62*, 2033 (1930).
[5] *R. Fornit*, Seifensieder-Ztg. *62*, 697 (1935).
[6] *M. T. Bogert, G. Powell*, Am. Perfum. *25*, 617, 620 (1930).
[7] *K. Bernauer, I. Shydrzyk*, J. Prakt. Chem. *155*, 310 (1940).
[8] *G. Sturz, J. L. Kraus*, C. R. Acad. Sci. *C 271*, 744 (1970).
[9] *R. Ahmad, B. C. L. Weedon*, J. Chem. Soc. *1953*, 2125.
[10] *S. Trippett, D. M. Walker*, Chem. Ind. (London) *1960*, 202.

Benzophenonedilithium as Complex with Tetrahydrofuran and Tetramethylethylenediamine

By *Borislav Bogdanović, Carl Krüger*, and *Bernd Wermeckes*[*]

While the structure and reaction behavior of alkali metal adducts of aromatic hydrocarbons are already well documented[1], only spectroscopic data are available on the structure and composition of the alkali metal ketyls and the dianions of aromatic ketones and thioketones[2]. We report here the synthesis and structure of a benzophenonedilithium compound which contains one molecule each of complexed tetrahydrofuran (THF) and tetramethylethylenediamine (TMEDA).

Our investigations are connected with studies on poly(alkali metal) complexes of 1,6,6aλ⁴-trithiapentalene[3] and related compounds. Crystalline complexes of this sort could previously not be isolated; benzophenonedilithium appeared to us to be the simplest model compound of these polymetalated systems. For the synthesis of the model compound *(1)*,



(1)

benzophenone was allowed to react with lithium sand in the molar ratio 1:40 in THF at 0 °C. In 7 d the ratio of lithium to ligand in the red solution slowly increased to 3.6:1. After removal of excess lithium, concentration of the now deep-violet solution, and addition of TMEDA, the mono-THF-

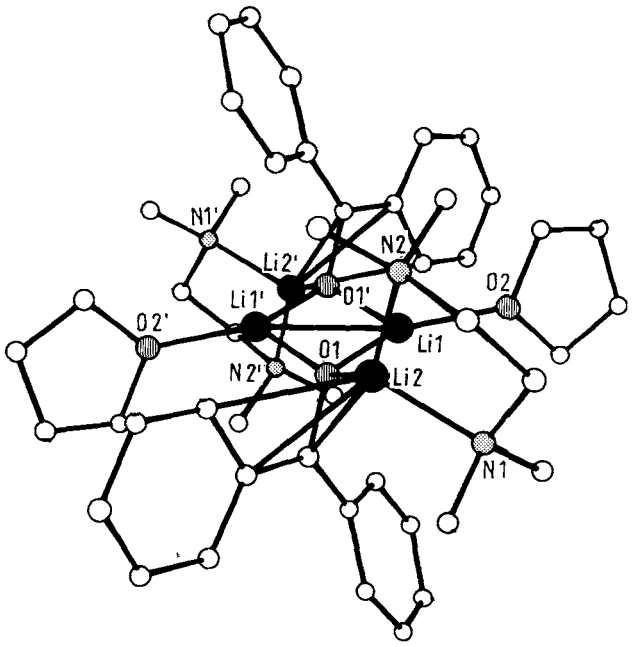


Fig. 1. Structure of the dimer of *(1)* in the crystal.

mono-TMEDA adduct of benzophenonedilithium *(1)* precipitates (yield 71%). It can be recrystallized from THF/TMEDA and forms violet crystals which are extremely sensitive to air and hydrolysis.

[*] Prof. Dr. B. Bogdanović, Priv.-Doz. Dr. C. Krüger, Dr. B. Wermeckes
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)

According to the X-ray structure analysis[4] *(1)* is a dimer (Fig. 1) with symmetry $\bar{1}$ (C_i). The oxygen atoms of the symmetry-related benzophenone moieties (O1, O1′) are bridged by a metal-metal contact of bonding dimensions (Li1—Li1′: 2.452(10) Å)[5] (see Fig. 2). The Li—O distances within this planar four-membered ring are equal (1.867(8) Å); the dihedral angle between the planar four-membered ring and the plane of the benzophenone moiety (O1C1C2C8) is 110.4°. Hence both lithium atoms (Li1, Li1′) of this metal-metal system interact with one lone pair of the carbonyl oxygen (three-center bonding), while the other lone pair is directed towards one of the "unique" lithium atoms (Li2). The latter, however, has an additional ion-pair interaction with the central planar part of the carbon skeleton of the benzophenone (C1, C2, C7) (dihedral angles O1C1C2C7: 2.7°, O1C1C8C13: 23.5°). Bonds of this type, with similar lengths, also exist in benzyllithium[6] or triphenylmethyllithium[7]. As expected Li1—O2 (1.919(8) Å) is shorter than Li—C (2.21—2.54). Two coordination sites on the almost tetrahedral Li2 are occupied by the nitrogen atoms of one TMEDA molecule, while a slightly angularly oriented THF molecule occupies a free site at Li1 and at Li1′.

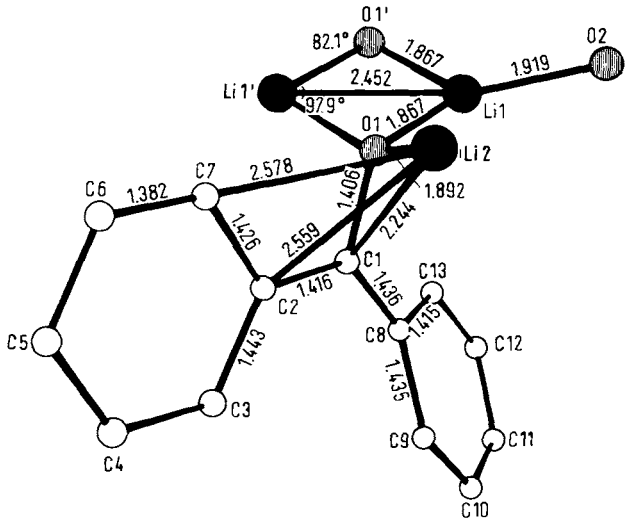


Fig. 2. Principal bond lengths [Å] and angles in *(1)* (substructure).

Received: April 1, 1980 [Z 581a IE]
German version: Angew. Chem. 92, 844 (1980)

CAS Registry number:
(1), 75112-28-6

Catalytic Synthesis of Magnesium Hydride under Mild Conditions

By *Borislav Bogdanović, Shih-tsien Liao, Manfred Schwickardi, Peter Sikorsky,* and *Bernd Spliethoff*[*]

The direct synthesis of magnesium hydride from the elements requires extremely long reaction times and drastic conditions[1]. Since hydrides of magnesium and its alloys and hydrides of intermetallic magnesium compounds are of potential use in reversible hydrogen storage devices[2], great efforts have already been directed at improving the hydrogenation of magnesium by addition of foreign metals or by alloying[1e, 2, 3]. In contrast, little is known about the use of homogeneous transition-metal catalysis for the hydrogenation of magnesium[4][***]. We report here on such a synthesis, which for the first time affords highly reactive magnesium hydride under mild conditions and which can also be carried out on a large scale.

Combinations of organic compounds of the main group elements with transition metal halides serve as suitable catalysts, which if necessary are activated by polycyclic arenes or amines; particularly active catalysts are obtained by reaction of anthracenemagnesium[5] with chromium, titanium, or iron halides in tetrahydrofuran (THF)[6]. Olive-green (Cr, Fe) or violet (Ti) THF solutions are formed, which already catalyze the hydrogenation of magnesium over days at 20 °C and normal pressure. To increase the rate of hydrogenation the catalysis can be carried out at 40—70 °C under H_2-pressure. As shown for the chromium catalyst (Fig. 1), for example, with this method and with a molar ratio of Mg:catalyst of 100:1 or 200:1, magnesium can be converted quantitatively into magnesium hydride within *ca.* 10 or 16 h, respectively, at 60—70 °C/80 bar.

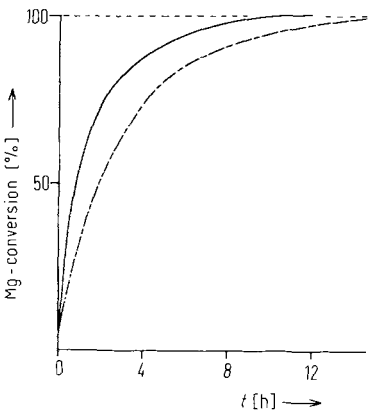


Fig. 1. Hydrogenation of magnesium with an anthracenemagnesium/$CrCl_3$ catalyst at 60—70 °C/80 bar; (——) Mg:Cr = 100:1, [Cr] = 0.086 mol/l; (– – – –) Mg:Cr = 200:1, [Cr] = 0.043 mol/l.

[1] *G. Stucky*, Adv. Chem. Ser. *130*, 56 (1974), and references cited therein.
[2] a) *V. Kalyanaraman, M. V. George*, J. Organomet. Chem. *47*, 225 (1973); b) *E. G. Janzen, C. M. Dubose, Jr.*, J. Phys. Chem. *70*, 3372 (1966); c) *B. Z. Askinazi, D. V. Ioffe*, Zh. Org. Khim. *3*, 367 (1967); Chem. Abstr. *66*, 115755 (1967); d) *Y. Minoura, S. Tsuboi*, J. Polym. Sci. *A-1*, *8*, 125 (1970).
[3] a) *B. Bogdanović*, DOS 2722221 (1977), Studiengesellschaft Kohle; Chem. Abstr. *91*, 39135 (1979); b) *B. Wermeckes*, Dissertation, Universität Bochum 1979.
[4] Crystallographic data: $a = 9.769(2)$, $b = 11.297(2)$, $c = 11.913(2)$ Å, $\alpha = 110.27(2)$, $\beta = 104.98(1)$, $\gamma = 92.67(2)°$; space group $P\bar{1}$, $Z = 1$, $\rho_{calc} = 1.084$ g cm^{-3}; 2680 reflections, of which 1812 observed; $R = 0.058$.
[5] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, J. Am. Chem. Soc. *98*, 74 (1976); *R. Zerger, W. Rhine, G. Stucky, ibid. 96*, 6048 (1974); *H. Dietrich*, Acta Crystallogr. *16*, 681 (1963); *M. Walczak, K. Walczak, R. Mink, M. D. Rausch, G. Stucky*, J. Am. Chem. Soc. *100*, 6382 (1978).
[6] *S. P. Patterman, I. L. Karle, G. D. Stucky*, J. Am. Chem. Soc. *92*, 1150 (1970).
[7] *J. J. Brooks, G. D. Stucky*, J. Am. Chem. Soc. *94*, 7333 (1972).

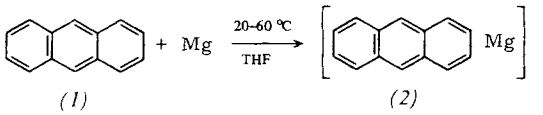
[*] Prof. Dr. B. Bogdanović, Dr. S. Liao [**], M. Schwickardi, Dipl.-Chem. P. Sikorsky, Ing. (grad.) B. Spliethoff
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)

[**] Alexander-von-Humboldt Fellow; permanent address: Institute for Chemical Physics of the Chinese Academy of Sciences, Talien (The Peoples Republic of China).

[***] In US-Pat. 3167218 (*E. van Tamelen, R. Fechter*, 1968) the production of alkali metal hydrides from the metals and hydrogen in the presence of, *e.g.* naphthalene and titanium tetraisopropylate is claimed, but only that of sodium hydride is described as example (as also in the later publication J. Am. Chem. Soc. *90*, 6854 (1968)). In the general description also the possibility of the hydrogenation of the alkaline earth metals and of aluminum is mentioned, as well as a series of further catalyst combinations. According to our own experiments, however, the catalysts recommended therein are unsuitable for the hydrogenation of alkaline earth metals and aluminum.

According to preliminary kinetic measurements the rate of hydrogenation is nearly proportional to the concentration of chromium or titanium catalyst and corresponds to a reaction of first order referred to magnesium[7]. In the case of the chromium catalyst (0.086 mol Cr/l) the rate of hydrogenation increases only slightly with increasing hydrogen pressure between 5 and 80 bar.

The following experimentally verified reactions may be regarded as possible steps of the homogeneously catalyzed hydrogenation of magnesium: (i) metallic magnesium reacts with anthracene in THF at 20 °C or above in the molar ratio 1:1 to give orange, sparingly soluble anthracenemagnesium *(2)* [eq. (a)]; (ii) in the reaction of *(2)* with $CrCl_3$ or $TiCl_4$ in THF, which leads to formation of the catalytically active species, free anthracene *(1)* is formed [eq. (b)]; (iii) in presence of the dissolved chromium or titanium catalyst, *(2)* is hydrogenated by hydrogen (at 30—60 °C/80 bar) to magnesium hydride [eq. (c)], with liberation of *anthracene (1)* (only small amounts of 9,10-dihydroanthracene were detected).



(1) *(2)* (a)

$$(2) + CrCl_3(TiCl_4) \xrightarrow[THF]{20\text{–}30\,^\circ C} Cr(Ti)\text{-cat.} + (1) \qquad (b)$$

$$(2) + H_2 \xrightarrow[THF]{Cr(Ti)\text{-cat.}} MgH_2 + (1) \qquad (c)$$

The reaction sequence eq. (a) and eq. (c) represents a catalytic cycle of magnesium hydrogenation *via* anthracenemagnesium *(2)* as intermediate. This assumption is supported by the experimental finding that the hydrogenation of *(2)* [eq. (c)] according to our method is considerably faster than the hydrogenation of elemental magnesium.

Thus, in this method a magnesium hydride/magnesium system is obtained which, because of the high dehydrogenation/hydrogenation rate (at 200—350 °C/1—50 bar) and high content of reversibly bound hydrogen in the magnesium hydride so produced (*ca.* 7 wt-%), is particularly suitable as a hydrogen storage system.

Procedure

All reactions carried out under argon. A suspension of magnesium powder (73.2 g, 3.0 mol) (Riedel-de Haën) in anhydrous THF (350 ml) is treated with ethyl bromide (0.3 ml) and, after 30 minutes' stirring, with 5.35 g (30.0 mmol) of *(1)*. After three hours' stirring (during which time *(2)* is formed) anhydrous $CrCl_3$ (4.75 g, 30.0 mmol) is added and stirring continued for a further 15—30 min until cessation of the weakly exothermic reaction. The olive-green suspension is transferred to a 1 l autoclave fitted with glass insert and magnetic stirrer and hydrogenated at 60—65 °C external temperature and a H_2-pressure of 80 bar; the rate of hydrogenation (Fig. 1) is measured *via* the drop in pressure in a hydrogen storage vessel. On completion of reaction the light-gray suspension is filtered through a glass frit (D4, diameter 9 cm)[8], and the MgH_2 washed twice with THF and pentane and dried in a high vacuum at 20 °C. One obtains 76.0 g of a pyrophoric magnesium hydride which is free from elemental magnesium; according to the elemental analysis and the amount of hydrogen liberated by hydrolysis the MgH_2 is *ca.* 94% pure (rest: THF, $MgCl_2$, catalyst[9].

Received: May 14, 1980 [Z 581 b IE]
German version: Angew. Chem. 92, 845 (1980)

CAS Registry numbers:
(1), 120-12-7; MgH_2, 7693-27-8; $CrCl_3$, 10025-73-7; $TiCl_4$, 7550-45-0

[1] a) *E. Wiberg, H. Goeltzer, R. Bauer*, Z. Naturforsch. *B 6*, 394 (1951); b) *T. N. Dymowa, Z. K. Sterlyadkina, V. G. Safronov*, Zh. Neorg. Khim. *6*, 763 (1961); Chem. Abstr. *55*, 23144 (1961); c) *J. Bousquet, J.-M. Blanchard, B. Bonnetot, P. Claudy*, Bull. Soc. Chim. Fr. *1969*, 1841; d) *C. M. Stander*, J. Inorg. Nucl. Chem. *39*, 221 (1977); e) *M. H. Mintz, Z. Gavra, Z. Hadari, ibid. 40*, 765 (1978).

[2] a) *J. J. Reilly, R. H. Wiswall*, Inorg. Chem. *6*, 2220 (1967); b) *ibid. 7*, 2254 (1968); c) *R. H. Wiswall*, Top. Appl. Phys. *29*, 201 (1978); d) *J. J. Reilly* in: Hydrides for Energy Storage. Pergamon Press, Oxford 1978, p. 301.

[3] a) *J. J. Reilly, R. H. Wiswall*, Proc. 7th IECEC Conf. (Am. Chem. Soc.) *1972*, 1342; b) *D. L. Douglass*, Metall. Trans. *6A*, 2179 (1975); c) see ref. [2d], therein p. 151; d) *B. Tanguy, J.-L. Soubeyroux, M. Pezat, J. Portier, P. Hagenmuller*, Mater. Res. Bull. *11*, 1441 (1976); e) *B. Darriet, M. Pezat, A. Hbika, P. Hagenmuller, ibid. 14*, 377 (1979); f) *M. H. Mintz, S. Malkiely, Z. Gavra, Z. Hadari*, J. Inorg. Nucl. Chem. *40*, 1949 (1978).

[4] a) *J. C. Snyder*, US-Pat. 3485585 (1969); Chem. Abstr. *72*, 45603 (1970); b) the hydrogenation of Mg at 20 °C/1 bar in THF with a VCl_4/Mg catalyst in THF has been reported: *B. Jezowska-Trzebiatowska, P. Sobota, J. Utko*, Bull. Acad. Pol. Sci. Ser. Sci. Chim. *24*, 331 (1976); this catalyst system, however, rapidly becomes inactive.

[5] *H. E. Ramsden*, US-Pat. 3354190 (1967).

[6] *B. Bogdanović*, DOS 2804445 (1979), Studiengesellschaft Kohle; Chem. Abstr. *91*, 159787 (1979).

[7] The kinetic measurements were carried out in a 2 l autoclave fitted with stirrer.

[8] The filtration is laborious; a much quicker filtration, particularly in experiments on a larger scale (up to 0.7 kg Mg), is possible with a pressure filter (Polypropylene cloth 2832, Verseidag).

[9] The procedure for the production of MgH_2 with $TiCl_4$ or $FeCl_2$ is analogous; the product is somewhat coarser and more easily filterable.

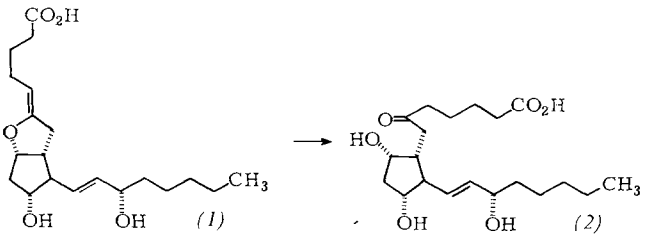
New Prostacyclin Analogues

By *Wilhelm Bartmann, Gerhard Beck, Jochen Knolle*, and *R. Helmut Rupp*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

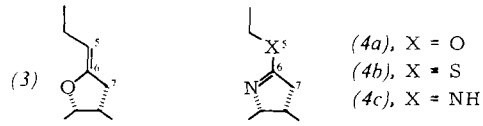
Prostacyclin (PGI_2) *(1)*[1] has been found in animal and human experiments to lower the blood pressure and to hinder platelet aggregation after intravenous administration[2]. Since it is less rapidly biologically deactivated than the "classical" prostaglandins E_2 and $F_{2\alpha}$ it has been considered as a circulating hormone affecting the circulation[3].

Aqueous solutions of pure *(1)* have a halflife of only 3 min at pH 7.5 and 37 °C[4]; *(1)* is hydrolyzed to 6-oxo-$PGF_{1\alpha}$ *(2)*.



It has been a preparative goal of various laboratories to synthesize chemically more stable analogues of *(1)*[5]. As far as can be seen, the biological action of *(1)* is closely connected with the electronic and steric parameters of the enol ether structure. Prostacyclin analogues differing considerably from the natural product in this partial structure are biologically less active[6].

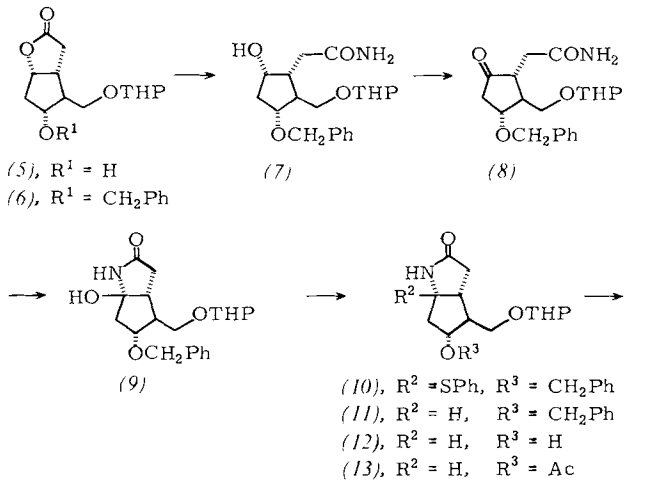
[*] Dr. W. Bartmann, Dr. G. Beck, Dr. J. Knolle, Dr. R. H. Rupp [+]
Hoechst AG
Postfach 800320, 6230 Frankfurt/M. 80 (Germany)
[+] To whom correspondence should be addressed.



(3) (4a), X = O; (4b), X = S; (4c), X = NH

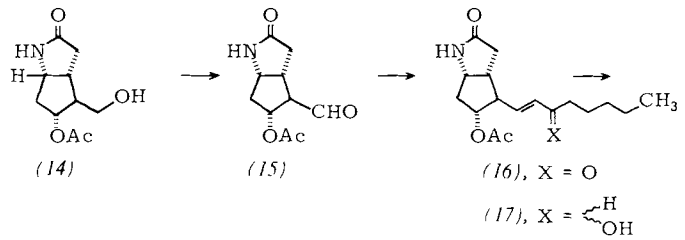
We now wish to describe the synthesis of prostacyclin analogues *(22)*, *(24)*, and *(26)* in which the enol ether structure *(3)* has been replaced by a β-hetero-imino group *(4)*.

Replacement of the C=C double bond by a C—X single bond should permit adoption of conformations resembling the *Z*-configuration of the natural product. It was expected that compounds having the partial structures *(4b)* and *(4c)* would be more resistant to acids than *(1)*. The starting material for the synthesis should be industrially available.

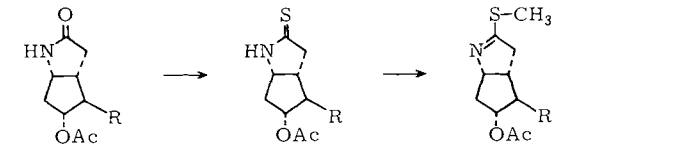


(5), R^1 = H; *(6)*, R^1 = CH_2Ph; *(7)*; *(8)*

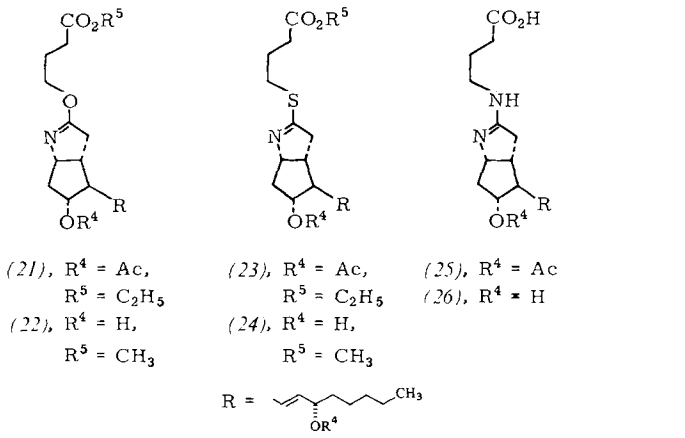
(9); *(10)*, R^2 = SPh, R^3 = CH_2Ph; *(11)*, R^2 = H, R^3 = CH_2Ph; *(12)*, R^2 = H, R^3 = H; *(13)*, R^2 = H, R^3 = Ac



(14); *(15)*; *(16)*, X = O; *(17)*, X = H, OH



(18), R^4 = Ac; *(19)*, R^4 = Ac; *(20)*, R^4 = Ac



(21), R^4 = Ac, R^5 = C_2H_5; *(22)*, R^4 = H, R^5 = CH_3; *(23)*, R^4 = Ac, R^5 = C_2H_5; *(24)*, R^4 = H, R^5 = CH_3; *(25)*, R^4 = Ac; *(26)*, R^4 = H

R =

Scheme 1.

Scheme 1 shows the transformation of the known synthon *(5)*[7] into the analogues *(22)*, *(24)*, and *(26)*.

After protection of the alcohol function in *(5)* (benzyl bromide/sodium hydride/50 °C) the lactone *(6)* is aminolyzed in methanol (autoclave, 36 h/130 °C/ammonia) and the resulting hydroxyamide *(7)* oxidized according to *Jones* to form the oxoamide *(8)* ($CrO_3/H_2O/H_2SO_4$/acetone/ −20 °C). Compound *(8)* slowly tautomerizes to the hydroxylactam *(9)*. Mild removal of the hydroxy group is accomplished by conversion of *(9)* into the phenylthio compound *(10)* which is also directly accessible from *(8)* (C_6H_5SH/$ClSi(CH_3)_3$/pyridine/CH_2Cl_2/reflux). Compound *(10)* can be desulfurized at room temperature with Raney nickel in *tert*-butyl alcohol to form *(11)* which gives the alcohol *(12)* on keeping for 5 h at 50 °C or on treatment with Pd/C/hydrogen in methanol at 25 °C.

After esterification of the alcohol function of *(12)* to form *(13)* (Ac_2O/pyridine/5 °C) and methanolysis of the tetrahydropyranyloxy group (CH_3OH/*p*-toluenesulfonic acid/ 25 °C) compound *(14)* is oxidized to *(15)* (dimethyl sulfoxide/oxalyl chloride/CH_2Cl_2/ −60 °C) and the crude product condensed according to *Horner-Emmons-Wittig* with dimethyl (2-oxoheptyl)phosphonate to produce the enone *(16)* (NaH/dimethoxyethane (DME)/25 °C). Reduction to *(17)* and its esterification (Ac_2O/pyridine/5 °C) led to the diacetate *(18)*, which affords the lactim ether *(22)* on reaction with ethyl ω-bromobutyrate (Ag_2O/xylene/120 °C) followed by removal of the acetate groups (K_2CO_3/CH_3OH/25 °C) from the product *(21)*.

The thiolactim ether *(24)* can be obtained by transformation of *(18)* into the thiolactam *(19)* (P_4S_{10}·4 pyridine/pyridine/80 °C), alkylation with ethyl ω-bromobutyrate (NaH/DME/25 °C) to form *(23)* and removal of the acetate groups (K_2CO_3/CH_3OH/25 °C).

The *S*-methyl thiolactim ether *(20)* preparable from *(19)* (NaH/DME/CH_3I/25 °C) is treated at 80 °C in methanol with γ-aminobutyric acid to form *(25)*. Hydrolysis of the acetate groups (K_2CO_3/CH_3OH/25 °C) leads to the amidine *(26)*.

Compounds *(22)*, *(24)*, and *(26)* exhibit interesting biological properties. Thus *(24)*, for example, inhibits platelet aggregation with an IC_{50}[9] value of 5×10^{-10} [M] and is more acid-resistant than prostacyclin *(1)*[8]. The three analogues were characterized by ^{1}H-NMR, IR, and mass spectra: *(22)* ($CDCl_3$): δ = 5.53 (2H, m, H—C=C), 4.25 (1H, m, H—C—N=C), 4.1 (1H, m, H—C—O), 3.8 (1H, m, H—C—O), 3.77 (3H, s, CO_2CH_3), 3.67 (2H, m, CH_2—O); *(24)*: ($CDCl_3$): δ = 5.58 (2H, m, H—C=C), 4.38 (1H, m, H—C=N—C), 4.08 (1H, m, H—C—O), 3.81 (1H, m, H—C—O), 3.67 (3H, s, CO_2CH_3), 3.1 (2H, m, CH_2—S); *(26)*: ($(CD_3)_2SO/CF_3CO_2D$): δ = 5.46 (2H, m, H—C=C), 4.31 (1H, m, H—C—N=C), 3.89 (1H, m, H—C—O), 3.8 (1H, m, H—C—O), 3.23 (2H, m, CH_2—N).

Received: March 25, 1980 [Z 577 IE]
German version: Angew. Chem. *92*, 850 (1980)

[1] *S. Moncada, R. Gryglewski, S. Bunting, J. R. Vane*, Nature *263*, 663 (1976).
[2] *K. C. Nicolaou, G. P. Gasic, W. E. Barnette*, Angew. Chem. *90*, 360 (1978); Angew. Chem. Int. Ed. Engl. *17*, 360 (1978).
[3] *R. J. Gryglewski*, Biochem. Pharmacol. *28*, 3161 (1979).
[4] *G. J. Dustin, S. Moncada, J. R. Vane*, Brit. J. Pharmacol. *62*, 414P (1978).
[5] *O. Kiyotaka, H. Nishiyama*, Tetrahedron Lett. *1979*, 3003, and references cited therein.
[6] *K. C. Nicolaou, W. J. Sipio, R. L. Magolda*, J. Chem. Soc. Chem. Commun. *1978*, 1067; *E. J. Corey, L. Szekely, C. S. Shiner*, Tetrahedron Lett. *1977*, 3529.
[7] *J. S. Bindra, A. Grodski, T. A. Schaaf, E. J. Corey*, J. Am. Chem. Soc. *95*, 7522 (1973).
[8] This experiment was performed by Dr. *U. Weithmann*.
[9] IC_{50} is that concentration at which the aggregation is 50% inhibited.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1010-0820 $ 02.50/0*

2-Vinylidene-2*H*-indene[**]

By *Reinhard Schulz, Armin Schweig, Curt Wentrup,* and *Hans-Wilhelm Winter*[*]

Until now, only one 2*H*-indene (isoindene), *viz.* 2,2-dimethyl-2*H*-indene, has been isolated and characterized[1]. Although the 2-methylene derivative (isobenzofulvene) is known as a reactive intermediate in dilute solution[2], no isolation or spectroscopic identification has been reported. However, the blue 2-(dimethylaminomethylene)-1,3-diphenyl-2*H*-indene stabilized sterically (and/or electronically) by substituents in positions 1 and 3 has been isolated[3].

We now wish to report the gas-phase and low temperature isolation of 2-vinylidene-2*H*-indene *(2)*. When cyclopropa[*b*]naphthalene *(1)*[4] was subjected to flash vacuum pyrolysis (30 × 2 cm quartz tube; 10^{-3}—10^{-4} torr), an intensely blue compound was collected at −196 °C on a cold-finger situated immediately after the exit from the oven. The blue color appeared at pyrolysis temperatures above *ca.* 400 °C, reached a maximum at *ca.* 600 °C, and had almost completely disappeared at 850 °C. The blue compound dimerized and/or polymerized as soon as diffusion commenced, *e.g.* in an ether matrix at −116 °C, or in the solid state at −100 °C (fading of the color in the course of *ca.* 5 min on warm-up between −100 and −80 °C).

(1) *(2)*

The blue compound was characterized by its IR spectrum at −196 °C, using a modified apparatus (10 × 1 cm pyrolysis tube) in which the products were condensed directly onto a turnable KBr disk attached to a liquid nitrogen cryostat (IR (−196 °C): 3030 w, 2960 w, 1935 vs, 1890 (sh), 1470 s, 1425 s, 905 s, 840 s, 800 vs, 745 s, 725 m cm^{-1}).

The very intense allene absorption at 1935 cm^{-1} is in agreement with the structure *(2)*. When the cryostat was warmed to −96 °C by the addition of toluene (room temperature), the 1935 cm^{-1} band disappeared with a halflife of *ca.* 8 min[5]. At the same time, the blue color disappeared.

The structure of *(2)* was obtained by variable temperature photoelectron spectroscopy (VTPES)[6]. For this purpose, the reaction *(1)*→*(2)* was carried out in the reactor (20 × 0.6 cm stainless steel pyrolysis tube; *ca.* 5×10^{-2} torr) of a modified PS18 photoelectron spectrometer. The mixture of pyrolysis product and starting material was ionized immediately after the exit from the reactor.

Figures 1a and 1b show the photoelectron spectra obtained at reactor temperatures of 25, 350, 500, and 700 °C. The spectrum of the starting material *(1)* has bands at ① 8.03 eV ($^2A_2(\pi)$), ② 8.54 eV ($^2B_1(\pi)$), and ③ 9.95 eV ($^2A_2(\pi)$, $^2A_1(\sigma)$) (assignment by CNDO/S[7] calculations). At pyrolysis temperatures above 350 °C, a new band ①' at 7.25 eV appeared. This reached a maximum at 500 °C, and had almost entirely disappeared again at 700 °C. The temperature dependence of this band largely parallels that of the formation of the blue allenic compound.

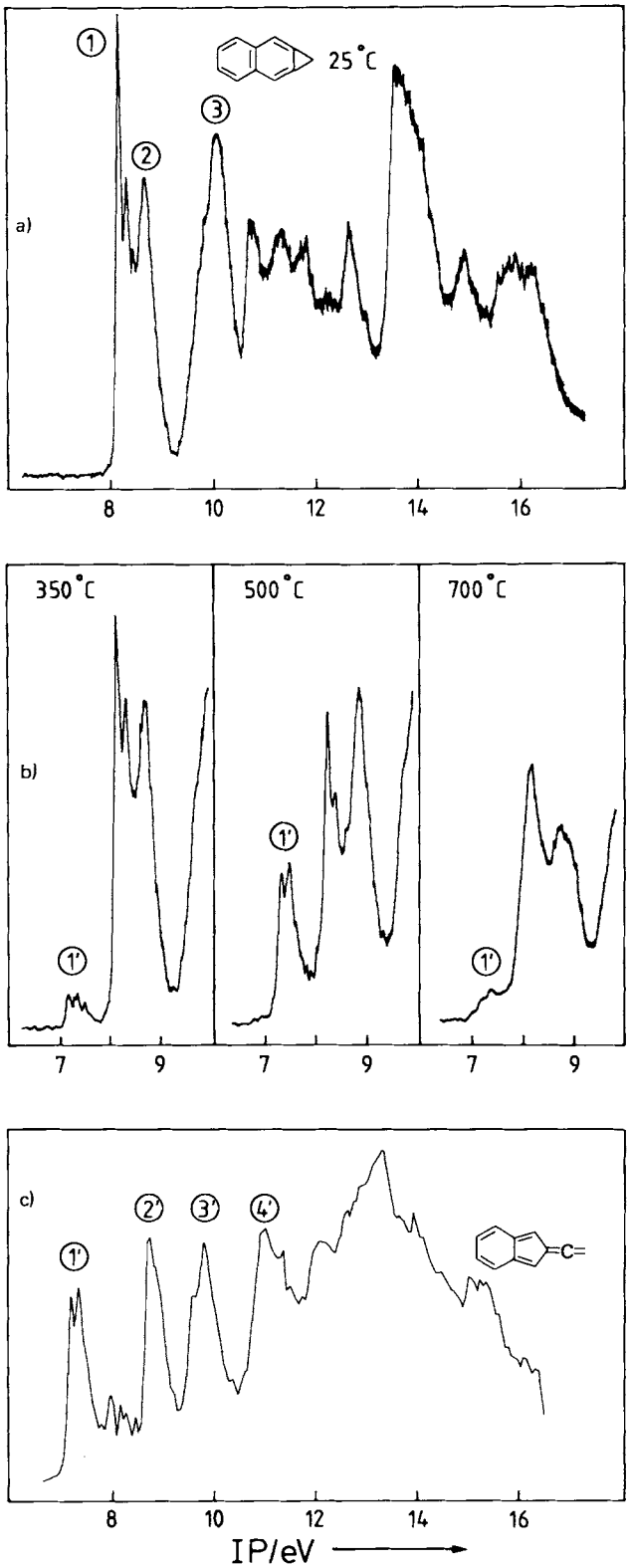


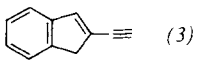
Fig. 1. He-I photoelectron spectra a) of *(1)* at 25 °C; b) of mixtures of *(1)* and *(2)* at 350, 500, and 700 °C; and c) of *(2)*. The last spectrum in Fig. 1c was calculated from the 500 °C spectrum by subtraction of the spectrum of *(1)*.

The formation of *ca.* 50% of the rearrangement product at 500 °C can be estimated from the relative band intensities. The remainder is largely unchanged starting material *(1)*. The spectrum of the rearrangement product was obtained by subtraction (Fig. 1c). It has bands at ①' 7.25 eV, ②' 8.83 eV, ③' 9.63—9.89 eV, and ④' 11.02 eV. The possibility that the species observed was 2-ethynyl-1*H*-indene *(3)*, the high-tem-

[*] Prof. Dr. C. Wentrup, Dipl.-Chem. H.-W. Winter
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)
Prof. Dr. A. Schweig, Dipl.-Chem. R. Schulz
Fachbereich Physikalische Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] $C_{11}H_8$ Intermediates, Part 4.—Part 3: *C. Wentrup, J. Benedikt,* J. Org. Chem. *45*, 1407 (1980).—Also: Part 88 of "Theory and Application of Photoelectron Spectroscopy". This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 87: *R. Schulz, A. Schweig,* Tetrahedron Lett. *1980*, 343.

perature rearrangement product of *(1)*[8], was excluded by recording a spectrum of this compound (8.04 eV ($^2A''(\pi)$), 9.03 eV ($^2A''(\pi)$), and 10.09–10.31 eV ($^2A''(\pi)$, $^2A'(\pi)$); assignment by MNDO[9] calculations).



(3)

The identification of the rearrangement product as 2-vinylidene-2*H*-indene *(2)* follows from the excellent agreement between the measured vertical ionization potentials (VIP) and those calculated for *(2)* by several methods[7, 9, 10] (Fig. 2).

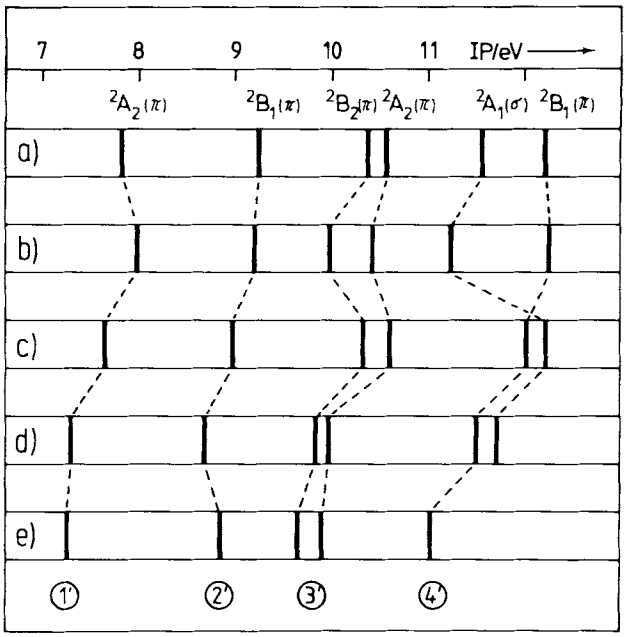


Fig. 2. Vertical ionization potentials (VIP) of *(2)*; calculated by a) CNDO/S [7]-Koopmans; b) CNDO/S PERTCI [10a]; c) LNDO/S [10b]-Koopmans; [d] LNDO/S PERTCI; and e) measured (see Fig. 1c).

Received: December 12, 1979 [Z 578 IE]
German version: Angew. Chem. *92*, 846 (1980)

CAS Registry numbers:
(1), 286-85-1; *(2)*, 75067-09-3; *(3)*, 74010-34-7

[1] *W. R. Dolbier, Jr., K. Matsui, H. J. Dewey, D. V. Horák, J. Michl*, J. Am. Chem. Soc. *101*, 2136 (1979).

[2] *H. Tanida, T. Irie, K. Tori*, Bull. Chem. Soc. Jpn. *45*, 1999 (1972); *P. L. Watson, R. N. Warrener*, Aust. J. Chem. *26*, 1725 (1973); *R. N. Warrener, G. J. Collin, G. I. Hutchison, M. N. Paddon-Row*, J. Chem. Soc. Chem. Commun. *1976*, 373; *R. N. Warrener, K. I. Gell, M. N. Paddon-Row*, Tetrahedron Lett. *1977*, 53.

[3] *K. Hafner, W. Bauer*, Angew. Chem. *80*, 312 (1968); Angew. Chem. Int. Ed. Engl. *7*, 297 (1968).

[4] *W. E. Billups, W. Y. Chow*, J. Am. Chem. Soc. *95*, 4099 (1973).

[5] Since the temperature of the condensate was not directly measured, the actual sample temperature could have been somewhat lower.

[6] *A. Schweig, H. Vermeer, U. Weidner*, Chem. Phys. Lett. *26*, 299 (1974); *W. Schäfer, A. Schweig*, Z. Naturforsch. *30a*, 1785 (1975); *R. Schulz, A. Schweig*, Angew. Chem. *92*, 752 (1980); Angew. Chem. Int. Ed. Engl. *19*, 740 (1980).

[7] *K.-W. Schulte, A. Schweig*, Theor. Chim. Acta *33*, 19 (1974).

[8] *C. Wentrup, E. Wentrup-Byrne, P. Müller, J. Becker*, Tetrahedron Lett. *1979*, 4249. We thank Dipl.-Chem. *J. Becker* for the preparation of a sample of *(3)*.

[9] *M. J. S. Dewar, W. Thiel*, J. Am. Chem. Soc. *99*, 4899 (1977).

[10] a) *H.-L. Hase, G. Lauer, K.-W. Schulte, A. Schweig*, Theor. Chim. Acta *48*, 47 (1978); b) *G. Lauer, K.-W. Schulte, A. Schweig*, J. Am. Chem. Soc. *100*, 4925 (1978); c) The VIPs were calculated for a geometry optimized with a MNDO program [9].

Synthesis of Cyclic Compounds from Triphenyl(phenyliminovinylidene)phosphorane and Carboxylic Acids

By *Hans Jürgen Bestmann, Gerold Schade*, and *Günther Schmid*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

Triphenyl(phenyliminovinylidene)phosphorane *(1)*[1] adds carboxylic acids *(2)*, primarily to give the nonisolable phosphoranes *(3)*, which are converted by $O \rightarrow N$-acyl migration into compounds *(4)*. On heating to 60 °C, compounds *(4)* rearrange by intramolecular *C*-acylation into acyl-*N*-phenylcarbamoyl ylides *(5)*[2].

When *(5)* is heated in boiling toluene it cleaves off phenyl isocyanate *(7)* in an equilibrium reaction, and the acyl ylide *(6)* is formed. *(7)* can be removed from the equilibrium by addition of an alcohol, so that the reaction sequence *(1)* + *(2)* → *(6)* is a general preparative method for the synthesis of acyl ylides *(6)* from free—inactivated—carboxylic acids *(2)*[3]. Table 1 shows some examples.

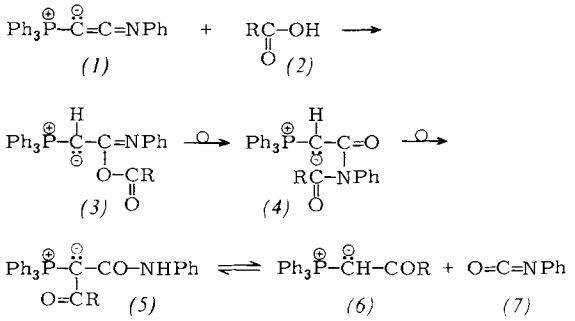


Table 1. Phosphoranes *(4)*, *(5)*, and *(6)* from ylide *(1)* and carboxylic acids *(2)* (yields not optimized).

	R	*(4)* M.p. (dec.) [°C]	*(4)* Yield [%]	*(5)* M.p. (dec.) [°C]	*(5)* Yield [%] [a]	*(6)* M.p. [°C]	*(6)* Yield [%]
a	CH_3	123	72	178	72	202	62
b	C_3H_7	131	71	162	71	162	54
c	Ph—CH=CH	116	51	192	51	148	59
d	Ph	[b]		182	74	181	69

[a] Referred to *(2)*. [b] Cannot be isolated pure.

Substituted carboxylic acids *(2)*, whose substituents can react with an ylide function, *e.g.* oxocarboxylic acids *(8)*, ought to occasion intramolecular ring closure reactions at the stage of *(9)*, *(10)*, or *(12)* [corresponding to *(3)*, *(4)*, *(6)*] on reaction with *(1)*. In the case of *(8)* these are intramolecular Wittig reactions. These cyclizations (ring closures A, B, C) lead to compounds of the type *(13)*, *(14)*, and *(15)*. From our findings the following general rules can be derived:

In the reaction of *(1)* with α-oxo acids the cyclization can proceed according to route A or B. One obtains either the isoimide *(13)* (X = null) or imide *(14)* (X = null) of a 2-substituted maleic acid. We found that the compounds *(13)* (X = null) can be quantitatively rearranged into *(14)* (X = null) with catalytic amounts of sodium azide in anhydrous methanol. The reaction of *(1)* with α-oxo acids thus opens up a general route for the synthesis of 2-substituted *N*-phenylmaleimides.

[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. G. Schade, Dr. G. Schmid
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

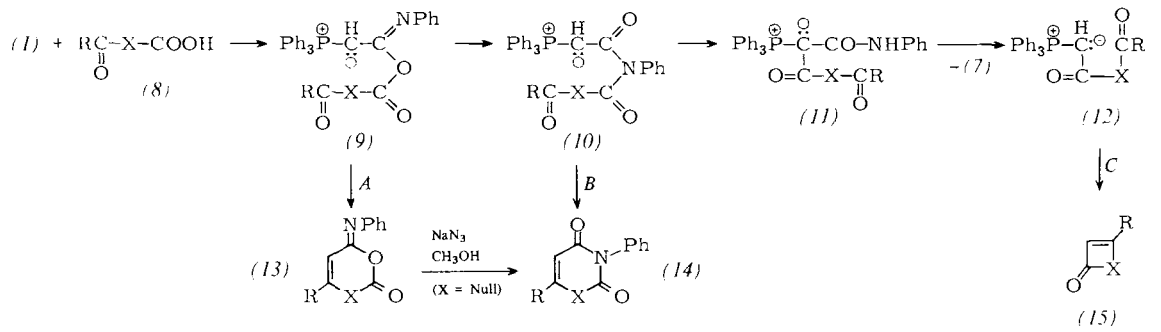


Table 2. Ring closure reactions by reaction of *(1)* with oxocarboxylic acids *(8)* (yields not optimized) [a].

Carboxylic acid *(8)*	*(11)* M.p. (dec.) [°C]	Yield [%]	Ring closure	Cyclic products	*(13)—(16)*	M.p. [°C] B.p. [°C/torr]	Yield [%]
R′—CO—COOH							
(8a), R′ = CH_3			*A*		*(13a)* [b]	106	42
(8b), R′ = Ph			*A*		*(13b)* [b]	128	69
R′—CO—COOH							
(8c), R′ = C_2H_5			*B*		*(14c)*	95	50
(8d), R′ = C_3H_7			*B*		*(14d)*	68	49
(8e)			*B*		*(14e)*	155	51
R′—CO—$(CH_2)_2$—COOH							
(8f), R′ = Ph	165—167	64	*C*		*(15f)*	82	78
(8g), R′ = C_4H_9	158—160	63	*C*		*(15g)*	50/0.05	80
(8h), *n* = 4	173—174	80	*C*		*(15h)*	50/0.02	75
(8i), *n* = 3	167—169	82	*C*		*(15i)*	40/0.02	60
(8j), *n* = 4	177—179	72	*C*		*(15j)*	60/0.01	85
(8k), *n* = 3	167—170	74	*C*		*(15k)*	60/0.05	67
(8l)	173—175	64	*C*		*(15l)*		
					(16)	38—39	82
(8m)	203—205	95	*C*		*(15m)*	65—66	55

[a] Known compounds are identical with authentic reference material; correct elemental analyses and molecular spectroscopic data (IR, NMR, mass spectra) for all unknown compounds. [b] *(14a)*, R′ = CH_3, and *(14b)*, R′ = Ph, were obtained from *(13a)* and *(13b)* by reaction with NaN_3/CH_3OH; m.p. 97 and 117 °C, respectively.

On reaction of *o*-formylbenzoic acid and *(1)*, 2-phenyl-2-benzazepine-1,3-dione *(14e)* is formed *via* ring closure B.

γ-Oxo acids react with *(1)* to give compounds of type *(11)*, which on heating immediately cyclize *via* acyl ylides *(12)* to cyclopentenones [ring closure C to type *(15)*, X = $(CH_2)_2$]. δ-Oxo acids can be analogously converted into cyclohexenones [type *(15)*, X = $(CH_2)_3$]. The annelations to *(15h—k)* are superior to other methods, *e.g.* the Robinson annelation, because the products are free from double-bond isomers[4] and of compounds which are formed by retro-aldol condensations[5]. Reaction of the oxocarboxylic acid *(8l)* proceeds *via* the corresponding compound *(11l)* to give the acyl ylide *(12l)*, which surprisingly reacts to give the "anti-Bredt" α,β-unsaturated ketone *(15l)*. Compound *(15l)* immediately adds the ethanol used for trapping the isocyanate to give the end product *(16)*[6] (see Table 2).

The finding that the acyl ylide *(12m)* formed in the reaction of *(8m)* forms the enol ether of a cyclic 1,3-diketone by Wittig reaction at the ester carbonyl group[7] is of special preparative interest.

Procedure

(15i): A suspension of *(1)* (10 g, 26.5 mmol) in anhydrous ethyl acetate (200 ml) is treated with a solution of 2-oxocyclopentaneacetic acid *(8i)* (3.8 g, 26.8 mmol) in ethyl acetate (20 ml). The solution is heated under reflux for 3 h. On cooling 11.3 g of *(11i)* crystallize out.

A solution of *(11i)* (10 g, 19.3 mmol) in 80 ml of anhydrous toluene, which contains 5 ml ethanol, is heated under reflux for 12 h. The solvent is removed and the residue digested with 50 ml pentane. Precipitated Ph_3PO is separated off and the previously unknown 4,5,6,6a-tetrahydro-2(1*H*)-pentalenone *(15i)* (1.41 g) isolated by bulb-to-bulb distillation.

Received: January 24, 1980 [Z 579 IE]
supplemented: August 8, 1980
German version: Angew. Chem. *92*, 856 (1980)

CAS Registry numbers:
(1), 21385-80-8; *(2a)*, 64-19-7; *(2b)*, 107-92-6; *(2c)*, 621-82-9; *(2d)*, 65-85-0; *(4a)*, 75066-52-3; *(4b)*, 75066-53-4; *(4c)*, 75066-54-5; *(5a)*, 13162-69-1; *(5b)*, 75066-55-6; *(5c)*, 75066-56-7; *(5d)*, 13162-68-0; *(6a)*, 1439-36-7; *(6b)*, 17615-01-9; *(6c)*, 13527-03-2; *(6d)*, 859-65-4; *(8a)*, 127-17-3; *(8b)*, 611-73-4; *(8c)*, 600-18-0; *(8d)*, 1821-02-9; *(8e)*, 119-67-5; *(8f)*, 2051-95-8; *(8g)*, 4316-44-3; *(8h)*, 1438-96-6; *(8i)*, 1460-38-4; *(8j)*, 2275-26-5; *(8k)*, 3296-45-5; *(8l)*, 39762-51-1; *(8m)*, 4376-18-5; *(11f)*, 75066-57-8; *(11g)*, 75066-58-9; *(11h)*, 75066-59-0; *(11i)*, 75066-60-3; *(11j)*, 75066-61-4; *(11k)*, 75066-62-5; *(11l)*, 75066-63-6; *(11m)*, 75066-64-7; *(13a)*, 75066-65-8; *(13b)*, 75066-66-9; *(14a)*, 3120-04-5; *(14b)*, 75066-70-5; *(14c)*, 3120-06-7; *(14d)*, 75066-67-0; *(14e)*, 75066-68-1; *(15f)*, 3810-26-2; *(15g)*, 53253-06-8; *(15h)*, 39163-29-6; *(15i)*, 72200-41-0; *(15j)*, 1196-55-0; *(15k)*, 1489-28-7; *(15l)*, 71370-30-4; *(15m)*, 42393-04-4; *(16)*, 75066-69-2

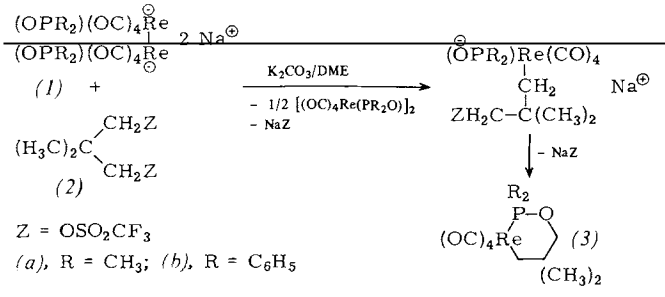
[1] *H. J. Bestmann, G. Schmid*, Angew. Chem. *86*, 274 (1974); Angew. Chem. Int. Ed. Engl. *13*, 273 (1974).
[2] Synthesis of the compounds *(5)* from acyl ylides *(6)* and phenyl isocyanate *(7)* cf. *S. Trippett, D. M. Walker*, J. Chem. Soc. *1959*, 3874.
[3] Synthesis of acyl ylides *(6)*: *H. J. Bestmann*, Angew. Chem. *77*, 651 (1965); Angew. Chem. Int. Ed. Engl. *4*, 645 (1965).
[4] *R. L. Augustine, J. A. Caputo*, Org. Synth. Coll. Vol. *5*, 869 (1973).
[5] *P. M. McCurry, R. K. Singh*, J. Org. Chem. *39*, 2317 (1974); *R. N. Lacey*, J. Chem. Soc. *1960*, 1639.
[6] *H. O. House, W. A. Kleschick, E. J. Zaiko*, J. Org. Chem. *43*, 3653 (1978).
[7] Cf. also: *K. Nickisch, W. Klose, E. Nordhoff, F. Bohlmann*, Chem. Ber. *113*, 3086 (1980).

First Insertion Reaction of Carbon Monoxide into a Rhenium-Carbon σ-Bond[**]

By *Ekkehard Lindner* and *Günter von Au*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 65th birthday

Carbon monoxide has great importance as a reactant in the hydroformylation of olefins[1]; this reaction is catalyzed by carbonyl-metal derivatives[2]. The lengthening of the C-chain of the metal-bound olefin occurs *via* labile σ-alkyl complexes, which insert CO into their M—C σ-bond. Such insertions with corresponding carbonyl-rhenium compounds have not previously been described[3]. We successfully performed this reaction with the six-membered rhenacycles *(3)* which we were able to obtain by heterolytic cleavage of the Re—Re bond in the dianionic, binuclear complexes *(1)*[4], with neopentylene bis(trifluoromethanesulfonate) *(2)*.



The colorless, thermally stable metallacycles *(3)* sublime in a high vacuum and are soluble in all common organic solvents. They were characterized by complete elemental analysis, IR, MS (Table 1), and ^{1}H-NMR spectra [*(3a)*, *(3b)* (C_6D_6 rel. to TMS): δ = 0.89, 1.01 (s, C(CH_3)$_2$), 0.92, 1.04 (d, J = 2.5, 3.1 Hz, P—Re—CH_2), 3.19, 3.51 (d, J = 17.6, 17.3 Hz, P—O—CH_2)], as well as by crystal structure analysis of *(3b)*[5].

Table 1. IR and MS data, and melting points of compounds *(3)*—*(6)*.

	(3a)	*(3b)*	*(4b)*	*(5b)*	*(6b)*
ν(CO) [cm^{-1}]	2978 m [a] 1998 s 1975 vs 1945 vs	2082 m [a] 2001 s 1984 vs 1943 vs	2113 m [b] 2046 m-s 2020 vs 1979 s	2048 vs [c] 1986 vs 1920 vs	2111 m [d] 2021 sh 2015 vs 1952 s
ν(SO_2)			1161 m [e] 1046 m		
ν(C=O)				1393 m [c]	1608 s [d]
m/e ($M^{\oplus}$) [f]	446	570	634 [g]	840	598
M.p. [°C]	8	117	132	112	≈96

[a] In *n*-hexane. [b] In CCl_4. [c] In toluene. [d] In $CHCl_3$. [e] In KBr. [f] Rel. to ^{187}Re. [g] Field desorption.

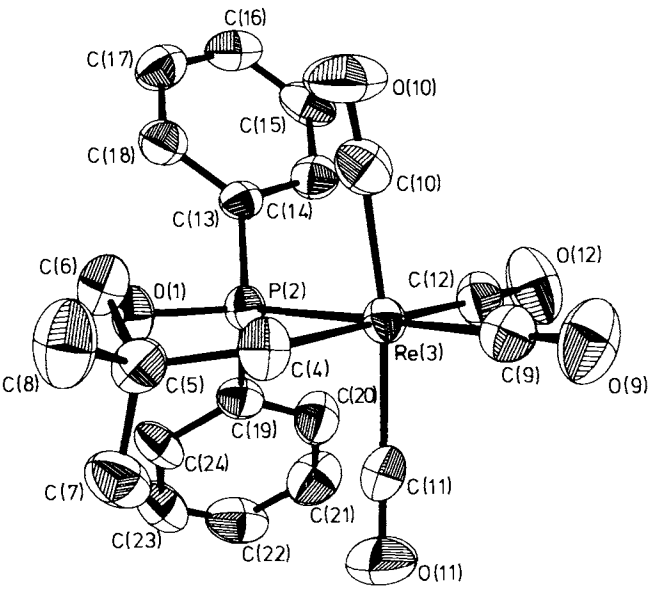


Fig. 1. ORTEP representation of *(3b)* (vibrational ellipsoids with 50% probability).

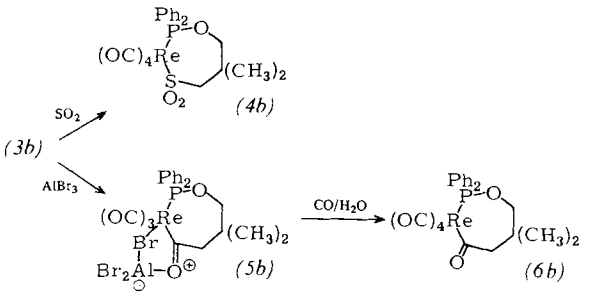
Bond lengths [pm]		Angles [°]	
Re3—C4	228.5(9)	P2—Re3—C4	89.8(2)
C4—C5	154.6(13)	Re3—C4—C5	123.2(6)
C5—C6	150.4(11)	C4—C5—C6	111.3(7)
C6—O1	147.3(12)	C5—C6—O1	113.3(7)
O1—P2	160.3(6)	C6—O1—P2	121.2(6)
P2—Re3	239.9(2)	O1—P2—Re3	116.0(2)

(3b) has a distorted chair conformation with a dihedral angle of 115.4° between the C5, C6, O1 plane and the approximate plane through O1, P2, Re3, C4, and C5. Thus the tetrahedral angle at C6 is only slightly enlarged. Due to the steric effect of both methyl groups, the same applies to the angle at C5, resulting in a considerable expansion of the tetrahedral angle at C4. This indicates a considerable ring strain, which leads to greater reactivity.

[*] Prof. Dr. E. Lindner, Dipl.-Chem. G. von Au
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Preparation and Properties of, and Reactions with Metal-Containing Heterocycles, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 5: *E. Lindner, H.-J. Eberle*, J. Organomet. Chem. *191*, 143 (1980).

Although in *(3b)* the Re3—C4 distance is clearly greater than the sum of the single bond radii, and SO_2 can easily cleave the Re—C σ-bond with ring expansion to thermally stable *(4b)*, the insertion of CO will not proceed until 100 °C



and 800 bar. However, if the metal-coordinated carbon monoxide in *(3b)* is activated with a Lewis acid, such as $AlBr_3$[6], then the colorless adduct *(5b)*, obtained in toluene, takes up CO at 20 °C without pressure. Subsequent hydrolysis with cleavage of the aluminum group, leads to the colorless, ring-expanded, insertion product *(6)*, which is thermally labile. In solution, CO is eliminated at 20 °C. In the spectra of *(4b)* and *(6b)*, in contrast to *(3b)*, ν(CO) is shifted characteristically to higher frequencies. *(4b)*, *(5b)*, and *(6b)* are soluble only in more strongly polar organic solvents.

Experimental

(3a, b): A solution of *(1a)* or *(1b)* (1.23 mmol) in dimethoxyethane (DME) (50 ml) is added dropwise to *(2)* (1.10 mmol) and K_2CO_3 (2 mmol) in DME (20 ml) at −10 °C [*(3a)*] or 20 °C [*(3b)*], and is heated for 10 h at 60 and 84 °C, respectively. After filtration (D4), *(3a)* and *(3b)* are purified on a chromatographic column (l = 0.3 m, diam. = 25 mm, silica gel, act. III, eluent: *n*-hexane). Final purification is by distillation (20 °C/10^{-2} torr) and recrystallization from *n*-hexane. Yield: 12—27%.

(4b): *(3b)* (0.38 mmol) in liquid SO_2 (10 ml) is left to react for 1 h at −40 °C. After removal of SO_2, analytically pure *(4b)* remains in quantitative yield.

(6b): *(3b)* (0.21 mmol) and $AlBr_3$ (0.21 mmol) are dissolved in toluene (20 ml) in the absence of air and moisture. After several minutes, when *(5b)* has formed, CO is bubbled through the solution for 1 h at room temperature. The solvent is removed and the solution hydrolyzed with aqueous $CHCl_3$, then filtered (D4). The solvent is removed under vacuum at −10 °C, and the residue of *(6b)* is washed with *n*-hexane. Yield: 45%.

Received: March 4, 1980 [Z 580 IE]
German version: Angew. Chem. *92*, 843 (1980)

CAS Registry numbers:
(1a), 69042-02-0; *(1b)*, 69042-03-1; *(2)*, 72610-41-4; *(3a)*, 75067-39-9; *(3b)*, 75067-40-2; *(4b)*, 75067-36-6; *(5b)*, 75067-41-3; *(6b)*, 75067-42-4; SO_2, 7446-09-5; $AlBr_3$, 7727-15-3

[1] *R. L. Pruett*, Adv. Organomet. Chem. *17*, 1 (1979).
[2] *C.-Y. Hsu, M. Orchin*, J. Am. Chem. Soc. *97*, 3553 (1975).
[3] *R. B. King, A. D. King, Jr., M. Z. Iqbal, C. C. Frazier*, J. Am. Chem. Soc. *100*, 1687 (1978).
[4] *E. Lindner, G. von Au, H.-J. Eberle*, Z. Naturforsch. *B 33*, 1296 (1978).
[5] *(3b)* crystallizes from *n*-heptane as triclinic crystals, space group $P\bar{1}$, a = 829.9(4), b = 970.0(2), c = 1376.9(3) pm, α = 92.85(2), β = 97.37(3), γ = 106.48(3)°, Z = 2, ρ_{calc} = 1.801 g cm^{-3}. The structure was solved with Patterson- and difference-Fourier syntheses and anisotropically refined (except H) with the program system SHEL-76 until R = 0.038, for 3250 independent reflections (θ = 3—25°). We would like to thank Mrs. *M. Gekeler* and Mr. *K.-P. Frank* for their help with the structure determination.
[6] *S. B. Butts, E. M. Holt, S. H. Strauss, N. W. Alcock, R. E. Stimson, D. F. Shriver*, J. Am. Chem. Soc. *101*, 5864 (1979).

Double Cycloaddition Yielding a Tricyclic Diphosphorane[**]

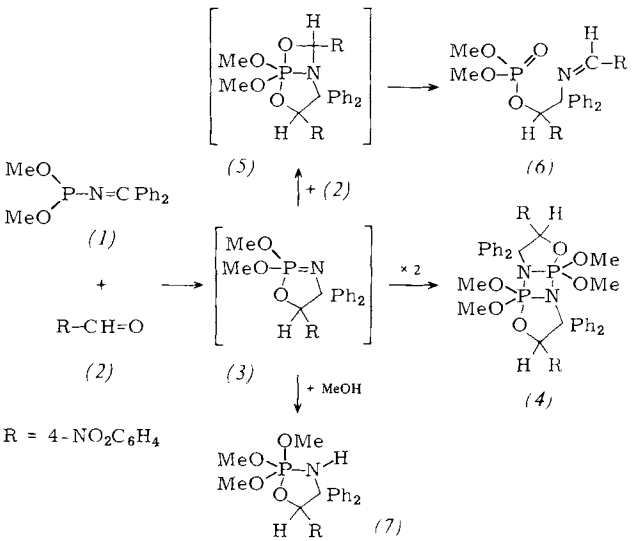
By *Alfred Schmidpeter, Werner Zeiss, Dietmar Schomburg,* and *William S. Sheldrick*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In criss-cross addition to a dienic four-membered chain, the first [3 + 2]-cycloaddition is followed by a second one, and a five/five-membered bicyclic species results. In the case of double addition to the three-membered chain of an enephosphane described below, the second addition is likewise a necessary consequence of the first one. The role of the second ene is assumed by P^{III} which increases its coordination number by two and becomes the P^{V} bridgehead of a four/five-membered bicyclic species.



(Methyleneamino)phosphanes[1] such as *(1)* represent a special case of 1,3-dipoles free of formal charges. They react with electron-deficient olefins and acetylenes *via* [3 + 2]-cycloadditions to form 1,2-azaphospholes and 1,2-azaphospholines, respectively[2]. Their reaction with carbonyl compounds is more complicated. We found that dimethoxy(diphenylmethyleneamino)phosphane *(1)* and *p*-nitrobenzaldehyde *(2)* afford a 2:2 and a 1:2 addition product in 40 and 30% yield, respectively, which prove to be the tricyclic diphosphorane *(4)* and the methyleneaminoethyl phosphate *(6)*. Both compounds must be regarded as the result of double cycloadditions: a [3 + 2]-addition forming the thermodynamically favorable PO bond leads, contrary to kinetic expectations, regiospecifically to the 1,3,2λ^5-oxazaphosphol-



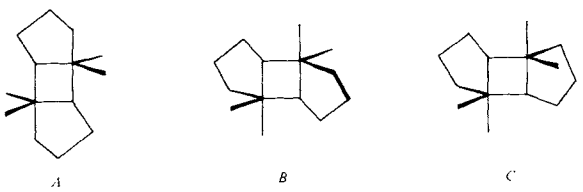
[*] Prof. Dr. A. Schmidpeter, Dr. W. Zeiss
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Priv.-Doz. Dr. W. S. Sheldrick, Dr. D. Schomburg
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[**] Four- and Five-Membered Phosphorus Heterocycles, Part 46. This work was supported by the Fonds der Chemischen Industrie.—Part 45: *K. C. Dash, H. Schmidbaur, A. Schmidpeter*, Inorg. Chim. Acta *46*, 167 (1980).

ine *(3)*. As a result of the proclivity of its P,N bond to undergo addition[3], compound *(3)* reacts further *via* [2+2]-cycloaddition with itself to form the dimer *(4)*[5], and with further *(2)* in the manner of a Wittig reaction[4] *via (5)* to give *(6)*[5].

If the reaction of *(1)* and *(2)* is performed in the presence of methanol (molar ratio 1:1:1), then *(3)* is trapped by addition of methanol to the P,N bond[6] forming the stable phosphorane *(7)*[5].

The tricyclic title compound *(4)* formed in one step from four acyclic building blocks is identified by the upfield shift of the phosphorus signal, $\delta^{31}P = -57.9$ and by the proton signals of the *cis*- and *trans*-OCH_3 groups which each constitute the X part of $[AX_3]_2$ spin systems: $\delta^1H = 2.92$ ($N = J(POCH) + J(PNPCOH) = 13.6$ Hz) and 3.63 ($N = 12.5$ Hz); OCHR: $\delta^1H = 5.88$ ($N < 1.5$ Hz). Assuming the bridgehead phosphorus to have trigonal-bipyramidal coordination and an axial-equatorial arrangement of all the rings, then three possible configurations (equivalent with regard to the polarity rule) result for *(4)*, *viz. A, B,* and *C* with equatorial, *trans*-axial, and *cis*-axial fusion, respectively; moreover, R may be in a *cis*- or a *trans* position (not shown).



The ^{1}H-NMR spectrum is compatible with each form and also with a mobile equilibrium between *A, B,* and *C*. X-ray structure determination[7] shows that *A* predominates in the crystal, although there is slight distortion towards *C* (Fig. 1).

The four-membered ring is planar and the five-membered rings exhibit an envelope conformation. The *cis* relationship of the groups R and the ring atoms on which they are located corresponds to the *cis* fusion of the five-membered rings (Fig. 1b). As a result of the small internal angles in the four- and five-membered ring at the phosphorus atom, the angle between the two methoxy groups is decreased. The mutual dependence of these two quantities[8] is confirmed by a comparison of the angles at the two crystallographically independent phosphorus atoms.

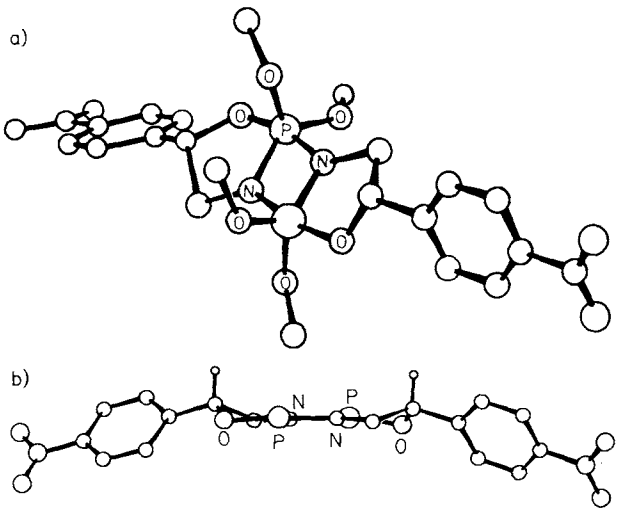


Fig. 1. Two views of the molecular structure of *(4)*. For the sake of clarity, the phenyl groups have been omitted, as have the methoxy groups in (b). The principal bond lengths [pm] and angles [°] are (standard deviations 0.4 pm and 0.2°; the two columns refer to the two crystallographically independent halves of the molecule):

					PNP	102.0	102.2
ax.	PO	169.4	169.0	ap./ap.	OPN	162.5	166.6
eq.	PO	159.0	159.7	ap./eq.	OPN	88.1	89.1
	PO	159.1	159.0		OPO	91.2	92.7
	PN	166.9	165.1		OPO	96.2	96.7
ax.	PN	178.2	176.2		NPN	77.4	78.3
					NPO	91.4	91.8
					NPO	99.3	93.5
				eq./eq.	OPO	105.7	110.8
					NPO	135.3	129.2
					NPO	118.8	119.3

Procedure

(4): (1)[1] (20 mmol) is stirred together with *(2)* (20 mmol) in ether (50 ml) under N_2 for 20 h. Compound *(4)*, which is sparingly soluble also in other solvents, precipitates as crystals which are separated and washed with ether until colorless; m.p. 175—176 °C.

(6): the evaporated filtrate is dissolved in dichloromethane and chromatographed on Al_2O_3. Compound *(6)* crystallizes from the concentrated eluate on stirring with pentane/ether; m.p. 195—196 °C.

(7): (1) (20 mmol) and methanol (20 mmol) in ether (50 ml) are stirred for 20 h with *(2)* (20 mmol). After concentration of the solution to one quarter of its volume, compound *(7)* precipitates as colorless crystals (45% yield); m.p. 135—140 °C (dec.) after recrystallization from dichloromethane with methanol.

Received: February 6, 1980 [Z 582 IE]
German version: Angew. Chem. *92*, 860 (1980)

CAS Registry numbers:
(1), 33027-80-4; *(2)*, 555-16-8; *(4)*, 75102-72-6; *(6)*, 75102-73-7; *(7)*, 75111-38-5

[1] *A. Schmidpeter, W. Zeiss,* Chem. Ber. *104*, 1199 (1971).
[2] *A. Schmidpeter, W. Zeiss,* Angew. Chem. *83*, 379 (1971); Angew. Chem. Int. Ed. Engl. *10*, 396 (1971); *A. Schmidpeter, W. Zeiss, H. Eckert,* Z. Naturforsch. *B 29*, 769 (1972); *W. Zeiss, A. Schmidpeter,* Tetrahedron Lett. *1972*, 4229.
[3] *A. Schmidpeter, J. Luber,* Phosphorus *5*, 55 (1974).
[4] The bicyclic [2+2]-cycloadducts of ketones to 1,2-azaphospholes, which are analogous to *(5)*, could, however, be isolated: *A. Schmidpeter, Th. von Criegern,* Angew. Chem. *90*, 64 (1970); Angew. Chem. Int. Ed. Engl. *17*, 55 (1978); *W. S. Sheldrick, D. Schomburg, A. Schmidpeter, Th. von Criegern,* Chem. Ber. *113*, 55 (1980).
[5] The isolated compounds *(4)*, *(6)*, and *(7)* have satisfactory C, H, N values. *(6)*, $\delta^{31}P = 21.6$; the methoxy groups are diastereotopic: $\delta^1H = 3.38$ ($J(POCH) = 11.6$ Hz) and 3.62 ($J(POCH) = 11.2$ Hz); OCHR: $\delta^1H = 6.38$ ($J(POCH) = 7.0$ Hz). *(7)*, $\delta^{31}P = -59.6$; the protons of the three methoxy groups give only a time-averaged doublet at 36 °C: $\delta^1H = 3.68$ ($J(POCH) = 12.6$ Hz). At −56 °C, however, the reduced rate of pseudorotation permits observation of the expected three resolved signals: equatorial *cis*, equatorial *trans*, axial, $\delta^1H = 3.91$, 3.81, and 3.54, respectively ($J(POCH) = 13.0$, 13.8, and 11.0 Hz).
[6] Acyclic phosphazenes are inert towards alcohols.
[7] *(4)*, triclinic crystals, $P\bar{1}$, with one molecule of diethylether in the unit cell, $a = 13.671(4)$, $b = 16.567(5)$, $c = 9.818(2)$ Å, $\alpha = 97.30(3)$, $\beta = 92.67(4)$, $\gamma = 96.71(4)°$; $Z = 2$; $\rho_{calc} = 1.34$ g cm^{-3}. The structure was solved by direct methods and difference Fourier syntheses, and refined to $R = 0.081$, $R_w = 0.070$, $R_G = 0.075$ for 4342 independent reflections (four-circle diffractometer, $F > 3.0\sigma(F)$). The positions of all the hydrogen atoms except the methyl protons could be located and refined with isotropic temperature factors.—A list of atomic coordinates and structure factors is available on request *(W. S. S.)*.
[8] *A. Schmidpeter, J. Luber, D. Schomburg, W. S. Sheldrick,* Chem. Ber. *109*, 3581 (1976).

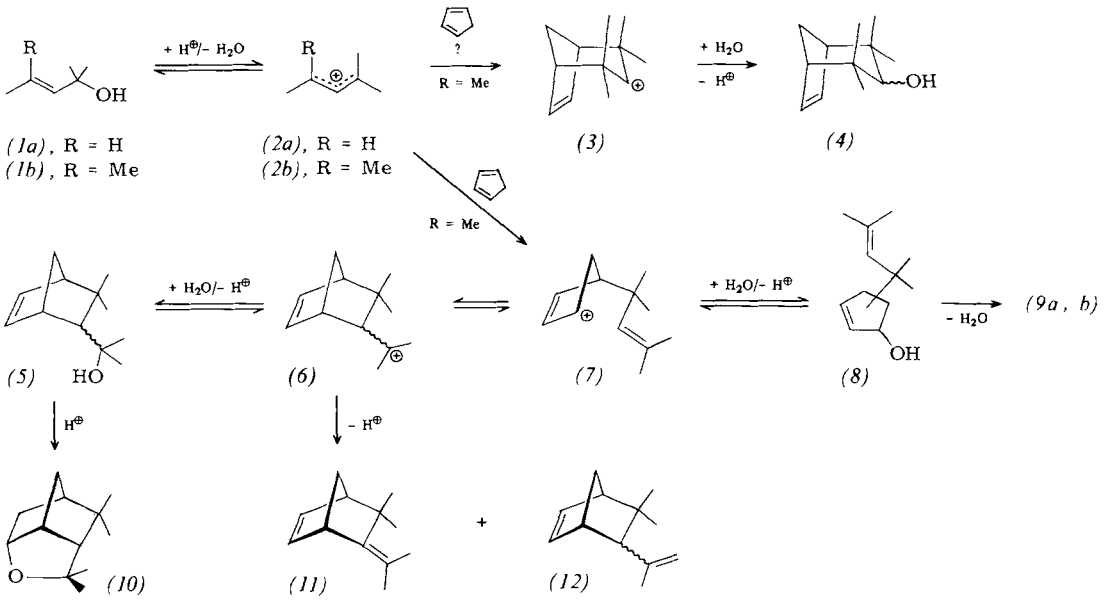
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0826 $ 02.50/0

Synthesis of Norbornenes from Cyclopentadiene and Allyl Alcohols in an Acidic Two Phase System[***]

By *Heidrun Ernst* and *H. M. R. Hoffmann*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Following the synthesis of bicyclo[3.2.1]oct-6-enes[1] from allyl cations and cyclopentadiene, a wide variety of seven- and five-membered rings has become accessible by combination of appropriate π systems[2]. Frequently, although by no means necessarily, the key electrophilic intermediate in these reactions has been a 2-alkoxyallyl cation or a related organometallic species.



We now report that another type of allyl cation, which lacks the potentially electron-releasing substituent at the central carbon of the allyl moiety but has stabilizing terminal substituents, reacts with conjugated dienes in a different manner. The two allyl cations investigated, *i.e.* the α,α,γ-trimethylallyl cation *(2a)* and the $\alpha,\alpha,\gamma,\gamma$-tetramethylallyl cation *(2b)* attack cyclopentadiene to give bridged cyclohexenes. For the sake of brevity only the reaction of 2,4-dimethyl-3-penten-2-ol *(1b)* and cyclopentadiene will be outlined here. Cation *(2b)* was generated in a novel way from the alcohol *(1b)* in a two-phase system consisting of aqueous acid and hydrocarbon solvent. Although cyclopentadiene has long been known to be very acid sensitive[3] and prone to dimerization and polymerization, it survived our experimental conditions at least partially to react with *(2b)*. The main products (30—40%) were the epimeric norbornene type alcohols *(5)* and a mixture of isomeric monocyclic allyl alcohols *(8)*, whereas the two bicyclic olefins *(11)* and *(12)* were formed in traces at 0—25 °C. The structures of *(5)*, *(11)*[4], and *(12)* were secured spectroscopically and by independent synthesis. $AlCl_3$-catalyzed reaction of mesityl oxide and cyclopentadiene gave the corresponding *endo/exo* Diels-Alder adduct[5] which was methylated with methylmagnesium iodide to give *(5)* and also methylenated to give *(12)*. Our reaction scheme is further supported by isolating the product alcohols *(5)* and *(8)*, subjecting them to the reaction conditions, and invoking the principle of microscopic reversibility. For example, when *(5)* was allowed to react with aqueous acid under two phase conditions at higher temperature, *i.e.* 50 °C, the bicyclic olefins *(11)* and *(12)*, cyclic ether *(10)*, and a tricyclic alcohol were formed as comparatively stable products. Significantly, another consecutive product was monocyclic alcohol *(8)* and its dehydration products *(9a, b)*. On the other hand, heating *(8)* at 50 °C under two phase conditions gave compounds *(11)* and *(12)*, the above-mentioned tricyclic alcohol, and the ether *(10)*.

Does the postulated allyl cation intermediate *(2b)* undergo cycloaddition to cyclopentadiene to give the bridged cation *(3)* having a seven-membered ring, analogous to the cycloaddition of the 2-methylallyl cation to cyclopentadiene[1a]? Reduction of 2,2,4,4-tetramethylbicyclo[3.2.1]oct-6-en-3-one[6] with $LiAlH_4$ gave the secondary alcohol *(4)*, which was not dehydrated after 1 h under two phase conditions (reflux). Forcing conditions (heating with $POCl_3$ and pyridine at 117 °C) gave 2,3,4,4-tetramethylbicyclo[3.2.1]octa-2,6-diene, formed by 1,2-methyl shift, and ring-contracted olefin *(12)*[1b]. As we found no trace of *(4)* in the product of the two phase reaction, we believe that the secondary carbenium ion *(3)* is not involved here, and that in any event, its formation would be energetically unfavorable. The formation of the norbornene type alcohol *(5)* is therefore formulated as a stepwise, Diels-Alder-like reaction with an allyl cation as a "dienophile". Presumably, the present work is also related mechanistically to recent studies of 1-alkoxydehydroallyl type cations (generated from propiolic ester and $AlCl_3$), which have been shown to attack appropriate π systems with formation of six-membered and also four-membered rings[7]. Finally, our simplified two phase procedure for generating allyl cations from allyl alcohols is of general preparative interest.

Experimental

(1b) (2.85 g, 25 mmol) and cyclopentadiene (3.3 g, 50 mmol) in pentane (5 ml) are stirred with water (5 ml) containing *p*-toluenesulfonic acid (2.4 g, *ca.* 13 mmol). After 7 h

[*] Prof. H. M. R. Hoffmann, Dr. H. Ernst (née Vathke) [**]
Institut für Organische Chemie der Universität
Schneiderberg 1 B, D-3000 Hannover 1 (Germany)

[**] New address: BASF Hauptlabor, D-6700 Ludwigshafen

[***] Cycloadditions of Allyl Cations, Part 23. We thank the Fonds der Chemischen Industrie and Deutsche Forschungsgemeinschaft for support of our work.—Part 22: *H. M. R. Hoffmann, J. Matthei*, Chem. Ber., in press.

at 0 °C (or 4 h at room temperature) the reaction solution is neutralized with aqueous $NaHCO_3$, the organic phase is separated and the aqueous layer is extracted three times with pentane. The combined organic phase is washed with water, dried (Na_2SO_4) and the solvent is evaporated to leave an oil which is filtered through silica gel (25 g) using pentane as an eluent (200 ml). Elution of the more polar alcohols with ether and bulb-to-bulb distillation gives the following typical composition of products: alcohols *(5)* and *(8)* (1.65 g, 37%, *(5)*:*(8)* = 1:2.4); *(8)* consists of at least three monocyclic isomers (GC, carbowax 20 M), *(5)* is an epimeric mixture (*endo*:*exo* = 2.5:1). The less polar olefin fraction (0.70 g) (from elution with pentane) contains mainly dicyclopentadiene, *(11)* (1%), *(12)* (1%), and two substituted cyclopentadienes *(9a, b)*.

endo-(12) and *exo-(12)* were synthesized independently by methylenation[8] of 6-acetyl-5,5-dimethyl-2-norbornene[5].

Received: May 13, 1980;
supplemented: September 12, 1980 [Z 584 IE]
German version: Angew. Chem. *92*, 861 (1980)

CAS-Registry numbers:
(1b), 56763-70-3; *(4)*, 75111-39-6; *exo-(5)*, 75111-40-9; *endo-(5)*, 75111-41-0; *(8)*, 75102-55-5; *(10)*, 75111-42-1; *(11)*, 75111-43-2; *exo-(12)*, 75111-44-3; *endo-(12)*, 75111-45-4; cyclopentadiene, 542-92-7

[1] a) *H. M. R. Hoffmann, D. R. Joy, A. K. Suter*, J. Chem. Soc. *B 1968*, 57; b) see also *H. M. R. Hoffmann, H. Vathke*, Chem. Ber., in press.
[2] *H. M. R. Hoffmann*, Angew. Chem. *85*, 877 (1973); Angew. Chem. Int. Ed. Engl. *12*, 819 (1973) and subsequent publications; *R. Noyori*, Acc. Chem. Res. *12*, 61 (1979).
[3] a) *A. Wassermann:* Diels-Alder Reactions. Elsevier, Amsterdam 1965; b) *J. P. Kennedy:* Cationic Polymerization of Olefins: A Critical Inventory. Wiley, New York 1975.
[4] 90 MHz ^{1}H-NMR (CCl_4, TMS): δ = 1.04 (s, 3H), 1.30 (s, 3H), 1.68 (s, 6H), 1.36—1.50 (m, 1H), 1.59—1.68 (m, 1H), 2.26—2.40 (m, 1H), 3.40—3.53 (m, 1H), 5.92—6.14 (m, 2H).
[5] *G. Buchbauer, G. W. Hana, H. Koch*, Monatsh. Chem. *107*, 387 (1976).
[6] *H. M. R. Hoffmann, K. E. Clemens, R. H. Smithers*, J. Am. Chem. Soc. *94*, 3940 (1972).
[7] *B. B. Snider, D. J. Rodini, R. S. E. Conn, S. Sealfon*, J. Am. Chem. Soc. *101*, 5283 (1979); *H. Fienemann, H. M. R. Hoffmann*, J. Org. Chem. *44*, 2802 (1979); *H. Mayr*, Habilitation thesis, Universität Erlangen-Nürnberg 1980.
[8] *K. Takai, Y. Hotta, K. Oshima, H. Nozaki*, Tetrahedron Lett. *1978*, 2417; see also *D. Hasselmann*, Chem. Ber. *107*, 3486 (1974).

Formation of Pyrrolnitrin and 3-(2-Amino-3-chlorophenyl)pyrrole from 7-Chlorotryptophan

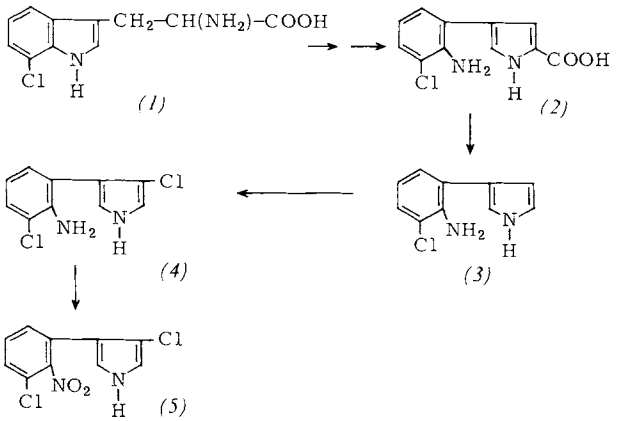
By *Karl-Heinz van Pée, Olga Salcher,* and *Franz Lingens*[*]

Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday

Several phenylpyrrole derivatives have been isolated from gram-negative *Pseudomonas* species and have been characterized; these include the antibiotic pyrrolnitrin *(5)*, aminopyrrolnitrin *(4)*[1] and 4-(2-amino-3-chlorophenyl)-2-pyrrolecarboxylic acid *(2)*[2]. 7-Chlorotryptophan *(1)*[3] was postulated as direct precursor of *(2)*[2]. At which stage of the biosynthesis is the second chlorine atom incorporated?

We report here on the formation of ^{36}Cl-labeled pyrrolnitrin from 7-chlorotryptophan *(1)* and on the isolation and characterization of the new phenylpyrrole derivative 3-(2-amino-3-chlorophenyl)pyrrole *(3)* from *Pseudomonas aureofaciens*, strain P[4].

Precultured cells from the early stationary growth phase of this strain of bacteria[4] were shaken with 2×10^{-3} M *(1)* and $Na^{36}Cl$ or D-tryptophan and $Na^{36}Cl$ for 5 days at 30 °C.



Ethyl acetate extracts were evaporated *in vacuo* and chromatographed on a silica gel 60-F_{254} precoated TLC plate with toluene as eluent. The pyrrolnitrin *(5)* that is formed can be determined with a UV thin layer scanner (calibrated with authentic *(5)*). The spots containing *(5)* were removed from the plate and the radioactivity measured in a dioxane liquid scintillator. The radioactivity of *(5)*—generated respectively by addition of *(1)* and $Na^{36}Cl$ and of D-tryptophan and $Na^{36}Cl$ to the cells—was in the ratio 54:100, *i.e.* one or two ^{36}Cl atoms, respectively, had been incorporated. Under otherwise equal conditions but in the absence of NaCl, the phenylpyrrole derivative *(3)* could be isolated. After an $OD_{560} = 2.0$ had been reached, 2.4×10^{-4} M 7-chlorotryptophan *(1)* was added. The fermentation was terminated after a further 24 h and the cell-free medium brought to pH 8.5 with ammonia. The ethyl acetate extract was evaporated *in vacuo* and chromatographed on silica gel 60 with toluene as eluent. The fractions with $R_f = 0.29$ in TLC (silica gel HF_{254}60, eluent toluene) and $R_f = 0.59$ (eluent toluene/dioxane (10:1), green color-reaction with van Urk's reagent[5]) were purified further by chromatography on silica gel 60 with toluene/dioxane (10:1) as eluent.

The band at longest wavelength in the UV spectrum of the new metabolites *(3)* shows—like the corresponding absorption of *(4)* and *(2)*—a strong hypsochromic shift on going from neutral to acidic medium. λ_{max} in MeOH, MeOH/0.1 N NaOH, and MeOH/0.1 N HCl is 303, 303, and 269, and 221, 221, and 230 nm, respectively.

The NH stretching vibration at 3300 cm^{-1} provides evidence of a pyrrole ring. In the mass spectrum (GC/MS)[6] the molecular ion appears as a doublet at $m/e = 192/194$ (intensity ratio 3:1). This is characteristic for a monochloro-substituted compound with an even number of N atoms.

From the spectral findings and the fact that compound *(3)* is formed by *P. aureofaciens* from 7-chlorotryptophan *(1)* we deduce the structure 3-(2-amino-3-chlorophenyl)pyrrole. *(3)* could be formed in the pyrrolnitrin biosynthesis from *(2)* by decarboxylation and chlorinated to aminopyrrolnitrin *(4)*. The proposed biosynthetic pathway must still be confirmed by enzymatic investigations of the individual steps.

Received: June 13, 1980 [Z 585 IE]
German version: Angew. Chem. *92*, 855 (1980)

CAS Registry numbers:
(1), 75102-74-8; *(2)*, 69275-12-3; *(3)*, 75102-75-9; *(4)*, 16386-65-5; *(5)*, 1018-71-9; D-tryptophan, 153-94-6

[1] *M. Gorman, D. H. Lively* in *D. Gottlieb, P. D. Shaw:* Antibiotics II. Springer, Berlin 1967.
[2] *O. Salcher, F. Lingens, P. Fischer*, Tetrahedron Lett. *1978*, 3097.
[3] *K.-H. van Pée, O. Salcher, F. Lingens*, Liebigs Ann. Chem., in press.
[4] *O. Salcher, F. Lingens*, Tetrahedron Lett. *1978*, 3101.

[*] Prof. Dr. F. Lingens, Dipl.-Chem. K.-H. van Pée, Dr. O. Salcher
Institut für Mikrobiologie der Universität Hohenheim
Garbenstr. 30, D-7000 Stuttgart 70 (Germany)

[5] *E. Stahl, J. Kaldewey,* Hoppe-Seylers Z. Physiol. Chem. *323*, 182 (1961).

[6] Capillary column SE 30/25 m; 80 eV; 220 °C. *m/e* = 192/194 (100%/33%, $M^{\oplus}$), 164/166 (66/22, *M* – HCNH), 156 (17, *M* – Cl), 129 (11, *M* – Cl–HCNH), 128 (16, *M* – HCNH—HCl), 102 (9, *M* – Cl –HCNH—HCN), 101 (8, *M* – HCNH—HCl—HCN).

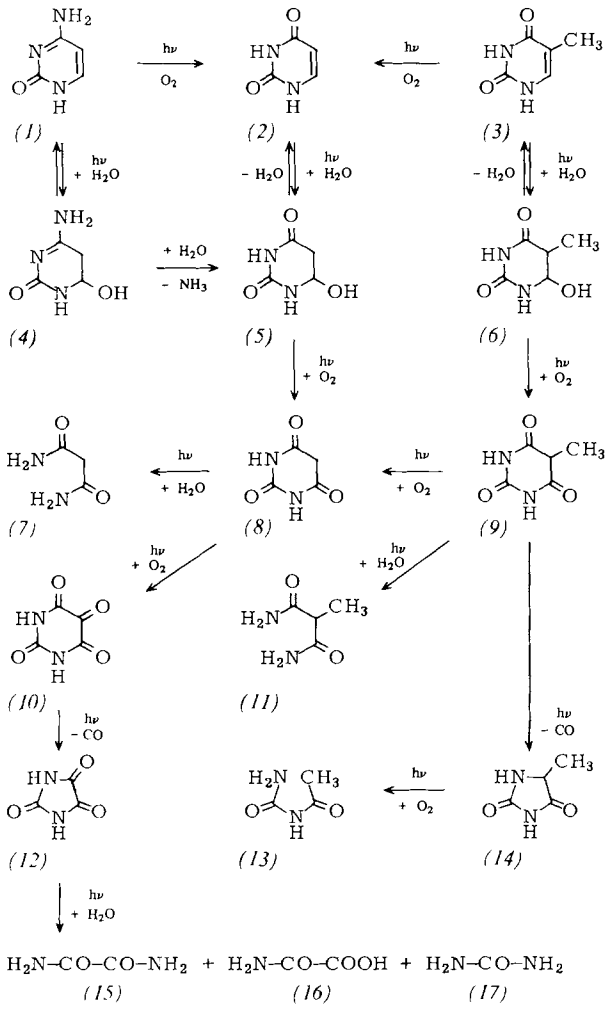
UV Irradiation of Nucleic Acids and Their Components in the Presence of Air[**]

By *Egon Fahr, Peter Fecher, Georg Roth,* and *Peter Wüstenfeld*[*]

Dedicated to Professor Alfred Roedig to the occasion of his 70th birthday

The UV irradiation of nucleic acids and their components has been investigated in great detail *in vitro* and *in vivo*[1]. Essentially, addition of water to the 5,6-double bond of the pyrimidine bases and dimerization of the latter to cyclobutane derivatives is observed. With few exceptions these investigations were carried out in the absence of air.

We have now been able to show that the UV irradiation of nucleic acids and of pyrimidine components of nucleic acids with the usual Hg low-pressure and medium-pressure lamps proceeds completely differently if carried out in aqueous solution in the presence of air.



Very little has been reported in the literature about the UV irradiation of these educts in the presence of air or oxygen. In the case of thymine, thymidine, uracil, uridine, and other pyrimidine derivatives no oxidation products were detected[2]. *Wang* and *Alcantara*[3a,c] report that thymine is oxidized to uracil *via* 5-hydroxy(methyl)uracil, 5-formyluracil, and 5-uracil carbonate. In the case of 1,3-dimethyluracil and 1,3-dimethylthymine CO-elimination to give *N,N*-dimethylmalonodiamide and *N,N*-dimethylmethylmalonodiamide could be demonstrated[4] (see also [3b]).

We have found that photochemical addition of water to cytosine *(1)*, uracil *(2)*, and thymine *(3)* affords the 6-hydroxydihydropyrimidine derivatives *(4)*, *(5)*, and *(6)*, respectively, of which *(4)* is converted by deamination into the corresponding uracil derivative *(5)*. Photochemical oxidation of *(5)* leads *via* barbituric acid *(8)* to alloxan *(10)*; that of *(6)* to methylbarbituric acid *(9)*. Photochemical elimination of CO from *(9)* and *(10)* affords methylhydantoin *(14)* and parabanic acid *(12)*, respectively. The photochemical hydrolysis of *(12)* gives oxamide *(15)*, oxalic acid monoamide *(16)*, and urea *(17)*, that of *(9)* methylmalonamide *(11)* and that of *(8)* malonamide *(7)*. The photochemical oxidation of *(14)* leads to acetylurea *(13)*.

Cytosine *(1)* affords the same irradiation products as uracil *(2)*, since it is either converted *via (4)* into *(5)* or by direct photochemical oxidation into uracil *(2)*. *(2)* can be detected in the irradiation solution of *(1)*.

The photochemical CO-elimination observed here is also displayed by cytidine, uridine, and thymidine as well as the pyrimidine components of polyuridylic acid and DNA, but not by the purine components of nucleic acids (adenine, guanine, adenosine, and guanosine were investigated).

In the earth's atmosphere there are *ca.* 400 million tons CO, which decomposes with a halflife of *ca.* 3 months (CO cycle of the earth's atmosphere[5]). CO emission into the atmosphere is 1.3—1.5 thousand million tons per annum, of which *ca.* 300 million tons originate from biological processes.

The formation of CO by higher plants, fungi, algae and microorganisms and their dependence on light has been demonstrated on a number of occasions[6]; the reactions responsible, however, are largely unknown. Possibly the photochemical elimination of CO from nucleic acids described here contributes to this CO production.

Experimental

Ca. 10^{-3} M solutions of the educts in water, through which a stream of filtered air was passed, were irradiated with VG-NN-15/22 Hg low-pressure lamps or TQ 718 Hg medium-pressure lamps (Original Hanau, Quarzlampen-Gesellschaft, Hanau). Wavelengths <210 were eliminated by filter-solutions.

The identification of the compounds *(1)—(3)*, *(7)*, and *(9)—(17)* in the irradiation mixtures was achieved by GC and TLC comparison with authentic material and by the use of precision mass spectrometry. The 6-hydroxydihydropyrimidine derivatives *(4)* and *(5)* were detected by cleavage of H_2O to give *(1)* and *(2)*, respectively. *(6)* cannot be detected directly. Its intermediary formation follows from the secondary products *(9)* and *(11)*. Barbituric acid *(8)* is oxidized photochemically to alloxan *(10)* so rapidly that it cannot be found in the irradiation mixture. CO-detection tubes (Drägerwerk AG, Gasanalysentechnik, Lübeck) were employed for the detection of CO.

[*] Prof. Dr. E. Fahr, Dr. P. Fecher, Dr. G. Roth, Dr. P. Wüstenfeld
Institut für Organische Chemie der Universität
Johann-Joachim-Becher-Weg 18—20, D-6500 Mainz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Received: June 20, 1980 [Z 586 IE]
German version: Angew. Chem. 92, 858 (1980)

CAS Registry numbers:
(1), 71-30-7; *(2)*, 66-22-8; *(3)*, 65-71-4; *(4)*, 10010-80-7; *(5)*, 1194-23-6; *(6)*, 13514-92-6; *(7)*, 108-13-4; *(8)*, 67-52-7; *(9)*, 2417-22-3; *(10)*, 50-71-5; *(11)*, 1113-63-9; *(12)*, 120-89-8; *(13)*, 591-07-1; *(14)*, 616-03-5; *(15)*, 471-46-5; *(16)*, 471-47-6; *(17)*, 57-13-6

[1] a) *E. Fahr*, Angew. Chem. *81*, 581 (1969); Angew. Chem. Int. Ed. Engl. *8*, 578 (1969); b) *S. Y. Wang*, Photochemistry and Photobiology of Nucleic Acids. Academic Press, New York 1976.

[2] *R. Beukers, J. Ijlstra, W. Berends*, Rec. Trav. Chim. Pays-Bas *78*, 879 (1959); *I. H. Brown, H. E. Johns*, Photochem. Photobiol. *8*, 273 (1968); *J. H. Fendler, G. Bogan, ibid. 20*, 323 (1974); *C. L. Greenstock, I. H. Brown, J. W. Hunt, H. E. Johns*, Biochem. Biophys. Res. Commun. *27*, 431 (1976).

[3] a) *R. Alcantara, S. Y. Wang*, Photochem. Photobiol. *4*, 473 (1965); b) *ibid. 4*, 465 (1965); c) *S. Y. Wang, R. Alcantara, ibid. 4*, 477 (1965).

[4] *S. Y. Wang*, J. Am. Chem. Soc. *80*, 6199 (1958); Nature *184*, B. A. 59 (1959).

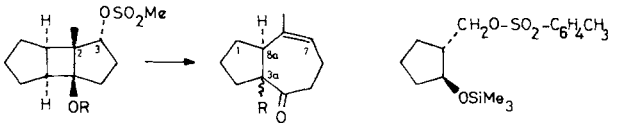
[5] *K. H. Liebl, W. Seiler* in *H. G. Schlegel, J. Gottschalk, N. Pfennig*: Proc. Symp. Microbial Production and Utilization of Gases. Verlag E. Goetze, Göttingen 1976, p. 215ff.

[6] *K. Bauer, R. Conrad, W. Seiler*, Biochim. Biophys. Acta *589*, 46 (1980), and references cited therein; *K. Bauer, W. Seiler, H. Giehl*, Z. Pflanzenphysiol. *94*, 219 (1979), and references cited therein.

Fluoride-Induced Fragmentation of Trimethylsilyloxysulfonates to Form *cis*-Coupled Hexahydroazulenones[**]

By *Lutz-F. Tietze* and *Ulrich Reichert*[*]

Cleavage reactions of the heterolytic fragmentation type[1] have great importance in the stereoselective synthesis of olefins[2], in the preparation of cyclic compounds of medium ring size[3], and in the formation of substituted ring systems of definite configuration[4]. A general and simple method is the base-induced fragmentation of the monosulfonates of 1,3-diols. However, this method has the great disadvantage that condensations[4] and isomerizations at the α-position to the newly formed carbonyl group can occur in a strongly basic reaction medium[5]. Thus, in the fragmentation of compounds of the structural type *(1)* with potassium *tert*-butoxide or potassium hydroxide mainly the thermodynamically stable *trans*-coupled bicyclic system of type *(4)* is formed. The fluoride-induced fragmentation[6] of the silyl ether *(2)*, on the other hand, leads exclusively to the *cis*-coupled hexahydroazulenone *(3)*. *(3)* corresponds to the substructure of the sesquiterpene of the eregoyazine type[7].



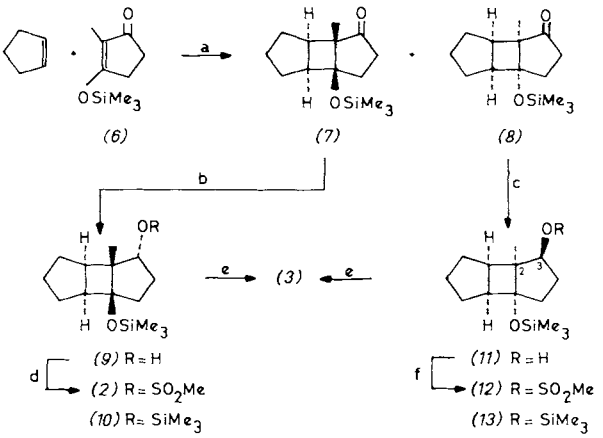
(1) R = H
(2) R = $SiMe_3$

(3) R = α-H
(4) R = β-H

(5)

For the synthesis of *(2)* a 35:1 mixture of cyclopentene and the trimethylsilyl ether *(6)*, which can be prepared in 91% yield by reaction of 2-methylcyclopentane-1,3-dione with hexamethyldisilazane/imidazole, was photolyzed at −60 °C (Scheme 1). After chromatography the cyclobutane derivatives *(7)* and *(8)* are obtained in a ratio of *ca.* 3:2 (total yield 51%). *(7)* and *(8)* were reduced to the crystalline alcohols *(9)* (m.p. 74 °C) and *(11)* (m.p. 71 °C)[8a], which on reaction with methanesulfonyl chloride gave the sulfonates *(2)* and *(12)*[8b]. In the case of *(11)* the reaction proceeded very slowly owing to strong steric shielding, and was still not complete after 100 h.

Reaction of *(2)* and of *(12)* with potassium fluoride in the presence of [18]crown-6 in dichloromethane gave the *cis*-coupled bicycle *(3)* as sole product in 78% and 76% yield, respectively. Thus, for the synthesis of *(3)* it is not necessary to separate *(7)* and *(8)*. The formation of the (*Z*)-C=C double bond in *(3)* is consistent with the *trans* arrangement of the substituents on C-2 and C-3 in *(2)* and *(12)*.



(6) *(7)* *(8)*

(9) R = H
(2) R = SO_2Me
(10) R = $SiMe_3$

(11) R = H
(12) R = SO_2Me
(13) R = $SiMe_3$

Scheme 1. a: high-pressure mercury lamp, quartz apparatus, 4 h, −60 °C; chromatography on silica gel with ether/pentane (1:3); 31% *(7)*, $R_F = 0.56$; 21% *(8)*, $R_F = 0.58$.—b: $LiAlH_4$, ether, 3 h, 42 °C (83%).—c: $LiAlH_4$, ether, 3 h, 42 °C (90%).—d: $MeSO_2Cl$, pyridine, dimethylaminopyridine (DMAP) [9], 8 h, 20 °C (86%).—e: KF, [18]crown-6, CH_2Cl_2, 4 h, 20 °C (78/76%).—f: $MeSO_2Cl$, pyridine, DMAP [9], 100 h, 20 °C (68%). The yields refer to isolated and analytically pure products.

(3) did not isomerize under the given reaction conditions, even after 48 h. Treatment of *(3)* with potassium *tert*-butoxide, on the other hand, led to a 1:4-mixture of *(3)* and *(4)*. The structures of *(3)* and *(4)* are in agreement with the analytical data (cf. [10]).

Experiments with other nucleofugal groups were less clear-cut. Thus, reaction of *(9)* with trifluoromethanesulfonic anhydride/pyridine gave the fragmentation product *(3)* directly in 50% yield together with 35% *(10)*; *(11)* afforded 46% *(3)* and 35% *(13)*. Presumably the trifluoromethanesulfonates are initially formed, at least partially, and then these fragment to *(3)* by nucleophilic attack of the trifluoromethanesulfonate ion at the silyl group. The trimethylsilyl trifluoromethanesulfonate formed in this reaction could then silylate unreacted *(9)* and *(11)* to *(10)* and *(13)*, respectively.

The scope of the above fragmentation reaction appears to be limited to strained cyclic systems. Thus the silyl ether *(5)*[11] does not react with potassium fluoride/[18]crown-6 within 24 h at 20 °C.

Received: May 13, 1980 [Z 568 IE]
German version: Angew. Chem. *92*, 832 (1980)

CAS Registry numbers:
(1), 74965-23-4; *(2)*, 74965-24-5; *(3)*, 74965-25-6; *(4)*, 74965-26-7; *(6)*, 1121-05-7; *(7)*, 74965-27-8; *(8)*, 74985-50-5; *(9)*, 74965-28-9; *(10)*, 74965-29-0; *(11)*, 74985-51-6; *(12)*, 74985-52-7; *(13)*, 74985-53-8; cyclopentene, 142-29-0

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. U. Reichert
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie.

[1] *C. A. Grob, P. W. Schiess*, Angew. Chem. *79*, 1 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1 (1967); *C. A. Grob, ibid. 81*, 543 (1969) and *8*, 535 (1969), and references cited therein.

[2] Examples from the field of natural products include, *inter alia*: *E. J. Corey, R. B. Mitra, H. Uda*, J. Am. Chem. Soc. *86*, 485 (1964); *R. Zurflüh, E. N. Wall, J. B. Sidall, J. A. Edwards, ibid. 90*, 6224 (1968).

[3] Entry to macrolides is also possible by double fragmentation: a) *D. Sternbach, M. Shibuya, F. Jaisli, M. Bonetti, A. Eschenmoser*, Angew. Chem. *91*, 670 (1979); Angew. Chem. Int. Ed. Engl. *18*, 634 (1979); b) *M. Shibuya, F. Jaisli, A. Eschenmoser, ibid. 91*, 672 (1979) and *18*, 636 (1979); c) see ref. [3] in [3a].

[4] a) *G. Kinast, L.-F. Tietze*, Chem. Ber. *109*, 3626 (1976); b) *L.-F. Tietze, G. Kinast, H. C. Uzar*, Angew. Chem. *91*, 576 (1979); Angew. Chem. Int. Ed. Engl. *18*, 541 (1979).
[5] *B. D. Challand, H. Hikino, G. Kornis, G. Lange, P. de Mayo*, J. Org. Chem. *34*, 794 (1969).
[6] The fluoride-induced fragmentation of a trimethylsilylcarbon compound has already been described: *H. Gerlach*, Helv. Chim. Acta *60*, 3039 (1977).
[7] *W. Vichnewski*, J. Org. Chem. *42*, 3910 (1977), and references cited therein.
[8] a) The relative configuration at C-3 in *(9)* and *(11)* was determined ^{1}H-NMR spectroscopically using the shift reagent Yb(fod)$_3$; b) the isomeric methanesulfonates *(2)* and *(12)* decompose in the pure form at room temperature. After 48 h a mixture of *(3)* and *(4)* could be isolated from the black oil in 16% yield.
[9] *G. Höfle, W. Steglich, H. Vorbrüggen*, Angew. Chem. *90*, 602 (1978); Angew. Chem. Int. Ed. Engl. *17*, 569 (1978).
[10] ^{1}H-NMR (100 MHz, $CDCl_3$): *(3)*: $\delta = 5.56$ (m, 7-H), 3.55 [m, $J_{3a,8a} = 9.5$ Hz (determined by decoupling experiments, irradiation at $\delta = 1.63$), 3a-H], 2.77 (m, 8a-H), 2.55 (br. s, 5-H_2), 1.70 (s, CH_3), 2.40—1.30 (m, 8 aliphatic H). *(4)*: $\delta = 5.56$ (m, 7-H), 3.04 (m, 3a-H), 2.95—2.65 (m, 8a-H), 2.39 (br. s, 5-H_2), 1.78 (s, CH_3), 2.40—1.30 (m, 8 aliphatic H).
[11] Synthesis by reaction of *trans*-(2-hydroxycyclopentylmethyl)-*p*-toluenesulfonate [4a] with trimethylsilyl chloride in pyridine/ether; yield 82%.

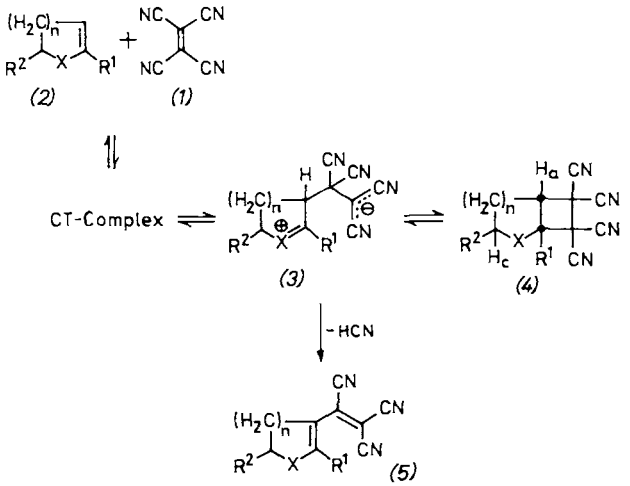
Thermal [2+2]-Cycloadditions of Tetracyanoethylene to Cyclic Thioenol Ethers[**][1]

By *Siegfried Fries* and *Klaus Gollnick*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Thermal [2+2]-cycloadditions of tetracyanoethylene *(1)* to *acyclic* thioenol ethers have recently been the subject of numerous reports[2].

We have now found that thermal [2+2]-cycloadditions of *(1)* to the *cyclic* thioenol ethers *(2a, b)* (3,4-dihydro-2*H*-thiopyrans) and *(2d-f)* (2,3-dihydrothiophenes) occur—*via* spontaneously formed, deep-blue CT complexes which disappear within minutes at room temperature and at about $-20\,^\circ C$, respectively—to give the corresponding tetracyanocyclobutane derivatives *(4)*, which generally crystallize analytically pure in 85—95% yield[3].



	n	X	R^1	R^2
a	2	S	H	H
b	2	S	CH_3	H
c	2	O	H	H
d	1	S	H	H
e	1	S	CH_3	H
f	1	S	CH_3	$CH(CH_3)_2$
g	1	O	CH_3	H

The oxygen analogues *(2c)* and *(2g)* react with *(1)* to give red CT complexes which are stable at $-20\,^\circ C$, but cyclize at $+20\,^\circ C$ within 4 h and ≈ 1 min, respectively, to the corresponding tetracyanocyclobutanes *(4c)* and *(4g)*. Obviously, 3,4-dihydro-2*H*-thiopyrans such as *(2a)* and 2,3-dihydrothiophenes such as *(2e)* react with *(1)* much more rapidly than their oxygen analogues. Under otherwise equal conditions the rates of cycloaddition (determined as the time elapsed up to disappearance of the CT complexes) of *(1)* to the cyclic thioenol ethers increase along the series *(2a)* < *(2b)* < *(2d)* < *(2f)* ≤ *(2e)*. Thus, 2,3-dihydrothiophenes react faster than 3,4-dihydro-2*H*-thiopyrans, and the methyl-substituted derivatives such as *(2b)* and *(2e)* react better than their unsubstituted parent compounds *(2a)* and *(2d)*, respectively. The relatively bulky isopropyl group in *(2f)* only moderately retards the rate of cycloaddition. Increasing solvent polarity promotes the cycloaddition; thus, the reaction rates of *(1)* + *(2a)* in tetrahydrofuran (E_T[4] = 37.4), dichloromethane ($E_T = 41.1$), and acetonitrile ($E_T = 46.0$) are in the ratio of about 1:2:10.

Increasing solvent polarity promotes not only the cycloaddition, but also the dissociation of the cyclobutane derivatives *(4d, f, g)* to their educts. The cycloreversion is easily recognized by the characteristic color of the CT complexes which appear on dissolution of the cyclobutanes in dimethyl sulfoxide or acetonitrile. Furthermore, elimination of hydrogen cyanide occurs; compounds *(5)*, however, were not intercepted. Formation of HCN is also observed in the reaction of *(1)* with the 2,3-dihydrothiophenes in acetonitrile at room temperature, whereas with 3,4-dihydro-2*H*-thiopyrans only cycloaddition reactions occur.

Our results can only be explained by assuming that in the rate-determining step zwitterionic intermediates of type *(3)* are formed, as is the case in the reaction of *(1)* with enol ethers [5]. Depending upon the solvent polarity, the zwitterions *(3)* then undergo competition reactions to give the cycloadducts *(4)* or eliminate HCN with formation of *(5)*. Alkyl substituents R^1 (such as CH_3) stabilize an intermediate carbenium ion and thus lower the energy of the transition state which leads to the zwitterion. The reaction of *(1)* with cyclic thioenol ethers is therefore accelerated by an α-methyl group as is the dissociation of the cycloadducts. The increased rate of cyclization of thioenol ethers with *(1)* and the enhanced cycloreversion of their cycloadducts as compared to the reactions of the corresponding oxygen derivatives are then due to the fact that sulfonium ions *(3)*, X = S, are more resonance-stabilized than the corresponding oxonium ions *(3)*, X = O. Since all steps of the cycloaddition reactions are reversible, we assume that the cycloadducts *(4)* exhibit the thermodynamically more stable *cis*-fusion of the rings.

Received: March 12, 1980 [Z 574a IE]
German version: Angew. Chem. *92*, 848 (1980)

CAS Registry numbers:
(1), 670-54-2; *(2a)*, 13042-80-3; *(2b)*, 13042-79-0; *(2c)*, 110-87-2; *(2d)*, 1120-59-8; *(2e)*, 4610-02-0; *(2f)*, 75066-71-6; *(2g)*, 1487-15-6; *(4a)*, 75066-72-7; *(4b)*, 75066-73-8; *(4c)*, 69798-90-9; *(4d)*, 75066-74-9; *(4e)*, 75066-75-0; *(4f)*, 75066-76-1; *(5a)*, 75066-77-2; *(5b)*, 75066-78-3; *(5c)*, 75066-79-4; *(5d)*, 75066-80-7; *(5e)*, 75066-81-8; *(5f)*, 75066-82-9; *(5g)*, 75066-83-0; *(4g)*, 75066-84-1

[*] Prof. Dr. K. Gollnick, Dr. S. Fries
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] From the Dissertation *S. Fries*, Universität München 1977.
[2] a) *J. K. Williams, D. W. Wiley, B. C. McKusick*, J. Am. Chem. Soc. *84*, 2210 (1962); b) *T. Okuyama, M. Nakada, K. Toyoshima, T. Fueno*, J. Org. Chem. *43*, 4546 (1978); c) *H. Graf, R. Huisgen, ibid. 44*, 2594 (1979).
[3] ^{1}H-NMR [$(CD_3)_2CO$]: *(4a)*: $\delta = 3.75$ (m, H_a), 4.90 (d, $J_{ab} = 9$ Hz, R^1 = H_b), 3.0 (m, 2H_c, R^2 = H_c); *(4b)*: $\delta = 3.72$ (m, H_a), 3.0 (m, 2H_c, R^2 = H_c), 2.00 (s, 3H, R^1 = CH_3); *(4d)*: $\delta = 4.50$ (m, H_a), 5.05 (d, $J_{ab} = 9$ Hz, R^1 = H_b), 3.25 (m,

$2H_c$, $R^2 = H_c$); *(4f)*: $\delta = 3.80$ (m, H_a), 4.05 (m, H_c), 2.00 (s, 3H, $R^1 = CH_3$), 1.05 (d, $J = 6$ Hz, 6H, $R^2 = CH(CH_3)_2$).

[4] *C. Reichardt:* Solvent Effects in Organic Chemistry. Verlag Chemie, Weinheim 1979, p. 242ff.

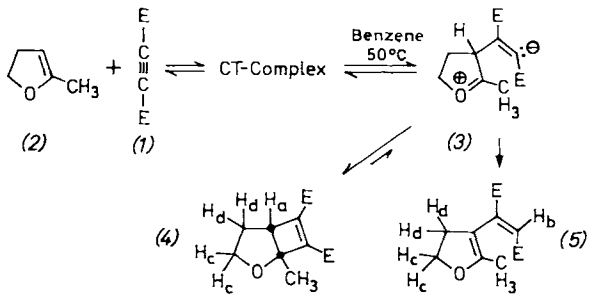
[5] Review: *R. Huisgen*, Acc. Chem. Res. *10*, 117 (1977).

Thermal Cycloadditions of Dimethyl Acetylenedicarboxylate to Cyclic Enol Ethers and Thioenol Ethers[**]

By *Klaus Gollnick* and *Siegfried Fries*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

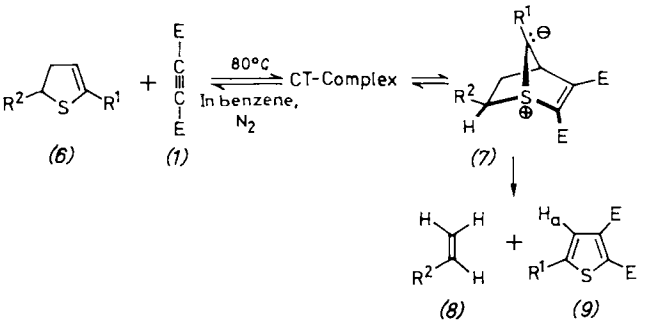
Cyclic enol ethers and thioenol ethers cycloadd to tetracyanoethylene (TCNE) in high yields under mild conditions[1]. On attempting to react dimethyl acetylenedicarboxylate *(1)*, $E = CO_2CH_3$, with 3,4-dihydro-2*H*-pyran, 2,3-dihydrofuran, or 5-methyl-2,3-dihydrofuran *(2)*, only the α-methylated enol ether *(2)* proved to be reactive enough to give *via* a pale yellow CT complex the [2+2]-cycloproduct *(4)*[2] as well as dimethyl 2-(2-methyl-4,5-dihydro-3-furyl)fumarate *(5)*[3].



Formation of *(5)* from the cycloadduct *(4)* is ruled out, since *(4)* is stable even in boiling toluene (110 °C). We assume that a zwitterionic intermediate *(3)* is formed from the CT complex, as was similarly discussed for [2+2]-cycloadditions with TCNE. Only then is the formation of *(5)* easily explained by prototropy in the dipole. The remarkable reaction-promoting influence of a methyl group, which has also been observed in the [2+2]-cycloaddition of *(1)* to 2-alkoxy-3,4-dihydro-2*H*-pyrans[4] and of TCNE to enol ethers and thioenol ethers[1], is then due to a stabilization of the oxonium ions of type *(3)*; alkyl groups thus lower the transition states which have to be passed in the rate-determining step that leads to the zwitterion.

The thioenol ethers *(6a—c)* and *(10a, b)* form yellow CT complexes on reaction with *(1)* in benzene. However, whereas the 3,4-dihydro-2*H*-thiopyrans *(10a, b)* are recovered unchanged from boiling benzene, the 2,3-dihydrothiophenes react with *(1)* in boiling benzene within several hours to give the alkenes *(8)* and dimethyl 2,3-thiophenedicarboxylates *(9)*[5].

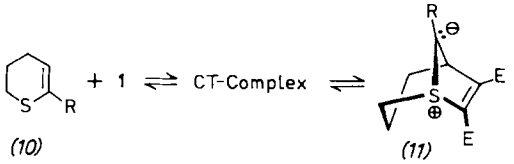
Of the three 2,3-dihydrothiophenes, *(6c)* reacts most rapidly. 3-Methyl-1-butene *(8b)* is apparently a better leaving group than ethylene. This was shown also in an attempt to react *(6a—c)* with methyl propiolate in boiling xylene



(6a), $R^1 = R^2 = H$ → *(8a)*, $R^2 = H$ + *(9a)*, $R^1 = H$
(6b), $R^1 = CH_3$, $R^2 = H$ → *(8a)*, $R^2 = H$ + *(9b)*, $R^1 = CH_3$
(6c), $R^1 = CH_3$, $R^2 = i\text{-}C_3H_7$ → *(8b)*, $R^2 = i\text{-}C_3H_7$ + *(9b)*, $R^1 = CH_3$

(140 °C), in which only *(6c)* underwent olefin elimination to give *(8b)*.

The results may be easily explained in terms of a *[2+3]-cycloaddition* of *(1)* to the thioenol ethers *(6)* to afford the bicyclic sulfonium ylides *(7)*, which subsequently react according to a retro-[2+3]-cycloaddition by elimination of an alkene *(8)* to give a 2,3-thiophenedicarboxylic acid ester *(9)*. The sulfonium ylide *(7)* may be stabilized by an overlap of the sp^3 anion orbital with a sulfur d-orbital[9]; in the oxygen analogue of *(7)*, however, the formation of a (p-d)π bond is impossible. The reaction of *(1)* with *(2)* therefore appears to prefer the energetically favored route *via* the 1,4-dipole *(3)*. *(1)* should also react with the 3,4-dihydro-2*H*-thiopyrans *(10a, b) via* CT complexes to give sulfonium ylides *(11)*, but this route proves to be a dead end, since the stabilization by a retro-[2+3]-cycloaddition to give *(1)* + *(10)* is apparently far more effective than by a fragmentation to 2,3-thiophenedicarboxylic ester + cyclopropane.



(a), R = H
(b), R = CH_3

Received: March 12, 1980 [Z 574b IE]
German version: Angew. Chem. *92*, 848 (1980)

CAS Registry numbers:
(1), 762-42-5; *(2)*, 1487-15-6; *(4)*, 75067-10-6; *(5)*, 75067-11-7; *(6a)*, 1120-59-8; *(6b)*, 4610-02-0; *(6c)*, 75066-71-6; *(8a)*, 74-85-1; *(8b)*, 563-45-1; *(9a)*, 14300-68-6; *(9b)*, 75067-12-8; *(10a)*, 13042-80-3; *(10b)*, 13042-79-0

[*] Prof. Dr. K. Gollnick, Dr. S. Fries
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *S. Fries, K. Gollnick*, Angew. Chem. *92*, 848 (1980); Angew. Chem. Int. Ed. Engl. *19*, 831 (1980).

[2] After chromatography on silica gel (CH_2Cl_2), 15% yield, crystalline, analytically pure. ^{1}H-NMR ($CDCl_3$): $\delta = 3.15$ (m, H_a), 4.10 (m, $2H_c$), 1.90 (m, $2H_d$), 1.60 (s, 3H, CH_3), 3.79 and 3.81 (each s, 3H, OCH_3).

[3] After chromatography on silica gel (CH_2Cl_2), 20% yield, oily substance, analytically pure. ^{1}H-NMR ($CDCl_3$): $\delta = 6.65$ (s, H_b), 4.40 (t, $J_{cd} = 9$ Hz, $2H_c$), 2.90 (t, $J_{cd} = 9$ Hz, $2H_d$), 1.67 (s, 3H, CH_3); 3.74 and 3.80 (each s, 3H, OCH_3). (In diethyl fumarate the olefinic protons appear at $\delta = 6.83$, in diethyl maleate at $\delta = 6.28$.)

[4] *S. S. Hall, A. J. Duggan*, J. Org. Chem. *39*, 3432 (1974).

[5] *(9a)*: 16% yield, analytically pure, m.p. 35 °C [6]; ^{1}H-NMR ($CDCl_3$): $\delta = 7.27$ (d, $J_{ab} = 4.5$ Hz, H_a), 7.46 (d, $J_{ab} = 4.5$ Hz, $R^1 = H_b$), 3.89 (s, 6H, $2OCH_3$); *(9b)*: 16% yield [from *(6b)*] or 37% yield [from *(6c)*], analytically pure, after distillation at 170 °C/15 torr [7]; ^{1}H-NMR ($CDCl_3$): $\delta = 6.93$ (q, $J = 1$ Hz, H_a), 2.50 (q, $J = 1$ Hz, 3H, $R^1 = CH_3$), 3.86 and 3.84 (each s, 3H, OCH_3); structure determination see [8].

[6] *J. Sicé*, J. Org. Chem. *19*, 70 (1954).

[7] *R. G. Jones*, J. Am. Chem. Soc. *77*, 4069 (1955).

[8] *K. Gollnick, S. Fries*, to be published.

[9] a) *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. Int. Ed. Engl. *8*, 639 (1969); b) *B. M. Trost, L. S. Melvin, Jr.*: Sulfur Ylides. Academic Press, New York 1975, p. 23.

Thermal Additions of Dimethyl Acetylenedicarboxylate to Cyclic Thioenol Ether 1-Oxides with Ring Expansion[**]

By *Klaus Gollnick* and *Siegfried Fries*[*]

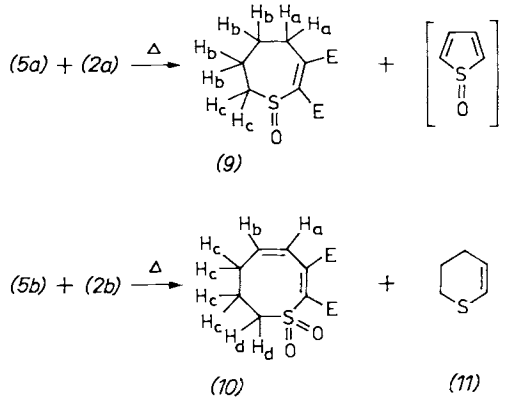
Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Cyclic thioenol ethers react with tetracyanoethylene (TCNE) to give [2+2]-cycloadducts[1a]. With dimethyl acetylenedicarboxylate *(1)*, $E = CO_2CH_3$, however, they undergo [2+3]-cycloaddition reactions to form unstable sulfonium ylides[1b].

Like their parent cyclic thioenol ethers, the 1-oxides afford colored CT complexes with TCNE; however, [2+2]-cycloadditions do not occur. With *(1)* and the 1-oxides of 2,3-dihydrothiophene *(2a)*, 3,4-dihydro-2*H*-thiopyran *(2b)* and its α-methyl derivative *(2c)* colored CT complexes are no longer observed. If, however, the components are heated for several hours in benzene at 80 °C or in toluene at 110 °C, dimethyl 6,7-dihydrothiepin-2,3-dicarboxylate 1-oxide *(5a)*, dimethyl 3,4-dihydro-2*H*-thiocin-7,8-dicarboxylate 1-oxide *(5b)* and its 6-methyl derivative *(5c)*[2], respectively, are isolated in about 10% yield (benzene) or 35% yield (toluene) (after chromatographic purification).

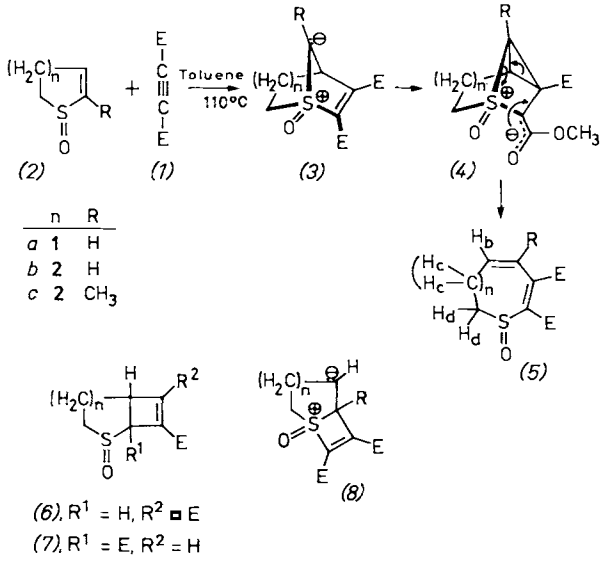
[2+2]-Cycloadditions to give cycloadducts of type *(6)* (with subsequent rearrangement *via (7)* to give *(5)*), and presumably also of type *(8)* are ruled out as a mode of formation[3]. On the other hand, a [2+3]-cycloaddition of *(1)* to *(2a—c)* to give the sulfonium ylide *S*-oxide *(3)* appears to be an attractive reaction route; in a similar way reactions of *(1)* and cyclic thioenol ethers afford bicyclic sulfonium ylides[1b]. However, whereas the latter undergo only retro-[2+3]-cycloadditions, the ylides *(3)* should be able to react further in an intramolecular Michael addition to give the tricyclic sulfonium ylide *S*-oxides *(4)*[4]. The tricycles *(4)* then rearrange to the monocyclic sulfoxides *(5)*. With the formation of *(3)* as the rate-determining step the observations that *(2c)* reacts essentially slower than *(2b)*, and that 2-isopropyl-5-methyl-2,3-dihydrothiophene 1-oxide no longer reacts, become intelligible[3].

The sulfoxides *(2a—c)* are stable for longer periods even in boiling xylene (140 °C). On the other hand, in the absence of solvents they rapidly disproportionate at higher temperatures into the thioenol ethers and the thioenol ether 1,1-dioxides. On heating 1:1 mixtures of the sulfoxides *(2b)* and *(5b)* in the absence of solvents, oxygen transfer takes place exclusively from *(2b)* to *(5b)* to give dimethyl 3,4-dihydro-2*H*-thiocin-7,8-dicarboxylate *(10)*[5] and the thioenol ether *(11)*. Under the same conditions, sulfoxides *(2a)* and *(5a)*, however, disproportionate by hydrogenation of *(5a)* to dimethyl 4,5,6,7-tetrahydrothiepin-2,3-dicarboxylate 1-oxide *(9)*[6] and by dehydrogenation of *(2a)* to the as yet unobtained monomeric thiophene 1-oxide[7]. Heating of the sulfoxides *(5a)* and *(5b)* above their melting points results only in resinification. These reactions may drastically lower the yields of *(5)*.



Received: March 12, 1980 [Z 574c IE]
German version: Angew. Chem. 92, 849 (1980)

CAS Registry numbers:
(1), 762-42-5; *(2a)*, 14852-21-2; *(2b)*, 16841-59-1; *(2c)*, 75067-13-9; *(5a)*, 75067-14-0; *(5b)*, 75067-15-1; *(5c)*, 75067-16-2; *(9)*, 75067-17-3; *(10)*, 75067-18-4; *(11)*, 13042-80-3; thiophene 1-oxide, 2657-73-0



	n	R
a	1	H
b	2	H
c	2	CH_3

[*] Prof. Dr. K. Gollnick, Dr. S. Fries
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fond der Chemischen Industrie.

[1] a) *S. Fries, K. Gollnick*, Angew. Chem. 92, 848 (1980); Angew. Chem. Int. Ed. Engl. 19, 831 (1980); b) *K. Gollnick, S. Fries*, Angew. Chem. 92, 848 (1980); Angew. Chem. Int. Ed. Engl. 19, (1980).

[2] *(5a)*: m.p. 132 °C (after chromatography on silica gel; CH_2Cl_2/CH_3OH (9:1); analytically pure; 34% yield); ^{1}H-NMR ($CDCl_3$): δ = 5.78 (m, J_{ab} = 8 Hz, J_{ac} = 1.9 Hz, R = H_a), 6.70 (m, J_{ab} = 8 Hz, H_b), 2.95 (m, 2 H_c), 3.60 (m, 2 H_d), 3.67 and 3.80 (each s, 3 H, OCH_3); IR (KBr): 1040—1070 cm^{-1} (S=O); *(5b)*: m.p. 108 °C (purification as in the case of *(5a)*; analytically pure 35% yield); ^{1}H-NMR ($CDCl_3$): δ = 5.82 (m, J_{ab} = 10 Hz, J_{ac} = 1.5 Hz, R = H_a); 6.57 (m, J_{ab} = 10 Hz, H_b), 2.38 (m, 4 H_c), 3.30 (m, 2 H_d), 3.68 and 3.85 (each s; 3 H, OCH_3); IR: 1045—1060 cm^{-1} (S=O); *(5c)*: m.p. 104 °C (purification as for *(5a)*, analytically pure, 36% yield); ^{1}H-NMR ($CDCl_3$): δ = 1.93 (d, J_{bCH_3} = 1 Hz, 3 H, R = CH_3), 6.23 (m, H_b), 2.30 (m, 4 H_c), 3.15 (m, 2 H_d), 3.68 and 3.85 (each s, 3 H, OCH_3); IR: 1040—1070 cm^{-1} (S O).

[3] *K. Gollnick, S. Fries*, to be published.

[4] In analogy to the transition *(3)* → *(4)* and the failure of an intramolecular Michael addition to take place with the bicyclic sulfonium ylides (see [1b]) $(CH_3)_2\overset{\oplus}{S}O—\overset{\ominus}{C}H_2$ reacts with the C=C double bond of α,β-unsaturated carbonyl compounds, whereas $(CH_3)_2\overset{\oplus}{S}—\overset{\ominus}{C}H_2$ does not; *E. J. Corey, M. Chaykovsky*, J. Am. Chem. Soc. 87, 1353 (1965).

[5] *(10)*: m.p. 123 °C (purification as for *(5a)* [2]); ^{1}H-NMR ($CDCl_3$): δ = 5.82 (m, J_{ab} = 10 Hz, J_{ac} = 1 Hz, H_a), 6.60 (m, J_{ab} = 10 Hz, H_b), 2.40 (m, 4 H_c), 3.40 (m, 2 H_d), 3.68 and 3.85 (each s, 3 H, OCH_3); IR: 1160, 1350 cm^{-1} (SO_2).

[6] *(9)*: m.p. 118 °C (purification as for *(5a)* [2]); ^{1}H-NMR ($CDCl_3$): δ = 3.45 (m, 2 H_a, 2 H_c), 2.10—2.70 (m, 4 H_b), 3.67 and 3.80 (each s, 3 H, OCH_3); IR: 1045—1060 cm^{-1} (S=O).

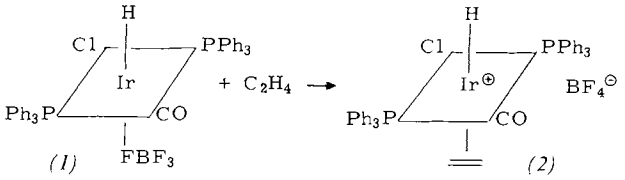
[7] a) *M. Prochazka*, Collect. Czech. Chem. Commun. 30, 1158 (1965); b) *K. Torsell*, Acta Chem. Scand. *B30*, 353 (1976).

A Cationic Ethylene(hydrido)iridium(III) Complex

By *Bernhard Olgemöller* and *Wolfgang Beck*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Hydridoolefin complexes of cobalt(III), rhodium(III), and iridium(III) occur as intermediates in the catalytic hydrogenation and hydroformylation of olefins[1]. We have been able to isolate the cationic iridium complex *(2)* by substitution of the tetrafluoroborate ligand in the hydride *(1)* by ethylene. Compound *(1)* has been prepared by oxidative addition of HBF_4 to the Vaska compound *trans*-$(Ph_3P)_2Ir(CO)Cl$[2].



The salt *(2)* is thermolabile (decomposition above 0 °C) and sensitive to moisture. The structure of its cation can be established unequivocally by ^{1}H-NMR spectroscopy. The signal of ethylene coordinated in *(2)* ($\delta_{C_2H_4}=4.37$ in CD_2Cl_2 rel. to $CHDCl_2=5.33$ at −43 °C) appears upfield from that of free ethylene ($\delta_{C_2H_4}=5.38$). The hydride absorption is observed as a triplet ($^2J_{PtH}=11$ Hz) at $\delta_H=-7.35$. A square-planar ethylene-hydrido complex, *viz. trans*-$[(Et_3P)_2Pt(C_2H_4)H]^{\oplus}$, has been known for some time[3]. Hydrido-d^6-metal compounds of—generally cyclic—oligoolefins have been reported on several occasions[4]. A cationic ethylene hydrido complex of rhodium[5] and dihydrido-monoolefin-iridium compounds have recently been described[6].

Reaction of the cationic iridium complex *(2)* with pentacarbonylrhenate(−1) in tetrahydrofuran leads in a reductive elimination *via* an isolable pale yellow intermediate to pentacarbonyl(ethyl)rhenium (MS: $m/e=355.97$, calc. 355.967)[7]:

$$(2) + Re(CO)_5^{\ominus} \xrightarrow[-BF_4^{\ominus}]{} C_2H_5Re(CO)_5 + (Ph_3P)_2Ir(CO)Cl$$

We assume the intermediate to have the structure of a bis-metalated ethane, as has been found for $(CO)_5ReCH_2CH_2Re(CO)_5$[8].

Synthesis of carbonyl(chloro)ethylene(hydrido)bis(triphenylphosphane)iridium(III) tetrafluoroborate (2)

All operations were performed under dry argon in dry solvents.—Dry C_2H_4 (molecular sieve) is passed at −40 °C through a suspension of *(1)* (750 mg, 0.86 mmol) in CH_2Cl_2 (10 ml). A clear solution is formed within 30 min, which is kept at this temperature for 1 h. On addition of cold *n*-pentane (40 ml), *(2)* precipitates as a colorless, finely crystalline powder. It is washed twice with *n*-pentane (2 × 10 ml) at −40 °C and dried at −30 °C *in vacuo*. The compound decomposes to ethylene and *(1)* above *ca.* 0 °C.

Received: April 8, 1980 [Z 587 IE]
German version: Angew. Chem. *92*, 863 (1980)

[*] Prof. Dr. W. Beck, Dipl.-Chem. B. Olgemöller
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

[1] *B. R. James*, Adv. Organomet. Chem. *17*, 319 (1979); *R. L. Pruett, ibid. 17*, 1 (1979). X-ray structure analysis revealed the *trans* structure of *(1)*.
[2] *W. Beck, B. Olgemöller, U. Nagel, H. Bauer, H. Löbermann*, J. Organomet. Chem., in press.
[3] *A. J. Deeming, B. F. G. Johnson, J. Lewis*, J. Chem. Soc. Chem. Commun. *1970*, 598.
[4] *R. H. Crabtree*, Acc. Chem. Res. *12*, 331 (1979); *J. Müller, H. Menig, G. Huttner, A. Frank*, J. Organomet. Chem. *185*, 251 (1980).
[5] *H. Werner, R. Feser*, Angew. Chem. *91*, 171 (1979); Angew. Chem. Int. Ed. Engl. *18*, 157 (1979), and references cited therein.
[6] *R. H. Crabtree, J. M. Miheleic, J. M. Quirk*, J. Am. Chem. Soc. *101*, 7740 (1979).
[7] The reactivity of *(2)* towards nucleophiles should be of general synthetic utility.
[8] *W. Beck, B. Olgemöller*, J. Organomet. Chem. *127*, C45 (1977).

One-Electron Oxidation of 1,2-Dithiacycloalkanes[**]

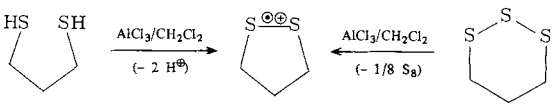
By *Hans Bock* and *Udo Stein*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The electron-rich sulfur-sulfur bond in disulfides XSSX changes considerably with the substituents X and the dihedral angle ω (XS—SX)[1-3]: thus the bond length d_{SS} varies between 188 and 222 pm (FSSF with $\omega=88°$ and S_7O with $\omega=6°$)[1,2] and the splitting of the sulfur electron pair ionization energies $\Delta IE_{1,2}$ between 0.2 and 1.8 eV (H_3CSSCH_3 with $\omega=85°$ and α-lipoic acid with $\omega=35°$)[1,3]. Donor-substituted disulfides exhibiting small dihedral angles should therefore be oxidizable to stable radical cations[4] in solution: during this transformation the electron density in the RS—SR bond is lowered and a favorable charge distribution is established by structural modifications such as bond contraction $\Delta d_{S^{\oplus\cdot}S}$ and flattening $\omega(RS^{\ominus\oplus}SR)\rightarrow 0°$[5].

The five-membered ring disulfide 1,2-dithiolane will be presented as an example (Fig. 1). Its unknown dihedral angle should be *ca.* 30°[3], the splitting $\Delta IE_{1,2}$ reaches 1.75 eV (!), and the "vertical" first ionization energy $IE_1^v=8.22$ eV is lowered by about 0.5 eV relative to diethyl disulfide[3]. Oxidation can be accomplished with $AlCl_3/CH_2Cl_2$—which generally requires $IE_1^v<7.9$ eV[6]—because "adiabatic" structural changes in solution effect additional stabilization of the incipient 1,2-dithiolate radical cation and thus lower the oxidation potential.

The energetically favorable 1,2-dithiolane radical cation is also formed on $AlCl_3/CH_2Cl_2$ oxidation of 1,3-propanedithiol with ring closure or of 1,2,3-trithiane with deposition of sulfur and ring contraction:



The equivalence of the adjacent methylene protons of the oxidized five-membered ring disulfide $(CH_2)_3S_2^{\odot\oplus}$ at 300 K (Fig. 1) confirms time-averaged planarity of the $CS^{\odot\oplus}SC$ group, and the large *g* factor of 2.0183 as well as the large ^{33}S isotope coupling constant evidence a pronounced spin density at the sulfur centers[7,8]. This interpretation of the ESR data is supported by INDO open-shell calculations; the bond contraction Δd_{S-S} should amount to about 10 pm[1].

Disulfides containing six- and seven-membered rings can be oxidized to the homologous 1,2-dithiane and 1,2-dithie-

[*] Prof. Dr. H. Bock, Dr. U. Stein
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

[**] Radical Ions, Part 44.—Part 43: *W. Kaim, H. Tesmann, H. Bock*, Chem. Ber., in press.

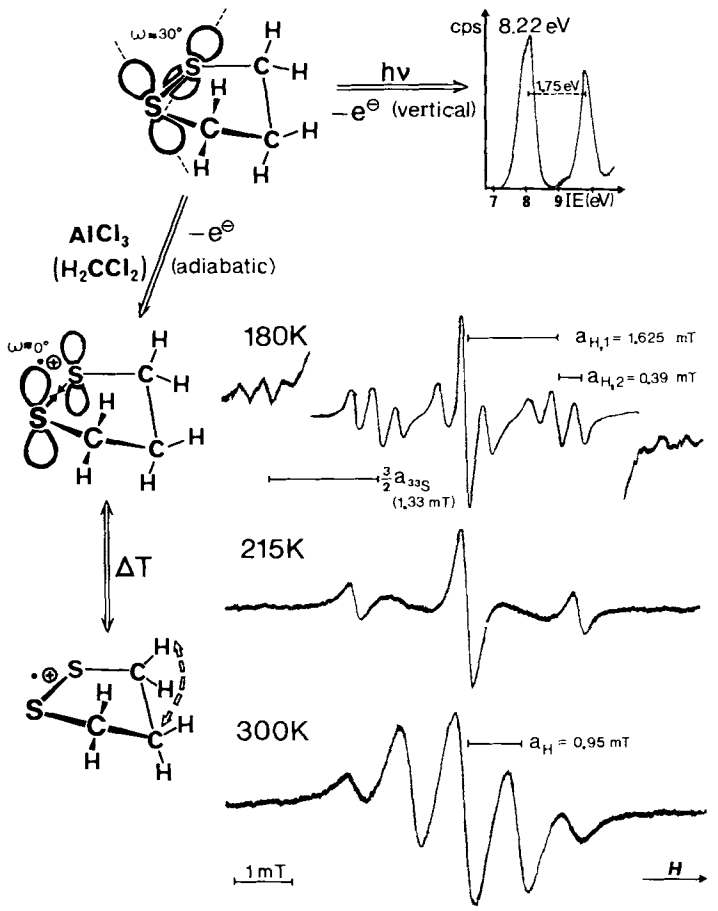
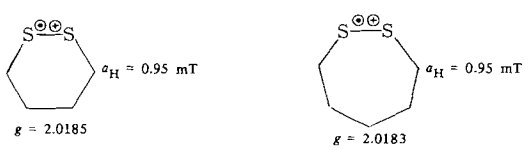


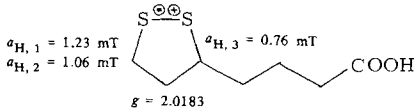
Fig. 1. The unstable compound 1,2-dithiolane can be prepared in benzene solution by oxidation of 1,3-propanedithiol with iodine in the dark and with addition of the polymerization inhibitor Et_3N. After removal of the solvent at 300 K, it can be evaporated into a photoelectron spectrometer by rapid heating to 350 K [1]. The first PE band with a "vertical" maximum at 8.22 eV is separated by 1.75 eV from the second ionization likewise assigned to sulfur electron pair combination, and its low energy foot extends to about 7.3 eV. One-electron oxidation with $AlCl_3/CH_2Cl_2$ affords a persistent radical cation whose $CS^{\oplus\oplus}SC$ skeleton is shown by optimized-geometry INDO open-shell calculations to be completely planar. The low temperature spectrum shows a triplet of triplets corresponding to the two different pairs of adjacent methylene protons. On edge amplification, the ^{33}S isotope coupling constants of 1.33 mT become visible; the factor $g = 2.0183$ is considerably higher than that for the free electron $g = 2.0023$. The central methylene bridge begins to invert above 200 K, and at 300 K a quintet is observed due to the four neighboring protons which are now equivalent on the NMR time scale. The temperature dependence of the line shape permits estimation of the activation barrier for the 1,2-dithiolane radical cation as 8 kJ/mol [1].

pane radical cations, which expectedly—the positive charge largely localized in the disulfide bridge is partly transferred by hyperconjugation to the adjacent methylene groups—exhibit comparable ESR spectra:



However, differences become apparent on replacement of H_2C by $(H_3C)_2C$ chain members: 4,4-dimethyl substitution of the 1,2-dithiolane radical cation raises the activation threshold for molecular fluctuation (Fig. 1) from 8 to 18 kJ/mol. Such a stiffening of the molecular skeleton is especially pronounced in the 4,4,6,6-tetramethyl-1,2-dithiepane radical cation, which merely shows a triplet for the two adjacent axial methylene protons at 300 K.

Selective $AlCl_3/CH_2Cl_2$ oxidation also permits transformation of biologically active compounds, such as α-lipoic acid which plays an important role as coenzyme in pyruvate decarboxylation[9], into their radical cations:



Received: May 5, 1980 [Z 588 IE]
German version: Angew. Chem. 92, 863 (1980)

[1] Dissertation *U. Stein*, Universität Frankfurt 1979. For dialkyl disulfides, the regressions $d_{SS} = 209 - 0.073\,\omega(CS—SC)$ with $SE = 1.3$ pm and $\Delta IE_{1,2} = 0.13 + 1.78|\cos\omega(CS—SC)|$ with $SE = 0.1$ eV result.

[2] Cf. *P. H. Laur* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry, Vol. III. Marcel Dekker, New York 1972, pp. 112f.; *R. Steudel*, Angew. Chem. *87*, 683 (1975); Angew. Chem. Int. Ed. Engl. *14*, 655 (1975). S_7O structure: *R. Steudel, T. Sandorf, R. Reinhard, ibid. 89*, 757 (1977) and *16*, 716 (1977), respectively.

[3] Cf. *H. Bock, G. Wagner*, Angew. Chem. *84*, 119 (1972); Angew. Chem. Int. Ed. Engl. *11*, 150 (1972); Chem. Ber. *107*, 68 (1974); *M. F. Guimon, C. Guimon, G. Pfister-Guillouzo*, Tetrahedron Lett. *1975*, 441; *B. Solouki, H. Bock*, Inorg. Chem. *16*, 665 (1977).

[4] *J. Gillbro* [Chem. Phys. *4*, 476 (1974)] as well as *R. L. Petersen, D. J. Nelson, M. C. R. Symons* [J. Chem. Soc. Perkin Trans. II *1978*, 225] were able to detect the unstable species $H_3CS^{\oplus\oplus}SCH_3$ after γ-irradiation. Complexes $R_2S^{\oplus\oplus}SR_2$ with "SS three-electron bond" are also known [*W. K. Musker, T. L. Wolford, P. B. Roush*, J. Am. Chem. Soc. *100*, 6416 (1978); *K.-D. Asmus*, Acc. Chem. Res. *12*, 436 (1979); and references cited therein].

[5] Compare, e.g., the MNDO hypersurface for the hydrazine radical cation $H_2N^{\oplus\oplus}NH_2$ [*H. Bock, W. Kaim, H. Nöth, A. Semkow*, J. Am. Chem. Soc. *102*, 4421 (1980)] which correctly predicts the bond contraction $\Delta d_{N,N} = 30$ pm and full planarity [*S. F. Nelsen, V. E. Peacock, C. R. Kessel*, J. Am. Chem. Soc. *100*, 7876 (1978)].

[6] Cf. *H. Bock, W. Kaim*, Tetrahedron Lett. *1977*, 2343; J. Organomet. Chem. *135*, C14 (1977); review: *H. Bock, G. Brähler, W. Kaim, M. Kira, B. Roth, A. Semkow, U. Stein, A. Tabatabai* in *J. Bargon:* Computational Methods in Chemistry. Plenum Press, New York 1980.

[7] Experimental correlation of g factors with S spin densities $\rho_S = -56.45 + 28.17\,g$ for radical ions of *S*-substituted π systems [Dissertation *G. Brähler*, Universität Frankfurt 1978] yields $\rho_S \approx 0.4$.

[8] The relation $a^{33}_S = Q_S\rho_S + 2Q_{CS}\rho_C$ [*M. Karplus, G. K. Fraenkel*, J. Chem. Phys. *35*, 1312 (1961)] with $Q_S = 3.3$ mT and $Q_{CS} = 0$ [Dissertation *G. Brähler*, Universität Frankfurt 1978] also yields a S spin density of $\rho_S \approx 0.4$.

[9] Cf., e.g., *F. Hucho*, Angew. Chem. *87*, 614 (1975); Angew. Chem. Int. Ed. Engl. *14*, 591 (1975); *J. K. Howie, J. H. Houts, D. T. Sawyer*, J. Am. Chem. Soc. *99*, 6323 (1977) and references cited therein.

The Significance of Isoselective Temperatures for the Existence of Linear Free-Energy Relationships[**]

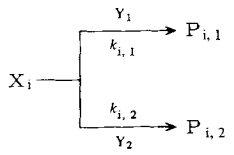
By *Bernd Giese* and *Woo-Bung Lee*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

In many cases of competing reactions of molecules X_i with the reaction partners Y_1 and Y_2 a coincidence of the selectivities $\log(k_{i,1}/k_{i,2})$ is observed in a narrow temperature range, the isoselective temperature T_{is}[1]. Above and below T_{is} the order of selectivities of the molecules X_i is exactly reversed.

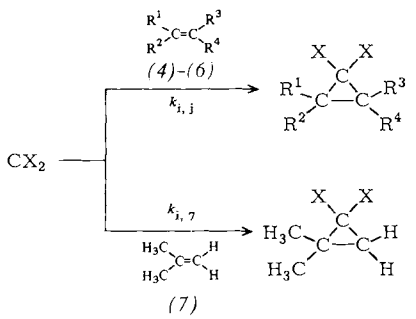
[*] Prof. Dr. B. Giese, W.-B. Lee
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.



If the competing pair Y_1/Y_2 is left unchanged, then different isoselective temperatures are observed for various classes of substances X_i. Thus T_{is} drops from 360 through 310 to 210 K in radical halogen abstractions in the $BrCCl_3/CCl_4$ competition system if there is a transition from alkyl radicals of the π-type *via* sp^2-hybridized σ-radicals to sp^3-hybridized bridgehead radicals[1,2].

The influence of the variation of reaction partners Y_j of the competing system on the isoselective temperature was previously unknown. To answer this question we have investigated the cycloadditions of the dihalocarbenes *(1)—(3)* with various pairs of the alkenes *(4)—(7)*[3].



(7)

X		R^1	R^2	R^3	R^4	
F	*(1)*	CH_3	CH_3	CH_3	CH_3	*(4)*
Cl	*(2)*	CH_3	CH_3	CH_3	H	*(5)*
Br	*(3)*	CH_3	H	H	CH_3	*(6)*
		CH_3	CH_3	H	H	*(7)*

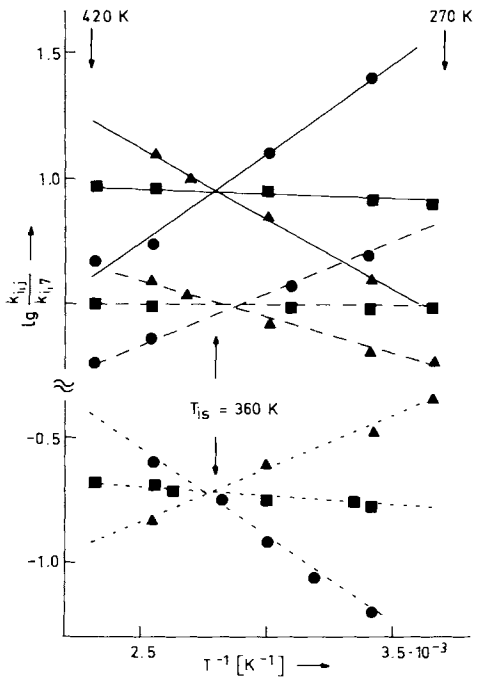


Fig. 1. Selectivities of the carbenes CF_2 (●), CCl_2 (■), and CBr_2 (▲) in cycloadditions with the alkene pairs *(4)/(7)* (solid lines), *(5)/(7)* (dashed lines), and *(6)/(7)* (dotted lines) between 270 and 420 K.

In Figure 1 the carbene selectivities measured between 270 and 420 K are plotted against T^{-1}. The three groups of lines show that different isoselective relationships exist for different alkene pairs[1]. Surprisingly, however, the selectivity lines for each competition pair intercept at 360 ± 10 K. Hence the substituents on the alkenes *(4)—(7)* have an influence on the isoselective relationship, but no influence on the isoselective temperature.

These astonishingly constant isoselective temperatures can only be due to special substituent effects. In fact, the reactivity of alkylated alkenes in cycloadditions with singlet carbenes at 298 K obeys a common linear free-energy relationship, as found by *Skell*[4] and *Moss et al.*[5]. If this dependence stems from a structure-reactivity correlation, then a linear relationships between these series of reactivities must also exist at other temperatures.

At the isoselective temperature the variation of the alkenes has exactly the same effect on the selectivity of the carbenes *(1)—(3)*. An interception of the carbene selectivities for a specific alkene pair must therefore be repeated in each of the other competing systems if there is a common linear free-energy relationship for the substituent effects.

Together with the results of radical substitutions in the $BrCCl_3/CCl_4$ competition system[2,6], these cycloadditions of the carbenes demonstrate that isoselective temperatures must be of the same order, if series of reactions between X_i and Y_j are to be correlated linearly. Thus, the determination of isoselective temperatures opens up an accurate and generally valid method for testing the description of substituent effects by linear free-energy relationships.

Received: March 18, 1980 [Z 589 IE]
German version: Angew. Chem. *92*, 864 (1980)

CAS Registry numbers:
(1), 2154-59-8; *(2)*, 1605-72-7; *(3)*, 4371-77-1; *(4)*, 563-79-1; *(5)*, 513-35-9; *(6)*, 107-01-7; *(7)*, 115-11-7

[1] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).
[2] *B. Giese, J. Stellmach*, Tetrahedron Lett. *1979*, 857; Chem. Ber., in press.
[3] Initial investigations had shown that the isoselective temperature in the competing system *(5)/(7)* fell in the range of measurement: *B. Giese, J. Meister*, Angew. Chem. *90*, 636 (1978); Angew. Chem. Int. Ed. Engl. *17*, 595 (1978); *B. Giese, W.-B. Lee, J. Meister*, Liebigs Ann. Chem. *1980*, 725.
[4] *P. S. Skell, M. S. Cholod*, J. Am. Chem. Soc. *91*, 7131 (1969).
[5] *R. A. Moss, C. B. Mallon, C. T. Ho*, J. Am. Chem. Soc. *99*, 4105 (1977).
[6] *B. Giese*, Angew. Chem. *88*, 723 (1976); Angew. Chem. Int. Ed. Engl. *15*, 688 (1976); *B. Giese, H.-D. Beckhaus, ibid. 90*, 635 (1978) and *17*, 594 (1978).

(Trifluoromethyl)fluorogermanates

By *David J. Brauer, Hans Bürger*, and *Reint Eujen*[*]

Since it was first synthesized, CF_3GeF_3 has been shown to react with excess aqueous KF forming $K_2[CF_3GeF_5]$[1]. We have now found that other trifluoromethylgermanium halides $(CF_3)_nGeX_{4-n}$, $n = 1—4$, X = F, Cl, Br, I[2,3] are remarkably stable towards H_2O and are decomposed only by $OH^{\ominus}$ with formation of HCF_3. Their miscibility with H_2O decreases with increasing CF_3 content n. They may be extracted undecomposed from the aqueous phase by organic solvents, such as ether.

The halide $X^{\ominus}$ (X = Cl, Br, I) may be precipitated quantitatively from aqueous solution as AgX without the CF_3Ge moiety being attacked. The addition of $F^{\ominus}$ *via* NaF or NH_4F leads to readily soluble (trifluoromethyl)fluorogermanates:

[*] Prof. Dr. H. Bürger, Dr. R. Eujen, Dr. D. J. Brauer
FB 9—Anorganische Chemie, Gesamthochschule-Universität
Gaussstr. 20, D-5600 Wuppertal 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1010-0836 $ 02.50/0

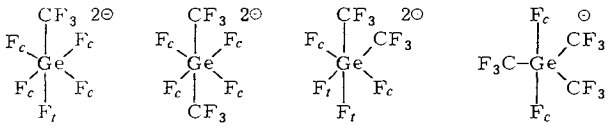
$$(CF_3)_nGeX_{4-n} \xrightarrow{F^{\ominus}} (CF_3)_nGeF_{6-n}^{2\ominus}$$

(1), $n=1$; *(2)*, $n=2$

$$(CF_3)_3GeX \xrightarrow{F^{\ominus}} (CF_3)_3GeF_2^{\ominus}$$

(3)

With $F^{\ominus}$ in excess, the intermolecular F-exchange is so slow that the coupling between CF_3- and GeF-groups is observable in the ^{19}F-NMR spectra (Table 1). The coupling patterns of the spectra, which are more readily interpretable than are those of the isoelectronic fluorophosphates[4], indicate that the six-coordinate, octahedral structures *(1)* and *(2a)* and five-coordinate, trigonal-bipyramidal structure *(3)* exist in solution.



(1) *(2a)* *(2b)* *(3)*

Table 1. ^{19}F-NMR spectra of (trifluoromethyl)fluorogermanates [a].

	$\delta(CF_3)$	$\delta(F_c)$	$\delta(F_t)$	$^3J(FF_c)$	$^3J(FF_t)$	$^2J(F_cF_t)$
(1)	−14.05	45.4	42.1	14.6	<0.3	23.7
(2a)	−14.13	47.1	—	14.5	—	—
(3)	−15.10	60.5	—	9.5	—	—

[a] Chemical shifts rel. CF_3COONH_4 int.; coupling constants in Hz.

In solution, the dianion *(2)* is present to more than 90% as the *trans*-isomer *(2a)*. The NMR evidence for the presence of the *cis*-isomer *(2b)* is uncertain because of the complexity of the $A_2BB'X_3X_3'$ spectrum; however, the moderately soluble potassium salt of *(2b)* could be crystallized from the mixture and characterized by an X-ray structure analysis. Solutions of *(3)* have to be saturated with NH_4F in order to suppress F-exchange. Only then are a triplet and decet observed in the ^{19}F-NMR spectrum in the ratio 9:2, with chemical shifts which deviate markedly from those of the hexacoordinated species *(1)* and *(2a)*. On dissolution in saturated NH_4F solution $(CF_3)_4Ge$ slowly decomposes, mainly to *(3)*. However, because of the F-exchange the NMR signal $\delta(CF_3) = -18.4$ shows no structurally diagnostic fine structure.

The X-ray structure analysis of $K_2[cis\text{-}(CF_3)_2GeF_4]$[5] shows that the distorted octahedral anion *(2b)* (Fig. 1) and the two cations have crystallographic symmetry C_2. The nearly identical GeF bond lengths are longer than in K_2GeF_6 (1.77 Å[6]); furthermore, the GeC bond lengths and FCF angle are respectively 0.052(5) Å longer and 4.5(3)° smaller than corresponding r_α values in $Ge(CF_3)_4$[7]. Each K

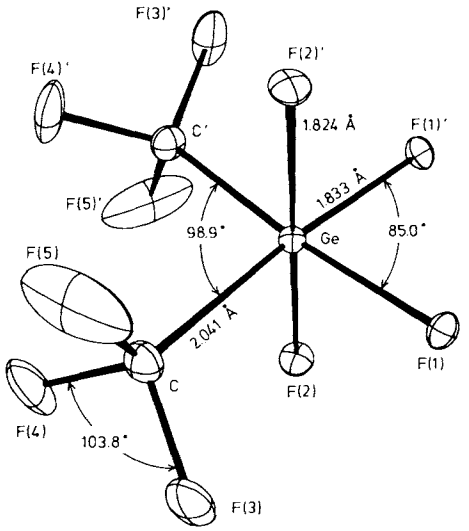


Fig. 1. Structure of *(2b)* in the crystal $K_2[cis\text{-}(CF_3)_2GeF_4]$.

atom has 10 nearest F atoms as neighbors, namely four or six F(Ge) atoms at 2.644(2) to 2.798(2) Å, and six or four F(C) atoms at 2.973(3) to 3.269(4) Å.

Procedure

A solution of NaF (235 mg, 5.6 mmol) in H_2O (2 ml) is treated with 650 mg (1.4 mmol) $(CF_3)_2GeI_2$. On vigorous shaking, the liquids slowly mix. After removal of the H_2O *in vacuo*, the solution is washed free of $I^{\ominus}$ with ethanol and the residue is dried in a vacuum. Yield: 380 mg (82%) $Na_2[(CF_3)_2GeF_4]$.

Received: January 24, 1980 [Z 590 IE]
German version: Angew. Chem. *92*, 859 (1980)

[1] *H. C. Clark, C. J. Willis*, J. Am. Chem. Soc. *84*, 898 (1962).
[2] *J. A. Morrison, L. L. Gerchman, R. Eujen, R. J. Lagow*, J. Fluorine Chem. *10*, 333 (1977).
[3] *R. J. Lagow, R. Eujen, L. L. Gerchman, J. A. Morrison*, J. Am. Chem. Soc. *100*, 1722 (1978).
[4] Gmelin Handbuch der Anorganischen Chemie, Suppl. Vol. *24*, p. 129ff. Springer Verlag, Berlin 1975.
[5] Colorless needles from $Na_2[(CF_3)_2GeF_4]$, KBr and H_2O; crystallographic data: $a=17.815(2)$, $b=11.474(1)$, $c=8.4782(6)$ Å, space group Ibca, $Z=8$, $\rho_{calc}=2.80$ g cm^{-3}. The anisotropic refinement of the structure with 746 observed data converged at $R=0.028$; for measurement and calculation methodology see: *D. J. Brauer, H. Bürger, K. Wiegel*, J. Organomet. Chem. *150*, 215 (1978).
[6] *J. L. Hoard, W. B. Vincent*, J. Am. Chem. Soc. *61*, 2849 (1939).
[7] *H. Oberhammer, R. Eujen*, J. Mol. Struct. *51*, 211 (1979).

Grundlagen der Kalorimetrie [Principles of Calorimetry]. By *W. Hemminger* and *G. Höhne*. Verlag Chemie, Weinheim 1980. xiv, 256 pp., bound, DM 88.00.

In view of the fact that no book in the German language dealing exclusively with calorimetry has appeared since *W. Roth* and *F. Becker*'s monograph (1956), although the importance of this method of measurement has been increasing continuously, the appearance of this book can only be welcomed.

The declared aim of this monograph is to provide information about the technical state of commercial apparatus and, with the aid of examples, to encourage the application of calorimetric methods. Accordingly, the book is divided into two parts, the first part being devoted to calorimetry and the second to calorimeters. The first part is preceded by a clear systematic classification of calorimeters subdivided according to the measurement principle, method of operation, and type of construction. This introductory matter must be welcomed, since it assists in throwing light on the jungle of nomenclature used in publications both as regards calorimeters themselves and the measurement principles. Other points of emphasis in the first part are the descriptions of the instruments for recording the measurements and the presentation of the thermodynamic principles, heat-transport phenomena, and the ambient and operating conditions. Finally, the evaluation of the measured curves is discussed in full. The second part is devoted to historical and current commercial apparatus. It is clear that the fundamental ideas in the field of calorimetry go back to such well-known workers as *Bunsen* and *Eucken*, and it is not a criticism to report that descriptions of individual examples of special apparatus available only to small research groups are not given.

The last section is intended to assist in the selection and evaluation of the suitability of calorimeters. Here there are some valuable pointers on the basis of which apparatus best suited to the solution of particular problems can be selected. The decision is helped by a list of addresses of the suppliers and associations concerned.

The book does not assume any special knowledge and is directed at practical research workers, advanced students, and interested industrial workers. Detailed and comprehensive accounts of individual solutions to problems cannot, therefore, be expected. However, for the group at which it is aimed this book is recommended reading.

Horst Klump [NB 519 IE]

Semisynthetic Proteins. By *R. E. Offord*. John Wiley & Sons, New York 1980. xi, 235 pp., bound, £ 17.00.

Protein semisynthesis is the use of fragments of naturally occurring proteins as easily available intermediates for building up proteins with new types of structures. If, for example, it is desired to investigate the effect of a single amino acid on the biological activity of a protein molecule, it is not necessary to build up the entire molecule step by step. Semisynthesis should always be considered in such cases if the molecular fragment to be replaced is located in a strategically favorable position of the amino-acid sequence, *e.g.* at the N-terminus; this end can be degraded stepwise, *e.g.* by the Edman method, and be replaced by acylation with suitable amino-acid and peptide derivatives (permutation). *Offord* is a pioneer in protein semisynthesis, and the present monograph summarizing his experience and that of his many friends and associates is therefore highly welcome. In it he has succeeded not only in presenting the theoretical principles of protein semisynthesis clearly and critically, but also in greatly facilitating the entry of newcomers into this field with proven laboratory procedures. The book is divided into eight chapters: Synthesis and Semisynthesis, Protecting Group Tactics for Splitting off Fragments, Cleavage and Separation of Protein Fragments, Protecting Group Tactics after Cleavage, Methods of Coupling, Cleavage of Protecting Groups and Purification, and Review of Published Papers on Protein Semisynthesis.

The book is most warmly recommended to biochemists, molecular biologists, pharmacologists, and chemists who wish to work in the field of protein semisynthesis.

Helmut Zahn [NB 521 IE]

Ullmanns Encyklopädie der technischen Chemie [Ullmann's Encyclopedia of Industrial Chemistry]. Edited by *E. Bartholomé, E. Biekert, H. Hellmann, H. Ley* (deceased), *W. M. Wiegert* (deceased), and *E. Weise*. Vol. 18: Petrolsulfonate bis Plutonium [Petroleum Sulfonates to Plutonium]. Verlag Chemie, Weinheim 1979. 4th edit., xvi, 738 pp., bound, DM 475.00.

Another volume[*] of the new edition of Ullmann has arrived. Its most comprehensive entries are on Pharmaka [Pharmaceuticals], Phosphor und seine Verbindungen [Phosphorus and its Compounds], Photographie [Photography], and Pigmente [Pigments]; together they make up two-thirds of the contents. The entry on Pharmaceuticals (107 pages) begins with a general part which, in addition to an introductory section on the action of pharmaceuticals, deals with the testing of drugs and the statutory regulations concerning their registration and marketing. This is followed by special entries on individual areas such as Antiepileptika [Antiepileptics], Kontrazeptiva [Contraceptives], Muskelrelaxantien [Muscle Relaxants], and Psychopharmaka [Psychopharmaceuticals]; here it must be observed that other, more extensive, areas of pharmaceuticals, *e.g.* antibiotics or heart and circulation agents, appear in other volumes under their own entries in accordance with their positions in the alphabet. Pharmazeutische Technologie [Pharmaceutical Technology] (25 pp.), *i.e.* the science of preparation forms of drugs (liquids for injection, tablets, ointments, *etc.*), an important field that is also known under the name of Galenik [Galenics], is also treated on its own. The entry on Photography (102 pp.) treats photographic chemistry in the form of a monograph, the processes of colour photography being illustrated in color. The Pigments entry (a total of 150 pp.) contains special sections on several inorganic and organic pigments, dealing not only with manufacturing processes but also with applications and toxicology. Among other things, it states that the world consumption of the most commonly used white pigment, titanium dioxide, in 1976 was 1.85×10^6 tons! Under Phosphorus and its Compounds (a total of 115 pp.) we find, besides elemental phosphorus, the phosphorus oxides, phosphorus acids, and phosphates, as well as the other organic and inorganic phosphorus compounds. The present volume also includes entries on Platinmetalle [Platinum Metals] and their compounds (32 pp.), Plutonium (10 pp.),

[*] Cf. Angew. Chem. Int. Ed. Engl. *19*, 148 (1980).

Phthalocyanine [Phthalocyanins] (20 pp.) (or interest particularly as dyestuffs), Phenolharze [Phenolic Resins] (13 pp.), and several intermediates (Phenol und seine Derivate [Phenol and its Derivatives], Phosgen [Phosgene], Phthalsäure und ihre Derivate [Phthalic Acid and its Derivatives]). We may also mention Pflanzenschutz, Toxikologie [Plant Protection, Toxicology] (37 pp.), an entry in which all toxicological aspects of the use of plant-protection agents are treated comprehensively; the toxicological characteristics of a large number of plant-protection agents are particularly interesting.

As usual with the Ullmann Encyclopedia, the individual entries have been written by outstanding specialists. Again as usual, the subdivision within the entries is clear and easy to understand, so that it is easy to find information on specific points. It is almost unnecessary to mention that the contents are always up to date (with some literature references up to 1979!).

All in all, a recommended and useful source of information for any chemist.

Ulfert Onken [NB 522 IE]

Chemistry through Models. By *C. J. Suckling, K. E. Suckling,* and *C. W. Suckling.* Cambridge University Press, Cambridge 1980. xii, 321 pp., bound, £ 5.95.

The use of models is so firmly rooted in our way of thinking that we often use models without being aware of the fact. Chemists in particular are forced to use models in many situations. However, "Chemistry through Models" appears to be the first attempt at a comprehensive account of the use of models in chemistry, an attempt that may be considered as successful.

Models are constructions of alternative, and usually simpler, forms of objects or concepts called prototypes. A piece of wood floating in water is a very simple physical model of the prototype "ship". The ideal gas law $pV = nRT$ is a conceptual model of the prototype "real gas", in which some important factors such as the interactions between the individual gas molecules and their intrinsic volumes are neglected. It can therefore be used only within an accurately delimited region to describe the properties of real gases.

The present book begins with two very detailed chapters in which models are defined, hints are given on their construction, and the advantages of the use of models are discussed, as are the dangers of their incorrect use. This is followed by chapters on conceptual models in chemistry (*e.g.* quantum-mechanical models such as the VB and the MO theories, linear free energy relationships, functional groups in organic chemistry, the periodic system of the elements in inorganic chemistry), and models of reacting systems (collision theory, transition-state theory, reaction mechanisms in organic chemistry, Woodward-Hoffmann rules, *etc.*). The use of models in the planning of syntheses, in spectroscopy, and in the elucidation of structures is explained next. The concluding chapter deals with models in biochemistry (biosynthesis, biomimetic reactions, study of complex enzyme systems, *etc.*), in the planning of new manufacturing plants, and in the development of new commercial products.

This review of the contents hopefully gives an idea of the broad scope of the book. Obviously, in view of the diversity of subjects treated, it was not possible to give an in-depth account of the problems in every case, but this disadvantage can be partly overcome by resorting to the literature references cited.

"Chemistry through Models" is a good introduction to the use of models in all fields of chemistry. It can be recommended to all chemists and advanced students who want an interesting guide to a complicated subject.

Kurt Hermann [NB 525 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Macromolecular Physics. Vol. 3. Crystal Melting. By *B. Wunderlich.* Academic Press, New York 1980. xiii, 363 pp., bound, $ 42.50.—ISBN 0-12-765603-0

Chemischer Pflanzenschutz Rückstände und Bewertung. Kommission für Pflanzenschutz-, Pflanzenbehandlungs- und Vorratsschutzmittel, Part XII. Deutsche Forschungsgemeinschaft. H. Boldt Verlag, Boppard 1980. 103 pp., brochure.—ISBN 3-7646-1786-1

Grundkurs Physik Band 2: Mechanik. By *M. Trümper.* Steinkopff Verlag, Darmstadt 1980. xviii, 207 pp., plastic, DM 20.80.—UTB 1058

Stabilitätsprüfung in der Pharmazie. By *W. Grimm* and *G. Schepky.* Editio Cantor, Aulendorf 1980. 397 pp., bound, DM 120.00.—ISBN 3-87193-052-0

Advances in Inorganic Chemistry and Radiochemistry. Vol. 23. Edited by *H. J. Emeléus* and *A. G. Sharpe.* Academic Press, New York 1980. ix, 441 pp., bound, $ 51.00.—ISBN 0-12-023623-0

DIN Taschenbuch 133. Normen über Siebböden und Kornmessung. Published by DIN Deutsches Institut für Normung e.V. Beuth Verlag, Berlin 1980/Bauverlag, Wiesbaden 1980. 256 pp., sewed, DM 59.00.—ISBN 3-410-11127-1 (Beuth Verlag); ISBN 3-7625-1305-8 (Bauverlag)

Hydrogen in Metals. Proceedings of the International Meeting "H in Metals", 1979 in Münster. Edited by *E. Wicke* and *H. Züchner.* Akademische Verlagsgesellschaft, Wiesbaden 1980. xvi, 838 pp., bound, DM 98.00.—ISBN 3-400-00432-4

Chemical Aspects of the Nuclear Fuel Cycle. Special issue of the journal "Radiochimica Acta". Edited by *R. G. Wymer.* Akademische Verlagsgesellschaft, Wiesbaden 1980. 131 pp., sewed, DM 45.00.—ISBN 3-400-00431-6

Advances in Chromatography. Vol. 18. Edited by *J. C. Giddings, E. Grushka, J. Cazes,* and *P. R. Brown.* Marcel Dekker, New York 1980. 312 pp., bound, SFr. 88.00.—ISBN 0-8247-6960-0

Marine Natural Products. Chemical and Biological Perspectives. Vol. 3. Edited by *P. J. Scheuer.* Academic Press, New York 1980. xii, 229 pp., bound, $ 28.00.—ISBN 0-12-624003-5

Trends in Enzyme Histochemistry and Cytochemistry. Ciba Foundation Symposium No. 73 (new series). Excerpta Medica, Amsterdam 1980. viii, 314 pp., bound, $ 53.75.—ISBN 0-444-90135-3

Einführung in die Physik. 2nd Edit. By *R. Fleischmann.* Physik Verlag, Weinheim 1980. xviii, 682 pp., bound, DM 79.00.—ISBN 3-87664-046-6

Sicherheit im Labor. einrichten — experimentieren — entsorgen. By *W. Wolff* and *M. Schwahn.* Diesterweg/Salle-Sauerländer, Frankfurt 1980. xii, 187 pp., ring-file, DM 38.00.—ISBN 3-425-05440-6

Elektrochemie II. In two volumes. Elektrodenprozesse, Angewandte Elektrochemie. By *C. H. Hamann* and *W. Vielstich.* Verlag Chemie, Weinheim 1980. taschentext 42/1 and 42/2. Each *ca.* 200 pp., sewed. Each DM 24.80.—ISBN Vol. 1 3-527-21081-4; Vol. 2 3-527-21082-2

Reaction Kinetics and Reactor Design. By *J. B. Butt.* Prentice-Hall, London 1980. 431 pp., bound, £ 14.25.—ISBN 13-753335-7

Komplexchemie experimentell. By *R. Demuth* and *F. Kober.* Diesterweg Verlag, Frankfurt 1980. *ca.* 280 pp., DM *ca.* 25.00.—ISBN 3-425-05365-5

Activated Carbon Adsorption of Organics from the Aqueous Phase. Vol. 1. By *I. H. Suffet.* John Wiley & Sons, New York 1980. *ca.* 700 pp., bound, $ 43.95.—ISBN 0-250-40269-6

Chlorofluorcarbons in the Environment. The Aerosol Controversy. Edited by *T. M. Sugden* and *T. F. West.* John Wiley & Sons, New York 1980. *ca.* 200 pp., bound, $ 46.30.—ISBN 085312-137-0

Fundamentals of Chemistry. 4th Edit. By *F. Brescia, J. Arents et al.* Academic Press, New York 1980. 735 pp., bound, $ 18.50.—ISBN 0-12-132392-7

Chemie. Technetium, Promethium und die natürlichen radioaktiven Elemente. Edited by *C. Keller* and *H. Möllinger.* Hüthig Verlag, Heidelberg 1980. *ca.* 345 pp., bound, DM *ca.* 48.00.—ISBN 3-7785-0630-7

The Hydrophobic Effect: Formation of Micelles and Biological Membranes. 2nd Edit. By *C. Tanford.* John Wiley & Sons, New York 1980. *ca.* 248 pp., $ 24.60.—ISBN 0-471-04893-3

Elektrochemie. Theoretische Grundlagen und Anwendungen. Band 1. By *G. Milazzo.* Birkhäuser Verlag, Basel 1980. *ca.* 400 pp., bound, ISBN 3-7643-1129-0—Chemische Reihe Band 26

Nucleic Acid-Metal Ion Interactions. Vol. 1. By *T. G. Spiro.* John Wiley & Sons, New York 1980. *ca.* 300 pp., $ 33.25.—ISBN 0-471-04399-0

Advances in Biochemical Engineering. Edited by *A. Fiechter.* Springer-Verlag, Berlin 1980. *ca.* 150 pp., bound, DM 83.00.—ISBN 3-540-09686-8
Vol. 16. Plant Cell Cultures I. *ca.* 150 pp., bound, DM 72.00.—ISBN 3-540-09807-0

Anorganische Chemie. 16th Edit. By *W. Klemm* and *R. Hoppe.* Walter de Gruyter, Berlin 1980. Sammlung Göschen 2623. 328 pp., DM 19.80.—ISBN 3-11-007950-X

Methods in Enzymology. Academic Press, New York 1980.
Vol. 64. Enzyme Kinetics and Mechanism. Part B: Isotopic Probes and Complex Enzyme Systems. Edited by *D. L. Purich.* 458 pp., $ 35.00.—ISBN 0-12-181964-7
Vol. 65. Nucleic Acids. Part I. Edited by *L. Grossman* and *K. Moldave.* 968 pp., $ 57.50.—ISBN 0-12-181965-5
Vol. 66. Vitamins and Coenzymes. Part E. Edited by *D. B. McCormick* and *L. D. Wright.* 816 pp., $ 55.00.—ISBN 0-12-181966-3

Solar-Elements. Research and Development. By *R. L. Bailey.* John Wiley & Sons, New York 1980. *ca.* 424 pp., $ 32.95.—ISBN 0-250-04346-3

Rodd's Chemistry of Carbon Compounds. 2nd Edit. Vol. IV: Heterocyclic Compounds. Part L. Elsevier, Amsterdam 1980. xxii, 552 pp., Dfl. 260.00.—ISBN 0-444-41768-0

Solution Equilibria. By *F. R. Hartley, C. Burgess,* and *R. M. Alcock.* John Wiley & Sons, New York 1980. *ca.* 400 pp., $ 49.50.—ISBN 0-85312-148-6

Erratum

The word "Super*nucleo*phile" in the title of the communication by *R. Bussas* and *G. Kresze* [Angew. Chem. Int. Ed. Engl. *19.* 732 (1980)] should read "Super*eno*phile".

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar,* **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Dr. Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 11
November 1980
Pages 841–946

Chemistry in Compressed Solutions

By William J. le Noble and Hartwig Kelm[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

Contrary to "common sense" impression, modest pressures often have quite large effects on reactions in solution.—The volume profile of a chemical reaction in solution is easily measurable with considerable precision by means of the effect of pressure on the rate and equilibrium constant. The factors that govern the magnitude of these pressure effects are similar to those that affect the entropy changes and there is a rough correlation between them; however, the volume parameters are much less subject to apparently random fluctuations, have much greater appeal to the solution chemist's intuition, and most important, the activation volume is the only transition state property that can readily be determined in absolute terms (rather than as a difference value). In this paper we outline the experimental approach to the measurement of volume changes in wet chemical reactions, interpret the volume quantities, discuss a number of simple model equilibria and reactions, point out a number of contributions in both mechanistic and synthetic chemistry, and make an attempt to foresee future developments.

1. Introduction

The application of high pressure to chemical reactions is based on a knowledge of physical properties in compressed media. Investigators in this area are especially indebted to Professor *E. U. Franck* and his collaborators for their efforts to measure the pressure response of virtually the entire gamut of physical properties of a variety of materials. A sample of their outstanding work and references to earlier reports may be found in Ref. [1].

1.1. Some Erroneous Impressions

The application of pressure to chemical reaction systems is indeed a very common one, both in the laboratory and in manufacturing plants. To those only superficially acquainted with this fact, the objective in these applications is almost always assumed to be an increase in the rates of the reactions, and/or a shift in the equilibria in the desirable direction. Indeed, in the gas phase, the rate and equilibrium changes can to a first approximation be calculated on the basis of two assumptions: that the rate and equilibrium constants are independent of the pressure, and that the ideal gas laws apply. Furthermore, in many instances the reaction may be occurring in a solution in equilibrium with a gas phase; in that case, Henry's law may allow evaluation of the concentrations of the reactants in the solution. Since it is also common knowledge that liquid compressibilities—and therefore, pressure-induced concentration changes in solution—are orders of magnitude smaller than the corresponding gas-phase properties, many chemists permanently retain the impression that no significant effects can be expected from the compression of liquid reaction systems. This impression is in fact invalid; indeed, rather large effects by relatively modest pressures are the rule rather than the exception in such systems, and it is the purpose of this paper to describe these effects

[*] Prof. Dr. W. J. le Noble
Department of Chemistry, State University of New York
Stony Brook, New York 11794 (USA)
Prof. Dr. H. Kelm
Institut für Physikalische Chemie der Universität
Robert-Mayer-Strasse 11, D-6000 Frankfurt am Main (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1111-0841 $ 02.50/0*

and their uses. It is intended primarily to convey an impression of the premises supporting the use of pressure on chemical reactions in solution, the methods employed, the results achieved, and the applications made possible by it; it is not intended to instruct the new practitioner in the technical details. Those desiring such instruction are referred to the Proceedings of the 1978 NATO Advanced Study Institute on High Pressure Chemistry[1], and to a comprehensive listing[2] of and comments on volume changes in chemical reactions[3].

1.2. Units and Physical Properties

It has become customary in high pressure chemistry in recent years to record pressure in MPa (megapascal) and GPa (gigapascal) units, the pascal being the new IUPAP unit of pressure. Accordingly, this paper will make use of these units. We note, perhaps superfluously, that a pascal equals one newton/m^2, and that 1 MPa equals 0.01 kbar, or about 10 atmospheres.

Almost all compounds have lower *densities* in the liquid state than in the solid and accordingly, pressure has the effect of *raising melting points.* This phenomenon is described by the well-known Clausius-Clapeyron equation. In most instances, the *melting point* is increased by a few tenths of a degree per MPa. As a consequence, a number of common solvents such as benzene, dimethyl sulfoxide, *tert*-butyl alcohol and others with freezing points near room temperature have only limited use in experiments under pressure; furthermore, it becomes virtually impossible to maintain the liquid state at room temperature with any fluid much above 5 GPa. Fortunately, the effects of interest to most chemists are steepest in the low end of the pressure range. Another fortunate circumstance is that water, the most common solvent of all, is more dense than ice at 0 °C and hence its *freezing point* is *lowered* by pressure; only at about 300 MPa does this trend reverse itself.

The *boiling point* is likewise raised, and in fact, very much more so than the melting point because of the relatively huge increase in density associated with this phase change. Pressure effects on the liquid *solubilities* of solids and gases are closely related to those on melting and boiling points. Thus, it would obviously be unwise to use saturated or nearly saturated solutions of solids under pressure; conversely, pressure is often used to keep effervescent gases in solution.

The *viscosity* of liquids is one of the most pressure-sensitive physical properties: it increases exponentially with pressure. This effect especially makes itself felt in diffusion-controlled reactions, in which the generation of lattice holes for the molecules of interest to move into is part of the activation process. Under high pressure conditions this step is obviously impeded, and such reactions are strongly retarded. Examples here are the termination step of polymerizations[4] and the energy transfer step in certain photophysical processes[5]. Under ordinary conditions, most bimolecular processes are totally independent of viscosity and, in fact, there is only one known instance of a reaction losing this independence under pressure: the displacement of bromide ion from ethyl bromide by eugenoxide ion in isopropyl alcohol-eugenol mixtures. This reaction, which is accelerated over most of the pressure range, as displacements normally are (see below), drops precipitously in rate when the pressure exceeds 2 GPa[6].

The increase in *liquid densities* at ambient temperatures in response to pressure is describable by the Tait equation

$$(V_0 - V_p)/V_0 = C\log(1 + B/P),$$

where B and C are constants characterizing the substance[7]. The effect is generally greatest in the more tenuous nonpolar liquids; increases up to 40% are observed for saturated hydrocarbons of low molecular weight at 1 GPa. Water, on the other hand, increases its density by only 20% over the same range; this fact may be attributed to the cohesion already present between the water molecules by virtue of their hydrogen bonds, which leads to a relatively high density even under atmospheric conditions. Water is said to possess a high internal pressure ($(\partial E/\partial V)_T$), and some efforts have been reported to relate solvent effects and pressure effects in nonionic reactions on the basis of simple additivity[8]; however, these attempts generally fail when their extrapolation to polar species is attempted. The assumption inherent in such correlations, *i.e.,* that a reacting molecule experiences a pressure from its solvent neighbors equal to that prevailing in the bulk solvent, is then bound to be inadequate.

Pressure causes increases in *dielectric constant* which can be described in terms of the Owen-Brinkley equation[9]; this has essentially the same form as the Tait equation. These changes are small but not unimportant: they allow a better test of the many supposed correlations between the rate and dielectric constants than measurements of solvent response, in which the chemical environment is also changed.

1.3. Apparatus

Generation and determination of pressure up to several GPa can be achieved without much effort. The apparatus normally employed consists of a generator, at least one manometer, a separator, and a pressure vessel. An intensifier is often used to produce the highest pressures. The scheme of a simple high pressure apparatus is shown in Figure 1.

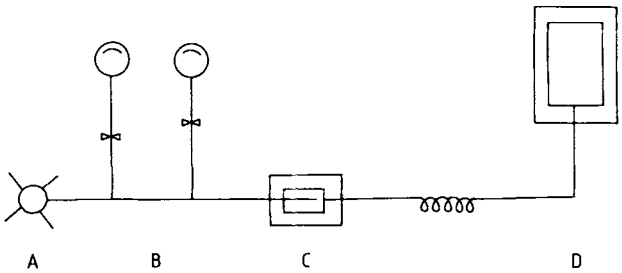


Fig. 1. Scheme of high pressure apparatus. A: generator; B: manometers; C: separator; D: reactor vessel.

Commercially available hand or motor driven generators usually produce pressures up to several tenths of a GPa, which in turn can be intensified by a factor of ten. For most studies in the liquid phase such pressures are sufficient. The pressures obtained are determined with the help of manometers also commercially available for various pressure ranges.

Oil is commonly used as a hydraulic fluid on the pressure generation side of the apparatus, whereas another fluid may be desired on the reactor side. In such cases a separator is

used that transfers pressure practically without loss. A piston system, a flexible tube or bellows, or the intensifier can be used for this purpose.

The solution to be studied is contained in a sample vessel, which must be made of inert materials, and which must completely separate the solution from the hydraulic fluid and yet transmit the pressure from the latter to the former while automatically adjusting its capacity. Its construction principle and size are determined by the method of analysis. The simplest version of such a vessel is a syringe containing the reacting solution, the pressure being transmitted *via* the plunger. Analytical samples can be taken from the syringe by means of a fine dosage valve. Pressure losses and interruptions of temperature constancy can—if desired—be avoided by slow pumping[10].

A large number of methods described in the literature can be used in conjunction with commercially available analytical instruments such as spectrophotometers for *in situ* analysis[11]. Ultraviolet-visible spectroscopy is perhaps the technique most frequently used; only small amounts of dilute reaction solutions (*ca.* 1—3 cm^3) are then required. A typical high pressure photometer cell is shown in Figure 2.

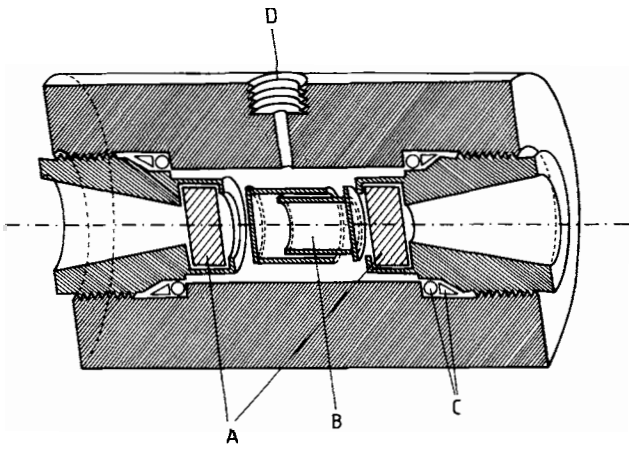


Fig. 2. Scheme of a high-pressure spectrophotometer cell (capacity *ca.* 1 to 3 cm^3): A: sapphire or quartz windows; B: "pillbox" containing reaction fluid; C: packings; D: hydraulic fluid.

It will be clear that charging the vessel and establishment of a constant pressure and temperature requires some time, perhaps 5 to 10 minutes. For reactions with half-lives below this range, special constructions have been proposed. These are essentially high pressure variations of the stopped-flow or relaxation methods[12]. The mixing of reagents under pressure is also possible[13]. In recent years NMR and ESR high pressure measurements have been employed for the study of fast degenerate reactions and equilibria[14].

No unusual safety precautions are necessary. In spite of the high pressures, the elastic energy that can be stored in liquids is relatively small when it is compared to gases, and when a leak develops it is usually more difficult to find it than to hide from it. Nevertheless, a complete and sudden rupture could under the worst circumstances pose a hazard that should not be ignored.

It should be pointed out that the high-pressure apparatus need not to be massive. Since the strength of vessels and tubing is determined by the ratio of external to internal diameter, it will be obvious that the size of the equipment is a function not only of the pressure but also of the sample size. Thus the mass of a vessel of several hundred cm^3 capacity designed for 2 GPa may weigh in the order of a hundred kilograms. The vessel shown in Figure 2 weighs only a few kilograms and the diamond cells designed for pressures of tens of GPa but very small (mg) samples may be carried in one's pocket.

1.4. Determination and Interpretation of Volume Changes

The pressure effects on chemical equilibria and reaction rates are described by the well-known equations:

$$(\mathrm{d}\ln K/\mathrm{d}P)_T = -\Delta\bar{V}/RT; \quad (\mathrm{d}\ln k/\mathrm{d}P)_T = -\Delta\bar{V}^{+}/RT$$

in which K and k represent the equilibrium and rate constants, $\Delta\bar{V}$ and $\Delta\bar{V}^{+}$ the reaction and activation volumes, respectively. Pressure-independent concentration units must be used for the calculation of the constants; if needs be, appropriate corrections have to be made.

The plots of $\ln K$ or $\ln k$ *versus* pressure may appear to be linear within experimental error, or they may show a more or less pronounced curvature. Since a theoretical description of these pressure dependencies is not possible at present, a number of empirical and semi-empirical functions have been proposed in order to describe the experimental data[1]. Depending on the type of function used and the statistical weight given to the individual points, one obtains slightly different results for the volume term at ambient pressure. Such variations are, however, seldom larger than the experimental error and choice of the evaluation procedure is not crucial.

In any molecular interpretation of $\Delta\bar{V}^{+}$, it should be remembered that the observed rate constant (k_{obs}) may represent a composite quantity because of the complexity of the mechanism. Even as simple a system of two opposing first order reactions

$$\mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{B}$$

leads to $k_{obs} = k_1 + k_{-1}$. The combination of a fast pre-equilibrium (*e.g.* a pre-protonation) with a rate determining step k_2

$$\mathrm{A} + \mathrm{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C} \xrightarrow{k_2} \text{products}$$

leads to $k_{obs} = k_1 k_2/k_{-1} = K k_2$. In such situations, the pressure dependencies of the equilibrium constants *and* of the rate constants are needed in order to give a complete description of the volume profile.

It has furthermore turned out to be advantageous and valid to a first approximation to split the individual volume quantities into an intrinsic and a solvation contribution:

$$\Delta\bar{V} = \Delta V_{intr} + \Delta V_{solv}; \quad \Delta\bar{V}^{+} = \Delta V^{+}_{intr} + \Delta V^{+}_{solv}$$

The intrinsic part results from the motion of the nuclei of the reacting species during the formation of the products or the transition state, *i.e.* from the formation or cleavage of bonds. This term represents the change in bond lengths and angles.

A change in polarity of the reactants during these processes causes the superimposed solvation contribution. Clearly the formation of a covalent bond between two atoms leads to a negative intrinsic contribution, whereas bond cleavage is characterized by a positive volume change; thus, bond-making processes are accelerated by pressure whereas bond-breaking is retarded.

If one considers the cleavage of a bond between two carbon atoms, the distance between them has to increase from *ca.* 1.5 Å to *ca.* 3.0 Å (the van der Waals distance). Given the cross section, for example, of a hydrocarbon chain, the increase in volume is about $+10$ Å^3, or about 10 cm^3 mol^{-1}. A more precise value cannot be given, because at the molecular level, the reaction will usually be accompanied by changes in bond angles and in void structure of the solution.

The intrinsic parts of the volumes of activation can be estimated in a similar manner, keeping in mind, however, that bonds are only partially formed or broken. Furthermore, the transition state does not necessarily lie midway in the reaction coordinate between reactants and products. There are, indeed, indications that covalent bond cleavage often occurs early and bond formation late; we return to this question in Sections 3.2 and 3.4. The normally expected contributions of $\Delta V^{\neq}_{intr}$ for these two processes range from $+3$ to $+8$ cm^3 mol^{-1} and from -7 to -12 cm^3 mol^{-1}, respectively.

Whenever such bond-making or bond-breaking processes are accompanied by the quenching or creation of charges or dipoles, the volume effects arising from them must also be estimated, since then not only the atoms of the reaction center are involved, but also an unknown number of solvent molecules in the neighborhood of these centers.

An exact appraisal of the ΔV_{solv} and $\Delta V^{\neq}_{solv}$ contributions would permit one to quantitatively describe solvent effects on equilibria and rates under pressure. Such a description is not possible at present, and one has to rely on estimates and experience.

The very short range interactions due to induced dipoles are very small; the volume effects can as a rule be neglected. The solvation contributions from the interactions of functional groups, *e. g.* hydrogen bonds, are larger; their quantitative estimation is based mostly on experimental data obtained with model systems.

The effects that stem from the appearance or disappearance of ionic charges and dipole moments can be estimated at least with respect to sign and even in a semiquantitative manner with the equations proposed by *Born* and *Kirkwood,* or rather by means of their pressure derivative given by *Drude* and *Nernst*[15]:

$$V_e = -(q^2/2rD^2)(dD/dP)$$

and

$$V_e = -(\mu^2/r^3)(3/(2D+1)^2)(dD/dP)$$

where V_e is the so-called electrostriction, q is the charge of the ion, μ the dipole moment, r the respective radius, and D is the dielectric constant. Based on the known value of (dD/dP) for water, the volume effect calculated is of the order of -1 to -2 cm^3 mol^{-1} for the development of a single ionic charge (or of a dipole moment of *ca.* 10 D); it becomes larger in nonaqueous solvents like methanol (-4 to -6 cm^3 mol^{-1}), acetone (-5 to -8 cm^3 mol^{-1}) or benzene (-20 to -30 cm^3 mol^{-1})[16]. Clearly charge delocalization reduces this effect. Such predictable solvation contributions will be shown to correspond to experimentally obtained volume data in later sections.

It may be worth while to point out that neither charges nor bond lengths and angles (and hence dipole or multipole moments) are influenced under pressure, as indicated by experimental evidence[17].

In the interpretation of volume data, it is vitally necessary to estimate the solvation contributions quantitatively in order to appraise the intrinsic part, the latter being the main criterion in the assignment of mechanisms. Additional caution should prevail when volume data to be used and compared were obtained at different temperatures.

1.5. Determination of Partial Molar Volumes and Partial Molar Volume Differences

When the density d is known for a solution of concentration c and for the solvent d_0, one can calculate the apparent molar volume ϕ of the solute in that solvent by means of

$$\phi = \frac{M}{d} - \frac{d-d_0}{d_0}\frac{1000}{c}.$$

The value obtained is often found to be somewhat dependent on the concentration. Such deviations are caused by solute-solute interactions which can be substantial if the mass fraction of the substrate is relatively large, or if the solute is charged. With large molecules, this may be the case even at low concentrations. For this reason, the partial molar volume at infinite dilution is used (ϕ^{∞}); it is obtained by extrapolating ϕ to zero concentration. With modern densimeters it is possible to measure the term $(d-d_0)$ to concentrations as low as 10^{-3} M, and to obtain ϕ^{∞} to an accuracy of the order of a few tenths of a cm^3 mol^{-1}. When the solute molecules are subject to association or dissociation, linear extrapolation can be expected only if the appropriate power function of c is used in the plot. For the best procedure to be employed, the original literature should be consulted[18].

Reaction volumes $\Delta\bar{V}$ for an equilibrium

$$A + B \rightleftharpoons C + D$$

can thus be determined if the necessary density data are available for all components. No high pressure measurements of K are necessary then, and in fact, the initial response of K to pressure changes $(d\ln K/dP = -\Delta\bar{V}/RT)$ can be calculated from such data. In many instances in which the reaction volumes have been determined either by means of the pressure dependence of the equilibrium constant, or from density data, the results agree very well. The density route is not available if substantial equilibration cannot be prevented.

For the ionization of weak electrolytes, the inescapable need for counterions actually supplies a solution to this problem: thus, the partial molar volumes of sodium acetate, hydrochloric acid, sodium chloride and acetic acid in water can be combined so as to yield the ionization volume:

$$\Delta\bar{V}_i = \bar{V}_{NaOAc} + \bar{V}_{HCl} - \bar{V}_{NaCl} - \bar{V}_{HOAc}$$

In other instances, however, one is obliged to make high-pressure measurements of the equilibrium constant. Spectroscopic techniques are the method of choice for covalent equilibria, and for ionic equilibria if the indicator approach is chosen; in that instance, one needs independent information concerning the volume profile for the ionization of the indicator itself. It is of course also desirable to verify that pressure does not modify the spectral characteristics of the pure components. Likewise, if the conductance method is to be used, one needs to keep in mind that other relevant properties of the system are sensitive to pressure too (the dielectric constant of the medium and the cell constant, to mention only two). However, these difficulties have largely been surmounted, and very extensive compilations of ionization volumes are now available[19]. Reaction volumes for reactions which essentially go to completion can be obtained either from partial molar volume data or by means of dilatometry.

2. Reaction Volumes

All chemical reactions approach an equilibrium composition. In some this composition is such that all components, including the starting materials, are simultaneously detectable in the final mixture; in others, the reaction is for all practical purposes complete. The method to be used in determining the reaction volume must be chosen according to the magnitude of the equilibrium constant, the rate of equilibration, the stability of the components *etc.* In this section, we discuss together, without further distinction, the reaction volumes both of traditional equilibria and complete reactions. Additional examples of reaction volumes are mentioned in Section 3, where they are compared with activation volumes.

2.1. Complexation

The small diameter of covalently bound hydrogen and the substantial length of the hydrogen bond combine to produce only a small volume decrease in the formation of such a bond: $\Delta\bar{V} = -4$ cm^3 mol^{-1}, on the average. This result was first deduced by *Drickamer et al.*[20] from the effect of pressure on the infrared spectra of alcohol solutions in hydrocarbons, and it has since then been confirmed by *Suzuki*'s studies of the complexation of phenol with dioxane[21], and of the dimerization equilibrium of carboxylic acids[22].

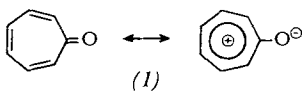
Similarly, small negative volume changes occur upon charge transfer complexation between neutral aromatic molecules such as chloranil and hexamethylbenzene[23]. Values of $\Delta\bar{V}$ of -5 to -10 cm^3 mol^{-1} are typically observed. They are in agreement with simple volume calculations based on X-ray data; since these calculations neglect electrostriction, the amount of charge transferred must be quite small.

The dominant effect of electrostriction on volume changes in solution first manifests itself when the members are charged. Thus, pressure strongly *inhibits* the complexation between *N*-methyl-4-carbomethoxypyridinium and iodide ions; $\Delta\bar{V}$ for this equilibrium is $+16$ cm^3 mol^{-1}[24]. Clearly, in this case the normal volume decrease that is expected upon complexation is more than offset by the release and relaxation of solvent molecules that occur when the charged members approach and in a sense neutralize one another. When only one of the members is charged, no pressure effect is observed at all ($\Delta\bar{V} \cong 0$); thus, the complexation of pentakis(methoxycarbonyl)cyclopentadienide ion with trinitrobenzene, and that of tropylium ion with hexamethylbenzene are pressure-independent equilibria[24]. The loss of solvation that occurs when one side of the ion is stripped to make room for the neutral partner compensates for the volume decrease that takes place in the complexation process.

2.2. Covalent Bond Formation

Covalent bonds are shorter than those produced by the weaker interactions discussed above, and more sizable volume decrease and pressure effects are observed, even with molecules of small diameter. Equilibrium studies of the hydration of carbonyl compounds under pressure have revealed that volume changes of -10 cm^3 mol^{-1} are quite typical[25]. Somewhat greater shrinking characterizes ketalization[26] and methanol addition to benzonitrile[27]. The addition of water to fumarate ion has a reaction volume of -10 cm^3 mol^{-1}[28], and so it is comparable to the hydration of the carbonyl functionality. The dimerization of NO_2 is greatly favored by pressure: $\Delta\bar{V} = -20$ cm^3 mol^{-1}. This pressure effect is larger than can be accounted for on the basis of covalent bond formation between two such small molecules, and it seems likely that the dimeric molecule contains local dipoles whose solvation may contribute to the overall result[29].

The molar volume decreases become much greater still when more than one covalent bond is formed. In the Diels-Alder reaction, for example, two new bonds result. The reaction volume has been determined in many instances—in some, by means of dilatometric experiments and in others, by means of partial volume determinations of the reactants and products. In the large majority of cases the shrinkage is as large as 30 to 40 cm^3 mol^{-1}[30–32]. Interestingly, the intrusion of electrostatic effects once again can greatly alter these numerical results. The cycloaddition product resulting from the reaction of cyclopentadiene with tropone, for example, appears to be only barely less voluminous than the compounds from which it was made: $\Delta\bar{V} = -5$ cm^3 mol^{-1}. The feature responsible for this exceptional case was revealed by individual partial molar volume measurements, which



(1)

showed tropone *(1)* to occupy much less space in solution than what is expected on the basis of a completely covalent structure; clearly, this molecule has a highly dipolar if not zwitterionic character, and the loss of the dipole counteracts the shrinkage due to bonding[33].

2.3. Ionization

The ionization volume of water has been determined as -22 cm^3 mol^{-1}[34]. This may seem impossible at first sight: the molar volume of water being only 18 cm^3 mol^{-1}. What happens is not that the ionizing molecules themselves shrink in any significant way, but that the bulk solvent around the newly formed ions solvates. This is a universal phenomenon;

there is no known instance in which a reaction producing ions from neutral molecules fails to lead to volume contraction.

A very large number of weak acids have been similarly examined[2], and the results can qualitatively be understood in terms of the aforementioned Drude-Nernst equation. Thus, the first ionization volume for hydrogen sulfide equals -16 $cm^3\ mol^{-1}$; clearly, a larger ionic size leads to less contraction. The q^2/r dependence manifests itself when delocalization of the charge characterizes the anion: phenol has an ionization volume of $-18\ cm^3\ mol^{-1}$, that of *p*-nitrophenol equals -10 $cm^3\ mol^{-1}$, and that of acetic acid, $-13\ cm^3\ mol^{-1}$; the much larger second $\Delta\bar{V}_i$ values of diprotic acids (phosphoric acid: $\Delta\bar{V}_{i,I}$: -14, $\Delta\bar{V}_{i,II}$: $-24\ cm^3\ mol^{-1}$) point in the same direction. The large solvent dependence of the ionization volume (embodied in the dielectric constant term) is shown by the fact that the values in methanol roughly double those in water. It is difficult to carry out such measurements in solvents much less polar than simple alcohols; however, in nonpolar media the volume decreases due to ionic solvation can be shown to become enormous (see Section 3.5).

An interesting aspect of the behavior of carbonic acid under pressure is that the volume change observed ($-27\ cm^3\ mol^{-1}$) indicates a process quite different from that of the otherwise closely related carboxylic acids. The difference is that the greatly increased ionization of carbonic acid under pressure reflects the effect of bond formation as well:

$$CO_2 + 2H_2O \rightleftharpoons HCO_3^{\ominus} + H_3O^{\oplus}$$

The base strengths of a large number of amines under pressure are also known, and since these data generally confirm but do not add to the conclusions just drawn, they need not be mentioned here.

Ion-pair equilibria are sensitive to pressure for the same reasons as acid-base equilibria, and the effects implicate the same factors. Monovalent ion-pairs in water are not known, but a number of divalent ion-pairs such as $MnSO_4$ and $MgSO_4$ have been studied in that solvent. The volume change that accompanies the dissociation of these pairs is about $-7\ cm^3\ mol^{-1}$[35]. If we consider ionization in terms of the Winstein Scheme

$$A-B \rightleftharpoons A^{\oplus}, B^{\ominus} \rightleftharpoons A^{\oplus} \,||\, B^{\ominus} \rightleftharpoons A^{\oplus} + B^{\ominus}$$

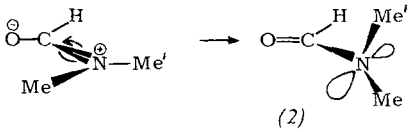
then according to the Drude-Nernst equation, the dissociation volume of a monovalent ion-pair in water should be only about -3 to $-4\ cm^3\ mol^{-1}$. This is but a small fraction of the ionization volume of a neutral monovalent species (generally about $-15\ cm^3\ mol^{-1}$); evidently, most of the electrostriction occurs in the first stage of the Winstein scheme.

The very large volume effects that accompany the charge separation in nonpolar solvents have been demonstrated by means of several ion-pair reactions. Thus, it has been deduced from the effect of pressure on the sodium hyperfine coupling constant that a volume contraction of $-15\ cm^3\ mol^{-1}$ occurs when naphthalenesodium tight ion-pairs in dimethylformamide are allowed to become loose[36]. This is a remarkably large value, if one considers that the ions are already formed at the start, that one of them must be highly delocalized, and that the separation is a minor one. Similar results have been obtained with alkali-metal fluorenides[37]. Complete separation brings about a proportionately larger volume decrease; thus, the dissociation of tetra-*n*-butylammonium picrate in ether has been claimed to have a $\Delta\bar{V}_d$ of $-125\ cm^3\ mol^{-1}$[38].

3. Activation Volumes

3.1. Conformational Changes

Only small pressure effects are observable when bonds undergo only partial deformations such as stretching and bending (biphenyl racemization[39]), or conformational changes (cyclohexane inversions[40]); the activation volumes are generally between $+2$ and $-2\ cm^3\ mol^{-1}$. In one instance, the methyl equilibration in dimethylformamide *(2)*, $\Delta\bar{V}^{\neq}$ is rather larger ($\sim +10\ cm^3\ mol^{-1}$). It would logically seem to be related to the partial loss of the dipole in the transition state;



(2)

however, the authors did not observe large solvent effects on this value, and they attribute the result at least partially to a pre-evacuation of the space needed to carry out the rotation[41].

3.2. Covalent Bond Formation and Cleavage

There are relatively few examples of such reactions that occur without large concomitant changes in dipole moment. The propagation step in free-radical polymerization is one of them. This reaction has been studied under pressure, especially by *Nicholson et al.*[4], *Weale*[3], and *Ogo et al.*[42] and their conclusions in general agree: the activation volume for this reaction is about $-10\ cm^3\ mol^{-1}$. While there are of course variations depending on the monomer involved, it is clear that the bond being formed is quite short already when the transition state is reached.

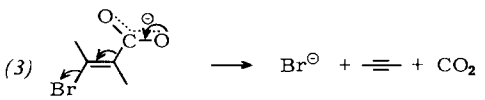
It might be supposed that the termination reaction of radicals should also be accelerated by pressure, but that is not so; it is in fact severely retarded. The reason for this is that this part of the polymerization reaction is diffusion controlled[4], and therefore inhibited by pressure in spite of the fact that the actual bond formation step is characterized by the usual volume decrease: the combination of radicals already together in a cage is accelerated. For instance, $\Delta\bar{V}^{\neq}$ for the recombination of *tert*-butoxy radicals equals $-4\ cm^3\ mol^{-1}$[43].

Covalent bond cleavage is retarded as expected; thus, the decomposition of di-*tert*-butyl peroxide is a well-known example with an activation volume of about $+10\ cm^3\ mol^{-1}$[44]. Since this type of reaction is often used to initiate polymerizations, it may be noted in passing that the pressure responses to all three steps in polymer formation (initiation, propagation, and recombination) conspire to generate fewer chains that grow more rapidly and are taken out of circulation less readily—in other words, to form polymers of greater density and higher molecular weights. This fact may find ap-

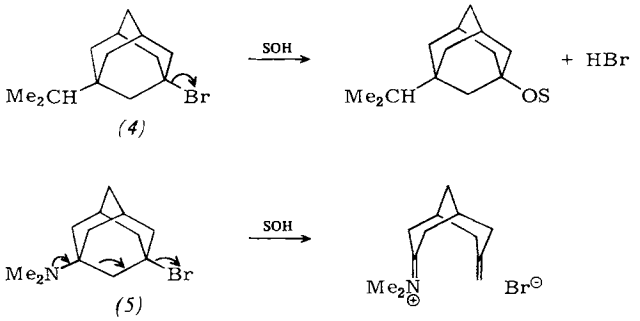
plication in the production of special polymers for which there are limited but critically important uses.

Bond cleavage in ions is complicated by the fact that the charge is often translocated in the process; however, experience has shown that this is a secondary consideration as long as no charge is neutralized, or new charges are formed. As an example one might mention the studies on decarboxylation by *Brower et al.*[45]: the loss of CO_2 from such ions as trichloroacetate has an activation volume of +6 to +10 cm^3 mol^{-1}, depending on the substrate.

Multiple bond fractures should show correspondingly larger volume changes. That is, *if* these bond reorganizations are concerted; if only one bond breaks in a rate controlling initial step, there is no reason to expect an unusually large volume increase in the transition state. Several results now available seem to bear this out. Thus, the fragmentation of 3-bromo-2-methylisocrotonate *(3)* has an activation volume of +18 cm^3 mol^{-1}[46]; when it is remembered that $\Delta\bar{V}^{\neq}$ in simple decarboxylation reactions averages +6 to +10 cm^3 mol^{-1}[45], concertedness in the reaction is clearly indicated.

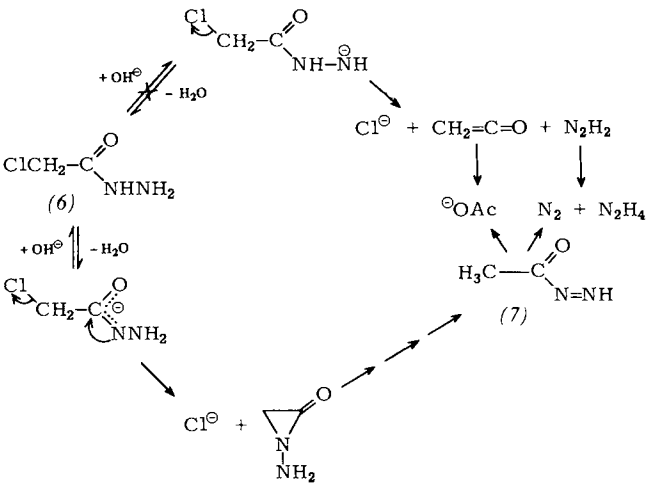


In the solvolysis of δ-aminoalcohol derivatives, the products are indicative of fragmentation, and the fact that the rate is up to 50000 times faster than the solvolysis rates of the corresponding carbon homomorphs (in spite of the induction by the nitrogen atom) strongly suggests that the bond cleavages are concerted[47]. Since charge formation occurs simultaneously, negative activation volumes are expected, but they should be less negative in the fragmentations than in the solvolyses.



This difference is indeed observed. Whereas the simple solvolysis of *(4)* (in 80% aqueous alcohol at 40 °C) has an activation volume in the range of -21 ± 2 cm^3 mol^{-1}, the fragmentations [*e.g.* of *(5)*] have one of -13 ± 2 cm^3 mol^{-1}[48] (SOH = alcoholic solvent). In one instance, the *N*-compound upon dissolution in aqueous alcohol does not lead to fragmentation products, but to substitution and elimination[47]. The rate is ten times slower than that of the carbon analog, and the activation volume is -23 cm^3 mol^{-1}[48].

In one fragmentation, the pressure effect was found to be opposite in sign to that expected: in aqueous alkaline solution, chloroacetyl hydrazide *(6)* fragments to chloride and acetate anions, and to nitrogen and hydrazine, *via* what was presumed to be a concerted fragmentation of the β-anion[49,50] similar to that of the anion *(3)*. However, $\Delta\bar{V}^{\neq}$ is -5 cm^3 mol^{-1}. A subsequent conventional investigation based on the effect of *N*-methyl substitution and on stopped flow experiments revealed that the reaction takes place *via* the α-anion and rate-limiting internal displacement. The intermediate acetyldiazene *(7)* was directly observed[51]. This is a nice example of the fact that deviations from expected pressure effects justify reinvestigations of reactions whose mechanisms have already been "established".



Very similar arguments can of course be applied in the case of the cycloaddition reactions. The schemes shown in Figure 3 for [2+2]- and [2+4]-cycloadditions indicate the three conceivable mechanisms for these reactions. The two-step process (A) with a biradical intermediate should result

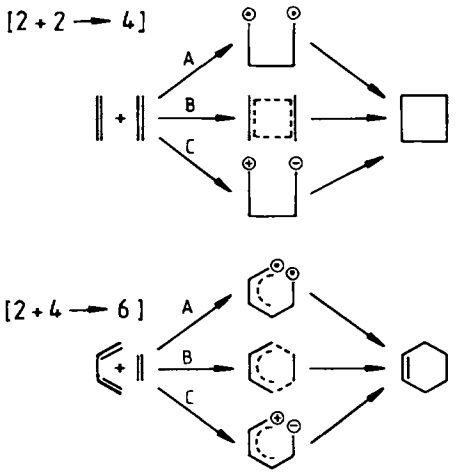


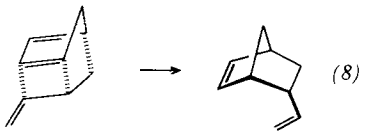
Fig. 3. Possible reaction mechanism of [2+2]- and [2+4]-cycloaddition reactions. A, B, C (see text).

in a moderately negative volume of activation accompanied by little or no solvent effect. The concerted route (B) is also nonpolar. A fairly large negative $\Delta\bar{V}^{\neq}$ is expected with no solvent variation. Finally, the polar two-step path (C) with the zwitterionic intermediate should lead to negative volumes of activation which in their magnitude depend on the solvent. Thus high pressure kinetics combined with solvent variation should in principle offer a possibility to differentiate between the three mechanisms.

It was already known in the thirties that the Diels-Alder reaction is unusually sensitive to hydrostatic pressure; the mechanistic implications have been discussed, especially by

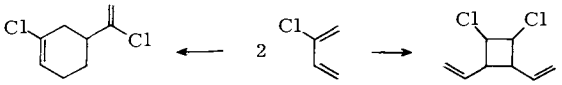
Walling and *Eckert*[52–55]. In fact, in recent years the Diels-Alder reaction has often been carried out under high pressure for synthetic reasons[56]. Evidently the reacting molecules have in the transition state already advanced well beyond the half-way point to the final volume; the reaction is indeed concerted.

Eckert's experiments in fact contain evidence for the unique feature of the secondary orbital interaction[57]: a weak bonding feature which is present in the transition state but not in the final product. It is thought that this feature is responsible for the predisposition of many of these reactions to produce *endo* products such as *(8)*, even though these are often the more hindered ones. In a number of such reactions, *Eckert* reported that the transition state is even smaller than the product.



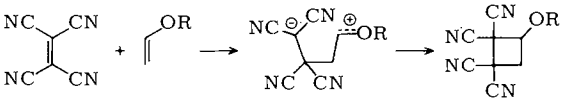
(8)

In some cases, allowed and forbidden cycloadditions occur in competition, and one can compare the rate of the presumably concerted cycloaddition directly with that of a stepwise analog. Indeed, *Stewart* has shown[58] that in the dimerization of chloroprene *(9)*, which produces both [2+4]- and [2+2]-products, pressure favors the former by a wide margin: $\Delta\Delta\bar{V}^{+} \approx 10$ cm^3 mol^{-1}.



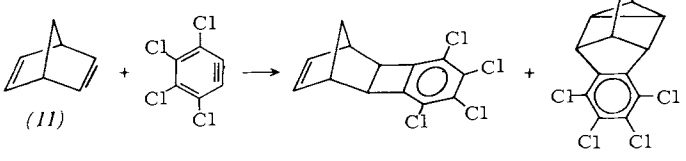
(9)

While the pressure effect appears to be a promising approach to the question of concertedness, one should be aware of the following pitfalls. For one, it is assumed that no zwitterionic character is present in either reactant, product, or transition state. That is not always true. For instance, in the cycloaddition of tetracyanoethylene to enol ethers, known to be stepwise and to involve a zwitterionic intermediate *(10)*[59], the activation volume in nonpolar solvents may have values as large as -50 cm^3 mol^{-1}[60]. That these large negative values are due in part to electrostriction and not to covalent bond formation is clear from the fact that the *reverse* of



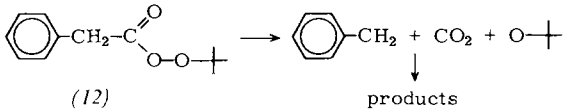
(10)

the last step also has a negative activation volume; this reaction is therefore less akin to homolysis than to solvolysis[61]. For similar reasons, in the competing cycloadditions of norbornadiene *(11)* and tetrachlorobenzyne, the [2+2]- is favored over the [2+4]-isomer[62]. If the zwitterionic character is present in one of the reactants, the disappearance of this feature as the cycloaddition progresses may make $\Delta\bar{V}^{+}$ less negative than would otherwise be expected. This is evidently the case in the 1,3-dipolar [4+6]-cycloaddition of tropone *(1)* to cyclopentadiene[33]. Although this is known to be a concerted reaction[63,64], the activation volume (-7 cm^3 mol^{-1}) is exceptionally small for a cycloaddition. Measurement of both the reaction volume and the partial molar volumes of all of the participating molecules, then showed that the tropone is responsible for the exceptionally small pressure enhancement of the rate: as noted in Section 2.2, the dipolar nature of this reactant disappears on the way to the transition state, and the volume decrease is accordingly reduced. This is a nice example of one of the principal advantages of the use of the activation volume over that of the other activation parameters: the availability of the corresponding initial state information makes it possible, when anomalous pressure effects are observed, to decide whether the anomaly is due to the initial or transition state.



(11)

It should not be assumed that bond cleavage is always characterized by large volume increases of 10 cm^3 mol^{-1} or more. Thus, it may be obvious from the near equality of the activation and reaction volumes in the Diels-Alder reaction that the corresponding cycloreversions would have quite modest activation volumes. This question is clearly related to the location of the transition state along the reaction coordinate. *Neumann et al.*[65] have found, for example, that the decomposition of peresters such as *(12)* may have activation volumes as low as 1 cm^3 mol^{-1} even though two bonds are breaking.



(12)

These fragile molecules obviously decompose with early transition states. The activation volumes for product formation in radical decompositions are much larger (>10 cm^3 mol^{-1}) in those cases in which the initial step is reversible, so that diffusion out of the initially formed cage is then part of the activation process.

The relation between $\Delta\bar{V}^{+}/\Delta\bar{V}$ and the transition state location in concerted reactions is a close though not a linear one. Both the volume changes *and* the location along the reaction coordinate are obviously related to the nuclear positions in the reacting molecules; on the other hand, the volume profile of the reaction may involve a "non-least motion" extremum that rules out the use of any linear relation between the two. Nevertheless, activation volumes are often used to make estimates, for example, of bond elongations in the transition state. *Hamann*[66] estimates on that basis that 25—50% extensions are common. Even now, however, one frequently encounters the rule of thumb that only a 10% extension occurs. The users of this rule are generally unaware that it originated with *Eyring et al.*[67], and that it, too, was based on a few of the earliest activation volume measurements!

In this connection, it may be useful to point out that there is a possible source of confusion in the terms "early" and "late", or "reactant-like" and "product-like", since these ex-

pressions depend on what parameter is used to make the comparison. The Diels-Alder reaction is a good example. This is generally described by organic chemists[68], because of its low activation energy, as a textbook example of a reaction with an early transition state; yet the fact that $\Delta\bar{V}^{\neq}$ and $\Delta\bar{V}$ are comparable requires that the transition state is late so far as nuclear locations are concerned. It seems evident that the nuclei are virtually already in place when the electrons begin to flow to form the new bonds. The Hammond postulate is another important principle related to transition state location; its connection with high pressure results is considered further in Section 3.4.

3.3. Neutral Displacement

In neutral displacement reactions

$$X—Y + Z \rightarrow \{TS\}^{\neq} \rightarrow X + Y—Z$$

the transition state is characterized either by an additional bond between Y and Z (S_N2- or A-mechanism) or by a broken Y—X bond (S_N1- or D-mechanism). Between these extreme configurations, a continuum of concerted bond-making/bond-breaking processes (interchange or I-mechanisms) can occur in which the more dominant of the two concurrent steps is often indicated by either an I_a- or I_d-symbol.

Since no major polarity changes are expected for this type of substitution reaction, the volumes of activation experimentally obtained consist mainly of the intrinsic contribution.

Among the examples, there are many radical abstraction reactions; for instance, the abstraction of a hydrogen atom from phenols by diphenylpicrylhydrazyl has an activation volume of -13 cm^3 mol^{-1}[17]. For the removal of a chlorine atom from CCl_4 by hydrocarbon radicals, $\Delta\bar{V}^{\neq}$ equals -15 cm^3 mol^{-1}[69]. The magnitude of these results suggests a rather close approach of the two reactants, *i.e.* a S_N2-like situation.

A rather impressive demonstration of the usefulness of the volume of activation as a mechanistic criterion was presented by *Merbach et al.*[70], who investigated the fast ligand exchange reactions

$$MX_5L + L^* \rightarrow MX_5L^* + L$$

for the systems M = Nb or Ta and X = Cl or Br. When L is an oxygen-ether, the complexes react *via* a dissociative mechanism with $\Delta\bar{V}^{\neq}$ values between $+15$ and $+30$ cm^3 mol^{-1}, whereas thio-, seleno-, and telluro-ethers indicate an associative behavior with $\Delta\bar{V}^{\neq}$ varying from -10 to -20 cm^3 mol^{-1}.

3.4. Displacements Involving Ions

In view of the large volume changes due to ionic solvation (electrostriction), considerable variations may be expected in pressure effects on ionic displacements depending on the charge type.

Those examples in which there is *no* net change in the number of charges would be expected to resemble neutral displacements. In coordination chemistry, the exchange of neutral ligands belongs to this type of reaction. The more labile solvent complexes, $MS_6^{2\oplus}$, of the divalent cations cobalt and nickel are believed to react *via* dissociative mechanism. In solvents like methanol, dimethylformamide and acetonitrile, the volumes of activation for the ligand-solvent exchange reactions turned out to be positive, ranging, indeed, from $+9$ to $+11$ cm^3 mol^{-1}[71].

Within the series of the rather stable complex ions $M(NH_3)_5OH_2^{3\oplus}$ (with M = Co, Rh, Ir, Cr), the volumes of activation for the corresponding water molecule exchanges amount to $+1.2$, -4.1, -3.2, and -5.8 cm^3 mol^{-1}[72-74], respectively. From these results it was proposed that contrary to earlier concepts, only the complexes of trivalent cobalt react by a dissociative mechanism (I_d), while the other central ions force an associative character on the substitution processes.

When both reactants are charged, the volumes of activation of ligand substitution reactions need to be interpreted in terms of their intrinsic and solvation contributions. In most cases, one can estimate the total volume of activation with respect to both sign and magnitude, for either a dissociative or an associative mechanism, and compare it with the experimentally obtained quantity. This allows one to make a decision as to the character of the rate determining step. For instance, the stepwise anation of $Cr(OH_2)_6^{3\oplus}$ by oxalate was investigated at pH 2.7, where only the aqua form of the complex is present and the oxalate exists mainly as $HC_2O_4^{\ominus}$. The volumes of activation for the formation of $Cr(C_2O_4)(OH_2)_4^{\oplus}$, $Cr(C_2O_4)_2(OH_2)_2^{\ominus}$, and $Cr(C_2O_4)_3^{3\ominus}$ turn out to be -2.2, -8.2, and -10.0 cm^3 mol^{-1}, respectively[75]. In case of a prevailing dissociative mechanism, each of the rate determining steps should be represented by a similar Cr—OH_2 bond breaking, resulting in a positive contribution to $\Delta V^{\neq}_{intr}$ and a negligible $\Delta V^{\neq}_{solv}$. An associative mechanism, preceeded possibly by an ion association, however, should lead to a negative $\Delta V^{\neq}_{intr}$ with a superimposing $\Delta V^{\neq}_{solv}$ varying in sign and magnitude. The experimental results can, in fact, only be reconciled with the second possibility.

A supplemental example of this line of reasoning is the anation of the pentacyano(aqua)cobaltate(III) ion:

$$Co(CN)_5(OH_2)^{2\ominus} + X^{\ominus} \rightarrow Co(CN)_5X^{3\ominus} + H_2O$$

For X = Br, I, NCS the volumes of activation were found to be $+8.4$, $+9.4$, and $+8.2$ cm^3 mol^{-1}[76]. Here only the common dissociative rate determining step of a Co—OH_2 bond cleavage is compatible with the results, since negative values are definitely expected for an associative mechanism.

The difficulty in interpreting high pressure effects of this type of reaction for organic substrates lies in the several complicating features, such as the effect of the dispersion of charge in the transition state and the degree of association of the ions in nonaqueous media. That charge dispersion is an important factor is clear from the effect of pressure on the displacement of bromide ion from ethyl bromoacetate by the dinegative thiosulfate ion: $\Delta\bar{V}^{\neq}$ is $+3.2$ cm^3 mol^{-1} in that case[77].

In displacement reactions in which charged products are formed from neutral substrates, electrostriction and covalent bond formation combine to produce pronounced shrinking. The best known example of this type is the Menschutkin

reaction; all of the numerous cases studied were accelerated by increased pressure. While many of these instances could be quoted as supporting the general impressions recorded above, special mention deserves to be made of three studies which have yielded particularly interesting results.

Two of these concern the solvent effect[78,79]: once again, Drude-Nernst behavior is observed, with the least polar media producing the greatest contractions. Figure 4 shows the variation of $\Delta\bar{V}^{+}$ with solvent for two Menschutkin reactions plotted as a function of the electrostriction parameter q_p. It can be seen that the contribution ΔV^{+}_{solv} is largest in nonpolar solvents, whereas ΔV^{+}_{intr} depends on the structure of the reactants.

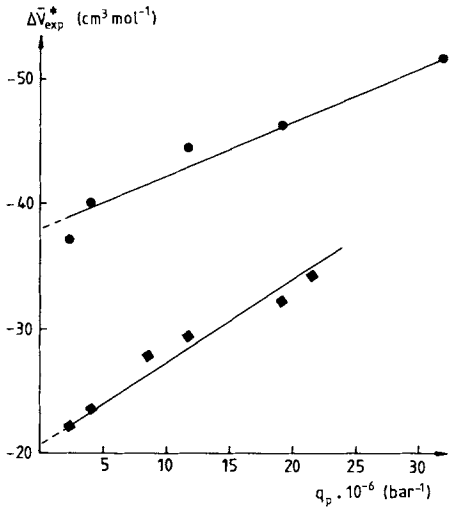


Fig. 4. Solvent dependence of $\Delta\bar{V}^{+}$ for the Menschutkin reactions: ● triethylamine + ethyl iodide and ■ pyridine + methyl iodide. The electrostriction parameter q_p is defined according to *Drude-Nernst*[15] as: $q_p = (3/(2D+1)^2)(dD/dP)$ with D being the dielectric constant of the solvent.

A second feature of great interest is that when Menschutkin reactions similar except in steric requirements are compared under identical conditions, the slower and more hindered reactions tend to be accelerated the most. Thus, a systematic study of the reactions of methyl, ethyl, and isopropyl iodides with pyridine, 2,6-dimethyl-, 2,6-diethyl-, 2,6-diisopropyl- and 2,6-*tert*-butylpyridines has revealed that $\Delta\bar{V}^{+}$ becomes steadily more negative as the hindrance is raised[80]; in fact, *Okamoto et al.*[81] have shown that the methylation of 2,6-di-*tert*-butylpyridine succeeds only under pressure. Several theories have been offered to account for this phenomenon; perhaps the most satisfying one is based on the fact that

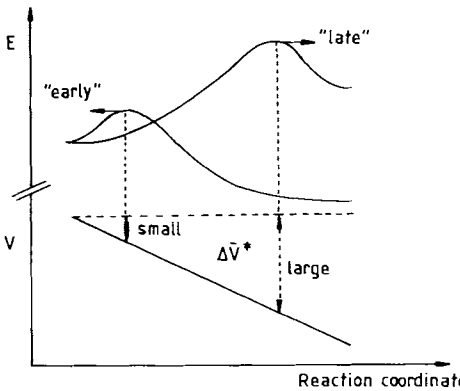


Fig. 5. Energy and volume profiles for an unhindered, fast Menschutkin reaction, and a hindered, slow one (with early and late transition state).

no anomalies are found in the initial and final state volumes[82]. Thus, the reaction volumes are all approximately the same, and the net result is that the activation volume becomes an increasingly larger fraction of the reaction volume as the crowding is raised. This suggests that the increase in hindrance leads to later transition states—precisely what is predicted on the basis of the well-known Hammond postulate (Fig. 5). It was subsequently found that in the corresponding reaction with methyl chloride, the $^{35}Cl/^{37}Cl$ isotope effect is indeed larger in the methylation of 2,6-lutidine than in that of pyridine[83].

3.5. Solvolysis

The solvolysis reaction is a good example of the dominance of ionic solvation over covalent bond making and breaking where the volume is concerned: even though a bond breaks, pressure invariably accelerates the reaction, generally by a wide margin. Again, the dominant contribution from ΔV^{+}_{solv} depends on the factors given in the Drude-Nernst equation; it ranges from -10 to -35 cm³ mol⁻¹.

In inorganic chemistry, the system studied most involves the hydrolysis of acido(pentaammine)cobalt(III) complexes

$$Co(NH_3)_5X^{(3-n)\oplus} + H_2O \rightarrow Co(NH_3)_5OH_2^{3\oplus} + X^{n\ominus}$$

The activation volumes for a series of X lie between -5 to -17 cm³ mol⁻¹[84] despite the assumption that breaking of the Co—X bond is presumably the initial step of the hydrolysis, thus contributing a positive ΔV^{+}_{intr}. A linear relationship as depicted in Figure 6 exists between the $\Delta\bar{V}^{+}$ values for X = Cl, Br, NO_3, SO_4, and dimethyl sulfoxide (DMSO) and the corresponding overall reaction volumes, $\Delta\bar{V}$. The slope is close to unity indicating that the leaving ligand $X^{\ominus}$ is

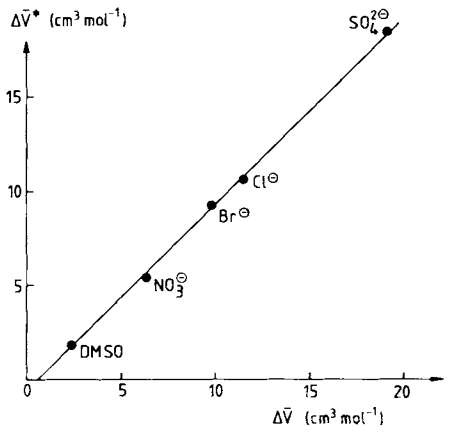


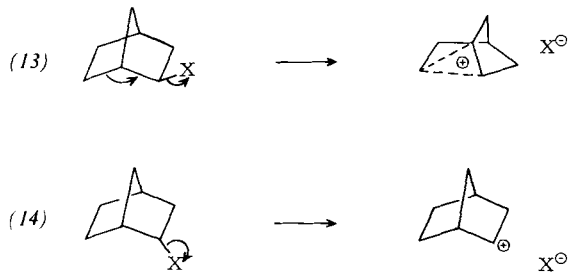
Fig. 6. Volume correlation $\Delta\bar{V}^{+}$ *versus* $\Delta\bar{V}$ for the hydrolysis reaction of $Co(NH_3)_5X^{(3-n)\oplus}$ (counterion: perchlorate).

almost fully detached in the transition state; *i.e.* a dissociative-(D)-mechanism is prevailing. In this case the volume of the transition state or intermediate can be considered as the sum of the solvated ligand X, with $\bar{V}(X^{n\ominus})$, and the five-coordinate common fragment with $\bar{V}\{Co(NH_3)_5^{3\oplus}\}$. The activation volume, $\Delta\bar{V}^{+}$, can thus be expressed as follows[85]

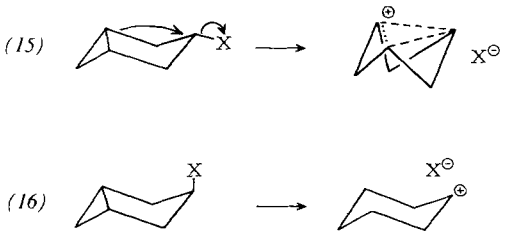
$$\Delta\bar{V}^{+} = \bar{V}\{Co(NH_3)_5^{3\oplus}\} + \bar{V}(X^{n\ominus}) - \bar{V}(Co(NH_3)_5X^{(3-n)\oplus})$$

The partial molar volumes of the individual ions $X^{\ominus}$ and $Co(NH_3)_5X^{(3-n)\oplus}$ can be determined by means of precision density measurements and by evaluation of the volumes of the respective counterions. This enables one to calculate the value of $\bar{V}\{Co(NH_3)_5^{3\oplus}\}$, which should be constant for the whole series if the D-mechanism is correct. In fact, it turns out to be 55 ± 1 cm^3 mol^{-1}. Thus, in this case of a predominantly dissociative mechanism, the combination of high pressure kinetics data with partial molar volume determinations permits the appraisal of the volume of reactive intermediates.

In this connection, high pressure has been brought to bear in an attempt to make a contribution to the question of the nonclassical ions. One of the highlights of organic chemistry of the nineteen sixties was the controversy about the validity of the concept of carbon participation in the formation of carbonium ions in solvolysis, and about the nature of the ions so formed. In some instances, this controversy has not been settled, even yet. As an example, we consider the 2-norbornyl derivative. Its *exo*-isomer *(13)* was claimed by *Winstein et al.*[86] to solvolyze with participation of other carbon atoms and formation of a symmetrical nonclassical ion, whereas the *endo*-isomer *(14)* behaves classically:

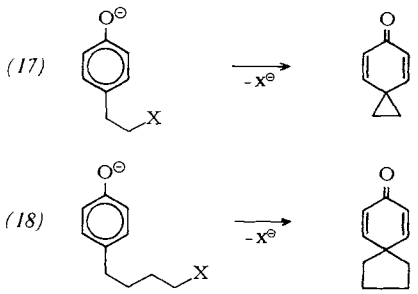


It is not possible here to take cognizance of the copious literature devoted to this question[87], and in this paper we can only allude to the pressure effect. In the *exo*-ion, the charge is dispersed between two carbon atoms, and hence that part of the activation volume that may be ascribed to the cation (roughly half) should be smaller than that of the *endo*-ion. The activation volumes for the two reactions were found to be about -14 and -18 cm^3 mol^{-1}, respectively, and hence this particular result supports carbon participation[88]. A similar result was found for the pair *(15)/(16)* shown below[89]:

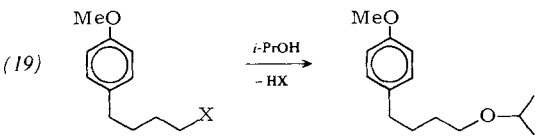


In his last review of this topic, *Winstein* listed these observations among those he felt supported the concept of carbon participation[90]; however, they do have one weakness. An activation volume less negative than normal in such reactions is indicated only if the positive charge becomes evenly distributed over at least two centers. If it becomes largely or completely *transferred* to one other atom, it is again localized albeit at an atom different from the one originally bound to the leaving group; if that be the case, there is no reason to anticipate an activation volume less negative than normal. This criterion can therefore be applied impartially only in instances in which symmetry *demands* charge dispersal, such as is the case in the two instances cited. The difference $\Delta\Delta\bar{V}^{\neq}$ furthermore is rather small, and hence accurate measurements under identical conditions are essential; this fact also rules out cases in which the pair of interest has an unusually large rate ratio (*i.e.* 10^3 or more: it will then be difficult to measure the two under the same conditions).

Nevertheless, there are continued indications that the effect is real. Thus, in cases involving the so-called $Ar^{\ominus}$-participation, no positive charge is formed at all, and the reactions are essentially internal S_N2-types. The activation volumes of *(17)* and *(18)* are then in the range of 0 to -5 cm^3 mol^{-1};



this compares with about -20 cm^3 mol^{-1} for the reaction of *(19)*[91].



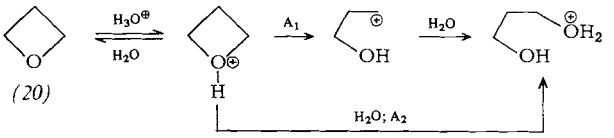
Sera has measured activation volumes of the solvolyses of *p*-substituted β-phenylethyl derivatives. In such reactions, it is now agreed, phenyl participation occurs when the substituent is an electron donor[92]. *Sera et al.*[93] find that the activation volume changes from -17 to -10 cm^3 mol^{-1} as the *p*-substituent is varied from *p*-nitro to *p*-methoxy. In a related experiment, the activation volume in the solvolysis of benzyl halides was found to become more negative when two large alkyl groups in the 2,6-positions interfere with the planarity and hence with charge dispersal.

3.6. Acid Catalyzed Solvolysis

Among the questions that have concerned high pressure chemists is that of solvent assistance, or whether the volume of activation can be used to probe solvolyses that may or may not be limiting. It does not appear to be so, with primary substrates such as β-cyclopentylethyl *p*-nitrobenzenesulfonate typically yielding $\Delta\bar{V}^{\neq}$ values quite similar to that of 2-adamantyl-*p*-nitrobenzenesulfonate[94] under identical conditions; the latter example is archtypical of secondary substrates hydrolyzing with a limiting S_N1-mechanism[95].

A closely related question has long puzzled organic chemists about the mechanism of acid-catalyzed hydrolysis of the CXC linkage in ethers, esters, acetals, amides, and so on:

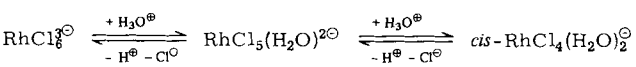
does the protonated species undergo unimolecular (A_1) bond cleavage to give a free carbenium ion in the rate-determining step followed by rapid reaction with solvent, or are these steps combined in a single, bimolecular reaction (A_2)? These two pathways are demonstrated by means of oxetane *(20)* as an example; it may be noted that the rate law—as in solvolysis—offers no distinction between these possibilities. Several



(20)

criteria have been applied to these reactions with this question in mind; among the more important are the solvent isotope effect (*i.e.* the use of D_2O) and the Hammett acidity function H_0. The results so obtained have never seemed very convincing; thus, in the case of oxetane, the use of these criteria led to the conclusion that it hydrolyzes *via* the A_1 mechanism[96]. That would mean a primary carbenium ion intermediate, in a solvent as nucleophilic as water. A straightforward prediction can be made on the basis of the pressure effect. The A_1 reaction is characterized by bond cleavage, and hence it should be pressure retarded; the A_2 pathway is basically one of displacement, and hence it should be promoted by hydrostatic pressure. This latter possibility is in fact observed; the activation volume is about -8 cm^3 mol^{-1}[97]. It may be noted in passing that the pre-equilibrium step involves no changes in either the total number of bonds or charges, and hence it should be affected by pressure in at most a minor way. A large number of cases has now been examined with this tool, especially by *Whalley et al.*, and a perfectly believable correlation between substrate and mechanism has emerged: while compounds such as ethers and simple esters solvolyze faster under pressure, others such as ortho-esters, acetals, *tert*-butyl ethers and so on are retarded[98]. The latter series is of course comprised of substrates capable of producing relatively stable carbenium ions.

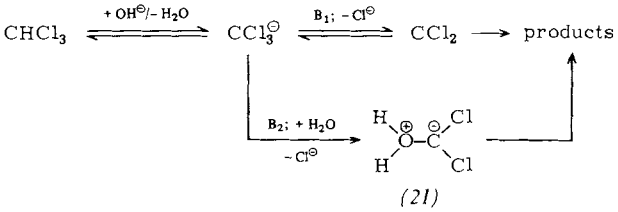
Similarly to the situation with organic substrates, the question again arises whether stepwise acid hydrolysis of complex ions involves a direct attack by a solvent water molecule or a primary dissociation of a metal-ligand bond. Based on earlier chloride exchange studies and on the steric course of the reaction, a D-mechanism was proposed for the acid catalyzed hydrolysis of the $RhCl_6^{3\ominus}$ ion.



The volumes of activation for the first two chloride removal steps amount to $+21$ and $+14$ cm^3 mol^{-1}, respectively[99]. Although one has to allow for the charge dispersal that occurs during the bond-breaking process, thus contributing a positive ΔV^{+}_{solv}, the large and positive values of $\Delta \bar{V}^{+}$ certainly contain a positive ΔV^{+}_{intr} as well.

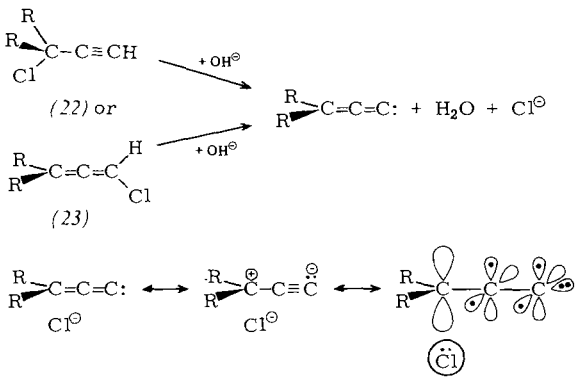
3.7. Base Catalyzed Solvolysis

A question similar to the one just considered arises in many base-catalyzed hydrolyses; the hydrolysis of chloroform may serve as example. In this case, the B_1 reaction would produce a free carbene, and the B_2 pathway would lead to a bound carbene (an oxygen ylide) *(21)*. It may be of interest to point out that *Hine*[100] in his classic paper on this reaction did not make a choice between these possibilities[100]. The observed rate constant was subsequently found to be proportional to the H_--function[101], which suggests that no solvent molecules become covalently bound in the transition state; but as noted above (Section 3.6), this criterion is subject to doubt. The activation volume is very large and positive, ($+16$ cm^3 mol^{-1}), so that it is certain that bond breaking must be taking place in the transition state[102]. The alternative B_2 path would in fact have led to a zwitterionic ylide *(21)* which because of its charges should be strongly solvated, and hence, characterized by contraction.



(21)

It is possible, of course, that carbenes are not always free molecules in all reactions in which carbenoid products form. The type of carbene considered, the solvent, leaving group and trapping agent all could conceivably alter the picture. These same studies have in fact unearthed one example of a complexed carbene[103]. The base-promoted solvolyses of tertiary propargyl halides *(22)* and of their isomeric allenic halides *(23)* are virtually unaffected by pressure, and it was concluded that these reactions produce not a free carbene, but one complexed with the leaving group in the same sense that ions are complexed in a pair. The zwitterionic character of the carbenic partner and the resulting electrostriction are thought to be responsible. In support of this conclusion, it was found that some internal return occurs; *i.e.*, during the



solvolysis of the acetylene derivative *(22)*, some of the allenic isomer *(23)* forms, and the yield of this product is almost independent of added chloride ions[104]. If the product *(23)* were formed *via* capture of chloride ions by a free carbene (external return), then the yield should have been increased by increasing the chloride ion concentration. The mechanism can of course also be tested stereochemically, and it has passed this test successfully[105].

The same question arises in other base-promoted reactions that produce interesting intermediates. *Brower* has employed

the high-pressure tool to demonstrate the freeness of dehydrobenzene in solution[106], and to dissect a number of carbanion reactions covering a spectrum of mechanisms[107]. We have used it to study the base-catalyzed reaction of chloramines. The evidence published in this case consists of base-catalyzed deuterium-exchange, correlation of the rate constant with the H_- function, and the fact that matrix-generated nitrene (NH) *does* react with water to produce hydroxylamine, which is the first observable product in the hydrolysis of NH_2Cl[108]. None of this evidence is completely convincing, however, and in fact, the rate law doesn't even rule out a simple S_N2 displacement reaction: the evidence that *Hine* had used to rule out such a mechanism for chloroform (a comparison of the rates of CH_xCl_{4-x}[100]) is not available in this instance. The activation volume is -3 cm^3 mol^{-1}. Furthermore, this same value applies to *N*-chloro(methyl)amine and *N*-chloro(dimethyl)amine; in the case of $(CH_3)_2NCl$, neither the B_1 nor the B_2 reactions are possible, and the conclusion is that the S_N2 mechanism is operating[109]. One might suppose that in analogy with the halomethanes, the B_1 pathway has its best chance among the halamines with the compounds NHX_2. It was found that difluoramine does indeed hydrolyze in aqueous base with an activation volume of about $+10$ cm^3 mol^{-1}[110]. Subsequent studies then showed that fluoronitrene (FN) could be trapped, that it is formed as a singlet, and that it has a triplet ground state[111]. The further fact that it is isoelectronic with oxygen makes it an enticing objective for further studies of its chemistry.

3.8. Rearrangements

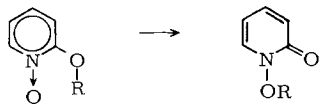
On the basis of the foregoing discussions, one should expect that pressure may either accelerate or retard rearrangements—the determining factor in whether bond-making or bond-breaking features dominate the mechanism. Simple steric changes and inversions, however, may be pressure independent.

Brower et al.[112] found that while the racemization of optically active sulfonium salts is usually virtually pressure-independent as might be expected from a simple sulfur inversion, in those instances in which a C—S fission could produce a stable carbenium ion— and hence in which an alternative mechanism for racemization might be operating—the racemization is indeed strongly inhibited by the application of pressure.

On the other hand, bond-making is clearly dominant in such concerted reactions as the Claisen[113] and Cope[114] rearrangements, which may be considered internal neutral displacements. $\Delta\bar{V}^{\neq}$ is about -15 cm^3 mol^{-1} in both cases.

The difference can be dramatically demonstrated with the rearrangement of ethers of type *(24)*.

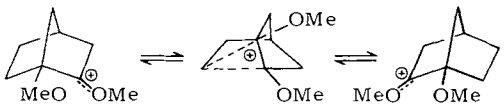
(24)



Pre-dissociation into radicals is the first step in the reaction when $R = CH(C_6H_5)_2$; it is retarded under pressure, with a $\Delta\bar{V}^{\neq}$ of $+10$ cm^3 mol^{-1}[115]. This is in stark contrast to the acceleration observed when $R = CH_2C_6H_5$ ($\Delta\bar{V}^{\neq} = -30$ cm^3 mol^{-1}). These conclusions are supported by the observation of CIDNP in the former reaction but not in the latter[116]. Pressure is therefore an important tool to ascertain concertedness in sigmatropic shifts, as it is in cycloadditions.

If the bond-breaking is of an *ionic* nature, the solvation that accompanies the approach of the transition state produces a *negative* activation volume. This is clear from an interesting and revealing result turned up by *Brower*[117]. He finds that the linkage isomerization in benzhydryl isothiocyanate is strongly accelerated by pressure. This reaction—observable only in ionizing media—therefore mimicks the pressure response of a concerted sigmatropic shift.

Charge dispersal may become the dominant feature in concerted sigmatropic shifts in ionic species if the reaction involves a relocation of the charge. This is the case in degenerate Wagner-Meerwein rearrangements. The equilibration of the 1,2-dimethoxynorbornyl ion—known to be classical[118]—was examined under pressure; it was found that the equilibration rate (as calculated from the NMR line shapes) was depressed by the application of pressure: $\Delta\bar{V}^{\neq} \approx +8$ cm^3 mol^{-1}[119]. The transition state *(25)* has the nonclassical and charge-dispersed structure in this instance.



(25)

Coordination compounds exhibit three types of rearrangements: linkage isomerization, geometric isomerization, and racemization. Linkage isomerizations are encountered with ambidentate ligands like NO_2, SO_2, SCN *etc.* One of the systems more extensively studied is the nitrito/nitro rearrangement of octahedral complexes:

$$M(NH_3)_5ONO^{2\oplus} \rightarrow M(NH_3)_5NO_2^{2\oplus}$$

The earlier studies[120] at ambient pressure had shown that at least for the cobalt(III) complex, the linkage isomerization is much faster than the hydrolysis reaction, and no exchange occurs between the bond ligand and free, labeled nitrite ions. The volumes of activation for M = Co, Rh, and Ir were found to be similar, *i.e.*, -6 ± 1 cm^3 mol^{-1}, suggesting a common

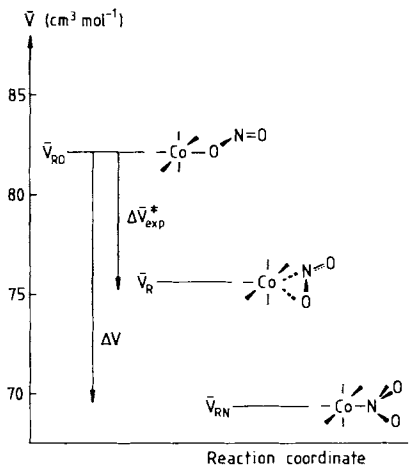


Fig. 7. Volume profile diagram for the linkage isomerization of $Co(NH_3)_5ONO^{2\oplus}$ (counterion: perchlorate).

mechanism[121]. Since the data are not at all similar to those obtained or expected for the corresponding hydrolyses reactions, an intramolecular rearrangement of the ligand is assumed with a transition state midway along the reaction coordinate, the overall volume of reaction being -12 cm^3 mol^{-1} for the cobalt complex ion. The total volume profile of the reaction emerging from these data is shown in Figure 7.

The linkage isomerization of the thiocyanato ligand attached to a planar four-coordinated palladium complex has been studied as part of a detailed investigation of this class of compounds. The two-pathway mechanism normally encountered for ligand substitution reactions of square planar complexes can be reduced to the solvolysis path (k_1) by steric crowding, *i.e.* by raising the bulkiness of the remaining ligands L (S = solvent):

$$ML_3X + S \xrightarrow{k_1} ML_3S + X$$

$$ML_3S + Y \xrightarrow{\text{fast}} ML_3Y + S$$

In fact, the rate constants and activation parameters for the solvolysis (or substitution through solvolysis) and the linkage isomerization of Pd(Et$_4$dien)SCN$^{\oplus}$ are identical, with $\Delta\bar{V}^{+}$ values of -10 ± 1 cm^3 mol^{-1}[122]. Unlike the nitrito/nitro isomerization, the linkage isomerization in this case proceeds through the well established hydrolysis route.

Conversions between the geometric *cis*- and *trans*-isomers of coordination compounds were studied with octahedral and square planar complexes as well. Isomerizations of *trans*-$Co(en)_2(OH_2)_2^{3\oplus}$ and *trans*-$Cr(C_2O_4)_2(OH_2)_2^{\ominus}$ were investigated in detail, with the result that the basic difference in mechanistic behavior between the complexes of trivalent cobalt and chromium was confirmed. Thus, the volume of activation for the isomerization of $Co(en)_2(OH_2)_2^{3\oplus}$ turns out to be $+6\pm1.5$ cm^3 mol^{-1} depending somewhat on ionic strength[123]. The relatively small and positive values were interpreted in terms of an I_d mechanism paralleling that of the water ligand exchange processes.

In contrast to this system, the isomerization of the *trans*-$Cr(C_2O_4)_2(OH_2)_2^{\ominus}$ shows a volume of activation of -16 cm^3 mol^{-1}[124]. This result could be conceived as an associative attack of a water molecule on the chromium center of the complex ion. However, the water exchange in this case is 150 times slower than the isomerization[125]. A rate-determining opening of an oxalato chelate ring with its charge concentration at the free end and a substantial contribution from electrostriction was therefore invoked.

Racemization reactions of a number of bis- and tris-oxalato complexes of chromium(III) show similar strong negative volumes of activation. Again, a ring-opening mechanism was suggested. The fact that all 12 oxygen atoms of $Cr(C_2O_4)_3^{3\ominus}$ were found to be equivalent in isotopic exchange studies supports the proposed mechanism[126].

Optically active cationic complex ions like $Cr(phen)_2(C_2O_4)^{\oplus}$, $Cr(bpy)_2(C_2O_4)^{\oplus}$, $Cr(phen)_3^{3\oplus}$, and $Cr(bpy)_3^{3\oplus}$ racemize with almost no pressure effect[127]. An internal twist mechanism is claimed to occur in which bonds are neither broken nor formed. This again shows that the volume of activation is an exceedingly useful criterion in mechanistic discussions.

3.9. Synthetic Applications

Pressure applications can be used to improve yields in those chemical syntheses in which the desired product formation has a markedly more negative volume of activation than the by-products; a difference in activation volume of *ca.* 10 cm^3 mol^{-1} can change a product ratio of 1:10 at ambient pressure into one of 10:1 at 1 GPa. Such circumstances may make a synthesis worthwhile.

And, in fact, examples of success are known: 0.7 GPa of pressure is enough to double the yield of *C*-alkylated phenols over *O*-alkylated isomer during the reaction of allyl chloride with aqueous sodium phenoxide[128]; the application of 1.4 GPa led to an increase from 2 to 65% in the cycloaddition of a steroidal diene in one instance[129]; as noted, *N*-methylation of 2,6-di-*tert*-butylpyridine, impossible altogether at atmospheric pressure, occurs with remarkable facility at 0.5 GPa, and so on. The Diels-Alder reaction in particular is one area that has attracted the attention of organic chemists as one that should be routinely considered a candidate for high-pressure execution[130]. Applications in inorganic synthesis have been reported by *Hagen et al.*[131].

4. Conclusions and Outlook

The principal uses of compressing chemical systems to date have been in mechanistic investigations. The volume of activation has intuitive appeal, a relatively favorable "signal to noise" ratio and an easy dissection into transition and initial state contributions, offering advantages over other activation parameters.

Additional possibilities now open to us include photochemistry[5, 132]. Thus, *Neuman et al.*[133] have already used high pressure to determine that α-fission has the greatest volume requirements among the various reaction paths into which carbonyl groups partition; *Weller et al.*[134] have determined that excimer formation prior to fluorescence can be diffusion controlled; *Hamann*[135] has calculated the ionization volume of excited *p*-nitrophenol from the effect of pressure on its Förster cycle, and it has been learned[136] that the pressure enhanced preference for covalent thermal [2+4]-cycloadditions over their [2+2]-analogs is reversed under photochemical conditions. Numerous other applications can be imagined and surely many are to be expected.

Something similar can be said for biochemistry[1, 137]. Some chemists are already using pressure to look for enzyme-mediated conversions subject to large-scale conformational changes in the catalytic process; others are scrutinizing the biomimetic catalysis of cyclodextrins and other enzyme models under pressure. There surely will be a useful high pressure input into problems surrounding the behavior of membranes; thus diffusion as revealed by spin labels is being investigated. The cyclization of squalene into steroid derivatives should benefit from high pressure conditions, as should numerous other forms of biomimicry.

The application of the next-higher-order pressures (of about 10 GPa where the $p\Delta\bar{V}^{+}$ term may well swamp the other parts of ΔG^{+}) is almost certain to lead to exciting new knowledge in even simple organic reactions[138]. The applications of relaxation and stopped-flow techniques under pressure are beginning to yield results[139], and the marriage of

high pressure and NMR techniques is sure to lead to knowledge of volume profiles in rapid degenerate equilibrations[14a]. Finally, small-scale technological applications are not ruled out either. Synthetic applications in the area of fine chemicals seem perfectly feasible; pharmaceuticals and special high molecular weight polymers are prominent among them.

The authors express their appreciation for the support of their own investigations in this field by the U. S. National Science Foundation (W. J. le Noble) and by the Deutsche Forschungsgemeinschaft (H. Kelm).

Received: September 17, 1980 [A 341 IE]
German version: Angew. Chem. *92*, 887 (1980)

[1] *H. Kelm:* High Pressure Chemistry. Reidel, Dordrecht 1978.
[2] *T. Asano, W. J. le Noble,* Chem. Rev. *78*, 407 (1978).
[3] For additional reviews and listing of data, see a) *P. W. Bridgman:* The Physics of High Pressure. Bell, London 1931; b) *P. W. Bridgman:* Collected Experimental Papers. Harvard University Press, Cambridge (Mass.) 1964; c) Discuss. Faraday Soc. *22*, (1956); d) *S. D. Hamann:* Physico-Chemical Effects of Pressure. Academic Press, New York 1957; e) *M. G. Gonikberg:* Chemical Equilibria and Reaction Rates at High Pressures. Israel Program for Scientific Translations, Jerusalem 1963; f) *R. S. Bradley:* High Pressure Physics and Chemistry. Vol. I and II. Academic Press, New York 1963; g) Proc. Olympia Symposium: The Physics and Chemistry of High Pressures, Gordon and Breach, New York 1963; h) *E. Whalley,* Adv. Phys. Org. Chem. *2*, 92 (1964); i) *S. D. Hamann,* Annu. Rev. Phys. Chem. *15*, 349 (1964); j) *K. E. Weale:* Chemical Reactions at High Pressures. Spon, London 1967; k) *W. J. le Noble,* Prog. Phys. Org. Chem. *5*, 207 (1967); l) *H. Heydtmann* in *H. Hartmann, J. Heidberg, H. Heydtmann, G. H. Kohlmayer:* Chemische Elementarprozesse. Springer, Berlin 1968, p. 331; m) *G. Kohnstam,* Prog. React. Kinet. *5*, 335 (1970); n) *C. A. Eckert,* Annu. Rev. Phys. Chem. *23*, 239 (1972); o) *R. C. Neuman,* Acc. Chem. Res. *5*, 381 (1972); p) *G. Jenner,* Angew. Chem. *87*, 186 (1975); Angew. Chem. Int. Ed. Engl. *14*, 137 (1975); q) *G. A. Lawrance, D. R. Stranks,* Acc. Chem. Res. *12*, 403 (1978); r) *D. A. Palmer, H. Kelm,* Coord. Chem. Rev., in press.
[4] *A. E. Nicholson, G. W. Norrish,* Discuss. Faraday Soc. *22*, 104 (1956).
[5] a) *A. H. Ewald,* J. Phys. Chem. *67*, 1727 (1963); b) *F. Tanaka, J. Osugi,* Rev. Phys. Chem. Jpn. *42*, 85 (1972); c) *R. Schmidt, H. Kelm, H.-D. Brauer,* Ber. Bunsenges. Phys. Chem. *81*, 402 (1977); d) *R. Schmidt, H.-D. Brauer, H. Kelm,* J. Photochem. *8*, 217 (1978); e) *R. Schmidt, H. Kelm, H.-D. Brauer, ibid. 11*, 145 (1979).
[6] *S. D. Hamann,* Trans. Faraday Soc. *54*, 507 (1958).
[7] See, for example, *S. W. Benson, J. A. Berson,* J. Am. Chem. Soc. *84*, 152 (1962); see also Ref. [3k], p. 230ff.
[8] *J. P. Snyder, D. N. Harpp,* J. Am. Chem. Soc. *98*, 7823 (1976).
[9] *H. S. Harned, B. B. Owen:* The Physical Chemistry of Electrolytic Solutions. 3rd Ed. Reinhold, New York 1958, p. 162.
[10] *B. T. Baliga, E. Whalley,* J. Phys. Chem. *73*, 654 (1969).
[11] There are of course many versions of how this can be done. For some examples, see a) *W. J. le Noble, A. R. Das,* J. Phys. Chem. *74*, 3429 (1970); b) *S. Claesson, S. Malmrud, B. Lundgren,* Trans. Faraday Soc. *66*, 3048 (1970); c) *K. Suzuki, M. Tsuchiya,* Bull. Chem. Soc. Jpn. *44*, 967 (1971); d) *F. Tanaka, M. Sasaki, J. Osugi,* Rev. Phys. Chem. Jpn. *41*, 18 (1972); e) *F. Tanaka, J. Osugi, ibid. 42*, 85 (1972); f) *F. K. Fleischmann, E. G. Conze, D. R. Stranks, H. Kelm,* Rev. Sci. Instrum. *45*, 1427 (1974); g) *W. J. le Noble, R. Schlott, ibid. 47*, 770 (1976).
[12] a) *K. R. Brower,* J. Am. Chem. Soc. *90*, 5401 (1968); b) *E. F. Caldin, M. N. Grant, B. B. Hasinoff, P. A. Trepolan,* J. Phys. E *6*, 349 (1973); c) *R. A. Grieger, A. D. Yu, M. D. Maissbluth,* Rev. Sci. Instrum. *44*, 1390 (1973); d) *A. Jost,* Ber. Bunsenges. Phys. Chem. *78*, 300 (1974); e) *K. Heremans* in [1], p. 311.
[13] a) *D. A. Palmer, R. Schmidt, R. van Eldik, H. Kelm,* Inorg. Chim. Acta *29*, 259 (1978); b) *R. A. Grieger, C. A. Eckert,* AIChE J. *16*, 766 (1970).
[14] NMR spectra: a) *H. Yamada, T. Ishihara, T. Kinugasa,* J. Am. Chem. Soc. *96*, 1935 (1974); b) *J. Jonas,* Rev. Sci. Instrum. *43*, 643 (1972); c) *J. von Jouanne, J. Heidberg,* J. Magn. Reson. *7*, 1 (1972); d) *E. Lang, R. Rauchschwalbe, H. D. Lüdemann,* High Temp. High Press. *9*, 519 (1977); e) *W. L. Earl, H. Vanni, A. E. Merbach,* J. Magn. Reson. *30*, 571 (1978); ESR spectra: f) *K. W. Böddeker, G. Lang, U. Schindewolf,* Angew. Chem. *81*, 118 (1966); Angew. Chem. Int. Ed. Engl. *8*, 138 (1969); g) *W. Z. Plachy, T. J. Schaafsma,* Rev. Sci. Instrum. *40*, 1590 (1969); h) *W. J. le Noble, P. Staub,* J. Organomet. Chem. *156*, 25 (1978).
[15] *P. Drude, W. Nernst,* Z. Phys. Chem. (Leipzig) *15*, 79 (1894).
[16] *E. Whalley,* J. Chem. Phys. *38*, 1400 (1963).
[17] *D. A. Palmer, H. Kelm,* Aust. J. Chem. *30*, 1229 (1977).
[18] *W. J. le Noble, T. Asano,* J. Org. Chem. *40*, 1179 (1975).
[19] *S. D. Hamann,* Mod. Aspects Electrochem. *9*, 47 (1974).
[20] *E. Fishman, H. G. Drickamer,* J. Chem. Phys. *24*, 548 (1956).
[21] *K. Suzuki, M. Tsuchiya,* Bull. Chem. Soc. Jpn. *48*, 1701 (1975).
[22] *K. Suzuki, Y. Taniguchi, T. Watanabe,* J. Phys. Chem. *77*, 1918 (1973).
[23] *A. H. Ewald,* Trans. Faraday Soc. *64*, 733 (1968).
[24] *A. H. Ewald, J. A. Scudder,* J. Phys. Chem. *76*, 249 (1972).
[25] *C. A. Lewis, R. Wolfenden,* J. Am. Chem. Soc. *95*, 6685 (1973).
[26] *D. G. Kubler, H. W. Young,* J. Org. Chem. *36*, 200 (1971).
[27] *M. Kurabayashi, K. Yanagiya, M. Yasumoto,* Proc. 4th Int. Conf. High Pressure *1974*, 663 (1975).
[28] *B. Andersen, P. E. Broe,* Acta Chem. Scand. *26*, 3691 (1972).
[29] *A. H. Ewald,* Discuss. Faraday Soc. *22*, 138 (1956).
[30] *R. A. Grieger, C. A. Eckert,* Trans. Faraday Soc. *66*, 2579 (1970).
[31] *K. Seguchi, A. Sera, K. Murayama,* Bull. Chem. Soc. Jpn. *47*, 2242 (1974).
[32] *C. Brun, G. Jenner,* Tetrahedron *28*, 3113 (1972).
[33] *W. J. le Noble, B. A. Ojosipe,* J. Am. Chem. Soc. *97*, 5939 (1975).
[34] *F. J. Millero, E. V. Hoff, L. Cahn,* J. Solution Chem. *1*, 309 (1972).
[35] *H. F. Fisher, D. F. Davis,* J. Phys. Chem. *69*, 2595 (1965).
[36] *W. J. le Noble, P. Staub,* J. Organomet. Chem. *156*, 25 (1978).
[37] *W. J. le Noble, A. R. Das,* J. Phys. Chem. *74*, 3429 (1970).
[38] *A. Persoons,* private communication.
[39] *D. R. McKelvey, K. R. Brower,* J. Phys. Chem. *64*, 1958 (1960).
[40] *H. D. Lüdemann, R. Rauchschwalbe, E. Lang,* Angew. Chem. *89*, 340 (1977); Angew. Chem. Int. Ed. Engl. *16*, 331 (1977).
[41] *R. Rauchschwalbe, G. Völkel, E. Lang, H. D. Lüdemann,* J. Chem. Res. (*S*) *1978*, 448.
[42] *M. Yokawa, J. Yoshida, Y. Ogo,* Makromol. Chem. *178*, 443 (1977).
[43] *R. C. Neuman, R. J. Bussey,* Tetrahedron Lett. *1968*, 5859.
[44] *C. Walling, G. Metzger,* J. Am. Chem. Soc. *81*, 5365 (1959).
[45] *K. R. Brower, B. Gay, T. Konkol,* J. Am. Chem. Soc. *88*, 1681 (1966).
[46] *W. J. le Noble, R. Goitien, A. Shurpik,* Tetrahedron Lett. *1969*, 895.
[47] *C. A. Grob, P. W. Schiess,* Angew. Chem. *79*, 1 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1 (1967).
[48] *W. J. le Noble, H. Guggisberg, T. Asano, L. Cho, C. A. Grob,* J. Am. Chem. Soc. *98*, 920 (1976).
[49] *C. A. Grob,* Angew. Chem. *81*, 543 (1969); Angew. Chem. Int. Ed. Engl. *8*, 535 (1969).
[50] a) *R. Buyle, A. Van Overstraeten, F. Eloy,* Chem. Ind. (London) *1964*, 839; b) *R. Buyle,* Helv. Chim. Acta *97*, 2449 (1964); c) *H. Paulsen, D. Stoye,* Chem. Ber. *99*, 908 (1966); d) *H. Paulsen* in *J. Zabicky:* The Chemistry of Amides. Wiley, New York 1970, Chap. 10.
[51] *W. J. le Noble, Y. S. Chang,* J. Am. Chem. Soc. *94*, 5402 (1972).
[52] *C. Walling, J. Peisach,* J. Am. Chem. Soc. *80*, 5819 (1958).
[53] See for example, a) *S. Seltzer,* J. Am. Chem. Soc. *87*, 1534 (1965); b) *M. Taagepera, E. R. Thornton, ibid. 94*, 1168 (1972).
[54] a) *S. W. Benson, J. A. Berson,* J. Am. Chem. Soc. *84*, 152 (1962); b) *C. Walling, H. J. Shugar, ibid. 85*, 607 (1963); c) *C. Walling, D. D. Tanner, ibid. 85*, 612 (1963); d) *S. W. Benson, J. A. Berson, ibid. 86*, 259 (1964).
[55] a) *R. A. Grieger, C. A. Eckert,* J. Am. Chem. Soc. *92*, 2918, 7149 (1970); Trans. Faraday Soc. *66*, 2579 (1970); see also b) *C. Brun, G. Jenner,* Tetrahedron *28*, 3113 (1972); c) *C. Brun, G. Jenner, A. Deluzarche,* Bull. Soc. Chim. Fr. *1972*, 2332.
[56] *W. G. Dauben, H. O. Krabbenhoft,* J. Org. Chem. *42*, 282 (1977).
[57] *R. Hoffmann, R. B. Woodward,* J. Am. Chem. Soc. *87*, 4388 (1965).
[58] *C. A. Stewart,* J. Am. Chem. Soc. *93*, 4815 (1971); *94*, 635 (1972).
[59] *R. Huisgen, G. Steiner,* J. Am. Chem. Soc. *95*, 5054, 5055, 5056 (1973), and references cited therein.
[60] a) *F. K. Fleischmann, H. Kelm,* J. Chem. Soc. Chem. Commun. *1973*, 3773; b) *J. von Jouanne, H. Kelm, R. Huisgen,* J. Am. Chem. Soc. *101*, 151 (1979).
[61] *W. J. le Noble, R. Mukhtar,* J. Am. Chem. Soc. *97*, 5938 (1975).
[62] *W. J. le Noble, R. Mukhtar,* J. Am. Chem. Soc. *96*, 6191 (1974).
[63] *R. B. Woodward, R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[64] *K. N. Houk, R. B. Woodward,* J. Am. Chem. Soc. *92*, 4143, 4145 (1970); *L. J. Luskus, N. S. Bhacca, ibid. 92*, 6392 (1970).
[65] *R. C. Neuman, J. V. Behar,* J. Am. Chem. Soc. *89*, 4549 (1967).
[66] See [3d], Vol. 2, Chap. 8.
[67] *A. E. Stearn, H. Eyring,* Chem. Rev. *29*, 509 (1941).
[68] *R. Huisgen, R. Schug,* J. Am. Chem. Soc. *98*, 7819 (1976); *G. Steiner, R. Huisgen,* Tetrahedron Lett. *1973*, 3769.
[69] a) *A. E. Nicholson, R. G. W. Norrish,* Discuss. Faraday Soc. *22*, 97 (1956); b) *V. M. Zhulin, I. K. Milyavskaya,* Bull. Acad. Sci. USSR (engl.) *1974*, 1411.
[70] *A. E. Merbach, H. Vanni,* Helv. Chim. Acta *60*, 1124 (1977).
[71] *S. T. D. Lo, M. J. Sisley, T. W. Swaddle,* Can. J. Chem. *56*, 2609 (1978).
[72] *H. R. Hunt, H. Taube,* J. Am. Chem. Soc. *80*, 2642 (1958).
[73] *T. W. Swaddle, D. R. Stranks,* J. Am. Chem. Soc. *94*, 8357 (1972).
[74] *S. B. Tong, T. W. Swaddle,* Inorg. Chem. *13*, 1538 (1974).
[75] *C. Schenk, H. Kelm,* J. Coord. Chem. *2*, 71 (1972).
[76] *D. A. Palmer, H. Kelm,* Z. Anorg. Allg. Chem. *450*, 50 (1979).

[77] *C. T. Burris, K. J. Laidler,* Trans. Faraday Soc. *51*, 1497 (1955).
[78] *H. Hartmann, H. D. Brauer, G. Rinck,* Z. Phys. Chem. (Frankfurt am Main) *61*, 47 (1968).
[79] *H. Hartmann, H. Kelm, G. Rinck,* Z. Phys. Chem. (Frankfurt am Main) *44*, 335 (1963).
[80] *W. J. le Noble, Y. Ogo,* Tetrahedron *26*, 4119 (1970).
[81] *Y. Okamoto, K. I. Lee,* J. Am. Chem. Soc. *97*, 4015 (1975).
[82] *W. J. le Noble, T. Asano,* J. Am. Chem. Soc. *97*, 1778 (1975).
[83] *W. J. le Noble, A. R. Miller,* J. Org. Chem. *44*, 889 (1979).
[84] a) *W. E. Jones, L. R. Carey, T. W. Swaddle,* Can. J. Chem. *50*, 2739 (1972); b) *W. E. Jones, T. W. Swaddle,* Chem. Commun. *1969*, 998; c) *D. L. Gay, R. Nalepa,* Can. J. Chem. *48*, 910 (1970).
[85] *D. A. Palmer, H. Kelm,* Inorg. Chem. *16*, 3139 (1977).
[86] *S. Winstein, D. Trifan,* J. Am. Chem. Soc. *74*, 1147, 1154 (1952).
[87] *H. C. Brown:* The Nonclassical Ion Problem. (With comments by *P. von R. Schleyer.*) Plenum Press, New York 1977.
[88] *W. J. le Noble, B. L. Yates,* J. Am. Chem. Soc. *87*, 3515 (1965).
[89] *W. J. le Noble, B. L. Yates, A. W. Scaplehorn,* J. Am. Chem. Soc. *89*, 3751 (1967).
[90] *S. Winstein,* Q. Rev. Chem. Soc. *23*, 141 (1969).
[91] *W. J. le Noble, B. Gabrielsen,* Tetrahedron Lett. *1970*, 45.
[92] a) *C. J. Lancelot, P. von R. Schleyer,* J. Am. Chem. Soc. *91*, 4291 (1969); b) *C. J. Lancelot, J. J. Harper, P. von R. Schleyer, ibid. 91*, 4294 (1969); c) *C. J. Lancelot, P. von R. Schleyer, ibid. 91*, 4296 (1969); d) *P. von R. Schleyer, C. J. Lancelot, ibid. 91*, 4297 (1969).
[93] *C. Yamagani, A. Sera,* Chem. Lett. *1972*, 741.
[94] *W. J. le Noble, A. Shurpik,* J. Org. Chem. *35*, 3588 (1970).
[95] *D. J. Raber, R. C. Bingham, J. M. Harris, J. L. Fry, P. von R. Schleyer,* J. Am. Chem. Soc. *92*, 5977 (1970).
[96] *J. G. Pritchard, F. A. Long,* J. Am. Chem. Soc. *78*, 2667 (1956); *80*, 4162 (1958).
[97] *W. J. le Noble, M. Duffy,* J. Phys. Chem. *68*, 619 (1964).
[98] *B. T. Baliga, A. K. Rantamaa, E. Whalley,* J. Phys. Chem. *69*, 1751 (1965).
[99] a) *D. A. Palmer, G. M. Harris,* Inorg. Chem. *14*, 1316 (1975); b) *K. E. Hyde, H. Kelm, D. A. Palmer, ibid. 17*, 1647 (1978).
[100] *J. Hine,* J. Am. Chem. Soc. *72*, 2438 (1950).
[101] *R. A. M. O'Ferrall, J. H. Ridd,* J. Chem. Soc. *1963*, 5035.
[102] *W. J. le Noble, M. Duffy,* J. Am. Chem. Soc. *86*, 4512 (1964).
[103] *W. J. le Noble,* J. Am. Chem. Soc. *87*, 2434 (1965).
[104] *W. J. le Noble, Y. Tatsukami, H. F. Morris,* J. Am. Chem. Soc. *92*, 5681 (1970).
[105] *W. J. le Noble, D. M. Chiou, Y. Okaya,* J. Am. Chem. Soc. *101*, 3244 (1979).
[106] *K. R. Brower,* private communication.
[107] *K. R. Brower, M. Muhsin, T. Konkol,* J. Am. Chem. Soc. *98*, 779 (1976).
[108] *M. Anbar, G. Yagil,* J. Am. Chem. Soc. *84*, 1790 (1962).
[109] *W. J. le Noble,* Tetrahedron Lett. *1966*, 727.
[110] *W. J. le Noble, D. N. Skulnik,* Tetrahedron Lett. *1967*, 5217.
[111] *W. J. le Noble, D. N. Skulnik, E. M. Schulman,* J. Am. Chem. Soc. *93*, 4710 (1971).
[112] *K. R. Brower, T. L. Wu,* J. Am. Chem. Soc. *92*, 5303 (1970).
[113] a) *C. Walling, J. Pellon,* J. Am. Chem. Soc. *79*, 4782 (1957); b) *K. R. Brower, ibid. 83*, 4370 (1961); c) see also *W. J. le Noble,* J. Phys. Chem. *67*, 2451 (1963).
[114] *R. C. Neuman, M. J. Amrich,* J. Am. Chem. Soc. *94*, 2730 (1972).
[115] *W. J. le Noble, M. R. Daka,* J. Am. Chem. Soc. *100*, 5961 (1978).
[116] *U. Schöllkopf, I. Hoppe,* Justus Liebigs Ann. Chem. *765*, 153 (1971).
[117] *K. R. Brower,* J. Am. Chem. Soc. *94*, 5747 (1972).
[118] *A. Nickon, Y. Lin,* J. Am. Chem. Soc. *91*, 6861 (1969).
[119] *W. J. le Noble, S. Bitterman, P. Staub, F. K. Meyer, A. E. Merbach,* J. Org. Chem. *44*, 3263 (1979).
[120] a) *R. K. Murmann, H. Taube,* J. Am. Chem. Soc. *78*, 4886 (1956); b) *F. Basolo, G. S. Hammaker,* Inorg. Chem. *1*, 1 (1962).
[121] *M. Mares, D. A. Palmer, H. Kelm,* Inorg. Chim. Acta *27*, 153 (1978).
[122] *M. Mares,* Dissertation, Universität Frankfurt 1978.
[123] *D. R. Stranks, N. Vanderhoek,* Inorg. Chem. *15*, 2639 (1976).
[124] *E.-G. Conze, H. Stieger, H. Kelm,* Chem. Ber. *105*, 2334 (1972).
[125] *H. Stieger, G. M. Harris, H. Kelm,* Ber. Bunsenges. Phys. Chem. *74*, 262 (1970).
[126] *J. A. Broomhead, I. Lauder, P. Nimmo,* J. Chem. Soc. *D 1969*, 652.
[127] *G. A. Lawrance, D. R. Stranks,* Inorg. Chem. *16*, 929 (1977).
[128] a) *W. J. le Noble,* J. Am. Chem. Soc. *85*, 1470 (1963); b) *W. J. le Noble, T. Hayakawa, A. K. Sen,* J. Org. Chem. *36*, 193 (1971); c) *K. R. Brower, R. L. Ernst, J. S. Chen,* J. Phys. Chem. *68*, 3814 (1964).
[129] *A. V. Kamernitzky, I. S. Levina, E. I. Mortikova, B. S. El'yanov,* Tetrahedron Lett. *1975*, 3235.
[130] a) *K. Seguchi, A. Sera, K. Murayama,* Tetrahedron Lett. *1973*, 1585; b) *W. G. Dauben, A. P. Kozikowski,* J. Am. Chem. Soc. *96*, 3664 (1974).
[131] *A. P. Hagen, H. W. Beck,* Inorg. Chem. *15*, 1512 (1976), and references cited therein.
[132] *F. Tanaka, M. Sasaki, J. Osugi,* Rev. Phys. Chem. Jpn. *41*, 18 (1971).
[133] *R. C. Neuman, C. T. Berge,* Tetrahedron Lett. *1978*, 1709.
[134] *P. Collman, A. Weller,* Ber. Bunsenges. Phys. Chem. *77*, 1871 (1973).
[135] *S. D. Hamann,* J. Phys. Chem. *70*, 2418 (1966).
[136] *W. J. le Noble, K. Tamura,* Tetrahedron Lett. *1977*, 495.
[137] *W. J. le Noble,* unpublished work.
[138] *I. S. Bengelsdorf,* J. Am. Chem. Soc. *80*, 1442 (1958).
[139] *A. Jost, K. G. Biphard,* Ber. Bunsenges. Phys. Chem. *79*, 850 (1975).

Stereospecific Polymerization of Propylene: An Outlook 25 Years after Its Discovery[**]

By Piero Pino and Rolf Mülhaupt[*]

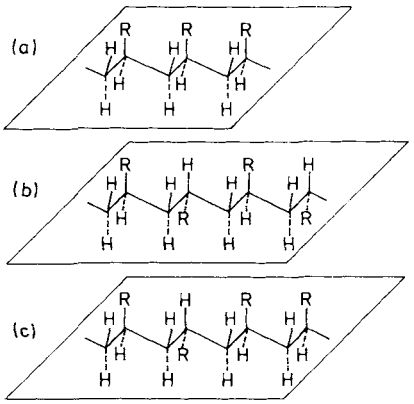
In 1955 *Natta* and his co-workers from the Istituto di Chimica Industriale del Politecnico di Milano reported the properties of highly crystalline polypropylene and other poly-α-olefins[1] which possess, at least in long sections of the main chain, asymmetric carbon atoms of the same absolute configuration (isotactic poly-α-olefins). The discovery of the new crystalline polymers was judged at that time "revolutionary in its significance"[2] and heralded a new era in polymer science and technology. Indeed, crystalline polypropylene, because of its relatively high melting point and its outstanding mechanical properties, has found very extensive application in the field of plastics films and fibers.—25 years after this publication, it is worthwhile examining the further developments following this discovery which has had such a great scientific and industrial impact, and the problems which are still open concerning the structure of the catalytic centers and the mechanism by which practically completely stereoregular polypropylenes are formed.

1. Historical Background

The absence of crystallinity in vinyl polymers synthesized by radical polymerizations was first pointed out by *Staudinger* who attributed this phenomenon to the formation of a large number of diastereoisomers of the linear macromolecules[3]. Some attempts to synthesize stereoregular macromolecules were first carried out by *Marvel* and co-workers[4] who could not detect any differences in the poly(methyl methacrylates) synthesized using optically active or nonchiral radical initiators. It was *Schildknecht* and his co-workers[5] who first obtained two different types of poly(vinyl ethers) by cationic polymerization under different conditions, one of which showed some crystallinity. Unfortunately, they apparently were unaware of a paper published by *Bunn*[7] in 1942 who had postulated the possibility that the main chains of vinyl polymers having sterically equivalent monomeric units can assume helical conformations. Therefore *Schildknecht* and co-workers, in searching for possible structures of a stereoregular vinyl polymer (Scheme 1), attributed a zig-zag planar conformation like the one already known for linear paraffins, to the main chain of the poly(vinyl ethers) in the crystalline state. That is why they were compelled to attribute alternate (*R*) and (*S*) absolute configurations to the asymmetric carbon atoms of the main chain in order to eliminate strong steric interactions between the relatively bulky side chains.

In 1950 *Morton*[8] used his "alfin" catalyst to prepare a high molecular weight polystyrene but he did not investigate its structure. In 1956, after isotactic polystyrene had been obtained and its structure identified by *Natta* and co-workers[1], *Williams*[9] showed that the polystyrene obtained by *Morton* was isotactic.

The work of *Natta* and co-workers in the field of poly-α-olefins began in 1952, as a consequence of a report by *Ziegler*[10] describing the possibility of synthesizing relatively low molecular weight linear polyethylenes by reaction of ethylene with trialkylaluminum compounds. In *Natta*'s opinion, Ziegler's "Aufbaureaktion", whereby the monomer inserts between the growing chain and a metal atom, should



Scheme 1. Zig-zag planar conformation of the main chain of vinyl polymers having different types of stereoregularity. a) Isotactic chain [1]; b) syndiotactic chain [6]; c) atactic chain [6].

permit far better control of the polymerization process than is possible in the usual ionic or radical polymerizations which were believed to occur by the addition of the monomeric molecules to the free end of the growing chain.

By the end of 1953 *Ziegler* discovered[11] that high polymers of ethylene can be obtained on the addition of a transition metal salt (*e.g.* $TiCl_4$) to the alkylaluminum catalyst. At that time work on the "Aufbaureaktion" with alkylaluminum compounds was already in progress in Natta's laboratory. *Natta* interpreted the effect of transition metal halides on the "Aufbaureaktion" by supposing that the transition metals activate the ethylene molecules prior to the insertion, and therefore greatly enhance the rate of propagation, while the rate of the termination processes remains substantially unchanged. He thought that the same principle might apply to propylene, which in the "Aufbaureaktion" yielded only oligomers, and tried to use the new Ziegler catalytic systems

[*] Prof. Dr. P. Pino, Dipl.-Chem. R. Mülhaupt
ETH-Zürich, Technisch-Chemisches Laboratorium
Universitätstrasse 6, CH-8092 Zürich (Switzerland)

[**] A large part of the information contained in this paper was presented at Hoechst AG, Frankfurt am Main, on June 8, 1979 and at a meeting of the Berlin section of the Gesellschaft Deutscher Chemiker on July 14, 1980.

(metallorganische Mischkatalysatoren) to obtain linear polymers of propylene. Polymers of this kind were unknown at that time but were expected to have elastomeric properties resembling those of polyisobutylene[12]. Indeed, in March 1954, using a $TiCl_4/Al(C_2H_5)_3$ catalytic system, *Natta* and his co-workers obtained a rubber-like polymer of propylene in the very first experiments. However, the product was not homogeneous and contained some white solid particles. Fractionation by solvent extraction surprisingly afforded four very different fractions[13]: The first one was an oily product soluble in acetone; the second was a rubber-like product soluble in diethylether; the third was a partially crystalline solid soluble in boiling heptane; and finally a white highly crystalline powder was obtained, which had a melting point higher than 160 °C, was insoluble in boiling heptane, and represented 30—40% of the total polymer. The series of solvents and the extraction conditions chosen effected a fractionation which was very efficient indeed, as was recently shown by ^{13}C-NMR spectroscopy (Fig. 1, cf. also Fig. 2)[176].

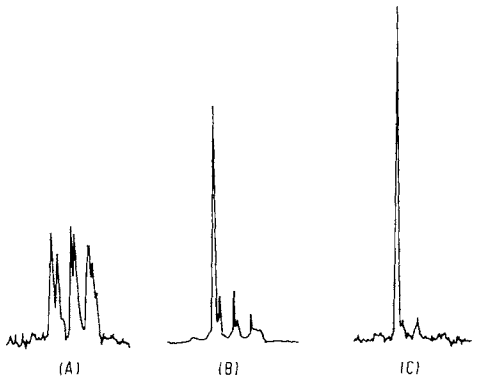


Fig. 1. ^{13}C-NMR spectra of polypropylene fractions obtained by extraction with solvents at their boiling temperature. (A) Acetone-insoluble, ether-soluble fraction; (B) ether-insoluble, heptane-soluble fraction; (C) heptane-insoluble fraction (solvent *o*-dichlorobenzene).

Initially the different properties of the fractions were attributed to differences in average molecular weight. However, thermal degradation of the crystalline fractions showed that low molecular weight polymers may also be crystalline[14]. The X-ray diffraction pattern of the crystalline products and density measurements showed that a zig-zag planar conformation of the main chain was not present in the solid state, and indicated the existence of a 3_1 helical conformation of the main chains[15]. Infrared spectra of the crystalline and amorphous fractions in solution and in the melt were very similar and indicated a head-to-tail structure of the main chain in both cases[1]. On the basis of the IR and X-ray data, it was possible to assign the correct structure of the new α-olefins polymers within a few months[16].

In the early fifties, propylene was polymerized with metal oxides in other laboratories[17-20]. However, only small quantities of the solid fractions were obtained, and it probably seemed uninteresting to invest too much time in investigating their structure. Furthermore, in one case, IR spectra, recorded only at room temperature on polymer films, were erroneously interpreted[19,20] and no X-ray studies were carried out. In another case[17,18], ethylene-propylene copolymers were often obtained as the major product, the ethylene very probably arising from propylene metathesis. Some of these polymers were characterized by X-ray diffraction and IR-spectroscopy but their structure was apparently not well understood[18].

It is interesting that, in 1955, *Natta*'s group[21] first proved the existence of isotactic polypropylene in the polymers obtained with various supported CrO_3 catalysts by comparing the spectroscopic and X-ray diffraction data of very small non-tacky polymer fractions thus obtained with the corresponding data already available in their laboratory for the polypropylenes prepared using the Ziegler catalyst.

2. Development of Catalysts for Polymerization of Propylene

The most frequently used catalysts for the synthesis of isotactic polypropylene is the product obtained by reacting a titanium halide with alkylaluminum compounds. However, partly to avoid conflict with existing patents and partly due to research efforts to clarify the polymerization mechanisms, a very large number of catalytic systems have been investigated.

We shall first outline the development of the classical Ziegler organometallic catalytic systems containing titanium halides and alkylaluminum compounds and then we shall briefly summarize some other types of catalytic systems which also produce isotactic polypropylene. The following discussion is by no means exhaustive and undoubtly reflects some personal biases of the authors about the relative importance of the approaches used by different groups.

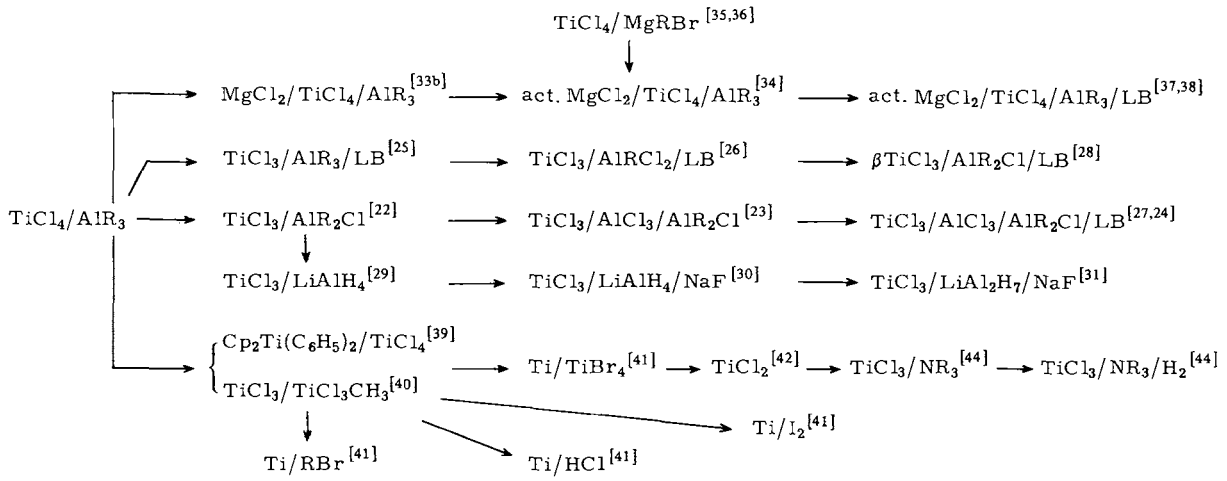
2.1. Development of Classical Titanium-Containing Catalytic Systems

An outline of the development of the catalytic systems, originally proposed by *Ziegler*[11], prepared from $TiCl_4$ and AlR_3 is presented in Scheme 2; in Scheme 3 a similar survey is shown for the $Ti(OR)_4/AlR_3$ catalytic systems.

The first important advance in the field[22] originated from *Natta*'s intuition that stereospecificity was connected with the regularity of the surface of the heterogeneous catalyst. Instead of preparing the catalyst by reaction of $TiCl_4$ with AlR_3, crystalline $TiCl_3$ prepared by reduction of $TiCl_4$ with hydrogen or with aluminum was suspended in a hydrocarbon medium and treated with a trialkylaluminum or a dialkylaluminum chloride. In this way the percentage of isotactic polypropylene in the polymerization product was increased from about 40% to about 90%.

A further improvement to this type of catalyst was made by researchers at Esso Research and Engineering Co., who used a solid solution of $AlCl_3$ in $TiCl_3$ instead of pure $TiCl_3$. Reacting this finely milled solid with aluminumalkyls gave a catalyst of higher activity[23]. A further increase in the percentage of isotactic polymer produced (up to 95%) was achieved by adding a Lewis base (*e.g.* an ester of an unsaturated carboxylic acid)[24] to the crystalline $TiCl_3$.

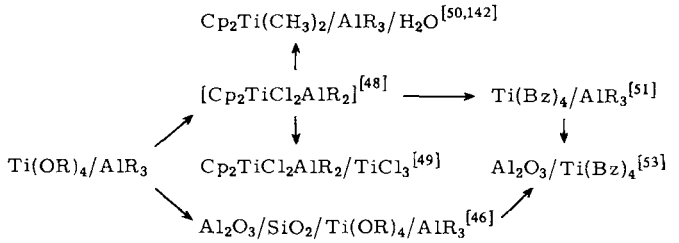
The use of Lewis bases to enhance catalytic activity was first proposed by *Razuvaev* and co-workers[25], and active catalytic systems were prepared from $TiCl_3$, $AlRCl_2$, and a Lewis base by *Coover* and co-workers[26]. More recently, treatment of the product resulting from reaction of $TiCl_4$ and $AlRCl_2$ with Lewis bases (mainly ethers) was found to give a



Scheme 2. Development of different types of titanium catalysts for the polymerization of propylene. LB = Lewis base.

$TiCl_3$-preparation with a larger surface area and with a much greater activity and high stereospecificity[27,28].

Catalysts of the same type which functioned at higher temperature (up to 200 °C) were obtained at Eastman Kodak[29] by reaction of $TiCl_3$ with $LiAlH_4$ and, in a further improvement, by adding NaF to the above mixture[30]. The best catalyst of this type seems to be a mixture of $TiCl_3$, $LiAl_2H_7$, and NaF[31].



Scheme 3. Development of different types of titanium catalysts for the polymerization of propylene. Bz = benzyl.

Parallel to the above developments, a series of attempts was made to support the $TiCl_4$ on different carrier materials. The first attempts were made with the classical large-surface supports used in heterogeneous catalysis, *i.e.* SiO_2[33a] or $MgCl_2$[33b]. However, no significant success was obtained along these lines until activated $MgCl_2$ was used as support[34-38].

Less important from an industrial point of view, but very interesting for the understanding of the nature of the catalytic centers, were the attempts to develop a catalyst containing only titanium as the metal component. Two groups[39,40] working independently obtained catalysts which are active in propylene polymerization by reacting $Cp_2Ti(C_6H_5)_2$ with $TiCl_4$[39] or by decomposing $TiCl_3CH_3$[40] to form a mixture of $TiCl_3$ with $TiCl_3CH_3$. Further developments in this field were the catalyst prepared by reacting elemental titanium with $TiBr_4$[41], with alkyl chlorides[41], with hydrogen chloride[41], or with iodine[41]. Also $TiCl_2$[42] and $TiCl_3$ treated with tertiary amines or with tertiary amines and hydrogen[43-45] were proposed as catalysts, but showed only very modest catalytic activity.

Among the original catalysts proposed by *Ziegler,* soluble systems, mostly containing no halogens, were examined in numerous investigations[50] (Scheme 3). This research finally led to the very active systems of the type $Cp_2Ti(CH_3)_2/AlR_3/H_2O$[142] which give the highest productivity for linear polyethylene (6×10^4 g polymer/g Ti × h × atm) and completely atactic polypropylenes (Fig. 2B). On the same line, catalytic systems were obtained from the reaction of $Ti(CH_2C_6H_5)_4$ with AlR_3[51] which yield organometallic complexes of relatively high molecular weight[52]. These complexes polymerize propylene and other α-olefins, yielding products containing a small amount of isotactic polymers.

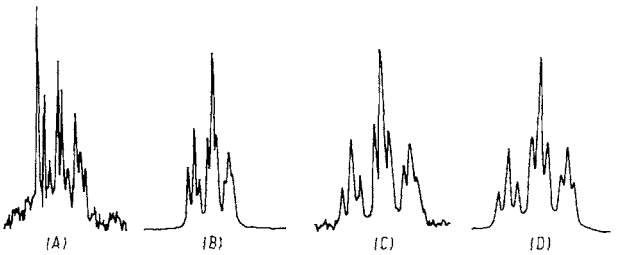


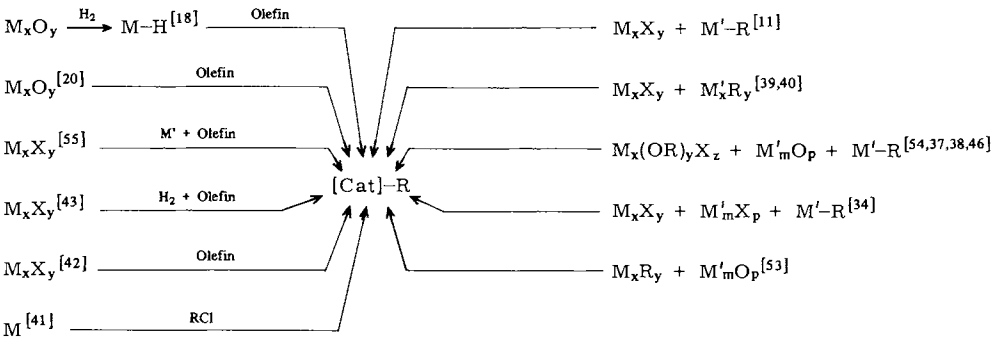
Fig. 2. ^{13}C-NMR spectra of ether-soluble polypropylenes. (A) Prepared with $MgCl_2/TiCl_4/Al(iC_4H_9)_3$/ethyl benzoate [176]; (B) prepared with $Cp_2Ti(CH_3)_2/Al(CH_3)_3/H_2O$ [142], product kindly made available by Professor *Sinn;* (C) atactic polymer prepared by epimerization of isotactic polypropylene with Pd catalysts at 270 °C (*U. W. Suter,* unpublished results); (D) calculated for a polypropylene with a Bernoullian distribution (molar fraction of m dyads corrresponding to the equilibrium composition is 0.48).

As soon as the activity of the soluble catalytic systems was recognized, attempts were made[46] to support the above soluble complexes. Titanium alcoholates and chlorotitanium alcoholates supported on Al_2O_3/SiO_2 in the presence of AlR_3 yielded small amounts of isotactic polypropylene, while only traces of polymer were obtained without support[46]. Highly crystalline polypropylene was obtained supporting the soluble complex $[Cp_2TiAl(C_2H_5)_2]_2$, which does not polymerize propylene, on $TiCl_3$[49]. Finally, an interesting class of catalytic systems was discovered in which Ti or Zr still attached to at least one benzyl group are chemically bound to the classical support Al_2O_3[53]. With these catalytic systems the use of organometallic compounds of aluminum can be avoided. The presence of a support increases the percentage of isotac-

tic polymer in the products; however, the synthesis of a high percentage of highly isotactic polypropylene has never been reported using this process. It is interesting to note that, with only the remarkable exception of the highly active soluble catalytic systems[50], all the other development lines finally led to catalysts in which titanium or, in general, the transition metal atoms are fixed to a solid support having a high surface area.

2.2. Pathways Leading to Stereospecific Catalysts for Olefin Polymerization

Scheme 4 summarizes the main pathways proposed to prepare catalysts for the synthesis of stereoregular poly-α-olefins. On the right side of the Scheme, catalysts containing in general more than one type of metal atom or ion are listed. Besides the typical Ziegler catalysts M_xHal_y/M'_mR_n[11] (M = transition metal; M' = main group metal), catalytic species supported on oxides[46] or on halides of the main group



Scheme 4. Methods of the synthesis of heterogeneous stereospecific catalysts [Cat]—R for the polymerization of α-olefins (M = transition metal; M' = main group metal; X = halogen).

elements have been proposed[34,54]. Furthermore, catalysts based on organometallic compounds of transition metals have been used in combination either with a halide of the same metal[39,40] as discussed for titanium catalysts in the previous section, or with a main group metal oxide[53].

On the left side of the Scheme 4, transition metals or transition metal compounds are shown which can form carbon-metal bonds *in situ*. In this family, $TiCl_4$ treated with aluminum and olefins[55], MoO_3/CoO pretreated with hydrogen[17,18], and CrO_3 supported on Al_2O_3/SiO_2[19,20] are, together with the $TiCl_4/AlR_3$ catalytic systems, the oldest representatives. Some catalysts of the above type are very active for ethylene polymerization but of no interest for propylene polymerization. In fact, although polymers of propylene were prepared very early with these catalysts, the yields of solid products were so low that they were not further investigated.

Other ways of producing catalysts for ethylene and α-olefin polymerization are the activation of metal halides with hydrogen and tertiary amines[43-45] or simply with olefins[42] and the activation of transition metals with alkyl halides[41].

3. Main Steps in the Development of Industrial Processes for Production of Isotactic Polypropylene

Despite the very large number of patents in the field, only relatively few have contributed to substantial progress in the industrial production of isotactic polypropylene[56-60]. In Table 1, some of the main improvements are listed in chronological order.

The original Ziegler catalytic systems had a relatively low productivity [up to *ca.* 20 g polypropylene/g Ti × h × atm][46]. A process based on this catalyst would have required three steps, *i.e.* polymerization, separation of the nonisotactic fractions (*e.g.* by solvent extraction), and purification of the isotactic polymers from the residues from the transition metal catalyst. The main improvements concern the increase of the polymer yield[32,61] and of the percentage of isotactic polymer[23,24,37] in the products, the medium in which the polymerization is carried out (saturated hydrocarbons, liquid monomer, gas phase[62]) and the regulation of the average molecular weight with H_2[63]. Further improvements concern the increase of the polymerization temperature[29-31] which, in principle, should allow the recovery of the polymerization enthalpy and finally the control of the polymer morphology.

The improvements connected with the developments on new catalysts have already been discussed in Section 2.1.

More recent developments concern mainly improvements in the catalyst productivity and have ultimately eliminated the need to purify isotactic polymers. A productivity of 520 g polymer/g Ti × h × atm was obtained by treating the $TiCl_3$ prepared from $TiCl_4$ and $AlCl_2(C_2H_5)$, with aliphatic ethers[27]. A greater improvement was obtained by supporting $TiCl_4$ on activated $MgCl_2$[37,38,61] or by producing a supported catalyst by reacting $TiCl_4$ with $Mg(OC_2H_5)_2$[54] or other magnesium compounds[35,36]. With these catalysts, a productivity of over 3000 g of polymer/g Ti × h × atm can be obtained; however, as with the non-supported catalyst, the percentage of isotactic polymer in the products is low (20—40%). A substantial improvement can be obtained by adding a Lewis base to the catalytic system (*e.g. N,N,N',N'*-tetramethylethylenediamine (TMEDA) in the solid component and ethyl benzoate in solution) (Table 2); in this way, the percentage of isotactic polymer can be increased to over 93%. In this case a productivity of 250 g polymer/g Ti × h × atm has been reported. In other cases productivities as high as 1300g/gTi × h × atm of polypropylene containing 90% isotactic polymer were reported[37].

Concerning the medium in which the polymerization is carried out, isotactic polypropylene is nowadays produced mainly in hydrocarbon suspension. However, as long ago as

Table 1. Important steps in the development of the industrial production of isotactic polypropylene with titanium catalysts.

Catalytic system	Conditions [a]	Fraction of isotactic polypropylene [%]	catalyst productivity g Polypropylene / g Ti × h × atm	Process steps [b]	Ref.
$TiCl_4/Al(C_2H_5)_3$ (1:3)	S	27	30	A + B + C	[47]
$\alpha TiCl_3/Al(C_2H_5)_2Cl$	S	87	25	A + C	[46]
$\alpha TiCl_3/AlCl_3/Al(C_2H_5)_2Cl$	S	80	120	A + C	[23]
$\beta TiCl_3/Al(C_2H_5)_3/H_2$	S	—	15	A + C	[63]
$TiCl_3/LiAl_2H_7/NaF$	S	90	70	A + B + C	[31]
$\beta TiCl_3/Al(C_2H_5)_2Cl$/methyl methacrylate	S	95	99	A + C	[24]
$TiCl_3/Al(C_2H_5)_2Cl$	G	72	320	A + C	[62]
$\beta TiCl_3/AlCl_3/Al(C_2H_5)_2Cl$/diisoamyl ether [c]	S	98	520	A + C	[32]
$TiCl_4/MgCl_2/Al(C_2H_5)_3$	F	21	3840	A + B	[61]
$TiCl_4$/ethyl *p*-toluate/$MgCl_2/Al(C_2H_5)_3$	F	91	755	A	[37]

[a] S, Polymerization in solvents; G, polymerization in the gas phase; F, polymerization in the liquid monomer. [b] A, Polymerization; B, separation of atactic fractions; C, purification of the isotactic polymers. [c] $\beta TiCl_3$ prepared from $TiCl_4$ and $AlCl(C_2H_5)_2$ and washed with aliphatic ethers.

in the fifties *Natta et al.* showed that propylene can be polymerized using a solid catalyst suspended in the gas phase[64] and, at the end of the sixties, a gas phase process for polypropylene was put into operation by BASF[62,65]. More recently, processes have come on stream in which the polymerization is carried out in liquid propylene; they seem to offer some advantages.

Table 2. Influence of Lewis bases on stereoregulation in propylene polymerization with supported $MgCl_2/TiCl_4/AlR_3$ catalytic systems.

Catalyst	Fraction of isotactic polypropylene [%]	g Polymer / g Ti × h × atm	Ref.
$TiCl_4/MgCl_2/Al(iC_4H_9)_3$	21	3840	[61]
$TiCl_4$(TMEDA)/$MgCl_2$/ $Al(C_2H_5)_3/C_6H_5COOC_2H_5$	93.5	250	[37]

Thanks to the outstanding properties of isotactic polypropylene[66,67] and improvements in the polymerization process, production is continuously growing and should reach a global level of well over 3×10^6 tons in 1980.

There are of course still many unsolved problems in the industrial production of polypropylene, the main one probably being the achievement of the control of the molecular weight distribution. This is connected with the preparation of catalysts in which the catalytic centers have similar chemical and steric structures. Highly active catalysts working at higher temperatures and giving a better control of polymer morphology would also certainly be welcome.

4. Fundamental Research on the Stereospecific Polymerization of Propylene and Other α-Olefins

Since the first announcement of the achievement of the stereospecific polymerization of propylene a large amount of fundamental research started all over the world with the aim of clarifying the two main novel aspects of this reaction, *i.e.* the mechanism of the reaction, which is characterized by an unusually high regiospecificity and stereospecificity, and the structure of the catalytic centers which are able to produce the stereoregular polymers.

To achieve the above aims, very different approaches have been adopted. They can be briefly summarized as follows:

A) Attempts to elucidate the mechanism of the reaction based on the investigation of
- Structure and stereochemistry of the synthesized polymers
- Model reactions
- Polymerization kinetics
- *"Ab initio"* or semiempirical calculations on models of catalytic centers

B) Attempts to elucidate the structure of the catalytic center based on the investigation of
- Reactions leading to the catalytic species
- Structure of the heterogeneous catalysts by various diffraction and spectroscopic techniques
- Synthesis of soluble coordination complexes having catalytic properties similar to the heterogeneous catalytic systems
- Relationship between structure of catalytic complexes and detailed structure of the polymers obtained

This effort has yielded a great amount of new knowledge not only in the field of polymer chemistry, but in many other fields of chemistry, such as organometallic chemistry, coordination chemistry, homogeneous and heterogeneous catalysis. However, although some features of the polymerization mechanism have been elucidated, important aspects of the polymerization reaction are still poorly understood and the detailed structure of the catalytic centers, not only in the heterogeneous polymerization catalysts but also in the homogeneous ones, is still unknown. The reasons for this lack of complete success are different for each of the approaches used, and will now be briefly summarized.

4.1. Polymerization Kinetics

Kinetic studies on heterogeneous catalytic reactions entail well known difficulties; in fact, kinetic measurements give only mean values for polymerization rates, from which it is impossible to determine the concentration of the active centers and the catalytic activity of each single catalytic center, which vary enormously from center to center.

The determination of the concentration of the catalytic centers has been attempted by several research groups[68-70]; only very few methods are available for such determinations, the one most commonly used being to poison the catalysts with radioactive carbon monoxide. Only a few catalytic systems (mainly based on Ti or V) have been investigated up to now.

Kinetic studies of polymerization in homogeneous phase[71,72] have shown that, even in the most thoroughly investigated catalytic complexes containing a bis(cyclopentadienyl)titanium group, the concentration of the catalytic species is too low to be detected by the available spectroscopic methods[71], and only precursors of the catalysts or non-catalytically active species in equilibrium with the catalytic centers can be studied.

Interesting reviews on the kinetic investigations have been published[73-77] and we shall not discuss this subject any further.

4.2. Spectroscopic and Diffraction Methods for the Investigation of Heterogeneous Catalysts

Although noteworthy progress has been made in the investigation of the structure of the surfaces of the heterogeneous catalysts during the past few years, the actual structure and the activity of single catalytic centers, even of the most stable heterogeneous catalysts, is far from being understood.

In the case of the typical Ziegler-Natta catalysts, the usual difficulties encountered in investigating heterogeneous catalysts are accompanied by further complications. Among these we mention only the relatively short life of the catalytic centers, compared with the catalyst lifetime, *e.g.* in ammonia synthesis, the continuous formation, at least in the $TiCl_3$ catalysts, of new surfaces by cleavage of the initial catalysts crystals, and the difficulty of investigating the catalyst after the reaction as it is often finely dispersed and completely buried in the bulk of the polymer.

Use of the various techniques and results obtained have been well documented in a number of papers and reviews[78-92] and will not be discussed here.

4.3. Theoretical Calculations on Models of the Catalytic Centers

Different types of calculations, including *ab initio*[97,98,101] calculations, semiempirical calculations[102], and calculations of nonbonded interactions at the active site[99,100] were attempted by different authors. The weak point of this approach, which was initiated by *Cossee* about 20 years ago[93-96], is the choice of the model on which calculations are made. As our knowledge of the structure of the catalytic centers is very scant (much scanter than the knowledge of the catalytic site of some enzymes), it only seldom happens that the calculations on models of catalytic centers lead to a better understanding of the experimental results and to the conception of new experiments. On the contrary, they offer very detailed explanations of the mechanism by which the models, that have been more or less arbitrarily chosen, could operate and they may give the impression to the unwary reader that the mechanism of stereospecific polymerization is fully known. Efforts along this line will become much more fruitful when more reliable models based on a better knowledge of the structure of the catalytic centers become available for these calculations.

4.4. Reactions Leading to the Catalytic Species

Great efforts in this direction were made especially in the period between the late fifties and the early seventies[103] but they did not bring any important advances in the understanding of the structure of the catalytic centers in the heterogeneous catalysts. The main difficulty here is that only a very few of the transition metal atoms (for Ti-containing nonsupported catalysts less than 1%) are actually catalytically active under steady-state conditions. In the reactions in which catalytic centers are formed, only the main products can be investigated, while products formed in smaller amounts (*e.g.* less than 1%) can hardly be investigated. Therefore a connection between the main reaction products must sometimes be postulated, or tacitly assumed, without actual proof that the main products and not small amounts of secondary products which form during the reaction, are in some way connected with the structure of the actual catalytic centers. This type of research will not be further discussed in this review.

4.5. Model Reactions

Investigation of model reactions of the two steps (π-olefin complex formation and insertion of a double bond into a metal-carbon bond) which are generally assumed to play a role in stereospecific polymerization has certainly contributed very significantly to our present understanding of the mechanism of stereospecific polymerization.

The vast amount of literature in this field includes the oligomerization of ethylene and α-olefins with organometallic derivatives of transition metals[104], syntheses and equilibria between diastereomeric olefin complexes in which the olefin is a monosubstituted ethylene[105,106], and rotameric equilibria in the same complexes connected with the rotation of the olefin around the metal olefin bonds[107]. Finally simple additions of organometallic compounds to the double bonds[108-110] are of interest as model reactions. Some of these model reactions will be considered in the following sections of this review.

4.6. Structure and Stereochemistry of the Synthesized Polymers

This line of research has afforded, in our opinion, the most valuable information, not only on the polymerization mechanism, but also on the origin of the stereospecificity of the process and on the structure of the catalytic centers. It includes the determination of the nature of the terminal groups of the polymer chains, research on the stereochemistry of the insertion reaction, and, finally, spectroscopic investigations of structural and steric irregularities in the polypropylene main chain in low molecular weight models and in polymers and copolymers of racemic α-olefins. These aspects will be the main topic discussed in the following sections.

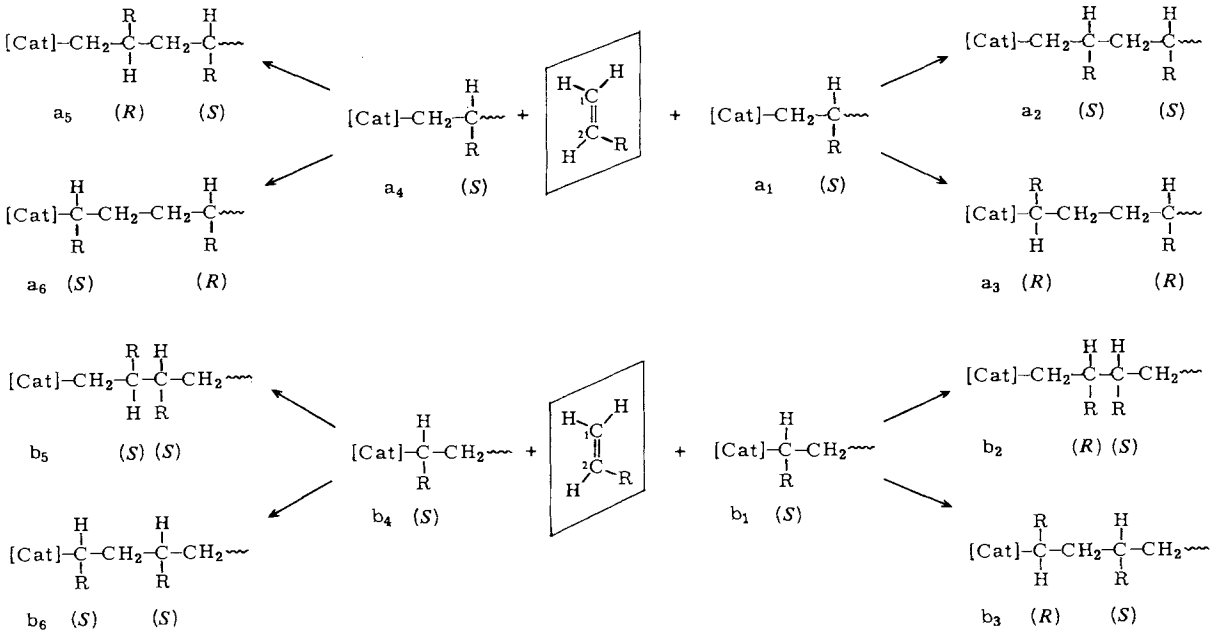
5. Research on the Mechanism of Stereospecific Polymerization Based on the Investigation of Structure and Stereochemistry of the Polymer Chains

5.1. Geometric Aspects of the Polymerization of α-Olefins

When ethylene dimerizes or polymerizes by an insertion reaction between a metal atom and the growing chain (*e.g.* as in the "Aufbaureaktion" discovered by *Ziegler*[10]), since ethylene is an olefin having D_{2h} symmetry, only one product can form in each step regardless of whether the stereochemistry is of the *cis* or *trans* type. The situation is completely different when an olefin having C_s symmetry undergoes the same reaction (Scheme 5). *Ziegler* had observed that in the dimerization of propylene the reaction is not completely regiospecific[112]; in fact, in the reaction of propylene with tri-*n*-propylaluminum, a small percentage of *n*-hexenes forms and therefore, small amounts of secondary alkylaluminum compounds must also be present in the reaction mixture in addition to primary alkylaluminum compounds. As practically no higher oligomers were formed, *Ziegler* did not consider the stereochemistry of the addition of the Al—R bond to an α-olefin, or the formation of corresponding diastereoisomers. Scheme 5 shows only the *cis* stereochemistry for the insertion reaction, which is the most probable in the addition of a M⇒C bond to a C=C double bond[113]; of course, a similar scheme could be conceived for an addition occurring with *trans* stereochemistry. Depending on the existence of a primary (a_1, a_4) or of a secondary group (b_1, b_4) bound to the metal (M) at the beginning of the step considered, a_2 and a_5 or b_2 and b_5 are formed by an insertion in which position 1 of propylene is linked to the metal atom of the catalyst and position 2 is linked to the growing chain end ("1—2" addition). a_3 and a_6 or b_3 and b_6 are formed by an insertion in which position 2 of propylene is connected with the metal atom of the catalyst ("2-1" addition). It is clear that a head-to-tail enchainment can be obtained by "1-2" addition to a primary metal alkyl (a_2 and a_5) or by a "2-1" addition to a secondary alkyl (b_3 and b_6). The type of enchainment is therefore regulated by the regioselectivity of the insertion reaction and the regularity of enchainment depends on regioselectivity at the two prochiral faces of the α-olefin, *i.e.* on the differences in energy between the activated complexes leading to a_2 or a_3, a_5 or a_6, b_3 or b_2, and b_6 or b_5.

The absolute configuration of the new asymmetric carbon atom which forms in each step depends both on the prochiral face of the α-olefin which reacts and on the regioselectivity of the addition ("1-2" or "2-1" type). For instance, if the asymmetric carbon atom next to the metal atom has an (*S*) configuration (a_1 or a_4), the new asymmetric carbon atom can have different absolute configurations, depending on the face attacked (compare a_2 with a_5 or a_3 with a_6) or, if the products arising from the same prochiral face are considered, on the type of addition (compare a_2 with a_3 or a_5 with a_6). Complete stereospecificity is achieved, *e.g.* when the same prochiral face of the olefin is always attacked and when the type of insertion ("1-2" or "2-1") is always the same. The same configuration of the asymmetric carbon atom formed during the insertion can also be achieved when a change in the face of the olefin reaction is accompanied by a change in the type of addition (compare a_2 and a_6 or a_5 and a_3).

In discussing the stereospecific polymerization of vinyl monomers, both regioselectivity and steric order must be kept in mind; possible relationships between the two phenomena have not been completely elucidated as yet; however, it is known that in other asymmetric reactions involving prochiral olefins, the same reaction on the two faces of the olefin can occur with different regioselectivity[114].



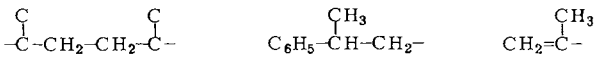
Scheme 5. Geometric aspects of the "Aufbaureaktion" of poly-α-olefins assuming a *cis* addition of the metal containing moiety ([Cat]) and of the growing chain end to the double bond. R = CH_3; $(CH_2)_x$—CH_3. The rules proposed by the IUPAC Commission on Macromolecular Nomenclature [111] are used in the formulas.

5.2. Early Research on the Stereospecific Polymerization of Propylene Yielding Isotactic and Syndiotactic Polymers

5.2.1. Isotactic Polypropylene

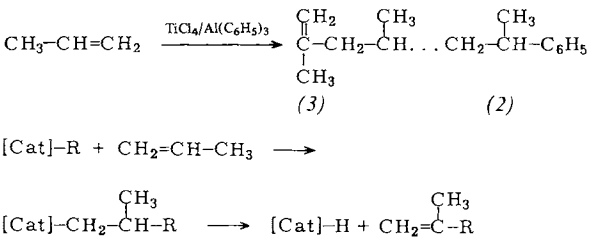
Although at the time of the discovery of the stereospecific polymerization the main aspects of the "Aufbaureaktion" in the presence of the alkyl derivatives of the metals of the three first groups of the Periodic Table were well understood, thanks to the research of *Ziegler* and of his co-workers, it was not obvious that the same mechanism should occur in the rapid polymerization of ethylene to very high polymers and particularly in the formation of stereoregular polymers of α-olefins in the presence of transition metals; in fact different hypotheses appeared in the literature in the fifties[115-120].

For the α-olefins the combination of X-ray and IR analyses showed very early that the polymers obtained with the Ziegler catalytic systems were substantially linear polymers with head-to-tail enchainments (absence of the IR band at 752 cm^{-1} corresponding to groups of type *(1)*). The regioselectivity was slightly lower for the amorphous than for the crystalline polymers.



(1) *(2)* *(3)*

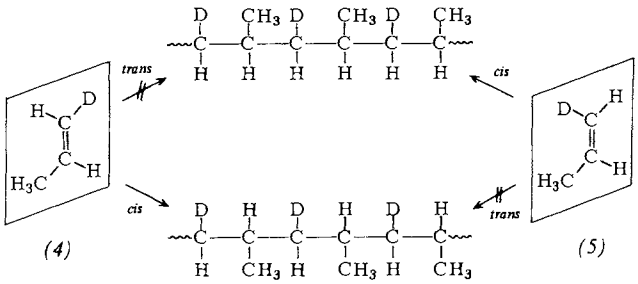
That the polymers form through an insertion reaction of the monomer into a metal to carbon bond was shown very early[121] by an IR investigation of the end groups of the polymer chains. In fact, with catalysts prepared from $TiCl_4$ and $Al(C_6H_5)_3$, end groups of types *(2)*[*] and *(3)* were found (Scheme 6). These results showed that α-olefin polymerization occurs through an insertion reaction similar to the one observed in the "Aufbaureaktion" with alkylaluminum compounds and that the insertion is practically of the 1-2 type, regioselectivity being very high, probably greater than 95% in the synthesis of both isotactic and atactic macromolecules.



Scheme 6. Top: formation of end groups of types *(2)* and *(3)*; bottom: polymerization by insertion and chain termination by hydride transfer.

Concerning the stereochemistry of the addition, it was realized that, given the high regioselectivity, the type of addition in the synthesis of the isotactic chains must always be the same, but it was only when diisotactic[**] polymers of deuterated propylene were synthesized[123] and their IR[124] and NMR[125] spectra interpreted that the knowledge of the stereochemistry reached its present state.

If we assume that the metal atom of the catalyst bearing the growing chain and the growing chain end add synchronously to the double bond of the incoming monomer, and if we consider that an *erythro*-diisotactic deuterated polypropylene is obtained from *cis*-1-deuterio propylene *(5)*, and correspondingly a *threo*-diisotactic polymer from the *trans* isomer *(4)*, the insertion reaction must occur through *cis* addition to the double bond (Scheme 7). Further confirmation of the above type of stereochemistry can be found in the structure of the *cis*-2-butene/ethylene copolymer[126,127] and from the NMR spectra of deuterated polypropylenes[135].



Scheme 7. Stereochemistry of addition to the double bond of the deuterated monomers *(4)* and *(5)*.

5.2.2. Syndiotactic Polypropylene

Hydrocarbon polymers having a substantial content of syndiotactic structure have been obtained up to now only in the case of propylene[131] and in the "1-2" polymerization of butadiene[177]. Only some of the aspects of the synthesis of syndiotactic polypropylene will be briefly discussed here.

Syndiotactic polypropylene was isolated for the first time by elution chromatography using highly isotactic polypropylene as the support, from ether-insoluble, heptane-soluble fractions of the polymers obtained with $TiCl_4/LiC_4H_9$ catalytic systems[131]. Fractions containing large amounts of syndiotactic structures in the chain were obtained later with $TiCl_4$/Na-alkyl catalytic systems[132]; however, the best results were obtained with soluble catalytic systems of the type VCl_4/AlR_2Cl/anisole[133].

By analogy with the polymerization of propylene to isotactic polymers and on the basis of the presence in the polymers of the alkyl groups initially bound to aluminum, a "1-2" type insertion mechanism was first postulated also in this case[132]. Only at the end of the sixties did NMR experimental evidence appear that showed that the stereochemistry of the addition reaction is of *cis* type, as in the case of the synthesis of isotactic polymers[125].

At the same time, data began to appear in the literature[130] indicating that with catalytic systems of the type $VCl_4/Al(C_2H_5)_2Cl$ the propylene insertion could be of the "2-1" type. Further indications in this direction came from the IR investigation of the ethylene propylene copolymers obtained with $VCl_4/Al(C_2H_5)_2Cl$ catalytic systems[137]. Finally, the existence of the "2-1" insertion mechanism for the polymerization of propylene to syndiotactic polymers with soluble

[*] Surprisingly, this fact has been overlooked by some authors [122] who postulate a hydride transfer from the tertiary carbon atom of the last monomeric unit of the growing chain to the metal atom as an important step in stereospecific polymerization.

[**] Diisotactic polypropylenes differ from isotactic ones by the existence of two asymmetric carbon atoms in the monomeric unit[123].

$VCl_4/Al(C_2H_5)_2Cl$ catalysts was definitely proven by end group determination. As a matter of fact, by cleaving the polymerization mixture with tritiated strong acids[136] it was shown that organometallic bonds do indeed exist at the end of the chains in the low temperature polymerization of propylene with $VCl_4/Al(C_2H_5)_2Cl$ catalytic systems both in the presence and in the absence of Lewis bases. However, the end groups thus formed, were not isopropyl groups, as in the case of isotactic polypropylene, but *n*-propyl groups, thus confirming the prevalence[138] of a "2-1" addition type in the synthesis of syndiotactic polypropylene at least with the catalytic system used.

The nature of the end groups corresponding to the first monomer insertion and the M—C bond in the synthesis of syndiotactic polypropylene[130] still needs to be confirmed.

At the present it is not clear if syndiotactic sequences can be formed only through a "2-1" type addition or if this is the preferred type of addition exhibited with soluble vanadium containing catalysts, but not necessarily with the heterogeneous titanium catalysts previously described[131,132]. In fact, the type of insertion is probably dependent, not only on the structure of the alkyl group bound to the metal, but also on the type of metal bound to the alkyl group. For example, in the case of addition of propylene to alkyllithium compounds, the presence of an isopropyl group bound to the metal was first believed[109] to induce a "2-1" type of addition. However, a more accurate investigation of this reaction showed[110] that also in this case the main reaction product arises from a "1-2" type of addition.

The existence of a connection between "2-1" type of addition and formation of long syndiotactic sequences would explain the known fact that while isolated syndiotactic dyads form with all the linear α-olefins with a "1-2" type of addition long syndiotactic sequences form only in the case of propylene. As a matter of fact, a low steric hindrance would be required for an addition of "2-1" type which should make possible the formation of long syndiotactic sequences[154].

5.3. Present Views on Regioselectivity in the Polymerization of α-Olefins

The early observation by *Natta et al.* of the predominance of a "1-2" type of addition in the polymerization of α-olefins significantly influenced polymer chemists' views on this problem for about 15 years and the findings on propylene polymerization with catalysts prepared from $TiCl_4$ or $TiCl_3/AlR_3$ were unduly generalized to the broad field of stereospecific polymerization. However, some clues indicating the incomplete regioselectivity of the "Aufbaureaktion" and related reactions started to appear in the literature as early as the fifties. *Ziegler* showed in 1952[112] that propylene dimerization with alkylaluminum compounds was not completely regioselective, and in 1959 it was demonstrated that in the reaction between $Al(iC_4H_9)_3$ and styrene in the presence of $Ni(acac)_2$, 30% of the products arise from the "2-1" addition of styrene to the $(iC_4H_9)_2Al—H$, which is the probable intermediate[134]. Furthermore, it was clear from the research of *Wilke* and co-workers on the propylene dimerization with organometallic nickel catalysts[128] and, later, from that of *Henrici-Olivé* and *Olivé*[129] on the dimerization of propylene in the presence of palladium catalysts, that propylene dimerization with transition metals can be far less regioselective than the "Aufbaureaktion" in the presence of main group elements.

An important contribution to the investigation of the regioselectivity in stereospecific polymerization was carried out by *Suzuki et al.*[130] who, on the basis of stoichiometric reactions between 1-pentene and different types of Ziegler catalysts, proposed that the insertion of 1-pentene into M—C bonds is mainly of the "1-2" type with typical $TiCl_3/AlR_3$ catalysts but mainly of "2-1" type with catalytic systems of the type $VCl_4/Al(C_2H_5)_2Cl$ which, with propylene, yield mainly syndiotactic polymers.

Zambelli's NMR-spectroscopic investigations on the regioselectivity of polypropylenes obtained with different catalytic systems[139–140] have shown that regioselectivity is lower with catalytic systems prepared from VCl_4 and $Al(C_2H_5)_2Cl$ than with $TiCl_3/Al(C_2H_5)_2Cl$ catalysts and decreases with increasing temperature[139] (Table 3).

Table 3. Regioselectivity of various catalytic systems in propylene polymerization [139, 148].

Catalyst	*T* [°C]	Fraction [a]	(CH_2CH_2)-sequences [g/100 g polymer]
$\delta TiCl_3/Al(C_2H_5)_2Cl$	15	A	[b]
		B	1.5
		C	—
$\beta TiCl_3/Al(C_2H_5)_2Cl$	15	A	2.5
		B	1
		C	—
$VCl_3/Al(C_2H_5)_2Cl$	15	A	1.5
		B	1.0
		C	—
$VCl_4/Al(C_2H_5)_2Cl$	−78	—	2.1
	−58	—	2.4
	−38	—	3.5
	−18.5	—	2.8
$VCl_4/Al(C_2H_5)_2Cl$/anisole	−38	—	3.3
	−18.5	—	4.4

[a] A, boiling pentane-insoluble, boiling hexane-soluble fraction; B, boiling hexane-insoluble, boiling heptane-soluble fraction; C, boiling heptane insoluble fraction. [b] Not determined.

The regioselectivity of the heterogeneous catalytic systems seems, however, to differ considerably, depending on the actual structure of the individual catalytic centers. Recent experiments[149] have shown that in fact the highly isotactic polypropylenes obtained with conventional $TiCl_3/AlR_3$ catalysts at 200—220 °C do not show detectable amounts of head-to-head sequences in their chains. Only when the polymerization temperature reaches 240 °C do the head-to-head sequences in the isotactic heptane insoluble fractions reach a concentration detectable by ^{13}C-NMR.

From the ^{13}C-NMR spectra of the polypropylenes prepared by *Sinn* and *Kaminsky*[142] it appears that a high regioselectivity (>90%)[143] exists also with soluble catalytic systems. The type of insertion does not seem to have been investigated in this case; however, a "1-2" type of addition seems very probable in view of the completely atactic structure of the polymers (Fig. 2B).

The origin of regioselectivity in Ziegler-Natta catalysis has never been discussed in detail. As previously proposed for other reactions catalyzed by transition metals[140], it might be

connected with the position of conformational equilibria in π-olefin complexes, which have been postulated as the first intermediates in the coordination polymerization, and with the different activation energies for the insertion reaction in which the different rotamers of the π-complexes react further in the polymerization process.

In conclusion, it appears that, depending on the type of catalyst used, regioselectivity in the polymerization of α-olefins can vary between 95—99% of "1-2" type and over 85% of "2-1" type. Unfortunately, because of the lack of sufficient knowledge of the factors influencing regioselectivity both with heterogeneous and homogeneous catalysts we are still far from reaching a control of regioselectivity that would allow us to synthesize polymers with a predetermined molar fraction of head-to-head or head-to-tail sequences in the main chain.

5.4. Present Views on Stereospecificity in the Polymerization of α-Olefins

Even 25 years after its discovery, polymerization of propylene to give isotactic polymers remains a unique example of stereospecificity in organic nonenzymatic reactions. In fact, as in some enzymatic reactions, the highest limit of stereospecificity which can be achieved, as shown by the stereoregularity of the polypropylene fractions insoluble in *n*-decane, is still unknown because of lack of sufficiently accurate experimental methods to measure it. The maximum stereospecificity achievable by polymerization of propylene to syndiotactic polymers has not been thoroughly investigated, but in any case it is smaller than that obtained in the synthesis of isotactic polypropylene and, in general, does not reach 95%.

Stereoregulation in stereospecific polymerization of α-olefins can arise from the interaction between entering monomer and growing chain, as in free radical polymerization, or from the interaction between monomer and metal atom (including its environment) or, finally, from both factors.

According to the present views, the origin of stereoregularity appears to be different for isotactic and for syndiotactic polymers; hence the two cases will be discussed separately.

5.4.1. Origin of Stereospecificity in the Synthesis of Isotactic Polymers

Taking into account the practically complete regioselectivity, which is revealed by the nondetectability of head-to-head/tail-to-tail enchainments, and the *cis*-stereochemistry of the reaction, the stereospecificity in the polymerization of α-olefins to isotactic polymers must be connected to the ability of the catalyst-growing polymer chain system, which we shall refer to as the "catalytic center", to discriminate sharply between the two prochiral faces of the α-olefin. To do this, the catalytic system must possess one or more chirality centers.

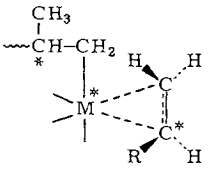
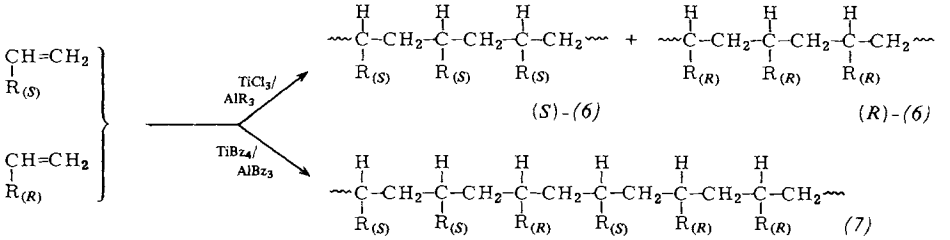


Fig. 3. Schematic representation of monometallic catalytic centers for isotactic polymerization. An asterisk indicates a chirality center.

Considering the simplest model of a monometallic catalytic center (Fig. 3), a chiral carbon atom certainly exists in the growing chain in β-position with respect to the metal atom; furthermore, the metal atom itself can be a chirality center[141] which, being bound to a solid surface, could maintain its absolute configuration during the insertion reaction.

The following facts indicate that the metal atom in the catalytic center is indeed chiral[*] and that chirality at the metal atom is the main stereoregulating factor in the polymerization of olefins to isotactic polymers.

Stereospecific catalytic centers are able to distinguish between the two antipodes of a racemic monomer, as shown by the existence of stereoselectivity in racemic α-olefin polymerization[168]. Homogeneous Ziegler type catalysts, as *e.g.* $Ti(CH_2C_6H_5)_4/Al(CH_2C_6H_5)_3$, do not show this property[144] and copolymers of (*R*) and (*S*) monomer *(7)* are formed which cannot be resolved by elution chromatography on an optically active support.

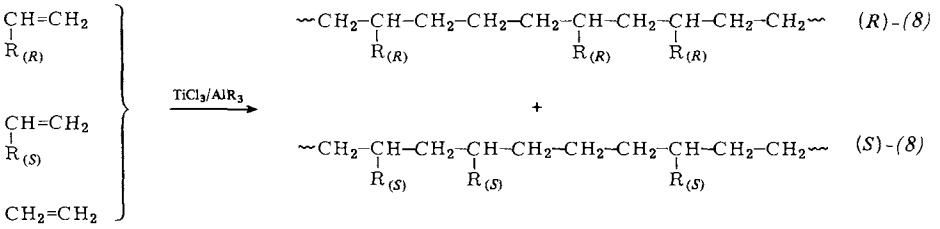


The copolymerization of racemic α-olefins with ethylene[145] is also stereoselective, *i.e.* it gives the copolymers (*R*)-*(8)* and (*S*)-*(8)* although the asymmetric carbon atom in the growing chain is at least δ-position with respect to the metal atom of the catalytic center.

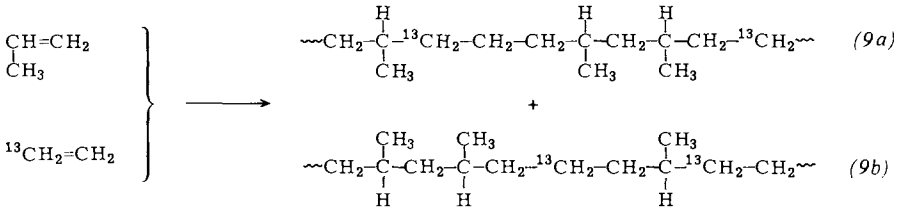
The copolymerization of a large excess of propylene with $^{13}CH_2{=}CH_2$ yields copolymers *(9a)* and *(9b)*, the ^{13}C-NMR spectrum of which shows only two bands attributable to isolated ethylene units. This fact indicates that the tertiary carbon atoms of the two propylene units separated by one ethylene unit arise from the addition of growing chain end and metal atom of the catalyst to the same prochiral face of the olefin[146].

When propylene polymerization is initiated with catalysts prepared from $TiCl_3$ and $Al(^{13}CH_3)_3$, the ^{13}C-enriched methyl group is present in the 2,4-dimethylpentyl terminal

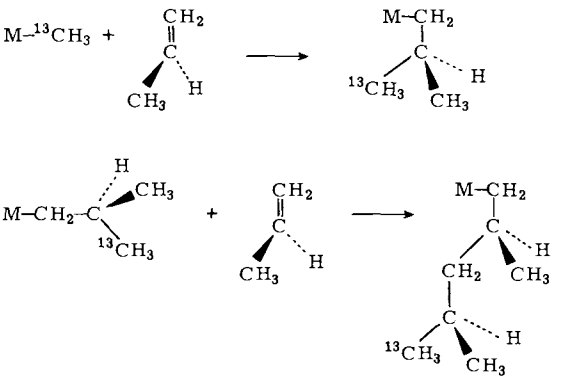
[*] Of course a chiral catalyst does not need to be optically active and, in the usual catalysts, it is believed to be racemic.



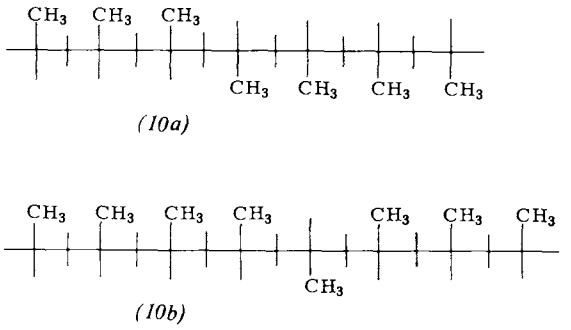
groups, as shown by ^{13}C-NMR and the stereochemistry of the end groups[*] indicates that the attack of the alkyl group and of the metal atom of the catalyst occurs at the same type of prochiral face of both the first and the second inserted propylene molecule[147].



In isotactic polypropylene chains, a low concentration (*ca.* 4%) of mmmr, mmrr, and mrrm pentads are found, but practically no pentads of the type mrmm have been detected (see Table 4)[148]. If the main stereoregulating factor were the last asymmetric carbon atom of the growing chain, an occasional steric error would be perpetuated, giving rise to sequences of the type *(10a)* and hence to a prevalence of mrmm pentads.



On the contrary, if the chirality at the metal atom is the main stereoregulating factor, an occasional steric error not involving a change of configuration at the metal atom would remain isolated, giving rise to pentads of the type mrrm, *(10b)* which have indeed been found. The degree of isotacticity and the type of steric errors of heptane-insoluble polymers obtained by different catalytic systems are reported in Table 4.



(10a)

(10b)

[*] The tertiary carbon atom of the isopropyl group is to be regarded as asymmetric since it is bound to a $^{12}CH_3$ and a $^{13}CH_3$ group.

Although the main stereoregulating factor has been identified from the experiments described above, the way in which this factor operates is still not well understood, mainly because of a lack of knowledge of the reaction step or steps corresponding to the insertion reaction. It is clear that the energy difference between the transition states leading to an isotactic dyad (m) or to a syndiotactic dyad (r) is, for some catalytic centers, at least 3 kcal/mol. Some polymerization experiments carried out at 240 °C in the presence of $TiCl_3$/AlR_3 catalytic systems and still yielding highly isotactic polymers (mmmm pentads content >97%) show, however, that for some catalytic centers the above difference reaches at least 4.3 kcal/mol[149]. This energy difference is mainly attributed to steric factors, the details of which are still far from being understood.

Table 4. NMR investigation of the boiling heptane-insoluble fraction of polypropylene [148] (prepared with various catalysts) (polymerization temperature 15 °C); m = *meso* (isotactic) dyads; r = racemic (syndiotactic dyads).

Catalyst	Hept.-insol. fraction [%]	Amount of pentad sequences [%] mmmm	mrmm	mrrm
$\delta TiCl_3/Al(C_2H_5)_2Cl$	88.5	≥85	—	≤2
$\beta TiCl_3/Al(C_2H_5)_2Cl$	47.5	≈90	—	≈2
$VCl_3/Al(C_2H_5)_2Cl$	57.5	74	6 [a]	≈3
$CrCl_3/Al(C_2H_5)_2Cl$	98.5	≈90	—	≈2
$ZrCl_4/Al(C_2H_5)_3$	22.5	≈90	—	≈2

[a] mmrm + rrmr.

This information about the mechanism of stereoregulation would be extremely valuable not only for the synthesis of catalytic centers having similar structures and activities, and of polymers with predetermined stereoregularity, but also, more generally, for a better understanding of asymmetric catalysis. In fact, the existence of chiral racemic catalysts having a high stereospecificity, which is evidenced by stereospecific polymerization, could open the way to the preparation of very efficient heterogeneous optically active catalysts for different asymmetric syntheses.

5.4.2. Origin of Stereospecificity in the Synthesis of Syndiotactic Polypropylene

The problem of stereospecificity in the synthesis of syndiotactic polymers has been little investigated up to now. As already mentioned, according to *Suzuki et al.*[130], a "2-1" type of insertion into a primary metal-alkyl bond like M—C_2H_5 or M—CH_3 should predominate with soluble catalysts, producing prevailingly syndiotactic polypropylene. According to *Zambelli*, on the basis of ^{13}C-NMR spectra, the first insertion of propylene on a primary metal carbon bond with $VCl_4/Al(CH_3)_2Cl$/anisole catalytic systems should be of the "1-2" type and it should be followed by a "2-1" type of insertion[138].

It now seems that the experimental facts can be understood by assuming that the stereospecificity in the synthesis of syndiotactic polypropylene originates from the presence of an asymmetric carbon atom of a secondary alkyl group directly bound to a metal[150]. Configurationally stable secondary alkyl-metal compounds are known in the case of mercury[151], iron[152], and rhodium[153] derivatives, and the stability of the M—C bond of VCl_4/AlR_2Cl catalysts in the syndiotactic polymerization which is not cleaved by methanol[136], supports the view that configurationally stable vanadium alkyls are present as catalysts.

A detailed model explaining how steric interactions in this type of *sec*-alkyl-vanadium compounds and in the corresponding postulated π complexes can effect steric control in syndiotactic polypropylene synthesis has recently been proposed[154]. This model also explains why homopolymerization of higher olefins to syndiotactic polymers does not occur with the same catalytic systems. Further research is needed to understand steric control of the syndiotactic type of polymerization in other catalytic systems, particularly in the heterogeneous ones.

Like the regiospecificity, the stereospecificity is also not very high in the synthesis of syndiotactic polypropylene, the difference between the energies of the activated complexes yielding isotactic or syndiotactic dyads being at most 2 kcal/mol[155].

6. Some Remarks on the Mechanism of Stereospecific Polymerization

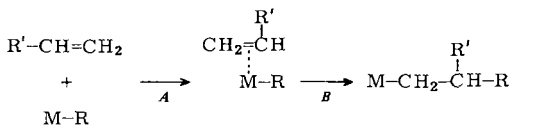
A thorough understanding of the origin of regioselectivity and stereospecificity in the polymerization of α-olefins would be necessary in order to rationally plan experiments to control the degree of stereoregularity, the average molecular weight, and the molecular weight distribution in the polymerization of α-olefins. To reach this understanding a more detailed knowledge of the reaction mechanism is required. Unfortunately, as in most catalytic processes, intermediates are very reactive and can only seldom be isolated. Most of our present knowledge is therefore based on indirect evidence and on investigations of model reactions. Regrettably, the scant experimental evidence is very often integrated into a large body of speculations and undue generalizations which further confuse the mechanistic picture.

We are not going to discuss in detail the mechanisms proposed up to now for the stereospecific polymerization, but we shall only present some facts mainly arising from the investigation of soluble catalysts and of model reactions and some speculations about the structure of the catalytic centers.

6.1. Experimental Evidence on the Mechanism of Propylene Polymerization with Ziegler Catalysts

Additions of organometallic compounds to olefins, which are the simplest models for the polymerization of α-olefins, are well described in the literature. They involve, in general, organometallic compounds of the metals of the first three groups of the Periodic System. In all these cases a planar four-center intermediate, as postulated for the addition of lithium alkyls to olefins[11], seems probable; however, a nonplanar intermediate complex has recently also been proposed[156]. An interaction between α-olefin and alkylmetal compound preceding the formation of the cyclic transition state and activating the olefinic double bond is conceivable, but has never been experimentally proved in the polymerization of α-olefins. Only in the case of alkylaluminum compounds has an interaction between a double bond present in one of the organic substituents and an aluminum atom been proven by IR spectroscopy[158].

To explain the much higher activity of Ziegler catalytic systems containing transition metal atoms, the possible activation of the olefinic double bond by chemiadsorption on the surface of a transition metal salt was already postulated by *Natta* in 1956[160]. Subsequently *Natta*[161], as well as *Ludlum et al.*[159] and *Carrick et al.*[157], proposed that the polymerization takes place through a coordination of the monomer to the catalyst followed by an insertion of the coordinated monomer into a metal to carbon bond (Scheme 8). *Cossee* then[93] proposed that the olefin forms a π-complex with a transition metal and is then inserted into one of its bonds with an alkyl group[93].



Scheme 8. Postulated two-step polymerization *A*, complexation; B, insertion.

Among the questions posed by experimental studies on the mechanism the following will be briefly discussed:

a) The type of metal atom on which the polymer chain is growing.
b) Formation of an olefin-catalyst complex.
c) Relative values of the activation energy for formation of the olefin-catalyst complex and for the actual insertion reaction.

a) In the original Ziegler catalytic systems, both transition metal atoms (*e.g.* Ti) and main group metal atoms (*e.g.* aluminum) were present. Therefore, the polymer chain can, in principle, grow either on the transition metal atom or on the main group metal atom. It was already shown in 1958[39,40]

that catalysts containing only titanium as metal component could polymerize both ethylene and propylene. This does not necessarily demonstrate that when, *e.g.*, titanium and aluminum are present in the catalyst, the chain still grows on titanium. It must be emphasized that simple titanium compounds like $Cl_3Ti—CH_3$ are not active in the stereospecific polymerization of propylene if $TiCl_3$ is not present, and that the classical Ziegler catalysts prepared from $TiCl_4$ and AlR_3 are much more active than the catalysts containing only titanium as the metal component. This problem has recently been solved, at least for the polymerization of ethylene with a soluble catalyst prepared from Cp_2TiCl_2 and $Al(C_2H_5)Cl_2$. In fact, using ^{13}C-enriched ethylene it was shown[71] that a complex containing titanium and aluminum is present and that the polymer chain grows by insertion of ethylene molecules into a Ti—C bond and not into an Al—C bond. From this and other experiments it now appears very likely that the polymer chain grows on the transition metal present in the catalyst; however, the question remains open if the olefin to be inserted is complexed to the same metal atom on which the chain grows.

b) Experimental evidence on the existence of a catalyst-olefin complex is very poor. No complex of this type has been isolated; among the indirect evidence appearing in the literature, we shall mention only the fact that in the stereospecific polymerization of substituted styrenes which is supposed to occur according to an anionic mechanism, a rate increase is found when electron donating substituents are present in a *para* position, contrary to what is known for anionic polymerization[163]. This fact indicates that the rate depends on the formation of a transition metal-monomer complex which is favored by electron donating substituents.

As a direct evidence for olefin π complex formation, *Ballard*[162] found an equilibrium constant of 0.01 for the equilibrium between the soluble catalytic complex *(11)* + ethylene shown below, however, for other systems, and particularly for heterogeneous catalysts, the situation could be very different.

$$Zr[CH_2—Si(CH_3)_3]_4 + C_2H_4 \rightleftharpoons [\text{Catalyst-Olefin complex}]$$
(11)

In the case of ethylene polymerization with the catalytic system $Cp_2TiCl_2/Al(C_2H_5)Cl_2$, *Fink*[71] was not able to detect by spectroscopic methods the formation of a π-complex, the concentration of which is therefore in this case lower than 1%.

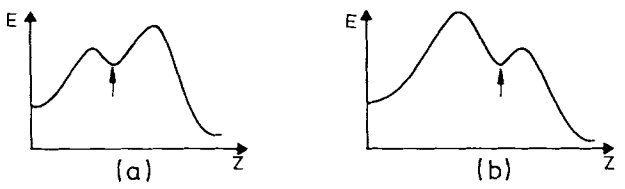
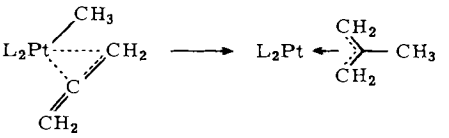


Fig. 4. Possible reaction paths for ethylene polymerization. a), b) see text. Arrow indicates catalyst-olefin complex.

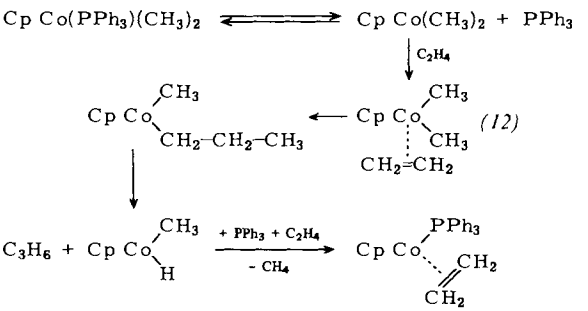
The failure to isolate an olefin catalyst complex, if it really is formed, can be explained in two ways (Fig. 4); either a rapidly established equilibrium exists between olefin-catalyst complex and free olefin and catalyst which, however, is largely displaced towards the dissociated species (Fig. 4a), or the activation energy for the insertion reaction of the π-complex is so low that the olefin-catalyst complex disappears at a rate which is very high, the steady state concentration of the olefin-catalyst complex being therefore very low (Fig. 4b).

c) To distinguish between the two possibilities of Figure 4, a knowledge of the relative activation energies for the catalyst-olefin complex formation and for the insertion of the complexed olefin is necessary. Unfortunately, very little is known about the insertion of a complexed olefin into a metal-to-carbon bond. The existence of a relatively high activation energy for an insertion reaction of a double bond into a metal-to-carbon bond was observed in the intramolecular reaction of a π-complexed allene molecule with a $Pt—CH_3$ bond (Scheme 9)[164]. However, since in the starting complex, the methyl group and the allene molecule are bound to the platinum atom in the *trans* position, it is not clear if the high activation energy is really required for the insertion reaction or if it is necessary to bring the two reacting moieties into the *cis* position.



Scheme 9. Insertion of a π-complexed allene into a $Pt—CH_3$ bond [164].

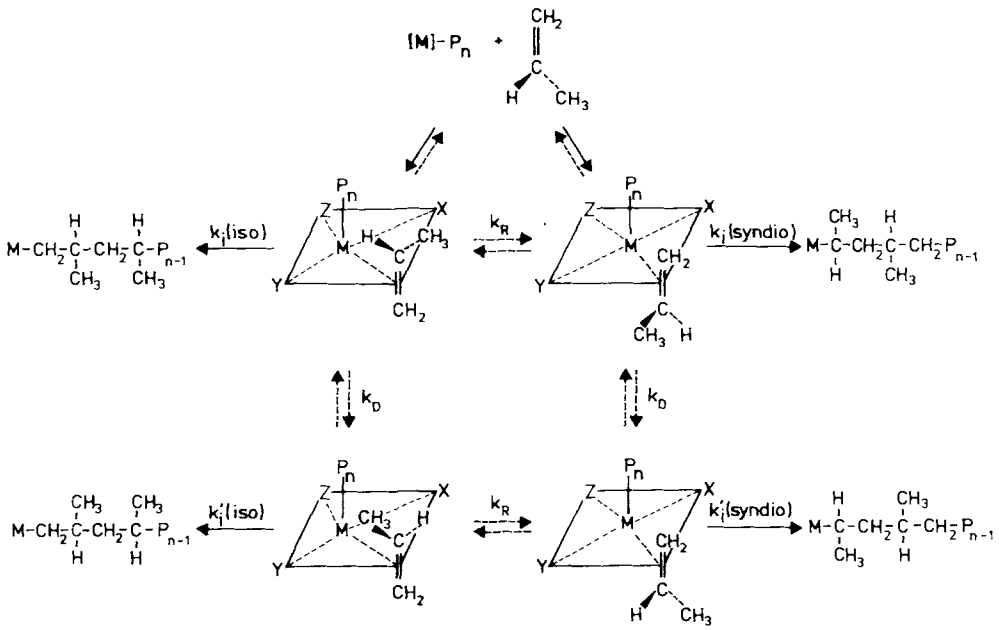
No insertion of a π-complexed ethylene into a $Co—CH_3$ bond was observed in the $[(CH_3)_3P]CoCH_3(C_2H_4)$[165]. However, such insertion into a $Co—CH_3$ bond was observed for the related complex *(12)* at 76 °C (Scheme 10)[166].



Scheme 10. Insertion of a π-complexed ethylene into the $Co—CH_3$ bond of complex *(12)* [166].

At present we can conclude that a two-step mechanism is very likely for the stereospecific polymerization even if not proven, and that a higher activation energy than that for the olefin-catalyst complex formation should be foreseen for the insertion reaction.

The working hypothesis we are using at the present is shown in Scheme 11; the double arrows correspond to reversible reactions, but not necessarily to rapidly achievable equilibria. According to this scheme, the position of diastereomeric and rotameric equilibria in the π-complexes and/or activation energy for the insertion reaction of the π-complexed olefin could cause the large regioselectivity and enantioface discrimination necessary for the synthesis of stereoregular poly-α-olefins.

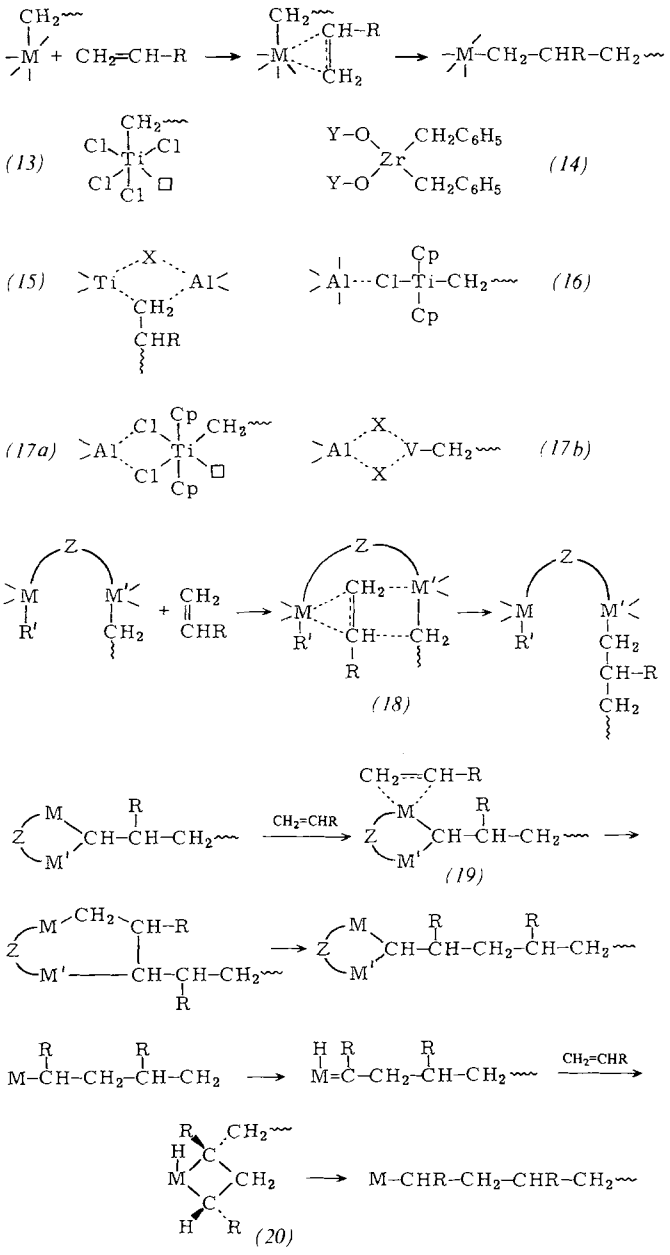


Scheme 11. Possible diastereomeric π-complexes and insertion reactions leading to isotactic or syndiotactic polypropylene; P_n = polymer chain, [M] = metal atom with ligands X and Y.

6.2. Speculations about the Structure of the Catalytic Centers and the Mechanism of their Catalytic Action

A great number of structures have been proposed for the catalytic centers[169,170]. The models are related to the different polymerization mechanisms proposed, which can be classified as shown in the Table 5 and Scheme 12. Monometallic centers such as *(13)* and *(14)* have been largely accepted, although compounds like $Cl_3Ti{-}CH_3$[39] and $Cp_2Ti(C_6H_5)_2$[40] are not catalytically active. Dimetallic models in which the growing polymer chain is linked to both metal atoms as in *(15)* were criticized by *Ziegler*[180] because in the "Aufbau-reaction" the monomeric trialkylaluminum that has no bridging alkyl groups is catalytically active, while the dimeric triethylaluminum bearing two such bridging alkyl groups is not catalytically active. Dimetallic centers of type *(17)* having two halogen bridges have been criticized since the titanium atom is not octahedrally coordinated in the soluble catalytic species obtained from Cp_2TiCl_2 and $AlC_2H_5Cl_2$[7]. Model *(19)* and the corresponding mechanism can be discarded because in the copolymerization of $CH_2{=}CD{-}CD_3$ and $CD_2{=}CD{-}CD_3$ with $TiCl_3/AlR_3$ catalysts only CH_2 and CD_2 were found in the isotactic polymer instead of the predicted CHD groups[167]. Model *(20)* can be criticized on the grounds that the synthesis of isotactic polypropylene occurs according to a "1-2" and not according to a "2-1" insertion, and for other reasons[147].

No direct proof exists to confirm the above structures, some of which are based on a series of interesting speculations and indirect evidence. While these structures have the merit of stimulating further experiments to prove some of their features, uncritical acceptance of one of them can hinder further progress in the field. Some of these structures might not be very far from the actual structure of some soluble nonstereospecific catalytic species; however, it is probable that the actual structures of the catalytic centers of the



Scheme 12. Models for catalytic centers and some proposed mechanisms for the α-olefin polymerization; M = M′ or M ≠ M′ X = Hal, Y = Si or Al, Z = org. or inorg. bridging ligands (see Table 5).

Table 5. Proposed mechanism and corresponding models of catalytic centers for the growth of the polypropylene chain (see Scheme 12).

Type of insertion reaction	Models for catalytic centers
Migration of the growing chain end to the complexed monomer	Monometallic centers *(13)* [93] and *(14)* Dimetallic centers [171] a) with growing chain as bridge between two metal atoms *(15)* [178] b) with one halogen as bridge between two metal atoms *(16)* [71] c) with two halogen atoms as bridges between two metal atoms *(17)* [179] d) with complexation of monomer to one metal atom M and chain growth at second metal atom M' *(18)*, $M \neq M'$ or $M = M'$ [168]
Growing chain end bound to two metal atoms; insertion of the complexed monomer into one of the metal-to-carbon bond followed by 1—3 migration of the other metal atom and of a hydrogen atom [52]	Dimetallic centers *(19)* [52]
Growing chain end bound by a double bond to the metal atom (carbene complex); insertion reaction through a metallacyclobutane intermediate [122]	Monometallic center *(20)* [122]

heterogeneous catalysts are much more complex and involve a greater number of metal atoms and ligands.

7. Trends in Research on Propylene Polymerization

Even now, most of the research in the field of propylene polymerization is carried out in industrial laboratories and only a small part of the work is published.

One of the main aims of industrial research is to obtain high purity polymers with very high yields and catalyst's productivity from processes that use higher polymerization temperatures, to facilitate temperature control in the reactors, and, eventually, to utilize the enthalpy of polymerization. Further aims are to control the molecular weight distribution and the morphology of the polymers and to synthesize poly-α-olefins that have a predetermined degree of stereoregularity.

The achievement of the above aims is mainly dependent on a better knowledge of the structure of the catalytic centers and on improved methods for their synthesis.

Research in this field is still mainly empirical in character; however, from the thousands of experiments that have been reported mainly in the patent literature, two main lines of research seem to emerge:

a) It is possible to obtain more active and more stable catalytic centers when the transition metal is bound to one or more —OX groups, where X is an element of the II, III, or IV group of the Periodic System.
b) It is possible, using suitable Lewis bases, to modify the stereospecificity of the catalytic systems. However, with most of the Lewis bases used, an increase in stereospecificity is often accompanied by a decrease in catalytic activity, especially in the case of supported catalysts.

Point a) has been mainly investigated by *Ballard* and co-workers[156,162] and by a few other authors[172,173], but some of the interesting results obtained by *Sinn* and co-workers[142] in the field of ethylene and propylene homogeneous polymerization might be related to it. Excellent reviews in this field have recently been published by *Sinn* and *Kaminsky*[50], by *Zacharov* and *Yermakov*[76], by *Ballard*[171] by *Caunt*[69], and by *Yamamoto* and *Yamamoto*[174].

Point b) has been the subject of a great number of patents and papers since the early days of stereospecific polymerization. The use of bases has also found important industrial applications: fluoride ion is used as a Lewis base in the Eastman Kodak propylene polymerization process[29,31] and carboxylic esters are used as the third component to improve the stereospecificity in some processes using the classical $TiCl_3/Al(C_2H_5)_2Cl$ catalytic system[24,25,32,37].

The dramatic effect of Lewis bases in improving stereospecificity has led to the use of the highly active Lewis base modified $TiCl_4/MgCl_2/AlR_3$ catalyst for the industrial synthesis of isotactic polypropylene[37,38] (Table 2).

The two main lines of research on the Ziegler type polymerization catalyst discussed in the present section must not be conceived as being completely separated; on the contrary, by overcoming possible psychological barriers, a fruitful cross-fertilization can take place, which might yield, in the near future, further progress in the field of the catalysts for the stereospecific polymerization of propylene.

8. Recent Investigations on the Role of Lewis Bases in Catalytic Systems Supported on $MgCl_2$

Some progress in the understanding of the role of the Lewis bases in this type of catalyst and of the nature of the catalytic centers has been made recently by investigating the stereoelective polymerization of racemic 4-methyl-1-hexene with $MgCl_2/TiCl_4/Al(C_4H_9)_3$ and (−)-menthyl anisate as chiral Lewis base[175]. The polymer obtained was separated into an amorphous (ethyl acetate-soluble) fraction and a crystalline (methylcyclohexane-soluble) fraction by solvent extraction (Table 6). The two fractions had optical activities of opposite sign, and the optical purity of the amorphous polymer increased, while that of the crystalline polymer decreased upon increasing the conversion. As expected, the optical purity of both fractions increased upon increasing the ratio of Lewis base to AlR_3.

These results indicate that catalytic centers having different stereospecificities exist in the above catalytic systems. Being of chiral-racemic nature, the highly stereospecific centers have different tendencies to complex the optically active Lewis base used. The complexation of the base decreases the activity of the catalytic centers; the centers forming less stable complexes and having one prevailing chirality polymerize one of the monomer antipodes more rapidly than the other. As a result, the synthesized polymer is optically active (stereoelective polymerization[181]).

The centers having a low stereospecificity have a larger Lewis acidity and are not stereoelective; therefore, they produce a stereoirregular polymer having the type of chirality prevailing in the nonpolymerized monomer and therefore opposite to that of the stereoregular polymers.

As found experimentally, the optical purity of both the nonpolymerized monomer and of the amorphous polymer must increase with increasing conversion.

Table 6. Stereoelective polymerization of racemic 4-methyl-1-hexene with $MgCl_2/TiCl_4/Al(iC_4H_9)_3/H_3COC_6H_4COO$-Ment [a] at 20—25 °C.

Lewis base Ti + Al [mol/mol]	Conversion [%]	Polymer fractions [b] B Yield [%]	B $[\alpha]_D^{25}$ (°) [c]	E $[\alpha]_D^{25}$ (°) [c]	Recovered monomer B Prevailing chirality	B e.e. [%]	B Prevailing chirality	B e.e. [%] [d]	E Prevailing chirality	E e.e. [%] [d]
0.112	58	10.86	0	− 6.00	(*S*)	0.73	—	0	(*R*)	1.06
0.409	15	6.5	+1.00	−20.67	(*S*)	0.297	(*S*)	0.27	(*R*)	3.47
0.538	65.5	4.5	+5.55	−10.08	(*S*)	2.21	(*S*)	1.48	(*R*)	1.69
0.797	43	6.9	+2.50	−10.40	(*S*)	2.71	(*S*)	0.67	(*R*)	1.77

[a] % Ti = 2.0; Al/Ti = 40; Ment = (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl. [b] *B*, acetone-insoluble, ethyl-acetate soluble polymer fraction; *E*, diisopropyl ether-insoluble, methylcyclohexane-soluble polymer fraction. [c] In methylcyclohexane. [d] Enantiomeric excess (optical purity) of a monomer giving rise to a polymer fraction having the same $[\alpha]_D^{25}$ and the same solubility (cf. *P. Pino et al.*, Polym. Lett. 5, 307 (1967).

This hypothesis was applied to propylene polymerization with similar catalytic systems and indeed it was found[176] that, on increasing the Lewis base/AlR_3 ratio from 0.01 to 0.3, a dramatic decrease of the heptane-soluble fraction takes place, while the amount of isotactic polymer produced per g of Ti per hour decreases only by about 25% (Fig. 5).

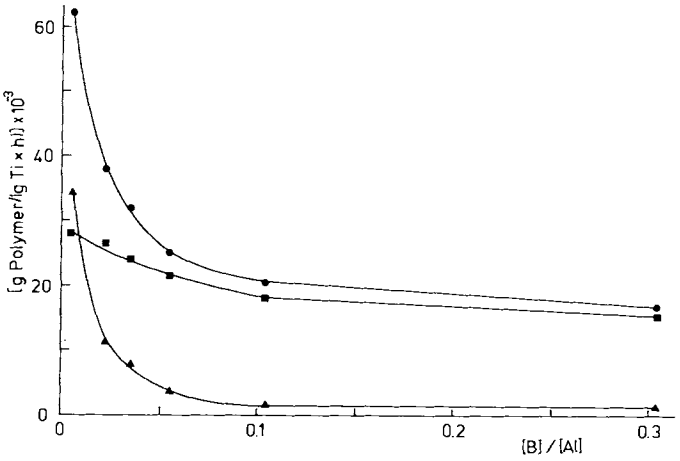


Fig. 5. Polymerization of propylene with the catalytic system $TiCl_4/MgCl_2/Al(iC_4H_9)_3$/ethyl benzoate. Catalyst's productivity at different ratios of [B]/[Al] [176]. [B] = molar concentration of ethyl benzoate; [Al] = molar concentration of triisobutylaluminum; ●, total polymer; ■, fraction insoluble in boiling heptane; ▲, fraction soluble in boiling heptane.

The ^{13}C-NMR spectra of the ether-soluble (Fig. 2A) and heptane-soluble fraction (Fig. 2B) obtained using different Lewis base/AlR_3 ratios shows that no fraction has a really atactic structure and that the ratio between the isotactic pentads (mmmm) and the syndiotactic pentads (rrrr) in the polymers significantly decreases when the Lewis base/AlR_3 ratio is increased (Fig. 6).

These results seem to indicate that even among the centers producing stereoirregular linear polypropylene, large differences exist in their Lewis acidity. The activity of the centers producing the (rrrr) pentads seems to be much less affected by the larger Lewis base/AlR_3 ratio, either because their Lewis acidity is smaller and they do not successfully compete with AlR_3 for the base present, or because they maintain their activity even after complexation with the base. We have already mentioned that some of the best catalysts for synthesizing syndiotactic polypropylene contain ethers[133].

These observations are in keeping with a competition between AlR_3 in solution and acidic centers on the solid surface for the complexation with the base, thus explaining why different Lewis base/AlR_3 ratios are necessary to obtain the same percentage of isotactic polymers, depending on the structure of the Lewis base and of AlR_3. These views are valid only for the catalytic systems mentioned above ($MgCl_2/TiCl_4/AlR_3$/Lewis base) and should not be extrapolated to similar catalytic systems without experimental confirmation. In fact, depending on the number of vacant sites in the catalytic centers, more than one base molecule per titanium atom might be necessary to stop the catalytic activity; in this case, centers containing only one molecule of base could still be catalytically active and could show a larger stereospecificity in the presence than in the absence of the Lewis base.

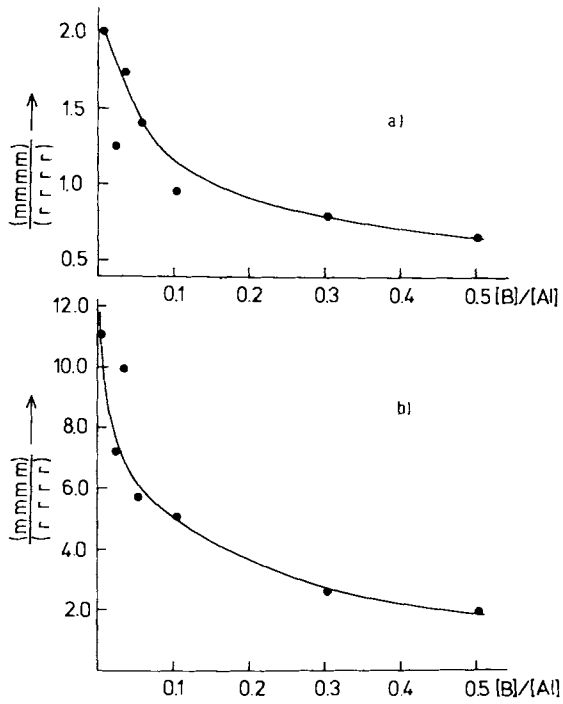


Fig. 6. Change in stereoregularity expressed as ratio of molar fractions of isotactic (mmmm) and syndiotactic (rrrr) pentads (a) in the ether-soluble and (b) in the heptane-soluble polypropylenes as a function of the ratio [B]/[Al] [176] (see legend of Fig. 5 for catalyst).

As shown by the above data, the $MgCl_2$-supported catalyst, despite the presence of the support which probably is far from being inert, yields interesting information on the nature of the catalytic centers, and Lewis bases can be used as probes to investigate their structure.

9. Final Remarks

The discovery of stereospecific polymerization of propylene has not only considerably stimulated the development

of polymer science, but also widely contributed to the development of various fields of chemistry.

In fact, due to the very early appreciation of the industrial relevance of propylene polymerization, numerous industrial laboratories have invested substantial efforts in the development of fundamental organometallic chemistry (in particular that of transition metals) and organometallic catalysis. Indeed, efforts to understand the mechanism of stereoregulation in stereospecific polymerization, although not comparable to the efforts devoted to the elucidation of enzymatic catalysis, have been much greater than those devoted to the understanding of other highly significant catalytic reactions, such as ammonia synthesis or the synthesis of hydrocarbons from carbon monoxide.

The knowledge of the existence of highly stereospecific catalysts for α-olefin polymerization could have stimulated the research on the possibility of application of similar catalytic systems to other organic syntheses. However, no significant progress has been reported in this field, with the exception of stereospecific dimerization and codimerization reactions. A possible reason for the delay of progress in this direction is the lack of sufficient knowledge of the factors on which stereospecificity is based.

Research on stereospecific polymerization has made a great contribution to our understanding of the relationships between homogeneous and heterogeneous catalysis; of interest for further progress in catalysis is also the idea of controlling the structure of the catalytic centers in heterogeneous catalysts by compounds (*e.g.* Lewis bases) which take part both in homogeneous equilibria (*e.g.* with Lewis acids) in solution and in heterogeneous equilibria (*e.g.* with groups having Lewis acidity) on the surface of an heterogeneous catalyst.

The contribution of the discovery of stereospecific polymerization to the development of polymer science is comparable to that provided by the understanding of free-radical polymerization and of polycondensation in the thirties. Besides the impetus to the development of new stereospecific syntheses of macromolecules, steric order in polymers afforded new parameters for acquiring a better knowledge of polymerization mechanisms.

Furthermore, the availability of a great number of new stereoregular polymers facilitated an understanding of the relationships between chemical structure and physical properties, including mechanical properties. In particular, the availability of polymers with perfectly defined chemical and steric structures allowed a better check on the results of conformational analysis and a better understanding of the significance of the conformational equilibria for the structure and properties of the polymers in crystalline state, in the melt, and in solution.

In spite of the great amount of research in the field of stereospecific polymerization that has been performed in the 25 years since its discovery, it appears that this subject will remain of paramount importance for the development of chemistry and of polymer science for a long time in the future.

Received: August 12, 1980 [A 339 IE]
German version: Angew. Chem. *92*, 869 (1980)

[1] *G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mazzanti, G. Moraglio*, J. Am. Chem. Soc. *77*, 1708 (1955).
[2] Letter from *P. J. Flory* to *G. Natta* dated January 21, 1955. We thank the Istituto di Chimica Industriale of Milan Polytechnic for a photocopy of this letter.
[3] *H. Staudinger:* Die hochmolekularen organischen Verbindungen. Springer, Berlin 1932, pp. 113f.
[4] *C. S. Marvel, R. L. Frank, E. Prill*, J. Am. Chem. Soc. *65*, 1647 (1943).
[5] *C. E. Schildknecht, S. T. Gross, H. R. Davidson, T. M. Lambert, A. D. Zoss*, Ind. Eng. Chem. *41*, 2104 (1948).
[6] *G. Natta*, Chim. Ind. (Milano) *77*, 1009 (1957).
[7] *C. W. Bunn*, Proc. R. Soc. *180*, 67 (1942).
[8] *A. A. Morton*, Ind. Eng. Chem. *42*, 1488 (1950).
[9] *J. L. R. Williams, J. Van Den Berghe, W. J. Dulmage, K. R. Dunham*, J. Am. Chem. Soc. *78*, 1260 (1956).
[10] *K. Ziegler*, Angew. Chem. *64*, 323 (1952).
[11] *K. Ziegler*, Belg. Pat. 533362 (German priority, Nov. 16, 1953).
[12] *R. E. Kirk, D. F. Othmer*, Encyclopedia of Chemical Technology, Vol. *11*. Interscience, New York 1953, p. 1.
[13] *G. Natta, P. Pino, G. Mazzanti*, Gazz. Chim. Ital. *87*, 528 (1957).
[14] *G. Natta, P. Pino, G. Mazzanti*, Chim. Ind. (Milano) *37*, 927 (1955).
[15] *G. Natta, P. Corradini*, Atti Accad. Nat. Lincei 4 (Ser. 8), 73 (1955).
[16] *G. Natta, P. Pino, G. Mazzanti*, US Pat. 3715344 (1973) (Italian priority June 8, 1954). Montecatini S.p.A.
[17] *E. Field, M. Feller*, US Pat. 2691647 (1954), Standard Oil Indiana.
[18] *A. Zletz*, US Pat. Appl. 462480 (filed Oct. 15, 1954), Standard Oil Indiana; Standard Oil Indiana, Brit. Pat. 820727 (1959).
[19] Phillips Petroleum, Austral. Pat. 864/54 (9. 12. 1954).
[20] Phillips Petroleum, Belg. Pat. 530617 (filed July 23, 1954).
[21] *G. Natta*, Chim. Ind. (Milano) *37*, 888 (1955).
[22] *G. Natta, P. Pino, G. Mazzanti*, Ital. Pat. 526101 (filed Dec. 9, 1954), Montedison. S.p.A.
[23] *E. Tornquvist, W. Seelbach, A. W. Langer, Jr.*, US Pat. 3128252 (1964) (filed April 16, 1956), Esso Research and Engineering. *E. Tornquvist, A. W. Langer, Jr.*, US Pat. 3032510 (1962) (filed June 27, 1958) Esso Research and Engineering Co.
[24] Mitsubishi Petrochem. Corp., Brit. Pat. 1092390 (1966).
[25] *G. A. Razuvaev, K. S. Minsker, G. T. Fedoseeva, V. K. Bykhovskii*, Polym. Sci. USSR *2*, 299 (1961).
[26] *R. L. McConnel, M. A. McCall, G. O. Cash, Jr., F. B. Joyner, H. W. Coover, Jr.*, J. Polym. Sci. *A 3*, 2135 (1965).
[27] *J. P. Hermans, P. Henrioulle*, DBP 2256789 (1973), Solvay.
[28] *J. P. Hermans, P. Henrioulle*, DBP 2213086 (1972), Solvay.
[29] *M. B. Edwards, H. J. Hagemeyer*, Brit. Pat. 930633 (1963) (US priority Aug. 28, 1958), Eastman Kodak.
[30] *H. J. Hagemeyer, Jr., M. B. Edwards*, Brit. Pat. 943206 (1963) (US priority Feb. 17, 1959), Eastman Kodak.
[31] *M. B. Edwards, K. V. Park, E. H. Carter, Jr.*, Fr. Pat. 1450785 (1966) (US priority July 22, 1964), Eastman Kodak.
[31a] *R. W. Lenz, F. Ciardelli:* Preparation and Properties of stereoregular Polymers, D. Reidel, Dordrecht 1980.
[32] *J. C. W. Chien* in [31a], p. 115.
[33a] *A. Orzechowski, J. C. MacKenzie*, Fr. Pat. 1349864 (1964) (US priority Jan. 18, 1960), Cabot Corp.
[33b] *N. W. Luft, C. Hulme, D. Y. Waddan*, US Pat. 2981725 (1967) (filed October 15, 1956) Shell Oil Co.
[34] *A. Mayr, P. Galli, E. Susa, G. DiDrusco, E. Giachetti*, Brit. Pat. 1286867 (1969), Montedison.
[35] *R. N. Haward, A. N. Roper, K. L. Fletcher*, Polymer *14*, 15 (1973).
[36] *K. Gardner, I. W. Parsons, R. N. Haward*, J. Polym. Sci. Polym. Chem. Ed. *16*, 1683 (1978).
[37] *U. Giannini, A. Cassata, P. Longi, R. Mazzochi*, Belg. Pat. 785332 (1972), Montedison. S.p.A.
[38] *U. Giannini, A. Cassata, P. Longi, R. Mazzochi*, Belg. Pat. 785334 (filed Dec. 27, 1972), Montedison. S.p.A.
[39] *P. Pino, G. Mazzanti*, Ital. Pat. 583219 (filed Oct. 8, 1958), Montedison. S.p.A.
[40] *C. Beerman, H. Bestian*, Angew. Chem. *71*, 618 (1959).
[41] *A. S. Matlack, D. S. Breslow*, J. Polym. Sci. *A 3*, 2853 (1965).
[42] *C. J. Benning, W. R. Wszolek, F. X. Werber*, Polym. Prepr. *3*, 138 (1962).
[43] *J. Boor, E. A. Youngman*, J. Polym. Sci. *B 2*, 265 (1964).
[44] *E. A. Youngman, J. Boor*, J. Polym. Sci. *B 3*, 577 (1965).
[45] *J. Boor*, J. Polym. Sci. *A-1, 9*, 617 (1971).
[46] *G. Natta, P. Pino, G. Mazzanti, P. Longi*, Gazz. Chim. Ital. *87*, 570 (1957).
[47] *G. Natta, P. Pino, G. Mazzanti, P. Longi*, Gazz. Chim. Ital. *87*, 549 (1957).
[48] *G. Natta, P. Pino, G. Mazzanti, U. Giannini*, J. Am. Chem. Soc. *79*, 2975 (1957).
[49] *G. Natta, G. Mazzanti*, Tetrahedron *8*, 86 (1960).
[50] *H. Sinn, W. Kaminsky*, Adv. Organomet. Chem. *18*, 240 (1980).
[51] *U. Giannini, U. Zucchini, E. Albizzati*, J. Polym. Sci. Polym. Lett. Ed. *8*, 405 (1970).
[52] *P. Pino, G. Consiglio, H. J. Ringger*, Justus Liebigs Ann. Chem. *1975*, 509.
[53] *D. C. H. Ballard*, Adv. Catal. *23*, 299 (1973).

[54] *R. Amtmann, B. Diedrich,* DBP 2043508 (1972), Hoechst.
[55] *M. Fischer,* DBP 874215 (1943), BASF.
[56] *K. Weissermel, H. Cherdron, J. Berthold, B. Diedrich, K. D. Keil, K. Rust, H. Strametz, T. Toth,* J. Polym. Sci. Symp. *51*, 187 (1975).
[57] *F. J. Karol* in *H. F. Mark, N. M. Gikales:* Encyclopedia of Polymer Science and Technology. Interscience, New York 1976, Suppl. Vol. 1, p. 120.
[58] *K. H. Reichert,* Chem.-Ing.-Tech. *49*, 626 (1977).
[59] *B. Diedrich,* J. Appl. Polym. Sci. Appl. Polym. Symp. *26*, 1 (1975).
[60] *S. Sivaram,* Ind. Eng. Chem., Prod. Res. Dev. *16*, 121 (1977).
[61] *P. Longi, U. Giannini, A. Cassata,* Belg. Pat. 774600 (1971), Montedison. S.p.A.
[62] *K. Wisseroth,* Chem.-Ztg. *101*, 271 (1977).
[63] Hercules Powder, Brit. Pat. 807204 (1959).
[64] *G. Natta, P. Pino, G. Mazzanti,* Ital. Pat. 566242 (1957), Montedison. S.p.A.
[65] *H. Mueller-Tamm,* Annu. Tech. Conf. Soc. Plast. Eng., Tech. Pap. 27th, *15*, 577 (1969).
[66] *H. P. Frank* in *H. Morawetz:* Polypropylene. Gordon and Breach, London 1968.
[67] *A. Valvassori, P. Longi, P. Parrini* in *E. G. Hancock:* Propylene and its Industrial Derivatives. Ernest Benn Ltd., London 1973, p. 156.
[67a] *J. C. W. Chien:* Coordination Polymerization. Academic Press, New York 1975.
[68] *Yu. I. Yermakov, V. A. Zakharov* in [67a], p. 91.
[69] *A. D. Caunt* in *C. Kemball:* Catalysis. Spec. Per. Rep. Chem. Soc., London 1977. Vol. 1, p. 256.
[70] *P. J. T. Tait* in [31a], p. 85.
[71] *G. Fink,* Habilitationsschrift, Technische Universität München 1976.
[72] *G. Fink, R. Rottler, D. Schnell, W. Zoller,* J. Appl. Polym. Sci. *20*, 2779 (1976).
[73] *T. Keii:* Kinetics of Ziegler-Natta Polymerization. Chapman and Hall, London 1972.
[74] *T. Keii* in [67a], p. 263.
[75] *P. J. T. Tait* in [67a], p. 155.
[76] *V. A. Zakharov, Yu. I. Yermakov,* Catal. Rev. Sci. Eng. *19* (1), 67 (1979).
[76a] *J. Boor, Jr.:* Ziegler-Natta Catalysts and Polymerization. Academic Press, New York 1979.
[77] See [76a], p. 464.
[78] *B. Ranby, J. F. Rabek:* ESR Spectroscopy in Polymer Research. Springer, Berlin 1977, p. 167.
[79] *L. A. Yatsenko, A. G. Boldyrev, J. G. Zhuchikhina, E. N. Kropacheva,* Kinet. Kata.. *20*, 1353 (1979).
[80] *A. G. Evans, J. C. Evans, J. Mortimer,* J. Am. Chem. Soc. *101*, 3204 (1979).
[81] *A. G. Evans, J. C. Evans, D. J. C. Espley, P. H. Morgan, J. Mortimer,* J. Chem. Soc. Dalton Trans. 1 *1978*, 57.
[82] *A. G. Evans, J. C. Evans, E. H. Moon,* J. Chem. Soc. Dalton Trans. 2 *1974*, 2390.
[83] *Y. Girard, M. Che, A. Guyot, H. Chanzy,* Makromol. Chem. *162*, 119 (1972).
[84] *J. Okura, T. Keii,* Nippon Kagaku Kaishi 2, 250 (1973).
[85] *E. H. Adema,* J. Polym. Sci. *C 16*, 3643 (1968).
[86] *A. S. Khlystov, A. R. Brodski, N. F. Noskova, D. V. Sokol'skii,* J. Phys. (Orsay), Colloq. *C-1*, 343 (1980).
[87] *A. P. Brodski, N. F. Noskova, A. S. Khlystov, M. P. Grechko, D. V. Sokol'skii,* 13 Vses. Chugaev. Soveshch. Khim. Kompleks. Soedin. *78*, 57 (1978).
[88] *G. A. Nesterov, V. A. Zakharov, E. Paukstis, E. N. Yurchenko, Yu. I. Yermakov,* Kinet. Katal. *20*, 429 (1979).
[89] *D. D. Eley, D. A. Keir, R. Rudham,* J. Chem. Soc. Faraday Trans. 1 *72*, 1685 (1976).
[90] *K. A. Klinedinst, M. Boudart,* J. Catal. *28*, 322 (1973).
[91] *N. Rosch, K. H. Johnson,* J. Mol. Catal. *1*, 395 (1976).
[92] See [76a], Chapter 8, pp. 180—211.
[93] *P. Cossee,* J. Catal. *3*, 80 (1964).
[94] *E. J. Arlman,* J. Catal. *3*, 89 (1964).
[95] *E. J. Arlman, P. Cossee,* J. Catal. *3*, 99 (1964).
[96] *E. J. Arlman,* J. Catal. *5*, 178 (1966).
[97] *O. Novaro, E. Blaisten-Barojas, E. Clementi, G. Giunchi, M. E. Ruiz-Vizcaya,* J. Chem. Phys. *68*, 2337 (1978).
[98] *G. Giunchi, E. Clementi, M. E. Ruiz-Vizcaya, O. Novaro,* Chem. Phys. Lett. *49*, 8 (1977).
[99] *A. Allegra,* Makromol. Chem. *145*, 235 (1971).
[100] *P. Corradini, V. Barone, R. Fusco, G. Guerra,* Eur. Polym. J. *15*, 1133 (1979).
[101] *P. Cassoux, F. Crasnier, J. F. Labarre,* J. Organomet. Chem. *165*, 303 (1979).
[102] *D. R. Armstrong, P. G. Perkins, J. J. P. Stewart,* J. Chem. Soc. Dalton Trans. 1 *1972*, (1972).
[103] See [76a], Chapter 4, pp. 80—128.
[104] *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Academic Press, London 1975, Vol. 2, p. 1.
[105] *G. Paiaro,* Organomet. Chem. Rev. *A 6*, 319 (1970).
[106] *R. Lazzaroni, P. Salvadori, P. Pino,* J. Organomet. Chem. *43*, 233 (1972).
[107] *J. Lewis et al.,* J. Chem. Soc. *A 1969*, 53.
[108] *K. Ziegler, H. G. Gellert,* Justus Liebigs Ann. Chem. *567*, 195 (1950).
[109] *P. D. Bartlett, S. Friedman, M. Stiles,* J. Am. Chem. Soc. *75*, 1771 (1953).
[110] *L. Lardicci, P. Salvadori, P. Pino, L. Conti,* Atti Accad. Naz. Lincei *40* (Ser. 8), 601 (1966).
[111] *A. D. Jenkins,* Pure Appl. Chem. *51*, 1101 (1979).
[112] *K. Ziegler, H. G. Gellert, K. Zosel,* Angew. Chem. *64*, 330 (1952).
[113] *F. A. Braude,* Progr. In Org. Chem. 3, 185 (1955).
[113a] *B. Pullman:* Catalysis in Chemistry and Biochemistry. Theory and Experiment. D. Reidel, Dordrecht 1979.
[114] *P. Pino, A. Stefani, G. Consiglio* in [113a], pp. 347—354.
[115] *C. D. Nenitzescu, C. Huch, A. Huch,* Angew. Chem. *68*, 438 (1956).
[116] *H. N. Friedlander, K. Oita,* Abstr. Pap. 130th Meeting Am. Chem. Soc. 1956, p. 138.
[117] *A. V. Topchiev, B. A. Krentsel, L. G. Sidorova,* Dokl. Akad. Nauk SSSR *128*, 732 (1959).
[118] *E. W. Duck,* J. Polym. Sci. *34*, 86 (1959).
[119] *R. Van Helden, H. P. Braendlin, A. F. Bickel, E. C. Kooijam,* Tetrahedron Lett. *1959*, 24.
[120] *A. Gilchrist,* J. Polym. Sci. *34*, 49 (1959).
[121] *G. Natta, P. Pino, E. Mantica, F. Danusso, G. Mazzanti, M. Peraldo,* Chim. Ind. (Milano) *38*, 124 (1956).
[122] *K. J. Ivin, J. J. Rooney, C. D. Stewart, M. L. H. Green, R. Mahtab,* J. Chem. Soc. Chem. Commun. *1978*, 604.
[123] *G. Natta, M. Farina, M. Peraldo,* Atti Accad. Lincei Rend. *25* (Ser. 8), 424 (1958).
[124] *T. Miyazawa, Y. Ideguchi,* J. Polym. Sci. *B 1*, 389 (1963).
[125] *A. Zambelli, M. Giongo, G. Natta,* Makromol. Chem. *112*, 183 (1968).
[126] *G. Natta, G. Dall'Asta, G. Mazzanti, I. Pasquon, A. Valvassori, A. Zambelli,* J. Am. Chem. Soc. *83*, 3343 (1961).
[127] *O. Natta, P. Corradini, P. Ganis, J. W. Bassi, G. Allegra,* Chim. Ind. (Milano) *44*, 532 (1962).
[128] *U. Birkenstock, H. Bönnemann, B. Bogdanović, D. Walter, G. Wilke,* Adv. Chem. Ser. *70*, 250 (1968).
[129] *G. Henrici Olivé, S. Olivé,* Angew. Chem. *87*, 111 (1975); Angew. Chem. Int. Ed. Engl. *14*, 104 (1975).
[130] *T. Suzuki, Y. Takegami,* Bull. Chem. Soc. Jpn. *43*, 1484 (1970).
[131] *G. Natta, I. Pasquon, P. Corradini, M. Peraldo, M. Pegoraro, A. Zambelli,* Atti Accad. Lincei Rend. *28* (Ser. 8), 539 (1960).
[132] *P. Longi, A. Roggero,* Ann. Chimica (Roma) *51*, 1013 (1961).
[133] *G. Natta, I. Pasquon, A. Zambelli,* J. Am. Chem. Soc. *84*, 1488 (1962).
[134] *G. Natta, P. Pino, G. Mazzanti, P. Longi, F. Bernardini,* J. Am. Chem. Soc. *81*, 2561 (1959).
[135] *A. Zambelli, G. Natta, J. Pasquon,* J. Polym. Sci. Part *C 4*, 411 (1963).
[136] *A. Zambelli, C. Sacchi,* Makromol. Chem. *175*, 2213 (1974).
[137] *A. Zambelli, C. Tosi, C. Sacchi,* Macromolecules *5*, 649 (1972).
[138] *A. Zambelli, P. Locatelli, E. Rigamonti,* Macromolecules *12*, 156 (1979).
[139] *A. Zambelli, C. Wolfsgruber, G. Zannoni, F. A. Bovey,* Macromolecules *7*, 750 (1974).
[140] *P. Pino, F. Piacenti, M. Bianchi* in *I. Wender, P. Pino,* Organic Synthesis *via* Metal Carbonyls. Wiley, New York 1977, p. 124.
[141] *G. Natta,* J. Inorg. Nucl. Chem. *8*, 589 (1958).
[142] *A. Andresen, H. G. Cordes, J. Herwig, W. Kaminsky, A. Merck, R. Mottweiler, J. Pein, H. Sinn, H. Vollmer,* Angew. Chem. *88*, 689 (1976); Angew. Chem. Int. Ed. Engl. *15*, 630 (1976).
[143] *P. Pino, U. W. Suter, P. Neuenschwander,* unpublished results. We thank Prof. *Sinn* for the sample of amorphous polypropylene produced by soluble titanium catalysts.
[144] *P. Pino, A. Oschwald, F. Ciardelli, C. Carlini, E. Chiellini* in [67a], p. 25.
[145] *F. Ciardelli, P. Locatelli, M. Marchetti, A. Zambelli,* Makromol. Chem. *175*, 923 (1974).
[146] *A. Zambelli, G. Gatti, C. Sacchi, W. O. Crain, Jr., J. D. Roberts,* Macromolecules *4*, 475 (1971).
[147] *A. Zambelli, P. Locatelli, M. C. Sacchi, E. Rigamonti,* Macromolecules, in press.
[148] *C. Wolfsgruber, G. Zannoni, E. Rigamonti, A. Zambelli,* Makromol. Chem. *176*, 2765 (1975).
[149] *P. Pino, O. Piccolo, F. Francalanci,* unpublished results.
[150] *A. Zambelli, G. Bajo, E. Rigamonti,* Makromol. Chem. *179*, 1249 (1978).
[151] *H. B. Charman, E. D. Hughes, C. Ingold,* J. Chem. Soc. *1959*, 2530.
[152] *R. W. Johnson, R. G. Pearson,* Chem. Commun. *1970*, 986.
[153] *D. Dodd, M. D. Johnson,* Chem. Commun. *1971*, 571.
[154] *A. Zambelli, G. Allegra,* Macromolecules *13*, 42 (1980).
[155] *A. Zambelli, P. Locatelli, G. Zannoni, F. A. Bovey,* Macromolecules *11*, 923 (1978).
[156] *D. G. H. Ballard,* Catalysis Proc. Int. Int. Symp. Elsevier, Amsterdam 1975, p. 521.
[157] *W. L. Carrick,* J. Am. Chem. Soc. *80*, 6455 (1958).
[158] *T. W. Dolzine, J. P. Oliver,* J. Am. Chem. Soc. *96*, 1737 (1974).
[159] *D. B. Ludlum, A. W. Andersen, C. E. Ashby,* J. Am. Chem. Soc. *96*, 1737 (1974).
[160] *G. Natta,* Angew. Chem. *68*, 393 (1956).
[161] *G. Natta,* Experientia Suppl. *7*, 21 (1957).
[162] *D. C. H. Ballard, D. R. Burnham, D. L. Twose,* J. Catal. *44*, 116 (1976).

[163] *F. Danusso, D. Sianesi*, Chim. Ind. (Milano) *44*, 474 (1962).
[164] *M. H. Chisholm, W. S. Johns*, Inorg. Chem. *14*, 1189 (1975).
[165] *H. F. Klein, R. Hammer, J. Wenninger* in [113a], p. 285.
[166] *E. R. Evitt, R. G. Bergman*, J. Am. Chem. Soc. *101*, 3973 (1979).
[167] *E. A. Atteya*, Thesis No. 5806, ETH Zürich (1976).
[168] *P. Pino*, Adv. Polymer Sci. *4*, 393 (1965).
[169] See [76a], pp. 236—341.
[170] *P. Pino, G. P. Lorenzi* in [31a], p. 1.
[171] *D. G. H. Ballard*, Adv. Catal. *23*, 263 (1973).
[172] *W. L. Carrick, R. J. Turbett, F. J. Karol, G. L. Karapinka, A. S. Fox, R. N. Johnson*, J. Polym. Sci. *A-1*, *10*, 2609 (1972).
[173] *D. R. Armstrong, R. Fortune, P. G. Perkins*, J. Catal. *42*, 435 (1976).
[174] *A. Yamamoto, T. Yamamoto*, Macromol. Rev. *13*, 161 (1978).
[175] *P. Pino, G. Fochi, U. Giannini*, to be published.
[176] *P. Pino, G. Guastalla, U. Giannini*, to be published.
[177] *G. Natta, L. Porri, G. Zanini, L. Fiore*, Chim. Ind. (Milano) *41*, 526 (1959).
[178] *P. Patat, H. Sinn*, Angew. Chem. *70*, 496 (1958).
[179] *G. Henrici-Olivé, S. Olivé*, Angew. Chem. *79*, 764 (1967); Angew. Chem. Int. Ed. Engl. *6*, 790 (1967).
[180] *K. Ziegler*, Angew. Chem. *71*, 623 (1959).
[181] *P. Pino, F. Ciardelli, G. P. Lorenzi, G. Natta*, J. Am. Chem. Soc. *84*, 1487 (1962).

Trinuclear Clusters of the Early Transition Elements

By Achim Müller, Rainer Jostes, and F. Albert Cotton[*]

Trinuclear clusters of the early transition elements, *i. e.* those elements situated on the left-hand side of the transition series, represent the simplest types of clusters. They characteristically have a pronounced formation tendency and high stability; they are therefore produced under a wide variety of conditions and their triangular M_3 skeleton is conserved in ligand exchange reactions. These clusters play a very important role in the chemistry of the respective elements, and especially those of the 4 d and 5 d series. Biochemical implications are of interest in connection with Mo^{IV}. This progress report presents a systematic account of the chemistry and the molecular and electronic structure of such compounds. A connection is also established with the crystal field treatment of mononuclear metal complexes.

1. Introduction

The chemistry of Werner complexes of type ML_n (M = a transition metal atom of the 3d series, L = a simple donor ligand without π-acceptor properties) is known in detail[1a]. Their molecular and electronic structures as well as ligand replacement reactions become intelligible with the aid of ligand field theory and related approximations as well as more rigorous treatments[1b]. Significantly, however, the early 4d and 5d metals in their lower oxidation states have virtually no aqueous chemistry (*e.g.*, $[M(H_2O)_6]^{2+}$ ions) comparable with that of the 3d transition series. It has not yet been properly emphasized in the chemical literature that under a variety of reaction conditions the heavier early transition elements very readily form isolated trinuclear clusters to which a variety of non-π-bonding ligands may be attached. The formation tendency for these trinuclear species, which dominate in the case of the early transition elements with intermediate oxidation states, is clearly very great. Numerous ligand substitution reactions are feasible at the central M_3 entity and the electronic energy levels may be discussed using relatively simple approximations comparable with crystal field analysis for mononuclear complexes. The formation of polynuclear structures with M—M bonds, especially by molybdenum, may be of importance in biochemistry, particularly because of the ready formation of these clusters in simple aqueous media at normal temperatures.

In this article we shall discuss the chemistry, structures, and bonding of these compounds in a systematic way. From an understanding of the electronic structure it is possible to elucidate the reactions and properties of the compounds. In view of the intense contemporary interest in all aspects of metal atom cluster chemistry, it seems pertinent to devote attention to these trinuclear clusters which are among the simplest and most accessible representatives.

2. Electron-Poor Trinuclear Clusters and Other Types of Transition Metal Clusters

We distinguish two broad classes of transition metal cluster compounds: "electron-rich" clusters formed by metals to the right side of the d-block in the periodic table, in which the metal atoms in low oxidation states are combined with π-acceptor ligands, and "electron-poor" clusters formed by the early transition elements, in which the metals atoms are in higher oxidation states and combined with ligands that are simple electron donors. The bonding in electron-rich clusters has been discussed in considerable detail[2], although not on the basis of quantitative calculations. Available theoretical treatments of the electron-poor clusters vary considerably in rigor. For many of them, essentially qualitative, symmetry-based analyses have been given[3-5] and in a few cases, namely $[Re_3X_{9+n}]^{n-}$ (X = Cl, Br; $n = 0, 3$)[6] and $[Mo_6Cl_{14}]^{2-}$ [6a] SCF-Xα-SW calculations have been carried out and the results tested against photoelectron spectroscopic data and other experimental facts. In a forthcoming article[7] the consist-

[*] Prof. Dr. A. Müller [+], Dipl.-Chem. R. Jostes
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld (Germany)
Prof. Dr. F. A. Cotton [+]
Department of Chemistry, Texas A & M University
College Station, Tex. 77843 (USA)
[+] To whom correspondence should be addressed.

ency of the simple and the more rigorous calculations will be discussed. For the clusters with which we are concerned in this article, however, no comprehensive work at any level of rigor has been published. An attempt to understand and calculate the electronic properties of some of these clusters using the Fenske-Hall method will be described elsewhere[8]. In this article we shall employ a more qualitative treatment, along the lines of the Cotton-Haas method[3], and treat all of the trinuclear electron-poor cluster compounds.

The term "electron-poor cluster" designates those clusters in which the number of metal-atom valence electrons is approximately equal to the number required to form single bonds between the adjacent pairs of metal atoms. For trinuclear clusters, this means a total of from five to eight electrons in the metal system, at least in a formal sense. In a simple, purely formal, shorthand, we may represent the M_3 system and the number of electrons, n, formally assigned to it as $\{M_3\}^n$. Clusters of this type are formed by the metals Ti, Zr, Nb, Ta, Mo, and W. The usual upper limit of $n=8$ for the number of electrons ($\{Mo_3\}^9$ cases are known but are rare) is significant because the next higher number of d-electrons in trinuclear clusters is 12 (as in Re_3X_9 and related species); in this case there is a clearly different electronic structure involving double bonds[6].

3. Preparation and Reactions of Cluster Compounds

Trinuclear clusters of the heavier early transition elements can be prepared by an *exceptionally varied range of reaction types*. Indeed, this characteristic in itself adds considerably to their significance for the chemistry of these elements.

In the case of *solid state structures*, stoichiometric amounts of the starting materials are usually caused to react at high temperatures. The following reaction types have been reported:

1) *Interaction of reactants containing the metals in the oxidation states required in the products:*

$$MoO_2 + M'O \rightarrow M'_2Mo_3O_8 \quad (M' = Mg,\ Mn,\ Fe,\ Co,\ Ni,\ Zn,\ Cd)^{[9,10]} \qquad (1)$$

2) *Comproportionation reactions:*

$$NbBr_5 + Nb \rightarrow Nb_3Br_8{}^{[11]} \qquad (2)$$

3) *Redox reactions:*

$$MoCl_3 + S_8 \rightarrow Mo_3S_7Cl_4{}^{[12]} \qquad (3)$$

Methods for preparing clusters *in solution* are of the following main types:

1) *Reactions of a compound whose metal is in the same oxidation state as the product:*

$$Mo^{IV}_{aq} + C_2O_4^{2-} \rightarrow [Mo^{IV}_3O_4(C_2O_4)_3(H_2O)_3]^{2-}{}^{[13]} \qquad (4)$$

2) *Solvolysis and oxidation of metal compounds in lower oxidation states:*

a) *Mononuclear reactants:*

$$W(CO)_6 + HOAc \rightarrow [W_3O_2(Oac)_6(H_2O)_3]^{2+}{}^{[14]} \qquad (5a)$$

b) *Binuclear reactants:*

$$W_2Cl_4(PnBu_3)_4 + HOAc \rightarrow [W_3O_3Cl_5(Oac)(PnBu_3)_3]^{[15]} \qquad (5b)$$

3) *Solvolysis and reduction of metal compounds in higher oxidation states:*

$$MoO_4^{2-} + S_x^{2-} \rightarrow [Mo_3S_{13}]^{2-}{}^{[16]} \qquad (6)$$

4) *Disproportionation reactions ($2M^V \rightarrow M^{IV} + M^{VI}$):*

$$(NH_4)_3[W_2O_4(C_2O_4)_{2.5}]\cdot 3H_2O + HF \rightarrow [W_3O_4F_9]^{5-}{}^{[17]} \qquad (7)$$

In addition, one may begin with a trinuclear cluster compound and carry out a ligand exchange reaction which preserves only the central M_3 unit or a redox reaction which preserves the central ligand sphere as well. An important example of a ligand exchange reaction is the following reversible process:

$$[Mo_3S_{13}]^{2-} \underset{S_x^{2-}}{\overset{+CN^-\ (-NCS^-)}{\rightleftharpoons}} [Mo_3S_4(CN)_9]^{5-}{}^{[18]} \qquad (8)$$

which may perhaps be a model reaction for the inhibition of xanthine oxidase by CN^-[19]. Neutral sulfur is transferred from the Mo—(S_2)—Mo bridges to CN^-, while the formal oxidation state of molybdenum is maintained (atom-transfer reaction from the activated S_2^{2-} ligand). Another noteworthy ligand exchange reaction allows the preparation of $[Mo_3S_{13}]^{2-}$ from $[Mo_3S_7Cl_4]$[12]:

$$Mo_3S_7Cl_4 \xrightarrow{+S_x^{2-}} [Mo_3S_{13}]^{2-}{}^{[20]} \qquad (9)$$

It should also be noted that molybdenum disulfur compounds with metal-metal bonds can undergo reductive elimination of S_2. This has been shown for $Cs_2[Mo_2(S_2)_6]$[21,22] which decomposes at relatively *low temperatures* accompanied by generation of S_2. The thermal decomposition of $(NH_4)_2[Mo_3S_{13}]\cdot nH_2O$ ($n=0$—2) leads to MoS_2, perhaps with coordinatively unsaturated trinuclear clusters as intermediates, without a change in the oxidation state of the metal[23] (the non-stoichiometric crystal water is lost at 50 °C).

On the basis of their electronic structures (see Section 5) it is to be expected that several clusters should undergo reversible redox reactions, as is clear, for example, from the existence of both $[Mo_3S_4Cp_3]^+$[24] and $[Mo_3S_4Cp_3]$[25]. The hexamethylbenzene derivatives of niobium and tantalum $[M_3X_6(C_6Me_6)_3]^+$ also show reversible redox reactions[26]; the oxidized, dipositive species is very reactive, but it can be isolated by crystallization with an oxidizing anion[27]. In solution, however, it dimerizes to form an octahedral cluster[26].

The variety of preparative methods shows that the trinuclear clusters are readily formed, and therefore play an important role in the chemistry of Nb, Mo, and W. This is especially evident from the ease with which they are formed from metal carbonyls, $Mo(CO)_6$ and $W(CO)_6$, by the action of organic acids [example (5a)][14,15], by reaction of MoO_4^{2-} with S_x^{2-} in H_2O [example (6)][16], or by reaction of $[Mo_3S_{13}]^{2-}$ with a large excess of CN^- [example (8)][18] (with retention of the central Mo_3S_4 unit!). The facile formation of $[Mo_3S_{13}]^{2-}$ under various conditions is a synergic effect of

the formation tendency of trinuclear Mo^{IV} clusters and the properties of S_2^{2-} ligands, which favor high coordination numbers and are suitable for stabilizing metal clusters by an optimum shielding[22]. $(NH_4)_2[Mo_3S_{13}]\cdot n\,H_2O$ ($n=0$—2) is even obtained *in nearly quantitative yield* by heating an aqueous solution containing MoO_4^{2-} saturated with $(NH_4)_2S_x$[16c]. Notable in this connection is also the formation of the cluster anion $[W_3O_4F_9]^{5-}$[17] through disproportionation of a W^V compound [example] (7)].

The species $[Mo_3O_4(C_2O_4)_3(H_2O)_3]^{2-}$[13] shown in example (4) demonstrates the tendency of Mo^{IV} in aqueous solution to form Mo_3 clusters in the presence of simple donor ligands. The extensive work of *Souchay, Lamache,* and coworkers and our own results[28] indicate that both hydrochloric acid and sulfuric acid solutions containing ≥ 3.5 M Mo^{IV} contain Mo_3 clusters (cf. also[57]). This is most clearly suggested by polarographic measurements, which show that Mo^{IV}_{aq} is reduced to Mo^{III} in two stages: reversible reduction by 2/3 electron per Mo precedes irreversible reduction by 1/3 electron per MO[28].

Our studies of the electronic structures of trinuclear clusters (see Section 5), especially those containing $[Mo_3O_4]$ central units, account for their stability in water in both the $\{Mo_3\}^6$ and $\{Mo_3\}^8$ configurations, namely, with both 2 and $2\frac{2}{3}$ electrons per Mo atom. The polarographic data are therefore to be understood in terms of the first, reversible reduction process taking the cluster from an $\{Mo_3\}^6$ configuration to an $\{Mo_3\}^8$ configuration, whereupon further reduction leads irreversibly to destruction of the cluster with formation of $[MoCl_6]^{3-}$. A trinuclear cluster structure for Mo^{IV}_{aq} cannot be excluded by EXAFS data[29]; however, a dinuclear complex was preferred. The first isolation of a crystalline substance, *viz.* $(NH_4)_5[Mo_3O_4F_9]\cdot NH_4F\cdot H_2O$[57], from mineral acid solution without addition of an additional complexing agent also suggests the presence of three-membered species.

Table 1 lists the known compounds together with their structural, optical, and magnetic properties, as well as a notation of the formal number of metal cluster electrons.

4. Complex Structures

For the trinuclear clusters under consideration there are three basic structures: without any μ_3-ligand, with one μ_3-ligand, and with two μ_3-ligands. These three structure types will henceforth be designated A, B, and C, respectively. Type B can assume two forms (B_1 and B_2), as will be seen.

Structure type A

This structure type, $[M_3X_6(C_6Me_6)_3]^{n+}$ with M = Ti, Zr, Nb, Ta and X = Cl, Br is depicted in Figure 1. The best-known representative of this type is $[Nb_3Cl_6(C_6Me_6)_3]^+$[26]. Each metal atom is coordinated in an approximately square-planar fashion with an additional η^6-C_6Me_6 ligand parallel to this plane.

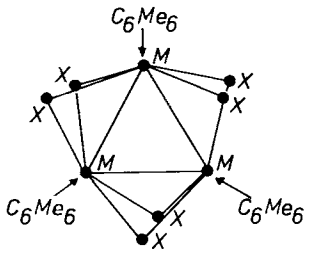


Fig. 1. Structure of clusters of formula $[M_3X_6(C_6Me_6)_3]$ (type A).

Table 1. Cluster compounds and their properties.

Compound	Structure type	Metal-metal distance [Å]	Number of electrons $\{M_3\}^n$	Electronic transitions [a] Color	Magnetism	Ref.
Ti_7Cl_{16}	B_1	2.954	6	black		[47] [b]
Nb_3Cl_8	B_1	2.81	7	6, 10, 15 [c]	$\mu_{eff}=1.86$	[48]
Nb_3Br_8	B_1	2.88	7	6, 9, 11 [c]	$\mu_{eff}=1.95$	[11]
Nb_3I_8	B_1	3.00	7	black	$\mu_{eff}=1.3$	[11]
$[Nb_3Cl_6(C_6Me_6)_3]^+$	A	3.334	8	23.8, 29.5, green [d]	diam.	[26, 30, 49]
$[Nb_3Br_6(C_6Me_6)_3]^+$	A		8	22.1, 26.5, brown [d]	diam.	[26, 30]
$[Nb_3Cl_6(C_6Me_6)_3]^{2+}$	A	3.335	7	purple [e]	ESR: $\bar{g}=1.996$	[27]
$[Ta_3Cl_6(C_6Me_6)_3]^+$	A		8	27.4, 34.7, brown-violet [d]	diam.	[26, 30]
$[Mo_3O_4F_9]^{5}$	B_1	2.502	6	19	diam.	[57]
$[Mo_3S_{13}]^{2-}$	B_2	2.722	6	18.5 (11) 21.5 (36) [f]	diam.	[16, 50]
$Zn_2Mo_3O_8$ [g]	B_1	2.524	6	black	$\mu_{eff}=0.34$	[9, 10]
$[Mo_3S_4Cp_3]^+$	B_1	2.812	6	dark green	diam.	[24]
$Mo_3S_4Cp_3$	B_1		7	black		[25]
$Mo_3S_7Cl_4$	B_2	2.745	6	red		[12]
$[Mo(Oac)_6(OEt)_2(H_2O)_3]^{2+}$	C	2.854	8	17 (3), 22 (3), 26 (3)		[51]
$[Mo_3O_4(C_2O_4)_3(H_2O)_3]^{2-}$	B_1	2.486	6	19 (3), 28 (7)		[13]
$[Mo_3O_4(acac)_3(EtO)_3]$	B_1	2.47	6	brown	diam.	[52, 53]
$[Mo_3OCl_3(Oac)_3(H_2O)_3]^{2+}$	B_1	2.550	8	dark blue		[54]
$[Mo_3S_4(CN)_9]^{5-}$	B_1	2.766	6	16.3 (5) [h]	diam.	[18]
$[W_3O_2(Oac)_6(H_2O)_3]^{2+}$	C	2.747	6	yellow		[14]
$[W_3O_2(O_2CEt)_6(H_2O)_3]^{2+}$	C	2.745	6			[14]
$[W_3O_2(O_2CCMe_3)_6(O_2CCMe_3)_2(H_2O)]$	C	2.76	6	yellow		[14]
$[W_3O_2(Oac)_6(Oac)_3]^-$	C	2.769	6	yellow		[14]
$[W_3O_4F_9]^{5-}$	B_1	2.514	6	dark red	diam.	[17]
$[W_3(OCH_2CMe_3)O_3Cr_3(O_2CCMe_3)_{12}]$	B_1	2.610	8	dark green [i]	W_3-unit diam.	[55]
$Zn_2W_3O_8$	B_1		6		$\mu_{eff}=0.35$	[38]
$[W_3O_3Cl(Oac)Cl_4(PBu_3)_3]$	B_1	2.609	6	red	diam.	[15]

[a] 10^3 cm^{-1}; ε values [10^2 l mol^{-1} cm^{-1}] in parentheses. [b] *H. Schäfer*, personal communication. [c] Electronic absorption spectrum: see [37]. [d] The color can only be explained by additional absorption bands not reported in ref. [26]. [e] The color may be due to the anion $(TCNQ)_2^{2-}$. [f] Electronic absorption spectrum: see [39]. [g] $Zn_2Mo_3O_8$ is the best characterized example of this type of compound; $M_2Mo_3O_8$ with M = Mg, Mn, Fe, Co, Ni, Zn, Cd [9]. [h] Electronic absorption spectrum: *A. Müller* and *U. Reinsch*, unpublished. [i] The color may be due to the Cr^{3+} chromophore in the compound.

There has so far been no information bearing on the structure and bonding of the known titanium and zirconium compounds of this type[30] and they are not, therefore, included in Table 1.

Structure type B

Structure type B_1 is depicted in Figure 2. It occurs with clusters $[M_3(\mu_3\text{-}X)(\mu_2\text{-}Y)_3L_9]$ having M = Ti, Nb, Mo, and W. Possible ligands are: X = Cl, Br, I, O, OCH_2CMe_3, S; Y = Cl, Br, I, O, S; L = F, Cl, Br, I, O, H_2O, OEt, O_2CCMe_3, CN, 1/3 Cp, 1/2 C_2O_4, 1/2 acac, 1/2 Oac, PBu_3[*].

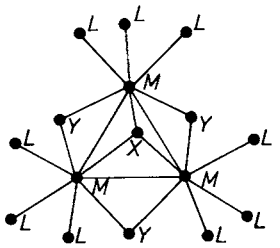


Fig. 2. Structure of clusters of formula $[M_3(\mu_3\text{-}X)(\mu_2\text{-}Y)L_9]$ (type B_1).

The coordination shell of each metal atom is a more-or-less distorted octahedron (MXY_2L_3 unit) as shown in Figure 3. A characteristic feature of the central unit $[M_3(\mu_3\text{-}X)(\mu_2\text{-}Y)_3]$ is that it can be regarded as an incomplete cube. A simple cluster of this kind, $[Mo_3S_4(CN)_9]^{5-}$ [18], is seen in Figure 4.

There is only one isolated cluster of type B that does not correspond to the general formula $[M_3(\mu_3\text{-}X)(\mu_2\text{-}Y)_3L_9]$,

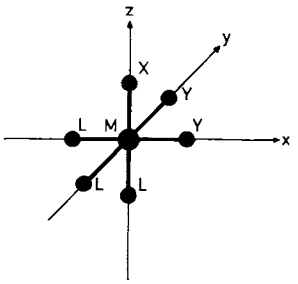


Fig. 3. Coordination and local coordination system of an isolated MXY_2L_3 unit.

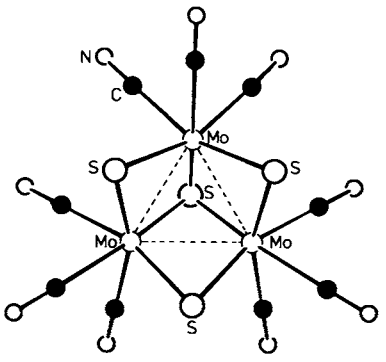


Fig. 4. Structure of $[Mo_3S_4(CN)_9]^{5-}$.

namely $[Mo_3S_{13}]^{2-}$, which has the central unit $[Mo_3(\mu_3\text{-}S)(\mu_2\text{-}S_2)_3]^{4+}$ and the structure presented in Figure 5. The

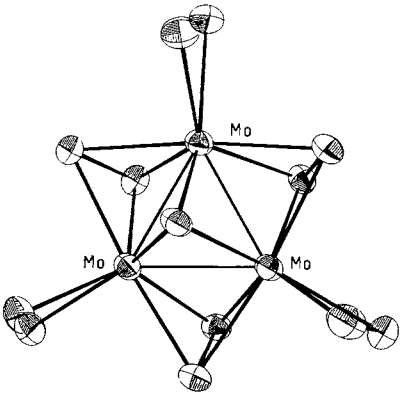


Fig. 5. Structure of $[Mo_3S_{13}]^{2-}$ (type B_2; ORTEP plot).

central unit just mentioned occurs also in a solid state structure[12]. If we neglect the M—M bonds, each molybdenum atom has a coordination number of seven. The shape of the coordination shell can be derived from the D_{2d} structure of $[Cr(O_2)_4]^{3-}$ [31] or $[Mo(O_2)_4]^{2-}$ [32], which is formed by two mutually perpendicular $M(O_2)_2$ units. The Mo atoms of the two different species of $[Mo_2(S_2)_6]^{2-}$ [33] found in the asymmetric unit of the crystal structure have nearly the same local symmetry, too (see Fig. 6).

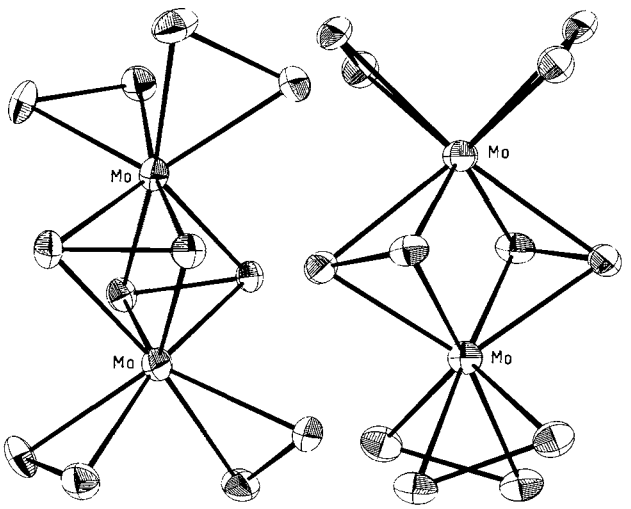
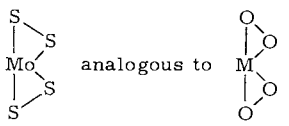


Fig. 6. Structure of the two independent anions $[Mo_2S_{12}]^{2-}$ in the asymmetric unit of the unit cell (ORTEP plot).

In $[Mo_3S_{13}]^{2-}$ we find a nearly planar unit



(with bridging S_2 groups) and, perpendicular to this, the planar unit



[*] When L = Cl, Br, I, or O, the ligands can form intermolecular bridges; when L = 1/2 C_2O_4, 1/2 acac or 1/2 Oac they form intramolecular bridges; L = CN or 1/3 Cp only for X = Y = S.

The occurrence of planar $M(X_2)_2$ units is fairly common with compounds having side-on bonded, diatomic ligands[34] (*e.g.* in $[Mo_4(NO)_4S_3(S_2)_5]^{4-}$[16c,35]). It should be noted that $[Cr^V(O_2)_4]^{3-}$ does exist as a monomeric complex, while a hypothetical $[Mo^V(S_2)_4]^{3-}$ (also with d^1 configuration) "dimerizes" under formation of $[Mo_2(S_2)_6]^{2-}$ with metal-metal bonds and sharing two S_2^{2-} ligands.

Structure type C

$[M_3(\mu_3\text{-}X)_2(\mu_2\text{-}O_2Y)_6L_3]$ clusters having the structure depicted in Figure 7 are known for the metals Mo and W[36]. Possible ligands are X = O, OEt; O_2Y = bridging bidentate ligands such as $MeCO_2$, $EtCO_2$, $tBuCO_2$; L = H_2O, $MeCO_2$, $tBuCO_2$.

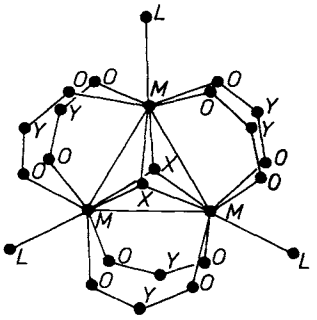


Fig. 7. Structure of clusters of formula $[M_3(\mu_3\text{-}X)_2(O_2Y)_6L_3]$ (type C).

The seven-fold coordination (*i.e.* neglecting M—M bonds) of each metal atom corresponds to that in the TaF_7^{2-} structure, namely, a capped trigonal prism (CTP) with C_{2v} symmetry, as shown in Figure 8.

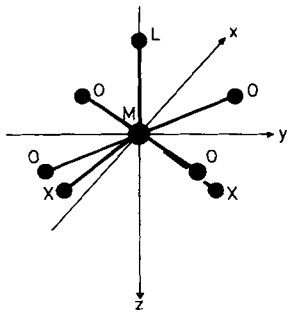


Fig. 8. Coordination and local coordination system of an isolated $MX_2(O_2Y)_4L$ unit.

5. Electronic Structures and Properties

Simplified MO calculations have been carried out for the observed structure types using a method much like that of *Cotton* and *Haas*[3] (see Section 8 for details). It can be shown (see ref.[8] for the full discussion) that this very simple method gives a satisfactory *qualitative* model for the bonding and explains most of the properties. Aside from the compounds $[Mo_3S_4Cp_3]^+$ and $[Mo_3S_4(CN)_9]^{5-}$ all the clusters of structure types B_1, B_2, and C are coordinated by ligands of the simple donor type. Ligands that are inherently capable of π-bonding (—O—, —S—, *etc.*) are, as a rule, in inter- or intramolecular bridging positions so that metal-ligand π-bonding may be neglected. This approximation makes it possible to subdivide the MOs into those which are responsible for metal-ligand bonding and those accounting for metal-metal bonding. With the compounds of structure type A such a subdivision is not possible because of the hexamethylbenzene ligands and therefore only compounds of structure types B_1, B_2, and C will be considered further. We may assume, however, that for clusters of structure type A the highest filled orbital has predominantly metal character; for $[Nb_3Cl_6(C_6Me_6)_3]^{2+}$ this is supported by the ESR spectrum[27].

Structure type B_1

A simplified description of the electronic structure of an MXY_2L_3 fragment as an octahedral complex shows that both the HOMO and the LUMO possess essentially metal d-character (corresponding to a crystal field splitting of the d orbitals into lower lying t_{2g} and higher lying e_g orbitals). While the e_g orbitals are directed towards the ligand atom centers the t_{2g} orbitals can interact only with the ligand π orbitals and if we neglect π bonding the t_{2g} orbitals may be regarded as pure metal orbitals. The three t_{2g} AOs (d_{xy}, d_{yz}, d_{xz}) on each metal atom can be combined within the symmetry (C_{3v}) of the entire molecule into the following symmetry-adapted MOs:

$1a_1$: $1/\sqrt{6}(d^1_{xz}+d^2_{xz}+d^3_{xz}+d^1_{yz}+d^2_{yz}+d^3_{yz})$
$2a_1$: $1/\sqrt{3}(d^1_{xy}+d^2_{xy}+d^3_{xy})$
a_2: $1/\sqrt{6}(d^1_{yz}+d^2_{yz}+d^3_{yz}-d^1_{xz}-d^2_{xz}-d^3_{xz})$
1e: $1/\sqrt{6}(2d^1_{xz}-d^2_{xz}-d^3_{xz})$; $1/\sqrt{2}(d^2_{xz}-d^3_{xz})$
2e: $1/\sqrt{6}(2d^1_{yz}-d^2_{yz}-d^3_{yz})$; $1/\sqrt{2}(d^2_{yz}-d^3_{yz})$
3e: $1/\sqrt{6}(2d^1_{xy}-d^2_{xy}-d^3_{xy})$; $1/\sqrt{2}(d^2_{xy}-d^3_{xy})$

Calculations of the orbital energies yield the MO scheme with three bonding MOs and one weakly bonding or nonbonding MO (Fig. 9).

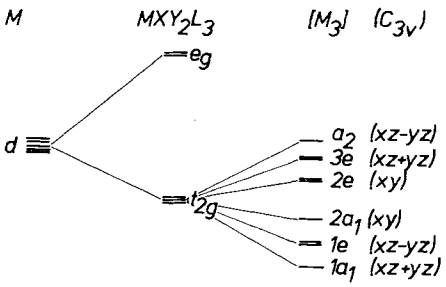


Fig. 9. MO scheme for the M_3 system of type B_1.

From the MO scheme it is understandable that clusters of structure type B_1 may exist with six, seven, or eight electrons in the metal system and that only those with seven electrons should be paramagnetic (with one unpaired electron). The estimated orbital energies suggest that electronic transitions within the metal system may cause absorption bands in the visible region. Such transitions are symmetry allowed and should, therefore, have higher intensities than the d-d transition of mononuclear species. Ligand→metal and metal→ligand charge transfer transitions are expected only at higher energies for the ligands that have been observed. In fact, clusters of structure type B_1, with six electrons, $\{M_3\}^6$, are red. For example, $[Mo_3O_4(C_2O_4)_3(H_2O)_3]^{2-}$ absorbs at 520 nm ($\varepsilon = 320$). On the other hand $[Mo_3OCl_3(Oac)_3(H_2O)_3]^{2+}$ with a $\{Mo_3\}^8$ configuration is blue. The observed colors

suggest the assignments $1e \rightarrow 2e$ for the transition causing the red color and $2a_1 \rightarrow 2e$ for that of the blue compound.

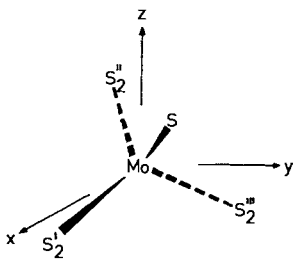
The existence of a low-lying unfilled metal cluster orbital in the $\{M_3\}^6$ cases is also indicated by the electronic absorption spectra of Nb_3Cl_8 and Nb_3Br_8 which show several bands in the near infrared and visible regions[37], by the black color of $Zn_2Mo_3O_8$[9], and by the weak paramagnetism of $Zn_2Mo_3O_8$[9,38] and $Zn_2W_3O_8$[38]. Because of the existence of six, seven, and eight-electron configurations, some degree of reversible redox behavior is to be expected for these compounds.

The observed increase in bond lengths on going from the $\{M_3\}^6$ to the $\{M_3\}^8$ configuration can be attributed mainly to ligand effects (see Section 6) and does not directly imply that the $2a_1$ orbital has antibonding character.

A description of the electronic structures of the compounds with strong ligands ($[Mo_3S_4Cp_3]^+$, $[Mo_3S_4(CN)_9]^{5-}$) using a simplified model of the isolated metal atom cluster is unlikely to be satisfactory for the same reason that a crystal field theory description of a mononuclear complex containing strong ligands is unsatisfactory. In both cases the strong π-bonding is too important to neglect. Because of appreciable delocalization of electron density out of the metal system and into π^* orbitals of the ligands there is a large increase (*ca.* 0.3 Å) in the metal-metal distances (see Table 1). The weaker metal-metal interaction leads to a red shift in the transitions of the metal system.

Structure type B_2

In the case of $[Mo_3S_{13}]^{2-}$ the coordination of each Mo atom can be regarded as a pseudotetrahedral arrangement of three S_2 groups and one S atom. (See also the detailed discussion of the molecular and electronic structure of $[Mo_3S_{13}]^{2-}$[39].) This pseudotetrahedral coordination implies that there should be a close similarity of the metal-ligand bonding to that in the tetrahedral MX_4^{n-} ions[40], such that the p_σ and p_π ligand orbitals of the MX_4^{n-} ion correspond to the π and π^* orbitals of the S_2^{2-} groups (see Fig. 10). On this basis there should be a splitting of the metal d orbitals,



S'_2—Mo—S''_2 103.05° S—Mo—S'_2 97.87°
S'_2—Mo—S'''_2 136.70° S—Mo—S''_2 120.05°
S''_2—Mo—S'''_2 103.05° S—Mo—S'''_2 97.82°

Fig. 10. Local coordination system of an individual $MoS(S_2)_3$ unit.

corresponding to that in a crystal field, into low-lying e and higher lying t_2 orbitals. The t_2 orbitals then point directly at the ligands, while the two e orbitals (d_{z^2} and $d_{x^2-y^2}$) on each metal center can be combined in accord with the C_{3v} symmetry of the whole molecule to give the following MOs:

a_1: $1/\sqrt{3}(d^1_{z^2} + d^2_{z^2} + d^3_{z^2})$
a_2: $1/\sqrt{3}(d^1_{x^2-y^2} + d^2_{x^2-y^2} + d^3_{x^2-y^2})$
1e: $1/\sqrt{6}(2d^1_{x^2-y^2} - d^2_{x^2-y^2} - d^3_{x^2-y^2})$; $1/\sqrt{2}(d^2_{x^2-y^2} - d^3_{x^2-y^2})$
2e: $1/\sqrt{6}(2d^1_{z^2} - d^2_{z^2} - d^3_{z^2})$; $1/\sqrt{2}(d^2_{z^2} - d^3_{z^2})$

A calculation of the orbital energies gives the MO scheme shown in Figure 11. Both clusters of structure type B_2 (cf. Table 1) have six electrons and these fill the bonding orbitals to give the configuration $1e^4a_1^2$. In this way the diamagnetism and the presence of Mo—Mo single bonds, as indicated by the vibrational spectrum and the interatomic distance, in $[Mo_3S_{13}]^{2-}$ are explained. The compound has been investigated by XPS, by means of which the oxidation state of the metal in this anion has been shown to be +4 (Mo $3d_{5/2}$: 230.1 eV). The Raman spectrum shows an intense line at 197 cm^{-1}, which has been assigned to a vibration with the character ν_s(Mo—Mo) + ν(Mo—S) by using ^{92}Mo and ^{100}Mo isotope substitution. The cyclic voltammogram shows two irreversible reduction waves, suggesting that the LUMO has antibonding character[39].

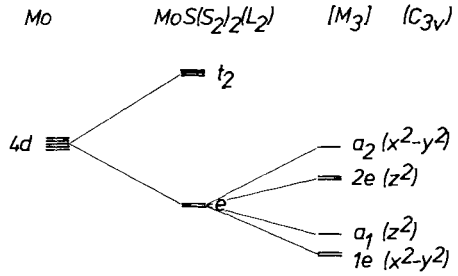


Fig. 11. MO scheme for the M_3 system of type B_2.

Explicit statements concerning the electronic structures of the type B_2 clusters are facilitated by the structural similarity between a Mo atom in $[Mo_3S_{13}]^{2-}$ and that of the Cr atom in $[Cr(O_2)_4]^{3-}$. According to an *ab initio* calculation[41] the highest (half) filled orbital of the latter ion is a nearly pure metal d orbital whose spatial orientation corresponds closely to that of a $d_{x^2-y^2}$ orbital. An orbital of this type on each of the three metal atoms in $[Mo_3S_{13}]^{2-}$ can be used to form bonding and antibonding MOs of 1e and a_2 types, respectively. The omission of one sulfur atom from a planar $Mo(S_2)_2$ fragment to leave a planar $MoS(S_2)$ unit makes another orbital of predominantly metal character available for metal-metal bonding. It is directed toward the center of the Mo_3 triangle and the three such orbitals can be combined to form a bonding a_1 MO and an antibonding 2e MO.

Structure type C

The local symmetry of one "triangular apex" ($MX_2(OY)_4L$) (cf. Fig. 7) is C_{2v}. Because of this low symmetry, a description of the electronic structure of such a cluster fragment is more difficult than for an octahedral one. According to a qualitative MO calculation[42], the CTP structure with C_{2v} symmetry has the d orbitals split into three higher-lying (but not, of course, degenerate) orbitals, $a_2(d_{xy})$, $a_1(d_{z^2})$, and $b_1(d_{xz})$, and two lower-lying orbitals, $b_2(d_{yz})$ and $a_1(d_{x^2-y^2})$. Within each group the energy ordering depends on the type of ligands and on the exact geometry. For a clus-

ter of structure type C the a_1 orbitals interact more strongly than the b_2 orbitals with the bridging O_2Y ligands and should therefore be higher in energy.

The d orbitals that should be most important for the metal-metal interactions can be combined under the restrictions of D_{3h} symmetry to form the following MOs:

d_{yz} a_2': $1/\sqrt{3}(d^1_{yz}+d^2_{yz}+d^3_{yz})$
$1e'$: $1/\sqrt{6}(2d^1_{yz}-d^2_{yz}-d^3_{yz})$; $1/\sqrt{2}(d^2_{yz}-d^3_{yz})$

$d_{x^2-y^2}$ a_1': $1/\sqrt{3}(d^1_{x^2-y^2}+d^2_{x^2-y^2}+d^3_{x^2-y^2})$
$2e'$: $1/\sqrt{6}(2d^1_{x^2-y^2}-d^2_{x^2-y^2}-d^3_{x^2-y^2})$; $1/\sqrt{2}(d^2_{x^2-y^2}-d^3_{x^2-y^2})$

The MO scheme for the entire metal cluster cannot be derived entirely unambiguously in this way because this would require a knowledge of the energy difference between the d_{yz} and $d_{x^2-y^2}$ atomic orbitals. Nevertheless, it is clear that the $1e'$ molecular orbital is the most strongly bonding and the $2e'$ molecular orbital is the most strongly antibonding. It is then understandable that six-electron systems (configuration $1e'^4a_1'^2$ or $1e'^4a_2'^2$) as well as eight-electron systems (configuration $1e'^4a_1'^2a_2'^2$) are both known. Clusters having either of these electron configurations should thus be diamagnetic.

While the electronic transition $a_1' \rightarrow a_2'$ is symmetry forbidden, the $a_1' \rightarrow 2e'$ and $a_2' \rightarrow 2e'$ transitions are symmetry allowed. This can explain why the compounds with $\{Mo_3\}^6$ configurations are yellow while those with $\{Mo_3\}^8$ configurations are red. For the $1e'^4a_1'^2a_2'^2$ configuration the HOMO is antibonding and in this way the longer metal-metal bonds in $[Mo_3(Oac)_6(OEt)_2(H_2O)_3]^{2+}$ compared to $[W_3O_2(O_2CR)_6L_3]$ may be understood.

6. Metal-Metal Distances

The metal-metal distances in the trinuclear clusters depend on the electron configurations $\{M_3\}^n$, on the coordination numbers, and definitely also on the type of ligands present. For instance, comparison of the Mo_3 and W_3 clusters with six-electron configurations and simple donor ligands (Table 2) reveals an increase of *ca.* 0.25 Å in the metal-metal bond lengths on going from those with coordination number 6 (average bond length 2.50 Å) to those with coordination number 7 (average bond length 2.75 Å). This can be attributed to the availability of more MOs with bonding character in the case of coordination number 6; in addition, somewhat better overlap makes the bonding orbitals somewhat lower in energy. The average bond lengths for similar Mo and W systems are very similar.

Table 2. Metal-metal bond lengths [Å] for the $\{M_3\}^6$ configuration—influence of the coordination number.

Coordination number	6	7
Mo	2.47—2.524	2.722–2.745
W	2.514—2.609	2.745—2.769

The influence of the electron configuration of the M_3 system can be seen by comparing the Mo_3 and W_3 clusters with coordination number 6 (Table 3). A change from the $\{M_3\}^6$ to the $\{M_3\}^8$ configuration appears to cause a slight increase, of about 0.05—0.10 Å, in the metal-metal distance. However, one must also be mindful of the fact that the ligands also influence the bond lengths. Thus, the Cl bridges in $[Mo_3OCl_3(Oac)_3(H_2O)_3]^{2+}$ apparently favor longer Mo—Mo distances than those in O-bridged systems. Similarly, in tungsten clusters of structure type B_1 a μ_3-O cap has a bond shortening effect as compared to a μ_3-OCH_2CH_3 cap. An extremely pronounced ligand effect on metal-metal bond lengths is seen along the series Nb_3Cl_8, Nb_3Br_8, Nb_3I_8.

Table 3. Metal-metal bond lengths [Å] for coordination number 6—influence of the electron configuration.

Electron configuration	$\{M_3\}^6$	$\{M_3\}^8$
Mo	2.47—2.524	2.550
W	2.514—2.609	2.610

Strong ligands exercise a very marked influence on the metal-metal bond lengths. While the typical bond lengths for B_1 type clusters with $\{M_3\}^6$ configurations are about 2.5 Å, the $[Mo_3S_4Cp_3]^+$ and $[Mo_3S_4(CN)_9]^{5-}$ clusters have bond lengths of around 2.8 Å (*i.e.* some 0.3 Å greater).

7. Summary and Outlook

In the presence of weak ligands without π-bonding properties the early transition elements—especially metals of the 4d- and 5d series in their middle oxidation states—form clusters. Frequently a d^n configuration leads to the formation of a dumbbell ($n=1$), triangle ($n=2$), tetrahedron ($n=3$), or octahedron ($n=4$)[16b].

As a group, the trinuclear clusters discussed in this article are distinguished by an exceptionally high formation tendency and high stability, so that they arise under very diverse conditions an preserve their integrity through various ligand-exchange reactions. These clusters are therefore of special significance for the chemistry of such transition elements in their middle oxidation states. For Mo^{IV} and W^{IV} the trinuclear clusters appear to be the most stable species in solution in the presence of non-π-bonding ligands. This may have biochemical implications for molybdenum. Niobium and probably tantalum clusters are found in solid state structures. Since the trinuclear clusters discussed here have chiefly anionic ligands they would have excessively high negative charges (*e.g.* $[Nb_3O_4X_9]^{8-}$) if they occurred as discrete species. Therefore, they occur preferentially as "polymeric" trinuclear clusters (as solids) which allows the total number of negative ligands (and hence negative charges) per metal atom to be smaller than for isolated species.

The clusters now known can be assigned to three structure types. It is interesting that those of types B_2 and C with $\{M_3\}^6$ configurations satisfy the 18-electron rule. A variety of properties (magnetic, optical, redox, and structural) can be systematically treated and understood using a simple MO scheme. Just as the metal-ligand interaction in mononuclear (Werner-type) complexes can be interpreted in terms of the electronic structure of one central atom, it is correspondingly possible to treat the trinuclear clusters by analyzing the electronic levels of the M_3 unit.

8. Appendix

In the method of *Cotton* and *Haas*[3] the energies of the molecular orbitals are expressed as functions of the overlap integrals and the valence orbital ionization potentials (VOIPs) for the metal atom orbitals. The overlap integrals were evaluated as linear combinations of the tabulated S_σ, S_π, and S_δ. Numerical values were calculated using a modified version of the programs written by *Cook*[43]. The following characteristic metal-metal distances were used: 2.50 Å for structure type B_1; 2.72 Å for structure type B_2; 2.75 Å for structure type C. Radial wave functions were those of *Roothaan* and *Synek*[44,45] of the multi-ζ-basis set type for the neutral Mo atom, and VOIPs for Mo 4d orbitals were the same ones as used for the calculation of MoS_2[46].

We thank the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Minister für Wissenschaft und Forschung (NRW) for financial support.

Received: March 19, 1980 [A 338 IE]
German version: Angew. Chem. *92*, 921 (1980)

[1] a) *F. A. Cotton, G. Wilkinson:* Advanced Inorganic Chemistry, 4th Ed. Wiley-Interscience, New York 1980; Anorganische Chemie, 3rd Edit., Verlag Chemie, Weinheim 1974; b) *C. J. Ballhausen:* Molecular Electronic Structures of Transition Metal Complexes. McGraw-Hill, New York 1979.
[2] *J. W. Lauher*, J. Am. Chem. Soc. *100*, 5305 (1978).
[3] *F. A. Cotton, T. E. Haas*, Inorg. Chem. *3*, 10 (1964).
[4] *D. L. Kepert, K. Vrieze* in *J. C. Bailar, H. J. Emeléus, R. S. Nyholm, A. F. Trotman-Dickenson:* Comprehensive Inorganic Chemistry, Vol. 4, p. 197. Pergamon Press, Oxford 1973; *J. F. Gibson, P. O. W. Meier*, J. Chem. Res. (*S*) *1978*, 66; *D. J. Robbins, A. J. Thomson*, J. Chem. Soc. Dalton Trans. *1972*, 2350; *S. F. A. Kettle*, Theor. Chim. Acta **3**, 211 (1965).
[5] *F. A. Cotton*, Inorg. Chem. *3*, 1217 (1964).
[6] a) *F. A. Cotton, G. G. Stanley*, Chem. Phys. Lett. *58*, 450 (1978); b) *W. C. Trogler, D. E. Ellis, J. Berkowitz*, J. Am. Chem. Soc. *101*, 5896 (1979); c) *B. E. Bursten, F. A. Cotton, J. C. Green, E. A. Seddon, G. G. Stanley, ibid. 102*, 955 (1980).
[7] *B. E. Bursten, F. A. Cotton, G. G. Stanley*, Isr. J. Chem., *19*, 132 (1980).
[8] *B. E. Bursten, F. A. Cotton, R. C. Najjar*, to be published.
[9] *W. H. McCarroll, L. Katz, R. Ward*, J. Am. Chem. Soc. *79*, 5410 (1957).
[10] *G. B. Ansell, L. Katz*, Acta Crystallogr. *21*, 482 (1966).
[11] *A. Simon, H. G. v. Schnering*, J. Less-Common Met. *11*, 31 (1966).
[12] *J. Marcoll, A. Rabenau, D. Mootz, H. Wunderlich*, Rev. Chim. Miner. *11*, 607 (1974).
[13] *A. Bino, F. A. Cotton, Z. Dori*, J. Am. Chem. Soc. *100*, 5252 (1978).
[14] *A. Bino, F. A. Cotton, Z. Dori, S. Koch, H. Küppers, M. Millar, J. C. Sekutowski*, Inorg. Chem. *17*, 3245 (1978).
[15] a) *P. R. Sharp, R. R. Schrock*, J. Am. Chem. Soc. *102*, 1430 (1980); b) *F. A. Cotton, T. R. Felthouse, D. G. Lay, ibid. 102*, 1430 (1980).
[16] a) *A. Müller, R. G. Bhattacharyya, B. Pfefferkorn*, Chem. Ber. *112*, 778 (1979); b) cf. also *A. Müller, S. Sarkar, R. G. Bhattacharyya, S. Pohl, M. Dartmann*, Angew. Chem. *90*, 564 (1978); Angew. Chem. Int. Ed. Engl. *17*, 535 (1978); c) *A. Müller, R. G. Bhattacharyya, W. Eltzner, N. Mohan, A. Neumann, S. Sarkar*, Proc. 3rd Int. Conf. Chemistry and Uses of Molybdenum, p. 59. Climax Molybdenum Comp., Ann Arbor 1979.
[17] *R. Mattes, K. Mennemann*, Z. Anorg. Allg. Chem. *437*, 175 (1977); *K. Mennemann, R. Mattes*, Angew. Chem. *88*, 92 (1976); Angew. Chem. Int. Ed. Engl. *15*, 118 (1976).
[18] *A. Müller, U. Reinsch*, Angew. Chem. *92*, 69 (1980); Angew. Chem. Int. Ed. Engl. *19*, 72 (1980).
[19] *R. J. P. Williams:* The Biological Role of Molybdenum. Bulletin of the Climax Molybdenum Co., London 1978; *V. Massey, D. Edmondson*, J. Biol. Chem. *245*, 6595 (1970); *J. S. Olson, D. P. Ballou, G. Palmer, V. Massey, ibid. 249*, 4363 (1974).
[20] *A. Müller*, unpublished.
[21] *A. Müller, A. Loewenschuss, D. Kuck, F. Königer*, to be published.
[22] *A. Müller, W. Jaegermann*, Inorg. Chem. *18*, 2631 (1979).
[23] *E. Diemann, P. J. Aymonino, A. Müller*, Z. Anorg. Allg. Chem., in press.
[24] *P. J. Vergamini, H. Vahrenkamp, L. F. Dahl*, J. Am. Chem. Soc. *93*, 6327 (1971).
[25] *W. Beck, W. Danzer, G. Thiel*, Angew. Chem. *85*, 625 (1973); Angew. Chem. Int. Ed. Engl. *12*, 582 (1973).
[26] *R. B. King, D. M. Braitsch, P. N. Kapoor*, J. Am. Chem. Soc. *97*, 60 (1975).
[27] *S. Z. Goldberg, B. Spivack, G. Stanley, R. Eisenberg, D. M. Braitsch, J. S. Miller, M. Abkowitz*, J. Am. Chem. Soc. *99*, 110 (1977).
[28] *P. Souchay, M. Cadiot, M. Duhameaux*, C. R. Acad. Sci. *C 262*, 1524 (1966); *M. Cadiot, M. Lamache-Duhameaux, ibid. C 264*, 1282 (1967); *M. Lamache-Duhameaux*, Rev. Chim. Miner. *5*, 459 (1968); *P. Souchay*, J. Inorg. Nucl. Chem. *37*, 1307 (1975); *M. Lamache*, J. Less-Common Met. *39*, 179 (1975); *R. Jostes, A. Müller*, unpublished.
[29] *S. P. Cramer, H. B. Gray, Z. Dori, A. Bino*, J. Am. Chem. Soc. *101*, 2770 (1979).
[30] *E. O. Fischer, F. Röhrscheid*, J. Organomet. Chem. *6*, 53 (1966).
[31] *J. Fischer, A. Veillard, R. Weiss*, Theor. Chim. Acta *24*, 317 (1972).
[32] *R. Stomberg*, Acta Chem. Scand. *23*, 2755 (1969).
[33] *A. Müller, W. O. Nolte, B. Krebs*, Angew. Chem. *90*, 286 (1978); Angew. Chem. Int. Ed. Engl. *17*, 279 (1978); Inorg. Chem. *19*, 2835 (1980).
[34] *A. Müller, R. Jostes, W. Jaegermann*, unpublished.
[35] *A. Müller, W. Eltzner, N. Mohan*, Angew. Chem. *91*, 158 (1979); Angew. Chem. Int. Ed. Engl. *18*, 168 (1979).
[36] The compound Nb_3S_4 [56] contains triangular Nb_3 units with μ_3-S ligands above and below the triangle. However, the Nb_3 units also form metal-metal bonds between themselves (which leads to metallic conductivity) and this compound cannot be considered as trinuclear cluster in the strict sense.
[37] *A. Broll, A. Simon, H. G. v. Schnering, H. Schäfer*, Z. Anorg. Allg. Chem. *367*, 1 (1969).
[38] *G. Tourne, H. Czeskleba*, C. R. Acad. Sci. *C 271*, 136 (1970).
[39] *A. Müller, R. Jostes, W. Jaegermann, R. G. Bhattacharyya*, Inorg. Chim. Acta *41*, 259 (1980).
[40] *A. Müller, E. Diemann, C. K. Jørgensen*, Struct. Bonding (Berlin) *14*, 23 (1973).
[41] *P. D. Dacre, M. Elder*, J. Chem. Soc. Dalton Trans. *1972*, 1426.
[42] *R. Hoffmann, B. F. Beier, E. L. Muetterties, A. R. Rossi*, Inorg. Chem. *16*, 511 (1977).
[43] *D. B. Cook:* Structures and Approximations for Electrons in Molecules. Ellis Horwood, Chichester 1978.
[44] *C. C. J. Roothaan, M. Synek*, Phys. Rev. *133*, A 1263 (1964).
[45] It is necessary to use a multiple zeta basis set because single and double zeta basis sets do not cover the metal-metal overlap region satisfactory.
[46] *R. Huisman, R. de Jonge, C. Haas, F. Jellinek*, J. Solid State Chem. *3*, 56 (1971).
[47] *H. Schäfer, R. Laumanns, B. Krebs, G. Henkel*, Angew. Chem. *91*, 343 (1979); Angew. Chem. Int. Ed. Engl. *18*, 325 (1979).
[48] *H. G. v. Schnering, H. Wöhrle, H. Schäfer*, Naturwissenschaften *48*, 159 (1961).
[49] *M. R. Churchill, S. W. Y. Chang*, J. Chem. Soc. Chem. Commun. *1974*, 248.
[50] *A. Müller, S. Pohl, M. Dartmann, J. P. Cohen, J. M. Bennett, R. M. Kirchner*, Z. Naturforsch. *B 34*, 434 (1979).
[51] *A. Bino, M. Ardon, I. Maor, M. Kaftory, Z. Dori*, J. Am. Chem. Soc. *98*, 7093 (1976).
[52] *M. Herceg, S. Šćavničar*, Croat. Chem. Acta *39*, 137 (1967); *S. Šćavničar, M. Herceg*, Acta Crystallogr. *21*, A 151 (1966).
[53] *D. Grdenić, B. Korpar-Čolig*, Proc. Chem. Soc. *1963*, 308.
[54] *A. Bino, F. A. Cotton, Z. Dori*, Inorg. Chim. Acta *33*, L 133 (1979).
[55] *V. Katovic, J. L. Templeton, R. E. McCarley*, J. Am. Chem. Soc. *98*, 5705 (1976).
[56] *A. F. J. Ruysink, F. Kadijk, A. J. Wagner, F. Jellinek*, Acta Crystallogr. *B 24*, 1614 (1968).
[57] *A. Müller, A. Ruck, M. Dartmann, U. Reinsch-Vogell*, Angew. Chem. and Angew. Chem. Int. Ed. Engl., in press.

Chemistry of Thiazyl Fluoride (NSF) and Thiazyl Trifluoride (NSF_3): A Quarter Century of Sulfur-Nitrogen-Fluorine Chemistry

By Oskar Glemser and Rüdiger Mews[*]

In memory of Hans von Wartenberg on the centenary of his birthday[1]

Since the first sulfur-nitrogen-fluorine compounds were synthesized 25 years ago[2], great progress has been made in this field of covalent fluorine chemistry[3–9]. The two small molecules thiazyl fluoride (NSF) and thiazyl trifluoride (NSF_3), are key substances; nearly all sulfur-nitrogen-fluorine compounds can be derived from them.

1. Synthesis of NSF and NSF_3

NSF and NSF_3 can be synthesized by many methods, *e.g.* by fluorination of S_4N_4 with AgF_2 or HgF_2 in tetrachloromethane[2,10,11]. However, in this reaction numerous side-products are formed, which are often difficult to separate. The reaction of imino(triphenyl)phosphoranes $Ph_3P{=}NR$ ($R = H$, $SiMe_3$) with SF_4[12] is better. For production on a preparative scale, we prefer the decomposition of compounds which already contain the N—S—F group[**]:

$$FCO{-}NSF_2 \xrightarrow[CsF]{20\,^\circ C} NSF + COF_2 \quad [13,14] \qquad (1)$$

$$Hg(NSF_2)_2 \xrightarrow[HV]{110\,^\circ C} 2\,NSF + HgF_2 \quad [15] \qquad (2)$$

NSF_3 can be obtained from either NSF or directly from $OCF{-}NSF_2$ with AgF_2:

$$NSF + 2\,AgF_2 \xrightarrow{20\text{–}110\,^\circ C} NSF_3 + 2\,AgF \qquad (3)$$

NSF (m.p. $-89\,^\circ C$; b.p. $+0.4\,^\circ C$) is a colorless, pungent gas at room temperature and at $<0.4\,^\circ C$ is a pale yellow liquid. It is extremely hygroscopic and cannot be stored at room temperature without decomposition. NSF_3 (m.p. $-72.6\,^\circ C$, b.p. $-27.1\,^\circ C$), on the other hand, is kinetically very stable, both as a gas and as a colorless liquid; it reacts with metallic sodium only at *ca.* $200\,^\circ C$[10].

2. Properties of NSF

NSF is isoelectronic with SO_2; as expected it has, like SO_2, a bent structure (Fig. 1)[16]. The photoelectron spectra[17–19] show a similar sequence of orbitals in both molecules.

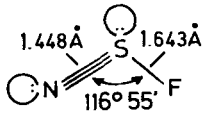


Fig. 1. Structure of NSF (not to scale). $f_{NS} = 10.94$ mdyn/Å [20–22]; dipole moment $\mu = 1.902$ D [20]; $\Delta H_f(NSF_{(g)}) = -20.92$ kJ/mol [23]; $\delta(^{19}F) = -234$ ($CFCl_3$) [22, 12].

From the electron and molecular structures of NSF, we deduce three possible primary reactions:

1. Reactions of the π-system (see Section 2.1): The S—N bond length is relatively short, and indicates multiple bonding, represented by the two canonical forms (*A*) and (*B*). We anticipate polymerization and addition reactions.

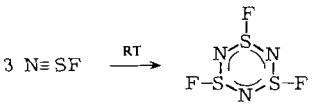
$$(A)\ :N{\equiv}S{-}F \longleftrightarrow {:}\overset{\ominus}{N}{=}\overset{\oplus}{S}{-}F\ (B)$$

2. Reactions with electrophiles (see Section 2.2): Electrophiles should be able to attack, as a consequence of the lone pairs on the N and S atoms. The relatively long and therefore strongly polar S—F bond should allow the addition of strong fluoro-Lewis acids.

3. Reactions with nucleophiles (see Section 2.3): Nucleophilic addition is favored at the coordinatively unsaturated S atom.

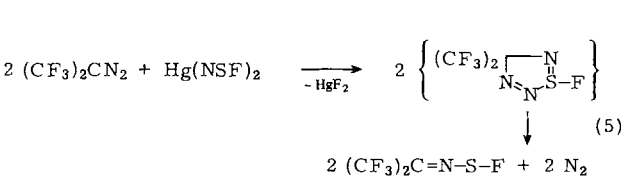
2.1. Reactions *via* the π-System

NSF forms a cyclic trimer at room temperature[11].



(4)

The reaction of the NSF-precursor, $Hg(NSF_2)_2$ [cf. Reaction (2)] with $(CF_3)_2CN_2$ is worthy of note. The primary step can be regarded as a dipolar addition of the diazo compound to the S—N bond of NSF; the stable product from reaction (5) contains sulfur with an oxidation number of $+2$[24]. Up to now, stable R=NSF compounds have not been obtained by any other method[25]. HgF_2 fluorinates $(CF_3)_2C{=}N{-}S{-}F$

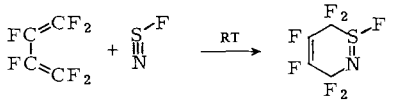


(5)

[*] Prof. Dr. O. Glemser, Doz. Dr. R. Mews
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] Abbreviations: HV = in vacuo, RT = room temperature, exc. = excess.

to give the sulfur difluoride imide $(CF_3)_2CF—N{=}SF_2$. $(CF_3)_2CN_2$ can also be regarded as a heterodiene instead of a 1,3-dipole. Genuine dienes, such as hexafluorobuta-1,3-diene, also react exothermically with cycloaddition[26] (alkylbutadienes react uncontrollably and ignite) [Reaction (6)].



(6)

Whether this [4+2]-cycloaddition is pericyclic, according to the Woodward-Hoffmann rules, or is a polar or nitrene-type addition in the primary step still needs clarification. It is interesting that on heating, the isoelectronic SO_2 adds chelatropically to the sulfur to form four-membered rings[27].

2.2. Reactions with Electrophiles

The site of electrophilic attack depends on the electrophile. Strong (hard) fluoro-Lewis acids attack at the fluorine to give thiazyl salts, for example:

$$NSF + BF_3 \rightarrow NS^{\oplus}BF_4^{\ominus}$$

According to *Pearson*, transition metal ions, $M^{2\oplus}$, can be classified as medium-hard acids. Here, the Coulomb interaction between the doubly-charged cation and the NSF dipole still dominates; these cations attack at the nitrogen. The HOMO/LUMO effect should be important only with soft acids, *e.g.* complexes of NSF with metals in low valencies; here an electrophilic attack on sulfur would be expected. However, we still lack proof of this type of reaction.

2.2.1. NSF as Complexing Ligand

Electrophilic attack on thiazyl fluoride by transition metal cations occurs at nitrogen[28,29]:

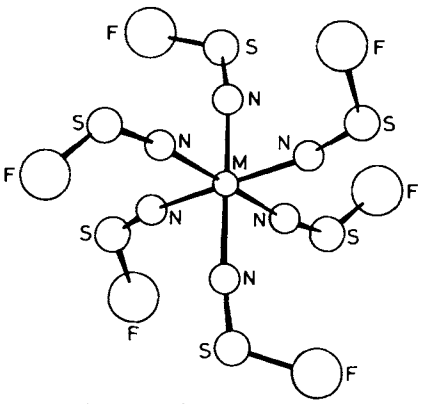
$$[M(SO_2)_2][AsF_6]_2 + 6\ NSF \xrightarrow[-2\,SO_2]{-20\,^{\circ}C} [M(NSF)_6][AsF_6]_2 \quad (7)$$
$$(M = Co, Ni)$$

A complex chemistry of this type using very weak bases and ligands sensitive to hydrolysis can be conducted in liquid SO_2. The solvent is bound—probably *via* S—to the central atoms only by weak σ-bonds; it can be concluded from the IR-data that hardly any π-back-bonding exists. Because of these weak bonds, SO_2 can be readily replaced—*e.g.* in Reaction (7) by NSF.

Table 1. S—N and S—F frequencies [cm^{-1}] as well as S—N and S—F distances [Å] of NSF and its Co- and Ni-complexes.

	NSF (g)	$[Co(NSF)_6]^{2\oplus}$	$[Ni(NSF)_6]^{2\oplus}$
ν_{SN}	361	1429	1438
ν_{SF}	641	655	655
d_{SN}	1.448	1.399(12)	1.404(5)
d_{SF}	1.643	1.569(12)	1.581(13)
∢ NSF [°]	116.5	115.0(0.7)	116.0(0.8)

From Table 1 it can be seen that the S—F and S—N bond frequencies are higher in the Co- and Ni-complexes than in NSF. Since this effect does not depend on mechanical coupling, it points to a reinforcement of the S—N and S—F bonds. This hypothesis was confirmed by X-ray structural analysis of the cations $[M(NSF)_6]^{2\oplus}$ (M = Co, Ni) (Fig. 2).



(M = Co, Ni)

Fig. 2. Structure of the cations $[M(NSF)_6]^{2\oplus}$ (M = Co, Ni) [28, 29]. See Table 1. Co—N = 2.093(11) Å, ∢Co—N—S = 170.8(10)°; Ni—N = 2.054(3) Å, ∢Ni—N—S = 168.6(2.5)°.

The central atom, M, is octahedrally coordinated by six NSF molecules *via* their N atoms. The decrease of the M—N distance on going from Co to Ni corresponds to the difference in the high-spin ionic radii. The M—N bond lengths are similar to those in the corresponding NH_3-complexes. The NSF angle alters little when complexed, in contrast to the S—N and S—F bonds, which are appreciably shortened. This unusual behavior is summarized (for some N—S—F compounds in different adducts), and explained in Section 3.1.1.

The introduction of NSF as a ligand into cationic carbonyl-metal compounds[30] is also achieved *via* SO_2-complexes:

$$[Re(CO)_5(SO_2)]^{\oplus}AsF_6^{\ominus} + NSF \rightarrow [Re(CO)_5NSF]^{\oplus}AsF_6^{\ominus} + SO_2 \quad (8)$$

The color of the deep-red cation $[Re(CO)_5NSF]^{\oplus}$ is due to a strong bathochromic shift of the NSF ligands, an effect which is not found with N-bound complexes (cf. Fig. 2). A similar shift occurs in the yellow starting material $[Re(CO)_5(SO_2)]^{\oplus}AsF_6^{\ominus}$ due to the SO_2 ligands, which are probably bound *via* sulfur. Whether this similar behavior indicates the same coordination of the atom, can only be clarified by X-ray structural analysis.

NSF is remarkably stabilized by complex formation. However, its reactivity is still so great that it reacts with both electrophiles and nucleophiles[31].

2.2.2. Formation and Reactions of the Cation $NS^{\oplus}$

Strong fluoro-Lewis acids, such as MF_5 (M = As, Sb) cleave NSF to give a fluoride ion and a thiazyl cation[32,33]; the reaction is best carried out in liquid SO_2[34].

$$NSF + MF_5 \xrightarrow{SO_2} NS^{\oplus}MF_6^{\ominus} \quad (M = As, Sb) \quad (9)$$

The S—N frequency is higher in $NS^{\oplus}$ than in NSF and, as expected, also higher than in the radical $NS^{\odot}$ (Table 2). Similar results are found with $NO^{\oplus}/NO^{\odot}$. Recently the formation of the cation $NS_2^{\oplus}$ was achieved[37].

Table 2. S—N frequencies [cm^{-1}] and S—N distances [Å] of NSF, $NS^{\oplus}$ and $NS^{\odot}$.

	NSF	$NS^{\oplus}$	$NS^{\odot}$
ν_{SN}	1361	1437	1205
d_{SN}	1.448	1.42(1)	1.4955
	[22, 16]	[35]	[36]
		1.44	
		[38—40]	

The thiazyl radical $NS^{\odot}$, ($X^2\pi$) has the electron configuration $1\sigma^2 2\sigma^2 3\sigma^2 4\sigma^2 1\pi^4 5\sigma^2 6\sigma^2 7\sigma^2 2\pi^4 3\pi^1$. The single electron is in an antibonding orbital; the expected bond strength increase occurs on ionization. A bond length of 1.44 Å was determined for $NS^{\oplus}$ ($X^1\Sigma^+$) from PE spectra[38], as well as from *ab-initio* calculations[39,40]. The X-ray structural analysis of $NS^{\oplus}Sb_2F_{11}^{\ominus}$ at −151.5 °C gave an N—S distance of 1.42 Å[35].

The cation $NS^{\oplus}$ is an interesting reagent for syntheses[34]. In $SOCl_2$ as solvent, $NS^{\oplus}$ reacts with S_4N_4 by insertion of an

$$S_4N_4 + NS^{\oplus}\ MF_6^{\ominus} \xrightarrow{SOCl_2} S_5N_5^{\oplus}\ MF_6^{\ominus} \quad (10)$$
(M = As, Sb)

$NS^{\oplus}$ moiety into the S—N bond of the starting material, to give a good yield of the yellow thiazyl salt (Reaction (10)). If liquid SO_2 is used as solvent, then a black polymer $(S_5N_5^{\oplus}AsF_6^{\ominus})_n$ is formed, along with other substances. The cation $S_5N_5^{\oplus}$ contained in the yellow salt, was first obtained by another method[41]. It has a planar ten-membered ring, which can be regarded as a 14π-electron system. An azulene-type molecular structure has been determined by X-ray analysis[42].

Insertion reactions into the polar S—Cl bonds occur with sulfenyl halides RSCl (R = CF_3, $(CF_3)_2C{=}N{-}$, Cl)[34], *e.g.* according to Reaction (11).

$$Cl{-}\overset{\delta\oplus}{S}{-}\overset{\delta\ominus}{Cl} + NS^{\oplus}\ MF_6^{\ominus} \xrightarrow{SO_2\,(l)} [N(SCl)_2]^{\oplus}\ MF_6^{\ominus} \quad (11)$$
(M = As, Sb)

The cation $[N(SCl_2)]^{\oplus}$ can also be obtained from NSF_3 and BCl_3 [see Reaction (48)][43]. In the yellow hygroscopic salts it has a planar *cis*-structure, *i.e.* the lone pairs on the N and S atoms are in a *cis*-configuration (Fig. 3).

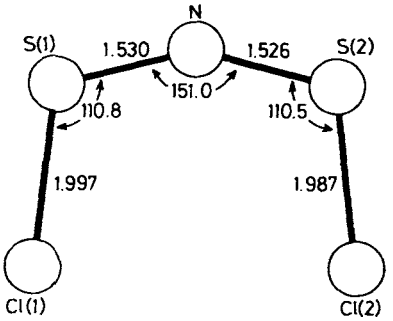


Fig. 3. Structure of the cation $[N(SCl)_2]^{\oplus}$.

The large SNS angle could indicate that the lone pair on nitrogen participates in the S—N bond[44].

2.3. Reactions with Nucleophiles

Nucleophilic attack occurs at the S atom, whereby either fluorine is substituted, or the coordination number is increased.

2.3.1. Substitution Reactions with Retention of the Formal S≡N Triple Bond

The formal triple bond is retained in only a few substitution reactions. So far only three compounds of the type N≡S—R (R = F, Cl, $ON(CF_3)_2$) have been reported; they all

$$2\ NSF + Hg[ON(CF_3)_2]_2 \xrightarrow[-HgF_2]{} 2\ N{\equiv}S{-}ON(CF_3)_2 \quad (12)$$
$$\downarrow$$
$$2/3\ \left[\begin{array}{l} \text{——}N{=}S\text{–} \\ \quad\quad | \\ (CF_3)_2NO \end{array}\right]_3$$

trimerize at room temperature [see also Reaction (4)]. The compound N≡S—$ON(CF_3)_2$ resulting from Reaction (12)[45], can, like NSF, be stabilized by being incorporated[46] into transition metal complexes [see *e.g.* Reaction (13)]. The orange-red salt is completely stable at room temperature.

$$[Re(CO)_5SO_2]^{\oplus}\ AsF_6^{\ominus} + N{\equiv}S{-}ON(CF_3)_2 \xrightarrow[-SO_2]{} [(CO)_5ReNSON(CF_3)_2]^{\oplus}\ AsF_6^{\ominus} \quad (13)$$

2.3.2. Nucleophilic Substitution and Subsequent Rearrangement

NSF was reacted with perfluoroalkenes[47,48] in the presence of CsF, in an attempt to replace the fluorine nucleophile by the perfluoro carbanion, to give disulfides and linear sulfenyl sulfur diimides [Reaction (14)].

$$N{\equiv}S{-}F + \rangle C{=}C\langle \xrightarrow{CsF} \{NSR_f\} \quad (14)$$
$$\downarrow$$
$$R_fN{=}S{=}N{-}S{-}R_f$$
$$(R_f = (CF_3)_2CF,\ (CF_3)_3C) \qquad + R_f{-}S{-}S{-}R_f + \cdots$$

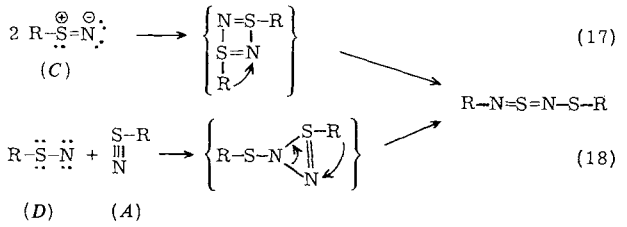
$$N{\equiv}S{-}F + F_3C{-}C{\equiv}C{-}CF_3 \xrightarrow{CsF} F_3C{-}CF_2{-}\overset{CF_3}{\underset{S{-}N}{\overset{|}{\underset{\|}{\overset{|}{N}}}}}{-}S + \cdots \quad (15)$$

If alkynes are used[49] [Reaction (15)], then cyclic sulfenyl sulfur diimides can be isolated, in which both ends of the —S—N=S=N— chain are bound to the same carbon atom. The electronegativity of R in thiazyl compounds RS≡N must obviously be high to enable a good overlap of the orbitals between N and S and the relatively short S—N distance for the formal triple bond. The bonding situation is illustrated by the canonical forms (*C*)—(*F*).

$$:N{\equiv}S{:}^{\oplus}\ R^{\ominus} \longleftrightarrow :N{\equiv}\ddot{S}{-}R \longleftrightarrow \ddot{N}^{\ominus}{=}\ddot{S}^{\oplus}{-}R \longleftrightarrow \ddot{N}{-}\ddot{S}{-}R \quad (16)$$
(*C*) (*D*) (*E*) (*F*)

As the electronegativity of R decreases, polar structures such as (*E*) and the nitrene structure (*F*) become important[50]. Even perfluorinated alkyl groups are incapable of stabilizing the formal triple bond. The secondary products from $\{R_fSN\}$ can be explained by the dimerization of polar or nitrene-type intermediates [Reactions (17) and (18)].

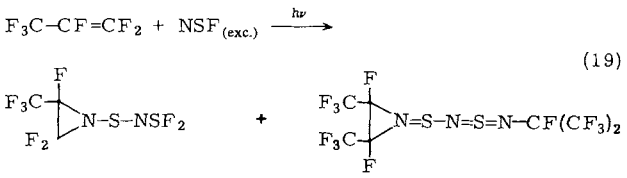
The formation of disulfides also indicates nitrene-type intermediates.



(17)

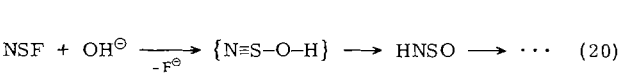
(18)

There is no clear evidence for nitrene reactions of NSF. Irradiation of excess thiazyl fluoride in the presence of hexafluoropropene[51] leads to sulfenylaziridenes [Reaction (19)].



(19)

Another type of rearrangement is found during hydrolysis. NSF is extremely hygroscopic and therefore somewhat difficult to handle. The coordinatively unsaturated sulfur atom is, as expected, easily attacked by the classic nucleophile water[52]; $F^{\ominus}$ is replaced by $OH^{\ominus}$. As shown by:



(20)

Thionylimide HNSO[10,53] is first formed, then hydrolytically cleaved. It decomposes *via* $S_2O_3^{2\ominus}$ to $HSO_3^{\ominus}$ and sulfur. The $HSO_3^{\ominus}$ ions then react with the remaining sulfoxylic acid to give trithionate $S_3O_6^{2\ominus}$ and hexathionate $S_6O_6^{2\ominus}$, both of which can be isolated as tetraphenylphosphonium salts.

2.3.3. Nucleophilic Addition with Increase of the Coordination Number

Nucleophilic attack on NSF by $F^{\ominus}$ in the presence of CsF gives the salt $Cs^{\oplus}NSF_2^{\ominus}$[54]. In the presence of elemental chlorine, $ClNSF_2$[14] is produced, an example of the sulfur difluoride imides $RNSF_2$, of which many are known[8]. The halogen derivatives $XNSF_2$ (X = F, Cl, Br, I) are better[15] synthesized by:

$$Hg(NSF)_2 + X_2 \rightarrow 2XNSF_2 + HgF_2 \qquad (21)$$

$ClNSF_2$ (b.p. 23.7 °C) is the most stable compound in this series. $FNSF_2$[55] is an isomer of NSF_3. The structure of $ClNSF_2$ was determined by electron diffraction (Fig. 4)[56]. The Cl atom is *cis* to the SF_2 group. In other words: the *cis*-arrangement of the lone pairs on the N and S atoms is sterically more favorable than a *trans*-arrangement. This arrangement is also observed with $F_3C{-}NSF_2$[57] and with other S—N—X compounds, *e.g.* $[N(SCl)_2]^{\oplus}$, XNSO[53], $(NSX)_3$, X = F, Cl (cf. Section 4).

Numerous organic sulfur difluoride imides can be obtained by addition of $ClNSF_2$ or $BrNSF_2$ to C=C double bonds[8]. The radical $^{\circ}NSF_2$ postulated in this reaction has been identified in a matrix[58]. Organic sulfur difluoride imides can also be obtained by the reaction of SF_4 with *e.g.* primary amines, silylated primary amines, cyanides, cyanates or thiocyanates[8].

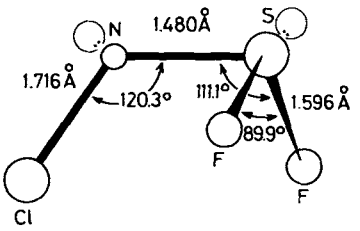
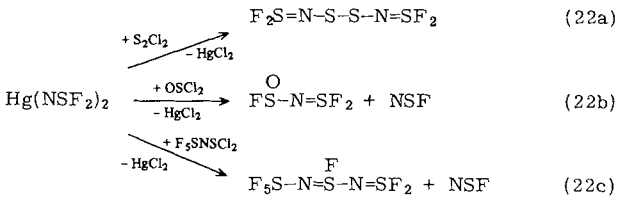


Fig. 4. Structure of $ClNSF_2$.

The NSF_2 group can also be directly transferred using $Hg(NSF_2)_2$[59] [Reaction (22)].

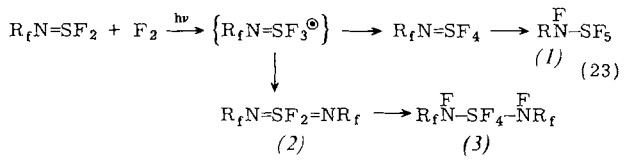


(22a)

(22b)

(22c)

In compounds of the type $RN{=}SF_2$, the N and S atoms are still coordinatively unsaturated. Therefore fluorination should lead to more highly coordinated species. We have recently[60] studied the photochemical reaction of $RN{=}SF_2$ ($R = C_2F_5$, SF_5) with fluorine in the gas phase, for which we postulate a radical mechanism [Reaction (23)]. Compounds *(1)* ($R_f = CF_3$, C_2F_5[61], FSO_2[62]) have already been prepared



(23)

by fluorination of $RN{=}SF_2$ in the presence of CsF. Compounds *(2)* were formed by uncatalyzed fluorination ($R_f = CF_3$, C_2F_5[61], SF_5[63]). Compounds with five-coordinate sulfur, such as $R_fN{=}SF_4$ are rare; however, we succeeded in isolating $C_2F_5N{=}SF_4$ (b.p. 25 °C) and in detecting traces of $F_5SN{=}SF_4$[64]. Compound *(3)* ($R_f = C_2F_5$) (b.p. 111 °C) is formed stereospecifically; only the *trans*-isomer is obtained.

The photochemical reaction of $RN{=}SF_2$ ($R = CF_3$, C_2F_5, iC_3F_7, $CF_2Cl{-}CF_2$, $CF_2Br{-}CF_2$, OCF) with OF_2[65] gives similar results. The $-N{=}SF_2$ group is isoelectronic with OSF_2, which reacts quantitatively with OF_2 to give O_2SF_2 and OSF_4[66]. Sulfur oxide difluoride imides and sulfur difluoride diimides are produced analogously by Reaction (24). $RN{=}SF_4$, isoelectronic with OSF_4, has been observed in only one case[65].

$$2\ RN{=}SF_2 + OF_2 \xrightarrow{h\nu} RN{=}\overset{O}{S}F_2 + \{RN{=}SF_4\} + RN{=}SF_2{=}NR + SF_4 \quad (24)$$

Compounds of type *(1)* [Reaction (23)] can also be produced according to Reaction (25), by low-temperature fluorination of NSF[14].

$$NSF + 3\ F_2 \xrightarrow{CsF} F_2N{-}SF_5\ (SF_6, NF_3) \quad (25)$$

In $F_2N{-}SF_5$, the sulfur is six-coordinate, and the nitrogen three-coordinate. The S—N bond of this compound is weak; this is confirmed by the relatively long S—N distance of 1.696 Å[67]. The molecule is therefore easily cleaved by further fluorination to give SF_6 and NF_3. On the other hand, the products and intermediates of Reactions (23)—(25) can also be regarded as derivatives of NSF_3 (cf. Section 3).

Derivatives of $RN{=}SF_2$ are easily produced by exchange of one or two F-atoms[68].

3. Properties of NSF_3

NSF_3 is isoelectronic with O_2SF_2, and like O_2SF_2 it has a distorted tetrahedral structure (Fig. 5) which was determined by *IR*[22,69], *NMR*[22], *Raman*[70] and *microwave* spectroscopy[71].

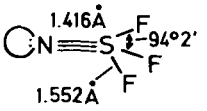


Fig. 5. Structure of NSF_3 (not to scale). $f_{NS} = 12.4$ mdyn/Å [22, 70, 72]; dipole moment $\mu = 1.91$ D [71]; $\Delta H_f^{\ominus}(NSF_{3(g)}) = -410$ kJ/mol [73]; $\delta(^{19}F)(CFCl_3) = 70.0$ [22, 74]; $\delta(^{14}N/^{15}N)(CH_3NO_2) = -243.4$ [74]; $J(F\text{-}^{14}N) = 26.4$ Hz; $J(F\text{-}^{15}N) = 37.5$ Hz.

From the electronic and molecular structures of NSF_3, we predict the following reaction possibilities:

1. Reactions with electrophiles (see Section 3.1): The lone pair on the N atom promotes electrophilic attack, so adducts are expected. The very short S—F distance, explained by π-back-bonding from occupied F(p) to empty S(d) orbitals, would hardly permit cleavage of $F^{\ominus}$ ions by strong fluoro-Lewis acids, as has been observed in the case of NSF. Therefore, NSF_3 should give adducts.

2. Reactions with the π-system (see Section 3.2): The very short S—N distance almost corresponds to a formal S≡N triple bond. Polymerization of the molecule, and addition to the S≡N triple bond should be observed.

Whilst NSF cyclotrimerizes to $(NSF)_3$, NSF_3 shows no similar reaction, *i.e.* the S—N bond behaves differently in NSF and NSF_3, although it can be described in both cases as a σ-bond and two π-bonds. The photoelectron spectra of NSF[17,18] and NSF_3[19] allow us to understand these results (Fig. 6).

The spectra are ambiguously interpreted in the literature; the following correlation would seem plausible: In NSF the HOMO is the σ-orbital of the lone pair on sulfur, then follow the two π-orbitals. NSF_3 has another set of orbitals: There are two degenerate π-orbitals as HOMOs and then a σ-orbital to which the lone pair on the nitrogen atom is assigned. Furthermore, it can be concluded from the measurements that the orbitals which contribute to the formal triple bond in NSF are on the N and S atoms, but in NSF_3 are more strongly concentrated on the N atom[19] (cf. also [75]). This difference in sequence and concentration of the orbitals in the two compounds probably causes the difference in chemical behavior.

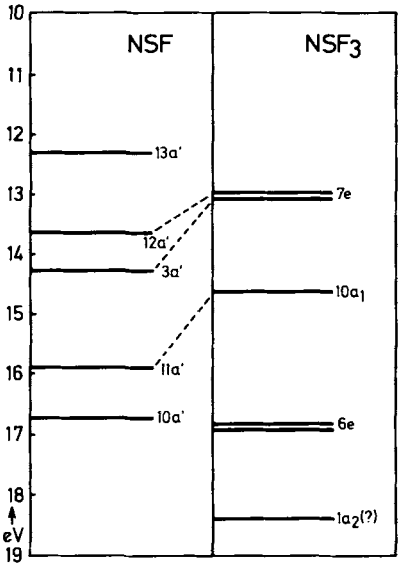


Fig. 6. Photoelectron spectra of NSF and NSF_3.

3. Reactions with nucleophiles (see Section 3.3): The partial charge of the S atom is lowered due to π-back-bonding, making nucleophilic attack on this still coordinatively unsaturated atom more difficult.

3.1. Reaction with Electrophiles

As with NSF, electrophiles such as fluoro-Lewis acids, cationic organometallic complexes and transition metal cations can be used. But the classic electrophile, the proton, as well as 'alkyl acids' ($R^{\oplus}$) are possible candidates. In all these reactions it is advantageous to use SO_2 as the solvent because it stabilizes the acids. NSF_3 is a stronger nucleophile, and so it displaces the SO_2 from these compounds. The given reactions are also valid for NSF_3-derivatives of the type NSF_2R.

3.1.1. Adduct and Complex Formation

In accordance with our prediction, fluoro-Lewis acids will only form adducts with NSF_3:

$$A + NSF_3 \rightarrow A{-}NSF_3 \quad (26)$$
$$(A = BF_3[76], AsF_5, SbF_5[133])$$

The stability of these adducts depends on the Lewis acid used. While liquid $F_3B{-}NSF_3$ completely dissociates into its components at room temperature, $F_5Sb{-}NSF_3$ is still not decomposed in the gas phase.

NSF_3 is thermally more stable than NSF, and therefore easier to incorporate into transition metal compounds as a ligand [Reactions (27)—(30)].

$$[M(CO)_5SO_2]^{\oplus}\,AsF_6^{\ominus} \xrightarrow[-SO_2]{+NSF_3} [M(CO)_5NSF_3]^{\oplus}\,AsF_6^{\ominus}\ [77] \quad (27)$$

(M = Mn, Re)

$$[C_5H_5Fe(CO)_2SO_2]^{\oplus}\,AsF_6^{\ominus} \xrightarrow[-SO_2]{+NSF_3} [C_5H_5Fe(CO)_2NSF_3]^{\oplus}\,AsF_6^{\ominus}\ [78] \quad (28)$$

$$[M(SO_2)_2]^{2\oplus}\,[AsF_6^{\ominus}]_2 \xrightarrow[-2\,SO_2]{+4\,NSF_3} [M(NSF_3)_4]^{2\oplus}\,[AsF_6^{\ominus}]_2\ [79] \quad (29)$$

(M = Mn, Fe, Co, Ni Cu)

$$AgAsF_6 + NSF_{3(exc.)} \xrightarrow{SO_2\,(l)} [Ag(NSF_3)_2]\,AsF_6 \xrightarrow[RT]{-NSF_3} [Ag(NSF_3)]\,AsF_6 \quad (30)$$

The $M^{2\oplus}$ ions bind a maximum of only four NSF_3 ligands (but six NSF ligands). According to Pauling's principle of electroneutrality, this could indicate that NSF_3 is a stronger σ-donor than NSF. A large increase in the S—N and S—F bond frequencies occurs in all adducts and complexes, an effect which we have already found with NSF complexes (where it is weaker), and which does not directly depend on the strength of the Lewis acid (Table 3).

Table 3. S—N and S—F frequencies [cm^{-1}] as well as S—N and S—F distances [Å] of NSF_3 and some of its complexes.

	NSF_3	$[Mn(NSF_3)_4]^{2\oplus}$	$[Re(CO)_5NSF_3]^{\oplus}$	$F_5As—NSF_3$
ν_{SN}	1515	1579	1643	1610
ν_{SF}	811, 775	880, 836	890, 847	888
d_{SN}	1.416	1.365(11)	—	1.383
d_{SF}	1.522	1.506(5)	—	1.439

This unusual effect points to a strengthening and shortening of *both* bonds in the adduct, since it cannot be explained by the coupling contributions[80]. Furthermore, we found that the stronger the bond between the central atom of the starting material and the N atom of NSF_3 is, the stronger the S—N bond becomes[81]. The X-ray structural analyses of $F_5As—NSF_3$ (Fig. 7)[82] and $[Mn(NSF_3)_4][AsF_6]_2$ (Fig. 8)[83] confirm the proposed shortening of the S—N and S—F bonds.

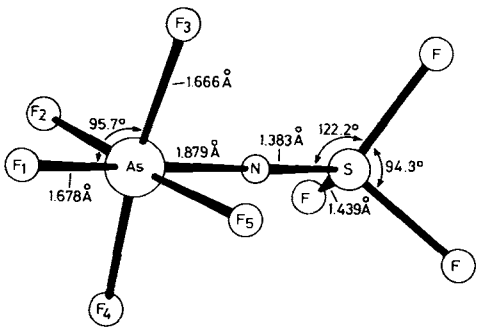


Fig. 7. Structure of $F_5As—NSF_3$.

According to preliminary results, there exists in $F_5As—NSF_3$ an exactly linear arrangement of F_{ax}—As—N—S with shorter S—N and S—F distances than in NSF_3[84]. In the octahedral complex $[Mn(NSF_3)_4][AsF_6]_2$, a Mn atom is located in the middle of a planar quadrangle formed by the N atoms of the four NSF_3 ligands. The fifth and sixth coordination positions are each occupied by fluorine atoms from the two AsF_6 groups. The S—N and S—F distances are considerably shortened. The Mn—N—S angle, like the Co—N—S angle (Fig. 2), deviates from 180°; further investigations will show whether or not this is due to steric factors. The As—F bond lengths indicate the presence of covalent interactions in the solid compound.

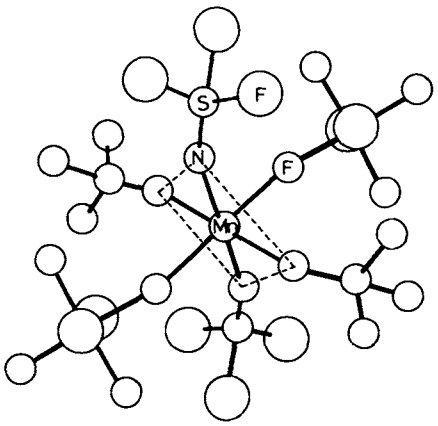


Fig. 8. Structure of $[Mn(NSF_3)_4][AsF_6]_2$. S—N = 1.365(11), S—F = 1.506(5), Mn—N = 2.187(8), Mn—F = 2.193(4), As—F_{ax} = 1.721(28), As—F_{eq} = 1.666(12) Å: ∢N—S—F = 121.4(1.3)°.

We explain the shortening of the S—N *and* S—F bonds in the NSF_3 adducts as follows: The lone pair on the N atom of NSF_3 has predominantly s-character. We assume, that when the adduct is formed, an sp-hybridization of the orbitals on the N atom occurs; this leads to a strengthening of the σ-bond and to a linear or almost linear central atom-S—N arrangement. Thus, charge-density is withdrawn from the S atom, whereby the S—F bond shortens due to further π-back-bonding. These considerations are also valid for the NSF complexes (Section 2.2.1).

3.1.2. Adducts and Complexes of NSF_3 Derivatives

Two types of NSF_3 derivatives (L), the species $N{\equiv}SF_2R$ ($R = NMe_2$, $(CF_3)_2CF$, OC_6H_5[85]) and $RNSOF_2$ ($HNSOF_2$[86], $H_3C—NSOF_2$[87], $NC—NSOF_2$[88], $NSF_2—NSOF_2$[85]), give the adducts F_5ML (M = As, Sb) and $[M(CO)_5L]^{\oplus}AsF_6^{\ominus}$ (M = Mn, Re).

The $N{\equiv}SF_2R$ group resembles the nitrile group in its ability to donate. In reactions with difunctional ligands, $N{\equiv}SF_2—NSOF_2$ or $N{\equiv}C—NSOF_2$, coordination takes place exclusively *via* the nitrogen of the $N{\equiv}S$ or $N{\equiv}C$ triple bond, respectively.

In the carbonyl transition-metal complexes of $N{\equiv}SF_2R$, the S—N and S—F frequencies, as in the NSF_3 complexes, are higher than in the uncomplexed molecules. This property leads to the conclusion that there is a linear or almost linear M—N—S arrangement, with shortened S—N or S—F distances. However, with fluoro-Lewis acids, such as AsF_5 or SbF_5, the S—F frequency increases, whilst the S—N frequency remains in the same region (Table 4).

We explain this as follows: In NSF_3 complexes the S atom apparently cannot accept a positive charge. In all cases the species $M—\overset{\oplus}{N}{\equiv}SF_3$ is formed, with a linear or almost linear M—N—S arrangement. However, substituents other than

Table 4. S—N and S—F frequencies [cm^{-1}] as well as $\delta(^{19}F)$ of NSF_2—$CF(CF_3)_2(L)$ and some of its adducts.

	L	$[Re(CO)_5L]^{\oplus}$	$F_5As \cdot L$	$F_5Sb \cdot L$
ν_{SN}	1502, 1475	1610, 1596	1496	1503
ν_{SF}	748, 722	832, 803	848, 819	863, 824
$\delta(^{19}F)$	−101.97	−92.00	−82.17	−79.3

fluorine lower the electronegativity of the SF_2R-group; the S atom is now able to accept a positive partial charge. Figure 9 shows the possible structures for adducts of NSF_2—NMe_2 with the strong acids SbF_5 and $CH_3^{\oplus}$.

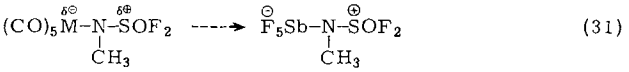


Fig. 9. Proposed structure for compounds with $-N{=}SF_2N(CH_3)_2$ groups.

Now the electron density on the S atom in $N{\equiv}SF_2R$ is certainly greater, and therefore the positive partial charge is smaller than in $N{\equiv}SF_3$. Weaker Lewis acids *e.g.* $[Re(CO)_5]^{\oplus}$ ions, cause a sp-hybridization of the orbitals of the N atom in $N{\equiv}SF_2R$, as in NSF_3; the influence on the bonding is the same. However, stronger Lewis acids of the type MF_5 (M = As, Sb), can withdraw more electron density from the bonding system of $N{\equiv}SF_2R$ than from NSF_3. The result is a sp^2-hybridization of the orbitals of the N atom (Fig. 9). A zwitterion is formed with the positive charge on the S atom of a non-linear M—N—S arrangement. As the partial positive charge is increased, ν_{SF} increases with increasing strength of the Lewis acid, and the S—F bond becomes shorter. There are two opposing effects regarding the S—N bond length: When the adduct is formed, the bond becomes shorter and stronger for the reasons discussed in Section 3.1.1. But, due to the altered hybridization of the orbitals on the N atom, the M—N—S arrangement becomes bent and the S—N bond longer.

Thus, the net result is that the length and strength of the S—N bond hardly alters.

The $RNSOF_2$ adducts all have nearly the same IR-spectra. That of H_3C—$NSOF_2$ has been chosen as an example and is given in Table 5. The coordination number of the N atom can be derived from the IR data. Furthermore, it can be seen that the bonding situation alters when the adduct is formed: The S—N bond contains more single bond character, ν_{NSO} becomes more or less decoupled, ν_{SN} is shifted to lower wavelengths, and $\nu_{as(NSO)}$ becomes more of a pure SO-vibration. This leads, depending on the acid strength, from compounds with partial charge to those with strongly zwitterionic character [arrow in (31)].



(31)

Table 5. IR data of H_3C—$NSOF_2$ (L) and some of its complexes [cm^{-1}].

	L	$[Mn(CO)_5L]^{\oplus}$	$F_5As \cdot L$	$F_5Sb \cdot L$
$\nu_{as(NSO)}$	1410, 1385	1390	1450	1450
$\nu_{sym(NSO)}$	1280	1215	1085	1092
$\nu_{as(SF)}$	920	940	948	950
$\nu_{sym(SF)}$	792	870	870	900

Again, as explained above, as the strength of the acid increases so the S atom becomes more positive, and the S—F bond becomes stronger—as shown by the trend of ν_{SF}[86].

The ideas developed here concerning the bonding in the adducts of H_3C—$NSOF_2$ have been confirmed by X-ray structural analysis[89] of F_5As—$N(CH_3)SOF_2$ (Fig. 10). The ligand is bound to the N atom, the S—N bond becomes longer in the adduct, the S—F bond shorter.

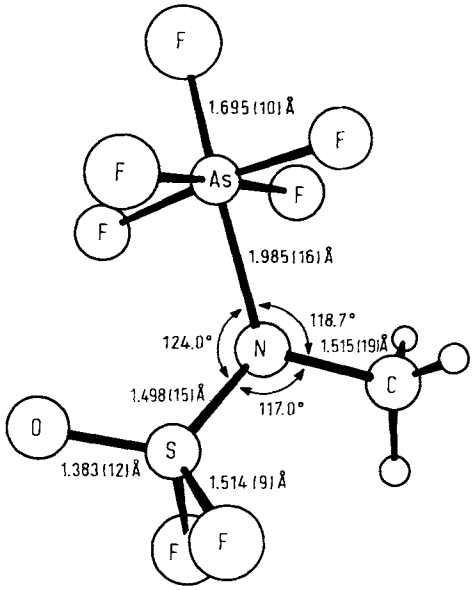
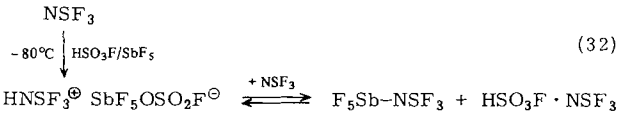


Fig. 10. Structure of F_5As—$N(CH_3)SOF_2$.

3.1.3. Formation of Cations from Thiazyl Trifluoride

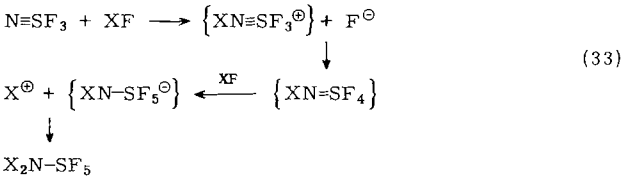
Protonation of NSF_3 occurs in the superacid system HSO_3F/SbF_5 according to Reaction (32).



(32)

The $HNSF_3^{\oplus}$ cation is detectable by NMR spectroscopy only up to −80 °C, then the equilibrium (32) is quickly established[90].

Cations of the type $XNSF_3^{\oplus}$ are probably the primary products of the addition of polar reagents XF (X = H, Cl) to the $S{\equiv}N$ triple bond in NSF_3 [Reaction (33)][91, 102].



(33)

None of the postulated intermediate products of this reaction could be isolated; for example, the $XNSF_3^{\oplus}$ cation would be immediately attacked by the $F^{\ominus}$ nucleophile to form $XN{=}SF_4$. Pentafluorosulfur amines are formed as the stable end products (see Section 3.2).

If the electrophilicity of the cations is lowered by introduction of X = alkyl, and by choosing large, weakly nucleophilic anions, then it is possible to isolate salts of these cations[92,93].

$$NSF_3 + ROSO^{\oplus}MF_6^{\ominus} \rightarrow [R{-}NSF_3]^{\oplus}MF_6^{\ominus} \quad (34)$$
$(R = CH_3,\ C_2H_5)$

$$NSF_2R + H_3COSO^{\oplus}AsF_6^{\ominus} \rightarrow [H_3C{-}NSF_2R]^{\oplus}AsF_6^{\ominus} \quad (35)$$
$(R = N(CH_3)_2,\ CF(CF_3)_2,\ NSOF_2)$

Especially remarkable is the cation $H_3C{-}NSF_3^{\oplus}$, which has the hitherto highest known S—N frequency (1788 cm^{-1}). X-ray structural analysis will show whether it contains the correspondingly shortest S—N distance[94].

3.1.4. Sulfur Tetrafluoride Imides

The cation $H_3C{-}NSF_3^{\oplus}$, obtained according to Reaction (34), reacts with $F^{\ominus}$ ions to give the tetrafluoride[92] (b.p. 21.8 °C):

$$H_3C{-}NSF_3^{\oplus}\,AsF_6^{\ominus} + NaF \xrightarrow[HV]{160\,^{\circ}C} H_3C{-}N{=}SF_4 \quad (36)$$

The NSF_4 group is isoelectronic with OSF_4. The expected trigonal-bipyramidal structure was confirmed by electron diffraction[95] (Fig. 11).

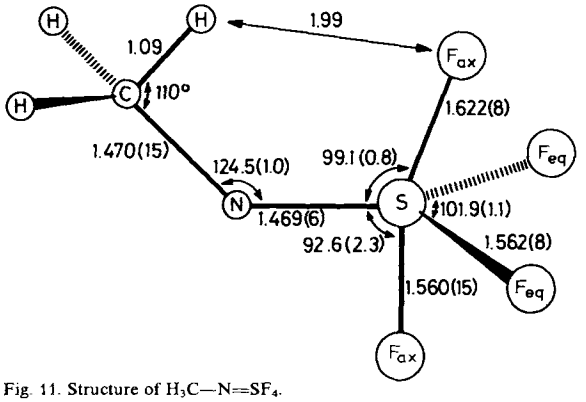


Fig. 11. Structure of $H_3C{-}N{=}SF_4$.

The $-CH_3$ group lies in the plane formed by the N and S atoms, and by the two axial fluorine atoms[96].

N-(perfluoroalkyl)sulfur tetrafluoride imides $R_f{-}NSF_4$, are accessible by fluorination of the corresponding sulfur difluoride imides $R_fN{=}SF_2$ [Reaction (23)] or by dehydrofluorination of *N*-(perfluoroalkyl)pentafluorosulfur amines $R_fNH{-}SF_5$[97]. It has recently been shown that perfluorinated sulfur tetrafluoride imide $FN{=}SF_4$ can be obtained from F_5S-NHF *via* this approach[97a].

3.2. Reactions *via* the π-System; Addition to the S≡N Triple Bond

Polar species such as XF (X = Cl, H)[91,102], add to the S≡N triple bond according to Reaction (33); according to the literature[102], also in the case of X = Cl only pentafluorosulfur amines are found, with no intermediate products such as sulfur tetrafluoride. However, if NSF_3 is used in excess, then cyclic $(ClNSF_4)_2$ is formed in small amounts [Reaction (37)]; this probably arises by dimerization of the monomeric tetrafluoride[98]. It is worth mentioning that sulfur in four-membered rings, as is the case here, has not yet been ob-

$$N{\equiv}SF_{3\,(exc.)} + ClF \longrightarrow \{Cl{-}N{=}SF_4\} \xrightarrow{ClF} F_5S{-}NCl_2 \quad (37)$$

$$1/2\ F_4S\begin{cases} Cl \\ N \\ N \\ Cl \end{cases}SF_4$$

served to have a coordination number of six. The proposed ring structure is supported by the ^{19}F-NMR spectrum, which has virtually two triplets at room temperature—originating from the axial and equatorial F atoms. The F atoms are coupled *via* the N atoms.

F_2 does not add in a similar manner. Surprisingly, fluorination of NSF_3 yields $F_5S{-}N{=}SF_4$, SF_6 and N_2[64] [Reaction (38)]. The compound $F_5S{-}N{=}SF_4$, can also be detected in traces in the photochemical reaction (23) of $F_5S{-}N{=}SF_2$ with F_2. A radical mechanism can thus be concluded for reaction (38)[99].

$$NSF_3 + F_2 \xrightarrow{RT} SF_6,\ N_2,\ F_5S{-}N{=}SF_4 \quad (38)$$

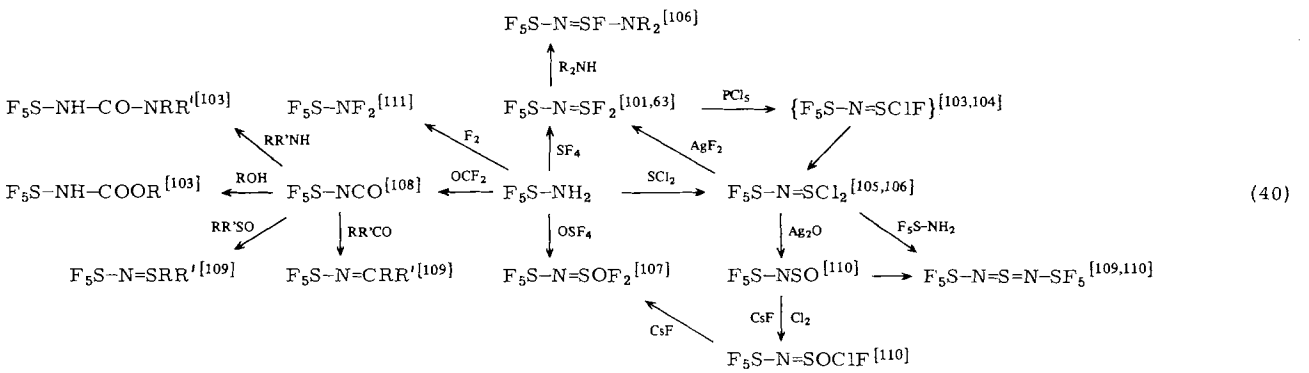
The bis(pentafluorosulfur) amines are obtained *via* $F_5S{-}N{=}SF_4$[100]:

$$(F_5S)_2NH \xleftarrow{HF} F_5S{-}N{=}SF_4 \xrightarrow{HgF_2} [(F_5S)_2N]_2Hg \quad (39)$$

The $(F_5S)_2N^{\ominus}$ ion, produced from the acid $(F_5S)_2NH$, is isoelectronic with the oxide $(F_5S)_2O$.

3.2.1. Other Pentafluorosulfur Amines

Pentafluorosulfur amine $F_5S{-}NH_2$, obtained by addition of HF to the S≡N triple bond of NSF_3 [Reaction (33)], serves as starting material for many further pentafluorosulfur amines, briefly summarized in Reactions (40).



(40)

$F_5S{-}N{=}SF_2$[101], $F_5S{-}N{=}SOF_2$[107], and $F_5S{-}NCO$[108] are synthesized directly from NSF_3 in the presence of HF; the reaction proceeds *via* $F_5S{-}NH_2$.

3.3. Reaction with Nucleophiles

Although $F^{\ominus}$ ions add to NSF to give $NSF_2^{\ominus}$ (Section 2.3.3), they do not add nucleophilically to NSF_3 to give stable $NSF_4^{\ominus}$ salts. However, NSF_3 reacts with F_2 in the presence of CsF, and with Cl_2 and HgF_2:

$$N{\equiv}SF_3 + CsF \longrightarrow \left\{Cs^{\oplus}NSF_4^{\ominus}\right\} \xrightarrow[-CsF]{F_2} F_5S{-}NF_2 \quad (41)$$

[112]

$$N{\equiv}SF_3 + HgF_2 \longrightarrow \left\{Hg(NSF_4)_2\right\} \xrightarrow[-HgCl_2]{Cl_2} F_5S{-}NCl_2 \quad (42)$$

[111]

The formation of $F_5S{-}NF_2$ by Reaction (41), and especially the simple synthesis of $F_5S{-}NCl_2$, are evidence for the NSF_4 anion being an intermediate.

In nucleophilic substitutions of NSF_3 with exchange of the fluorine atoms, the S≡N triple bond can be preserved (Section 3.3.1), or the primary product can rearrange (Section 3.3.2).

3.3.1. Substitution with Retention of the S≡N Triple Bond

Reactions of NSF_3 with amines[113,114] or with alcohols[114] give compounds which still contain the formal S≡N triple bond [Reactions (43) and (44)].

$$NSF_3 + 2\,R_2NH \xrightarrow[Et_2O]{20^{\circ}C} N{\equiv}SF_2{-}NR_2 + R_2NH \cdot HF \quad (43)$$

$$NSF_3 + C_6H_5OH \xrightarrow[Et_3N]{20^{\circ}C} N{\equiv}SF_2{-}O{-}C_6H_5 + Et_3N \cdot HF \quad (44)$$

S-Perfluoroalkyl derivatives can be synthesized by reaction with alkenes in the presence of CsF[115,48], *S*-aryl derivatives can be obtained *via* aryllithium compounds[116].

$$NSF_3 + \rangle C{=}C\langle + CsF \xrightarrow{90^{\circ}C} \left\{Cs^{\oplus}R_f^{\ominus}\right\} \xrightarrow{-CsF} N{\equiv}SF_2R_f \quad (45)$$

($R_f = (F_3C)_2CF$[115], $(F_3C)_3C$[48])

$$NSF_3 + ArylLi \xrightarrow[Et_2O]{-78^{\circ}C} NSF_2Aryl + LiF \quad (46)$$

The two alkyl derivatives rearrange at around 100 °C to give sulfur difluoride imides $R_fN{=}SF_2$. Very little is known about the physical and chemical properties of *S*-aryl compounds. The reaction with aryllithium compounds and lithium amides also leads to disubstituted derivatives of the type $NSFR_2$ (R = aryl, $N(C_6H_5)_2$) as well as to a bis(difluorothiazyl) compound [Reaction (47)][116].

$$2\,NSF_3 + Li{-}C_6H_4{-}Li \longrightarrow N{\equiv}S(F)_2{-}C_6H_4{-}S(F)_2{\equiv}N + 2\,LiF \quad (47)$$

3.3.2. Substitution with Rearrangement of the Primary Product

Stability of NSF_3: In contrast to NSF, NSF_3 is kinetically very stable; it resists hydrolysis by dilute acids and does not react with metallic sodium below *ca.* 200 °C[10]. NSF_3 closely resembles SF_6 in its behavior. In both fluorides there is a certain localization of electron density on the S atom, due to π-back bonding from the F atoms, which makes nucleophilic attack on this atom more difficult. However, electrophilic attack proceeds very rapidly. SF_6 reacts rapidly with $AlCl_3$[117], and NSF_3 reacts rapidly with BCl_3 [Reaction (48)] to give the cation $[N(SCl)_2]^{\oplus}$[43] [cf. Reaction (11)].

$$NSF_3 + BCl_3 \rightarrow [N(SCl)_2]^{\oplus}BCl_4^{\ominus} + (NSCl,\ N_2,\ Cl_2,\ BF_3,\ BF_2Cl) \quad (48)$$

$NSCl_3$ does not seem to be capable of existence, probably because the S—Cl bond energy is insufficient to incorporate all six valence electrons of sulfur.

Hydrolysis: A nucleophilic attack on the S atom in NSF_3 by $OH^{\ominus}$ ions, is possible using hot alkali [Reaction (49)][118].

$$N{\equiv}SF_3 \xrightarrow[-F^{\ominus}]{+OH^{\ominus}} \left\{\begin{array}{c} H \\ \uparrow\downarrow O \\ N{\equiv}S{-}F \\ F \end{array}\right\} \longrightarrow HN{=}S(=O){-}F \xrightarrow[-F^{\ominus}]{+OH^{\ominus}} \quad (49)$$

$$H_2N{-}SO_2F \xrightarrow[-F^{\ominus}]{+OH^{\ominus}} H_2N{-}SO_3H \xrightarrow[H^{\oplus}]{+H_2O} NH_4^{\oplus}\,HSO_4^{\ominus}$$

The first hydrolysis product is sulfur oxide difluoride imide $HNSOF_2$, whose presence was proven by precipitation of the tetraphenylphosphonium salt[119]. The second hydrolysis product, H_2NSO_2F, is related to $NSF_2{-}NHSO_2F$ [see Reaction (61)].

$HNSOF_2$ (Fig. 12a), which we described as a complex ligand (Section 3.1.2), is the parent compound of the $RNSOF_2$ series; R can be an inorganic as well as an organic group. As an acid, $HNSOF_2$ forms salts; worthy of note are the Cs[14], Ag[120] and Hg[121-123] salts, because they react with elemental halogens to give the *N*-halogen derivatives $XNSOF_2$ (X = F, Cl, Br, I)[14,121,124], for example:

$$Hg(NSOF_2)_2 + X_2 \rightarrow 2\,XNSOF_2 + HgF_2 \quad (50)$$

The halides $XNSOF_2$ and $XNSF_2$ have very similar properties. Thus, the structures of $ClNSOF_2$ (Fig. 12b) and $ClNSF_2$ (Fig. 4) are closely related to one another, and the structures of $HNSOF_2$ (Fig. 12a) and $ClNSOF_2$ (Fig. 12b) nearly agree. It should be pointed out that the structures of the isoelectronic species $HNSOF_2$, $OSOF_2$ and NSF_3 hardly differ from one another.

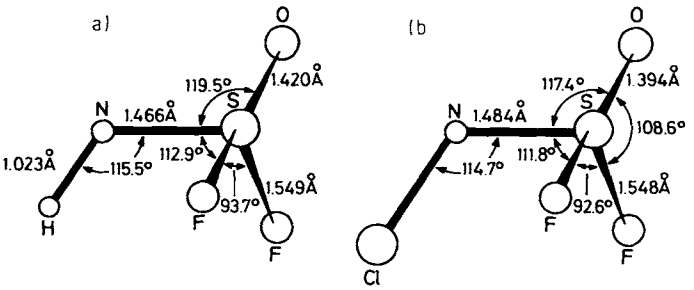


Fig. 12. Structure of a) $HNSOF_2$ (determined by microwave spectroscopy [127]) and b) $ClNSOF_2$ (determined by electron diffraction [126]).

In $HNSOF_2$ and $ClNSOF_2$, as in $ClNSF_2$, the —NH or ClN— group is *cis* to the SF_2— group, or: the lone pair on the N atom and the S=O double bond prefer the sterically favorable *cis*-arrangement. Many organic derivatives of sulfur oxide difluoride imide can be obtained by addition of $ClNSOF_2$ to C=C double bonds[128-130]. As with compounds of the type $RNSF_2$, organic sulfur oxide difluoride imides can also be produced by reaction of OSF_4 with, for example, primary amines, silylated amines, cyanates, and cyanides[8]. The reaction of $RN{=}SF_2$ with OF_2 [Reaction (24)] should also be mentioned.

Many inorganic sulfur oxide difluoride imides *e.g.* $B(NSOF_2)_3$, $[B(NSOF_2)_4]^{\ominus}$, $Sb(NSOF_2)_3$, $Si(NSOF_2)_4$, $OP(NSOF_2)_3$, and $SP(NSOF_2)_3$, can be synthesized *via* $Hg(NSOF_2)_2$—or often better *via* $AgNSOF_2$—with the corresponding chlorides[125,131-139].

$$MCl_n + n/2\ Hg(NSOF_2)_2 \xrightarrow{CH_2Cl_2} M(NSOF_2)_n + n/2\ HgCl_2 \quad (51)$$

The $NSOF_2$ group can also act as a ligand in transition metal complexes. Its tetraphenylarsonium derivative reacts with palladium acetate [140]:

$$4\ (C_6H_5)_4AsNSOF_2 + Pd(OAc)_2 \xrightarrow{CH_3OH} [(C_6H_5)_4As]_2[Pd(NSOF_2)_4] + 2\ (C_6H_5)_4AsOAc \quad (52)$$

The $NSOF_2$ group can be introduced into carbonyl transition metal complexes by using the silver salt $AgNSOF_2$[141] [Reaction (53)]. Below room temperature, $M(CO)_5NSOF_2$ (M = Mn, Re) is obtained. The Mn-compound dimerizes at

$$[Mn, Re](CO)_5Br + AgNSOF_2 \xrightarrow[<RT]{CH_2Cl_2} [Mn, Re](CO)_5NSOF_2$$

$$[Mn, Re](CO)_5NSOF_2 \xrightarrow{70\,^{\circ}C} [Mn(CO)_4NSOF_2]_2$$

$$[Mn, Re](CO)_5NSOF_2 \xrightarrow[90\,^{\circ}C]{\text{heptane}} [Re(CO)_4NSOF_2]_2 \quad (53)$$

room temperature with elimination of CO to give $[Mn(CO)_4NSOF_2]_2$, whose structure was determined[142,143] (Fig. 13). $[Re(CO)_4NSOF_2]_2$ m.p. 150 °C (decomp.) is formed analogously at 90 °C.

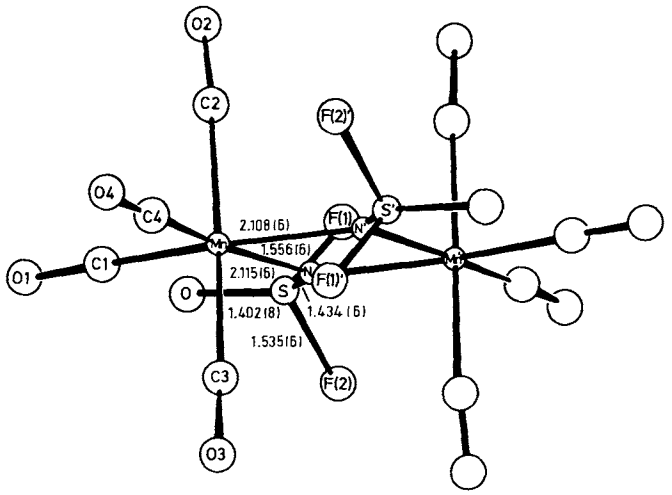


Fig. 13. Structure of $[Mn(CO)_4NSOF_2]_2$ (m.p. 130 °C, decomp.).

In the $NSOF_2$ bridges of the Mn compound (Fig. 13), the S—O and S—F distances are very short and similar to those in $HNSOF_2$ and $ClNSOF_2$ (Fig. 12), as well as in $Re(CO)_5NSOF_2$ (Fig. 14)[144]. The S—N distance is shorter

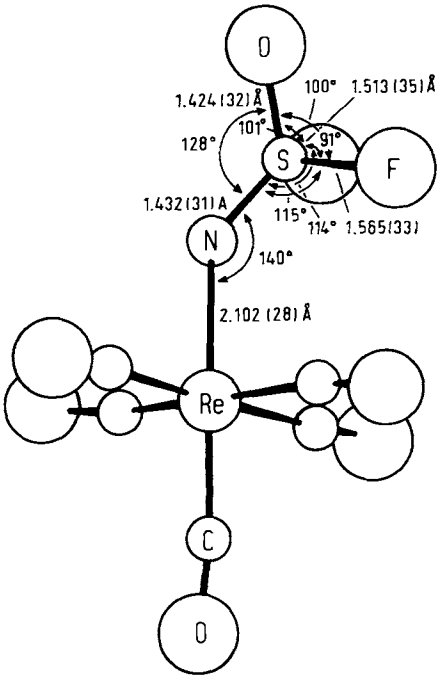


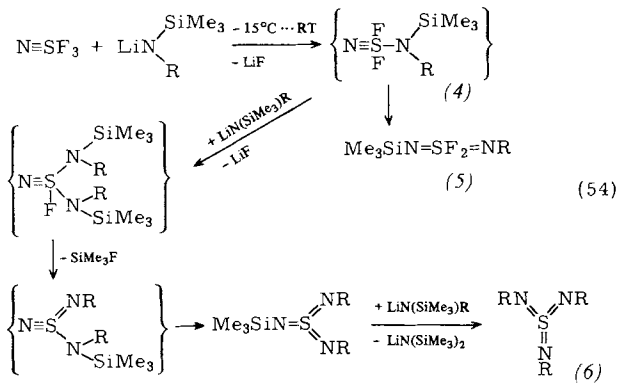
Fig. 14. Structure of $Re(CO)_5NSOF_2$ (m.p. 70 °C).

than in NSF and indicates strong (d-p)π bonds between sulfur and nitrogen. The central part of the structure containing the Mn, N and S atoms is nearly planar, the Mn_2—N_2 ring is exactly planar. All Mn—N bonds are equal and somewhat longer than the sum of the covalence radii. A Mn—Mn bond can be ruled out; the small NMnN' angle of 76° points rather to a repulsive interaction. The *cis*-arrangement of the $Re(CO)_5$— group to the F atoms in $Re(CO)_5NSOF_2$ is surprising. In this respect, the compound behaves like all $RNSOF_2$ and $RNSF_2$ species[145]. Reactions of $[Mn(CO)_4NSOF_2]_2$ which involve retention or opening of the four-membered Mn_2N_2 ring are known[146].

Other similar species, such as $C_5H_5Fe(CO)_2NSOF_2$ and $C_5H_5Cr(CO)_2NSOF_2$, can be produced from iodides or chlorides in accordance with Reaction (53)[147].

Reaction with LiN(SiMe$_3$)R, (R = SiMe$_3$, CMe$_3$)[148-150]: The reaction of NSF_3 with $LiN(SiMe_3)R$ gives $S(NSiMe_3)_3$ (b.p. 204 °C), $S(NCMe_3)_3$ (m.p. 52.5 °C), $S(NSiMe_3)(NCMe_3)_2$ (m.p. 110 °C), as well as $Me_3SiN{=}SF_2{=}NR$ (R = $SiMe_3$, b.p. 158 °C; R = CMe_3, m.p. 11 °C), according to choice of R and choice of reaction conditions. In this reaction, the NSF_3 molecule is attacked electrophilically at the F atom by Li, and nucleophilically at the S atom by the lone pair of the N atom, *i.e.* the silylated amide is acting as an acid as well as a base. We assume that an intermediate product *(4)* results from the cleavage of LiF; this then forms the very stable *(5)* by the migration of the $SiMe_3$ group.

With more silylated lithium amide, the intermediate product *(4)*, but not the diimide *(5)*, reacts. The final product is the sulfonylimide *(6)*, a derivative of the unknown sulfur triimide, which is isoelectronic with SO_3.



(54)

$(R_3SiN)_2SO$[151] occupies an intermediate position between SO_3 and sulfur triimide; it is obtained from OSF_4 and $LiN(SiR_3)_2$. The aza-analogues of the type $(R_3CN)_2S{=}NX$ (X = R'SO_2, F_5S, R_f[152], POF_2[153]) [Reaction (55)], are of interest; they all contain three-coordinate sulfur which has an oxidation number of +6, and have a "Y-triene" structure[154]. The bulky $SiMe_3$ group as well as the CR_3 group, stabilize low coordination states. Compounds $(RN)_3S$ with *e.g.* R = CH_3 or iC_3H_7, polymerize[150]. The molecular structure of $(tBuN)_3S$ was determined by X-ray structural analysis at −130 °C (Fig. 15)[149]. Here, as in the isoelectronic SO_3, the sulfur has a trigonal-planar coordination[155]. The σ-bonds between the S atom and the N atoms lie almost in a plane. This results in a sterically favorable arrangement for the formation of 3pπ(S)—2pπ(N) bonds. The S—N bond lengths vary between those of a single and a double bond.

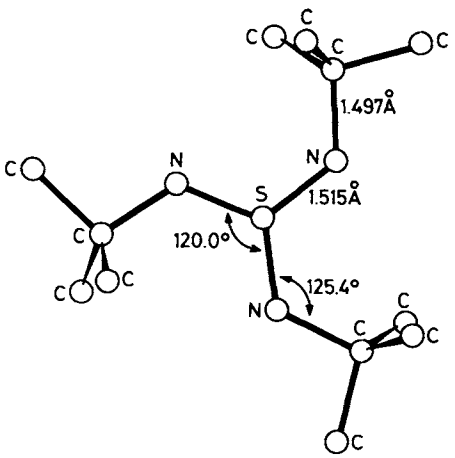
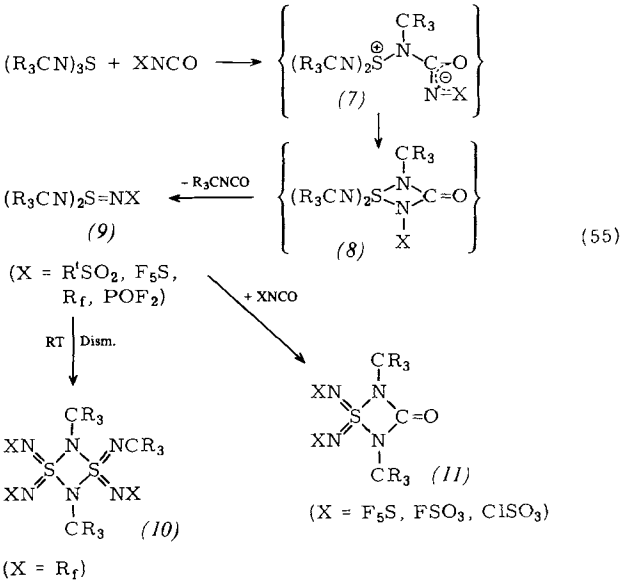


Fig. 15. "Y-triene" structure of $[(CH_3)_3CN]_3S$.

Reactions of $(Me_3SiN)_3S$ and $(R_3CN)_3S$: In both types of "Y-trienes", the S-atom is screened by the bulky Me_3Si or R_3C groups, so that its electrophilic character is ineffective. The characteristic reaction of three-coordinate sulfur compounds should—as known from SO_3—be an increase in coordination number. However, this only occurs if initially one of the N atoms is electrophilically attacked. Of interest are the reactions with isocyanates and *N*-sulfinylamines which lead to new four-membered SN-[156,157] or SNC-ring systems[152] *via* compounds with three-coordinate sulfur, *i.e.* Reactions (55) and (56).

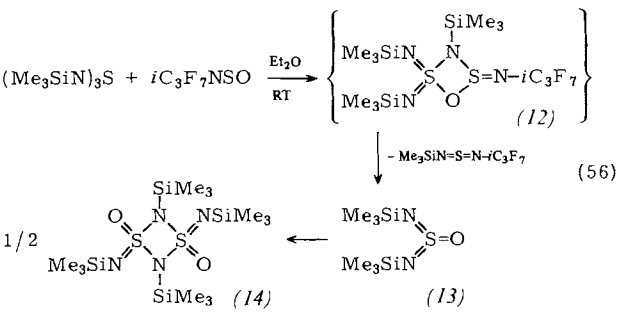
The Y-trienes *(9)* are produced *via* the betaines *(7)* and unstable thiadiazetidinones *(8)*; they then react with excess XNCO to give the stable species *(11)*. Without a suitable co-reactant, the Y-trienes form cyclodiaza-λ⁶-thianes *(10)*.



(55)

(X = R_f)

The reactions with *N*-sulfinylamines proceed *via* similar intermediate products. The intermediate *(13)*, which is probably produced *via (12)*, dimerizes to *(14)*. The structure



(56)

of *(14)*, determined at −120 °C (Fig. 16)[157], is centrosymmetric and contains a planar S_2N_2 ring with transannular S...S and N...N distances of only 2.477 and 2.257 Å, respectively. The N atoms in the ring have pyramidal configurations. The geometry of the ring depends on the nature of the ligands; thus, the four-membered ring of derivative *(10)* is non-planar[157].

Reactions with $Me_3SiN{=}SF_2{=}NSiMe_3$: The cleavage of the Si—N bond in $Me_3SiN{=}SF_2{=}NSiMe_3$ by fluorides and

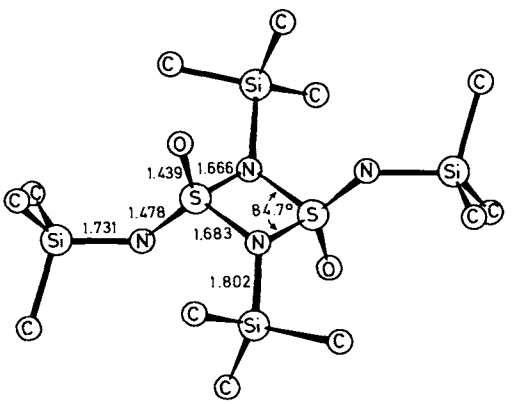


Fig. 16. Structure of the cyclodiaza-λ⁶-thiane (14).

acid anhydrides usually leads to sulfur difluoride diimides. For example, the reaction of $(F_2PO)_2O$ or $(CF_3CO)_2O$ is in accordance with Reaction (57). The monosubstituted products can be detected by NMR spectroscopy.

$$Me_3SiN{=}SF_2{=}NSiMe_3 + ROR \xrightarrow[-\,Me_3SiOR]{0\,^\circ C} \{Me_3SiN{=}SF_2{=}NR\} \quad (57)$$

$$\{Me_3SiN{=}SF_2{=}NR\} \xrightarrow[-\,Me_3SiOR]{+\,ROR} RN{=}SF_2{=}NR$$

(R = F_2P^{O} [158], F_3CC^{O} [159])

An essentially more complicated result is observed with COF_2[159], because the reactive OCF group is inclined to give secondary reactions [Reaction (58)].

$$Me_3SiN{=}SF_2{=}NSiMe_3 + OCF_2 \longrightarrow \{Me_3SiN{=}SF_2{=}NC(O)F\} \quad (58)$$

$$\{Me_3SiN{=}SF_2{=}NC(O)F\} \xrightarrow{+\,OCF_2} FC(O)N{=}SF_2{=}NC(O)F,\ FC(O)N{=}SF_2{=}N{-}C(O){-}N{=}SF_2{=}NC(O)F,$$

$$MeSiN{=}SF_2{=}N{-}C(O){-}N{=}SF_2{=}NSiMe_3$$

The difluoride diimide does not give the expected SF_3-derivative with SF_4, but *N*-(nitridodifluorosulfur) sulfur difluoride imide[160], the first sulfur-nitrogen compound containing single, double, and triple S—N bonds. This is probably formed according to Reaction (59), whose mechanism can be considered as the inversion of that of Reaction (54).

$$Me_3SiN{=}SF_2{=}NSiMe_3 + SF_4 \xrightarrow[-\,Me_3SiF]{RT} \left\{ F_3S(F)(N{-}SF)(N{-}SiMe_3) \right\} \quad (59)$$

$$\left\{ F_3S(F)(N{-}SF)(N{-}SiMe_3) \right\} \xrightarrow[-\,Me_3SiF]{RT} N{\equiv}SF_2{-}N{=}SF_2$$

The formation of the end product is easily understood from the geometry of the intermediate. An excess of SF_4 gives a mixture of *cis*- and *trans*-bis(difluorosulfinylimino)sulfur tetrafluoride $F_2SN{-}SF_4{-}NSF_2$ [Reaction (60)][161]. These compounds with six-coordinate sulfur, as

$$Me_3SiN{=}SF_2{=}NSiMe_3 \xrightarrow{+\,SF_4} \underset{trans}{F_3S(NSF_2)_2} + \underset{cis}{F_3S(NSF_2)_2} \quad (60)$$

$$N{\equiv}S{-}N{=}S(F)_2 \xrightarrow{+\,SF_4} F_3S(NSF_2)_2$$

well as $N{\equiv}SF_2{-}N{=}SF_2$, rapidly polymerize at room temperature and react explosively with water. The analogous $N{\equiv}SF_2{-}N{=}S(O)F_2$ (b.p. 93 °C) is formed from OSF_4 and $Me_3SiN{=}SF_2{=}NSiMe_3$; it attacks rubber and ignites with damp cellulose[162]. It reacts with SF_4 at 120 °C (CsF) to give a mixture of *cis*- and *trans*-$F_2SN{-}SF_4{-}NS(O)F_2$, which can be stored for days at room temperature in a glass vessel without decomposition[161].

Hydrolysis of NSF_2NSOF_2: Reactions of $NSF_2{-}NSOF_2$ offer an interesting comparison between the reactivity of the $N{\equiv}SF_2{-}$ and $NS(O)F_2{-}$ groups. When hydrolyzed[162], the $NS(O)F_2{-}$ group is attacked [Reaction (61)]; the hydrolysis product can be trapped as the tetraphenylarsonium salt. Three tautomeric forms (*G*), (*H*) and (*K*), can be formulated for the free salt, which has hitherto not been isolated. According to the bond lengths in the anion, determined by X-

$$N{\equiv}S(F){-}N{=}SF_2(O) \xrightarrow[-\,F^{\ominus}]{+\,OH^{\ominus}} \{N{\equiv}SF_2{-}NS(O)F(OH)\} \longrightarrow \quad (61)$$

$$N{\equiv}S(F){-}N{=}S(F)(O){-}OH \qquad N{\equiv}S(F){-}NH{-}S(F)(O){-}F \qquad HN{=}S(F){-}N{=}S(F)(O){-}F$$

(*G*) (*H*) (*K*)

ray analysis[163] (Fig. 17), (*H*) is the most important tautomer $[d(N_1S_1) < d(N_2S_2) < d(N_2S_1)]$. The two isoelectronic groups $N{\equiv}SF_2{-}$ and $-SO_2F$ form two tetrahedra connected by the same N atom; the structure is very similar to that of inorganic μ-oxoanions $X_2O_7^{y\ominus}$.

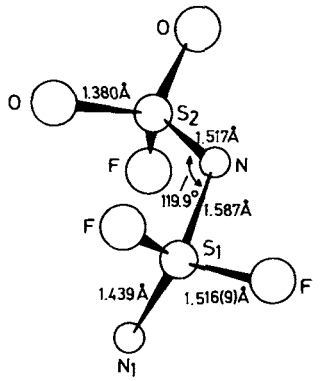


Fig. 17. Structure of the $NSF_2{-}NSO_2F^{\ominus}$ ion.

In this connection, one should remember the hydrolysis of NSF_3, which proceeds *via* the non-isolable $H_2N{-}SO_2F$ [Reaction (49)]. The acid generated by hydrolysis of $NSF_3{-}NSOF_2$ [Reaction (61)] can be formulated as $HNR{-}SO_2F$ with $R = NSF_2$; the structure of its anion (Fig. 17) can be regarded as proof of the occurrence of $H_2N{-}SO_2F$.

Just how versatile the chemistry of sulfur-nitrogen-fluorine acids, such as $NSF_2{-}NH{-}SO_2F$, can be, is shown for example, by the far better investigated isoelectronic $HN(SO_2F)_2$[164], which can also be produced by hydrolysis of $FSO_2{-}N{=}SOF_2$ (formed from H_2NSO_2F and OSF_4). The range of application reaches from organometallic to noble-gas chemistry. The $N(SO_2F)_2$ group can be introduced as a ligand into transition metal complexes *via* the silver salt[165, 166]. Substitution reactions using ligands such as

$$M(CO)_5Br + AgN(SO_2F)_2 \xrightarrow[-\,AgBr]{CH_2Cl_2} M(CO)_5N(SO_2F)_2 \quad (62)$$

(M = Mn, Re)

$$C_5H_5Cr(NO)_2Cl + AgN(SO_2F)_2 \xrightarrow[-\,AgCl]{} C_5H_5Cr(NO)_2N(SO_2F)_2 \quad (63)$$

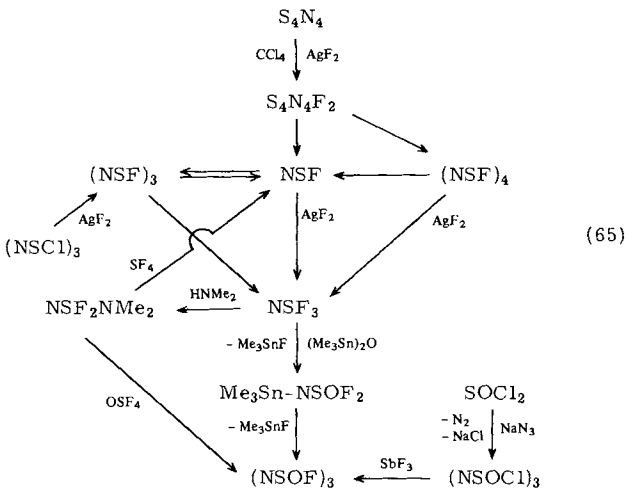
CH_3CN, Ph_3P and Ph_3As[166], have been carried out on the complexes obtained by Reactions (62) and (63). The reaction with XeF_2 [Reaction (64)], gives the remarkable $FXeN(SO_2F)_2$, the first xenon species with a Xe—N bond[167].

$$XeF_2 + HN(SO_2F)_2 \xrightarrow[0\,^\circ C/4\ h]{CF_2Cl_2} FXeN(SO_2F)_2 + HF \quad (64)$$

4. Cyclic Compounds[3, 5, 8, 9, 168–171]

From the abundance of compounds containing sulfur, nitrogen and fluorine, we want to pick out $(NSF)_4$, $(NSF)_3$ and $(NSOF)_3$, since the chemistry of these three compounds is closely related to that of NSF and NSF_3, as shown by Reaction scheme (65).

Fluorination of S_4N_4 using AgF_2 in CCl_4, produces the eight-membered ring $(NSF)_4$[2], probably, as new work



(65)

shows, *via* the intermediate $N_4S_4F_2$[172]. Up to now, $(NSF)_4$ could only be synthesized from S_4N_4, which also has an eight-membered ring. At 300 °C *in vacuo*, or when heated in CCl_4, $(NSF)_4$ dissociates into NSF, which then trimerizes, as already known, to give the six-membered ring $(NSF)_3$[173]. Its formation by decomposition of $S_4N_4F_2$ is also conceivable. Preparatively, the Cl→F exchange of $(NSCl)_3$ using AgF_2[174], is better.

The fluorination of NSF and its cyclic derivatives gives NSF_3, which reacts with hexamethylstannoxane to give $Me_3Sn—NSOF_2$. The decomposition of this sulfur oxide difluoride imide at room temperature leads quantitatively to $(NSOF)_3$[132]. Other sulfur oxide difluoride imides decompose likewise under certain reaction conditions into $(NSOF)_3$ as well as polymeric rubber-like $(NSOF)_x$, which is isoelectronic with $(PNF_2)_x$[171].

$(NSOF)_3$ can be obtained by fluorination of $(NSOCl)_3$ using SbF_3. Furthermore, by starting from NSF_3, it is possible to obtain $(NSF)_3$ and $(NSOF)_3$ *via* the amine $NSF_2(NMe_2)$. The amine reacts with SF_4 as well as with OSF_4 to give $F_5S—NMe_2$ along with NSF in the first case, and $(NSOF)_3$ in the second[107].

Figure 18 shows the structures of $(NSF)_4$[175], $(NSF)_3$[176] and α-$(NSOCl)_3$[177], determined by X-ray analysis. The structure of α-$(NSOF)_3$ *(cis)* is not yet known, but it may correspond to the structure of α-$(NSOCl)_3$[178].

The $(NSF)_4$ molecule is a puckered eight-membered ring, with alternating S—N bond lengths of 1.66 and 1.54 Å; two F atoms are axial, two are equatorial. The structures of $(NSF)_3$ and $(NSOCl)_3$ are very similar to each another; the six-membered rings have a chair configuration with uniform S—N bond lengths of 1.593 and 1.571 Å, respectively. The halogen atoms are axial *(cis)*; the lone pairs on the N and S atoms of $(NSF)_3$ occupy equatorial *(trans)* positions, like the O atoms and lone pairs on the N atoms of $(NSOCl)_3$.

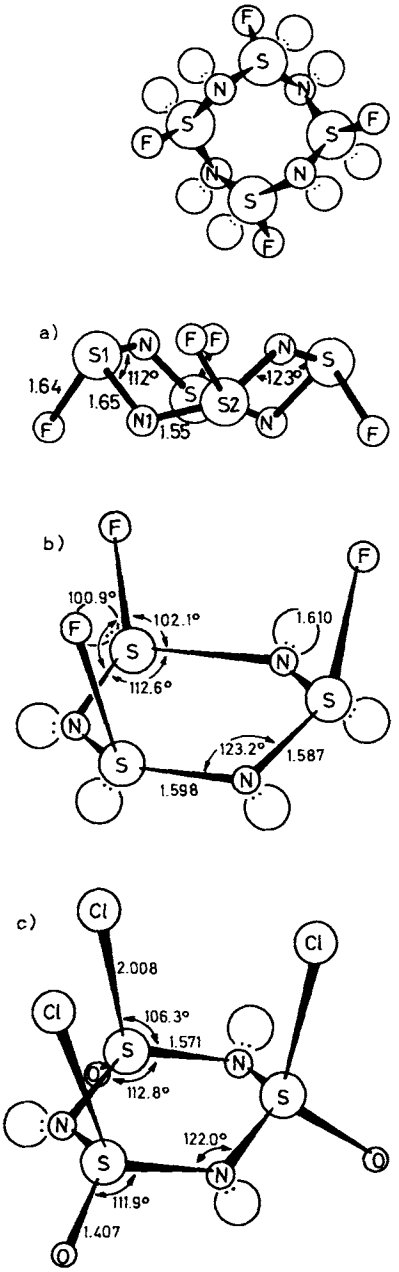


Fig. 18. Structure of a) $(NSF)_4$, b) $(NSF)_3$ and c) α-$(NSOCl)_3$.

The angles at the N and S atoms are almost the same in all three ring systems (similar hybridization of the orbitals). Thus, the chair configuration of the six-membered ring of $(NSF)_3$ becomes the puckered, compact structure of the eight-membered $(NSF)_4$ ring, which, for steric reasons has axial and equatorial F atoms. This is probably due to the repulsive effect of their lone pairs, which are somewhat displaced from one another (Fig. 18a), so that the NSF angles of 91.8° (F—S1—N1) and 106.2° (F—S2—N2) alternate. The same repulsive effect causes the lengthening of four of the eight S—N bonds[179].

The uniform S—N bond lengths in $(NSF)_3$ and $(NSOCl)_3$ could, according to *Dewar et al.*[180], be caused by three islands of delocalized SNS-π-bonds [(d-p)π][171], which originate from three-centered two-electron π-bonds between an N atom and two S atoms. Transannular interaction between the S atoms (Fig. 18) probably occurs in the rings[181].

The repulsive effect of the lone pairs, especially on the π-bonds of the ring, reaches a minimum in the *cis*-structure found for $(NSF)_3$. However, in $(NSOCl)_3$, the repulsive action of the electrons in the S=O double bond is certainly weaker than that of the lone pairs on the S atoms; *i.e.* $(NSOCl)_3$ can form other isomers than the *cis*-form. In accordance with this, only the *cis*-form is found for $(NSF)_3$, whilst in $(NSOCl)_3$ and $(NSOF)_3$, *cis*- and *trans*-isomers have been observed. The *cis*-isomer however, should be the most energetically favorable configuration. This we could prove by an isomerization reaction: At room temperature, in the presence of $F^{\ominus}$ ions (NH_4F, KF) in acetonitrile, pure *cis*- or pure *trans*-$(NSOF)_3$ gave an equilibrium mixture of 75% *cis*- and 25% *trans*-$(NSOF)_3$[182], by an S_N2 reaction with inversion at sulfur (Fig. 19). From the temperature dependency of the equilibrium constant, the conversion enthalpy was found to be $\Delta H_c = 5.5 \pm 1.4$ kJ/mol[182].

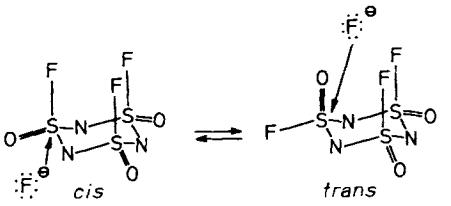


Fig. 19. Equilibrium mixture obtained from the isomerization of *cis*- or *trans*-$(NSOF)_3$.

$(NSF)_3$ should be more stable than $(NSF)_4$, due to the delocalized π-bonds. This was confirmed by the chemical behavior [see *e.g.* Reactions (66) and (67)].

$$(NSF)_4 + 2\,MF_5 \rightarrow N_3S_3F_2^{\oplus}MF_6^{\ominus} + NS^{\oplus}MF_6^{\ominus} \quad (66)$$

$$(NSF)_3 + MF_5 \rightarrow N_3S_3F_2^{\oplus}MF_6^{\ominus} \quad (67)$$

(M = As, Sb)

The cation $N_4S_4F_3^{\oplus}$ is unstable, the eight-membered ring loses an NS unit to form the more stable cation $N_3S_3F_2^{\oplus}$; only the $MF_6^{\ominus}$ salts of this cation are produced from the reaction of $(NSF)_3$ with Lewis acids MF_5[183]. However, $(NSF)_4$ is less sensitive than $(NSF)_3$ to hydrolysis. Nucleophilic attack on the S atom is more difficult with the tetramer than with the trimer, due to its compact structure. The trimer is, like its starting material NSF, strongly hygroscopic.

So far, our experiments show that of the three ring systems $(NSF)_4$, $(NSF)_3$, and $(NSOF)_3$, only the last is suitable for substitution reactions with retention of the ring structure[184]. The delocalized π-bond stabilizes the S—N ring; the S=O double bond and the eventual back-bonding by the F atoms produce a certain electron density on the S atom, which, as in the case of NSF_3, makes nucleophilic attack on this atom more difficult. Moreover, the S atom in $(NSOF)_3$ has a higher coordination number than in $(NSF)_4$ and $(NSF)_3$.

4.1. Some Reactions of $(NSOF)_3$[171]

Fluorination of $(NSOCl)_3$ by SbF_3 yields a mixture of *cis*- and *trans*-isomers of $(NSOF)_3$, along with a little $(NSOF)_2(NSOCl)$ and $(NSOF)(NSOCl)_2$, each of which form three isomers[185]. A mixture of *cis*- and *trans*-$(NSOCl)_3$ is best synthesized[186] according to Reaction (68). As was anticipated, $(NSOF)_3$ is relatively resistant to attack by water.

$$SOCl_2 + NaN_3 \xrightarrow[CH_3CN]{-35\,^{\circ}C} \{N_3SOCl\} + NaCl \xrightarrow[-N_2]{0\cdots30\,^{\circ}C} 1/3\,(NSOCl)_3 \quad (68)$$

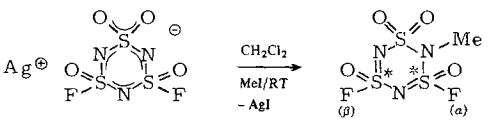
Only boiling sodium hydroxide solution hydrolyzes it to amidosulfuric acid and ammonia[187]; an intermediate product can be precipitated as the tetraphenylphosphonium salt (*cis*- and *trans*-form) according to Reaction (69)[188, 189]:

$$(NSOF)_3 + OH^{\ominus} + Ph_4PCl \xrightarrow[12\,h]{100\,^{\circ}C} Ph_4P^{\oplus}[N_3S_3O_3F_2O]^{\ominus} + HCl + F^{\ominus} \quad (69)$$

The remarkable cyclic anion $[N_3S_3O_3F_2O]^{\ominus}$ can also be obtained by alcoholysis of $(NSOF)_3$ in the presence of NMe_3.

$$(NSOF)_3 + MeOH + 2\,NMe_3 \xrightarrow[Et_2O]{-20\,^{\circ}C} NMe_4^{\oplus}[N_3S_3O_3F_2O]^{\ominus} + NMe_3HF \quad (70)$$

The free acid can be isolated as the oxonium salt $H_3O^{\oplus}[N_3S_3O_3F_2O]^{\ominus}$, by ion exchange and subsequent evaporation of the aqueous solution[188]. The silver salt is obtained with Ag_2CO_3; it reacts with alkyl iodides[190] according to Reaction (71).



(71)

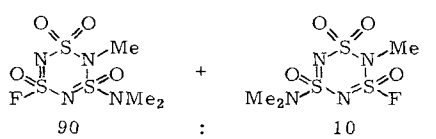
The proposed structure is based on the ^{19}F-NMR spectrum[191]. The compound has two asymmetrical S atoms; their chirality was demonstrated with the help of the chiral 2-butanol[192] using ^{19}F-NMR.

An analogous reaction[193] to (70) is observed with the amino derivative $N_3S_3O_3F_2NMe_2$:

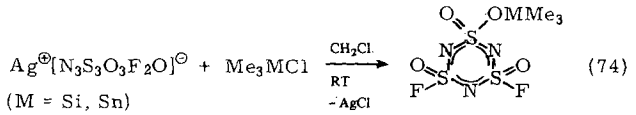
$$N_3S_3O_3F_2NMe_2 + MeOH + 2\,NMe_3 \xrightarrow[CH_3CN]{60\,^{\circ}C} NMe_4^{\oplus}[N_3S_3O_3F(O)NMe_2]^{\ominus} + NMe_3HF \quad (72)$$

After preparation of the free acid, and its conversion to the silver salt, it reacts with MeI to give two isomers in the ratio of 9:1 [Reaction (73)]. The principal isomer shows no coupling in its ^{19}F-NMR spectrum; therefore, the methyl groups on the ring and the SOF-group are in a 1,4-position.

$$Ag^{\oplus}[N_3S_3O_3F(O)NMe_2]^{\ominus} \xrightarrow[MeI/RT]{CH_2Cl_2} \quad (73)$$



The silver salt reacts in quite a different way with organometallic halides[193] [Reaction (74)], the cation $Me_3M^{\oplus}$ is bound to an O atom of the anion. The ^{19}F-NMR spectrum

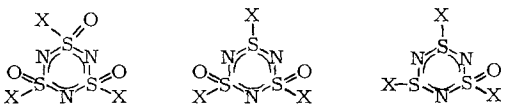


(74)

shows both F atoms to be equivalent (*cis* form), and in the ^{29}Si-NMR spectrum there is no coupling with fluorine. In addition, the chemical shift lies in the region for Si—O bonds. The O—M bond is energetically favorable here.

Ammonia in ether reacts with $(NSOF)_3$ to give $N_3S_3O_3F_2NH_2$, from which various derivatives $N_3S_3O_3F_2R$ can be made, with *e.g.* $R = NSF_2$, $NSOF_2$, $NSCl_2$, $NPCl_3$, $N{=}CHPh$[194, 195].

$(NSOF)_3$ reacts with secondary amines to give tri-, di-, and monosubstituted products[196, 197], depending on the experimental conditions; primary amines usually give only mono-, and rarely trisubstituted products. Primary amines form adducts with the substitution product; the free amine is obtained by cleavage of the adduct in an ether suspension, using hydrogen chloride[197]. Ring systems can be produced from $(NSOF)_3$, which contain sulfur with coordination numbers of three and four, with corresponding oxidation numbers of +4 and +6.

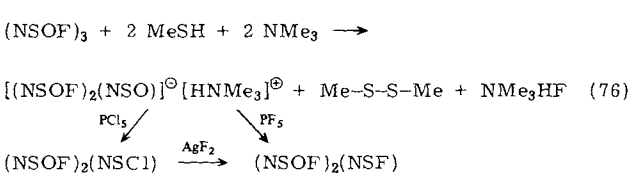


(75)

(15) *(16)* *(17)*

X = F, Cl	X = F, Cl	X = F, Cl
$(NSOX)_3$	$(NSOX)_2(NSX)$	$(NSOX)(NSX)_2$
$(NSOCl)_2(NSOF)$		
$(NSOCl)(NSOF)_2$		
cis-trans-isomers	*cis-trans*-isomers	no isomers

The ring system (15) was briefly mentioned in Reaction (68). The species *(16)* is obtained in good yield[188] by Reaction (76). An alternative method is the reaction of



(76)

$N_3S_3O_3F_2NH_2$ with $SOCl_2$[195]. Further compounds of the type *(16)* and *(17)* were obtained by reaction of $S_3N_2O_2$ with liquid chlorine[198, 199] and subsequent selective fluorination with SbF_3.

In agreement with our thoughts on the occurrence and non-occurrence of isomers of $(NSOF)_3$ and $(NSF)_3$, we find *cis-trans* isomers in the case of *(15)* and *(16)*, which, respectively contain three and two S(O)F groups; *(17)*, which only has one S(O)F group, forms no isomers.

5. Conclusion

The present review article identifies the two molecules NSF and NSF_3 as key compounds in sulfur-nitrogen-fluorine chemistry. Not only almost all known linear fluorinated "thiazenes" (azathienes), but also cyclic oligomers and polymers can be derived from them by addition reactions at the formal S≡N triple bond and by substitution and rearrangement reactions. The types of derivatives are multifarious: they embrace purely "inorganic" to "almost organic" species, organometallic compounds, complexes, and salts. The numerous possible reactions and the novel types of bonding that are observed give a good indication of how this area of chemistry is capable of extension, both from the standpoint of the chemistry of the main group elements—which has recently attracted revived interest—as well as by the use of sulfur nitrogen-fluorine compounds as unusual ligands in transition metal complexes. It is especially worth mentioning that reactions with these complex ligands are possible[31].

X-ray structural analyses and spectroscopic data provide information on the character of the bonding between sulfur and nitrogen. We have found relatively long as well as very short SN bonds; we plan to check which factors influence the SN bond length and those upon which the geometry of the R—SN moiety depends[200]. Finally, it should also be mentioned that the physiological properties of the species mentioned here have scarcely been investigated.

We thank the co-workers cited in our publications, who have contributed by their research to the development of this area. The work of our research group was supported by the Deutsche Forschungsgemeinschaft, the Stiftung Volkswagenwerk, the Fonds der Chemischen Industrie and the Akademie der Wissenschaften in Göttingen as well as by the Mittel des Landes Niedersachsen.

Received: June 11, 1980 [A 340 IE]
German version: Angew. Chem. *92*, 904 (1980)
Translated by Gillian L. Shaw, Offenburg

[1] Prof. Dr. *H. von Wartenberg* (1880—1960); cf. Angew. Chem. *72*, 179 (1960).
[2] *O. Glemser, H. Schröder, H. Haeseler*, Naturwissenschaften *42*, 44 (1955); Z. Anorg. Allg. Chem. *279*, 28 (1955); *O. Glemser, H. Schröder, ibid. 284*, 97 (1956).
[3] *O. Glemser*, Angew. Chem. *75*, 697 (1963); Angew. Chem. Int. Ed. Engl. *2*, 530 (1963); Prep. Inorg. React. *1*, 227 (1964); Endeavour *28*, 86 (1969); Int. J. Sulfur Chem. *C6*, 35 (1971).
[4] *O. Glemser, U. Biermann*, Nachr. Akad. Wiss. Goettingen, Math.-Phys. Kl. II, Nr. 5, p. 65 (1968).
[5] *O. Glemser, M. Fild* in *V. Gutmann:* Halogen Chemistry. Vol. 2. Academic Press, London 1967, p. 1.
[6] *S. P. von Halasz, O. Glemser* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry. Marcel Dekker, New York 1971, p. 209.
[7] *H. W. Roesky* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry. Marcel Dekker, New York 1971, p. 13.
[8] *O. Glemser, R. Mews*, Adv. Inorg. Chem. Radiochem. *14*, 333 (1972).
[9] *R. Mews*, Adv. Inorg. Chem. Radiochem. *19*, 185 (1976).
[10] *O. Glemser, H. Richert*, Z. Anorg. Allg. Chem. *307*, 313 (1961).
[11] *O. Glemser, H. Meyer, A. Haas*, Chem. Ber. *97*, 1704 (1964).
[12] *R. Appel, E. Laßmann*, Chem. Ber. *104*, 2246 (1971).
[13] *A. F. Clifford, C. S. Kobayashi*, Inorg. Chem. *4*, 571 (1965).
[14] *J. K. Ruff*, Inorg. Chem. *5*, 1787 (1966).
[15] *O. Glemser, R. Mews, H. W. Roesky*, Chem. Ber. *102*, 1523 (1969).
[16] *W. H. Kirchhoff, E. B. Wilson, Jr.*, J. Am. Chem. Soc. *85*, 1726 (1963).
[17] *D. O. Cowan, R. Gleiter, O. Glemser, O. Heilbronner, J. Schäublin*, Helv. Chim. Acta *54*, 1559 (1971).
[18] *R. N. Dixon, G. Duxbury, G. R. Fleming, J. M. V. Hugo*, Chem. Phys. Lett. *14*, 60 (1972); *P. Rosmus, P. D. Dacre, B. Solouki, H. Bock*, Theor. Chim. Acta *35*, 129 (1974).
[19] *D. O. Cowan, R. Gleiter, O. Glemser, E. Heilbronner*, Helv. Chim. Acta *55*, 2418 (1972).
[20] *R. L. Cook, W. H. Kirchhoff*, J. Chem. Phys. *47*, 4521 (1967); *A. M. Mirri, A. Guarnieri*, Spectrochim. Acta *A 23*, 2159 (1967).
[21] *A. Müller, N. Mohan, S. J. Cyvin, N. Weinstock, O. Glemser*, J. Mol. Spectrosc. *59*, 161 (1976).
[22] *H. Richert, O. Glemser*, Z. Anorg. Allg. Chem. *307*, 328 (1961).

[23] *J. W. Larson, G. K. Johnson, P. A. G. O'Hare, N. N. Hubbard, O. Glemser,* J. Chem. Thermodyn. *5*, 689 (1973).

[24] *J. Varwig, H. Steinbeisser, R. Mews, O. Glemser,* Z. Naturforsch. *B 29*, 813 (1974).

[25] *F. Seel, W. Gombler, R. Budenz,* Z. Naturforsch. *B 27*, 78 (1972). Amidosulfoxy acid fluorides ($R_2N{-}S{-}F$) can be stabilized somewhat by steric screening: *G. V. Röschenthaler, R. Starke, ibid. B 32*, 721 (1977).

[26] *W. Bludssus, R. Mews,* J. Chem. Soc. Chem. Commun. *1979*, 35.

[27] *W. L. Mock,* J. Am. Chem. Soc. *88*, 2857 (1966); *S. D. McGregor, D. M. Lemal, ibid. 88*, 2858 (1966).

[28] *B. Buss, P. G. Jones, R. Mews, M. Noltemeyer, G. M. Sheldrick,* Angew. Chem. *91*, 253 (1979); Angew. Chem. Int. Ed. Engl. *18*, 231 (1979); Acta Crystallogr. *B 36*, 141 (1980).

[29] *G. Hartmann, P. G. Jones, R. Mews, G. M. Sheldrick,* Z. Naturforsch. *35b*, 1191 (1980).

[30] *R. Mews,* Angew. Chem. *87*, 669 (1975); Angew. Chem. Int. Ed. Engl. *14*, 640 (1975).

[31] A fluoride ion can be cleaved from the complex obtained by Reaction (8), as with free NSF, by using fluoro-Lewis acids at $-30\,^{\circ}C$ in liquid SO_2 (*R. Mews, C. S. Liu,* unpublished):

$$[Re(CO)_5NSF]^{\oplus}AsF_6^{\ominus} + AsF_5 \rightarrow [Re(CO)_5(NS)]^{2\oplus}[AsF_6^{\ominus}]_2$$

If silylamines or halides are used, the fluorine can be exchanged to form, for example, $[Re(CO)_5NSN(CH_3)_2]^{\oplus}$ or $[Re(CO)_5NSCl]^{\oplus}$ (*R. Mews,* unpublished).

[32] *O. Glemser, W. Koch,* Angew. Chem. *83*, 145 (1971); Angew. Chem. Int. Ed. Engl. *10*, 127 (1971).

[33] *O. Glemser, W. Koch,* An. Asoc. Quim. Argentina *59*, 143 (1971).

[34] *R. Mews,* Angew. Chem. *88*, 757 (1976); Angew. Chem. Int. Ed. Engl. *15*, 691 (1976).

[35] *W. Clegg, O. Glemser, K. Harms, G. Hartmann, R. Mews, M. Noltemeyer, G. M. Sheldrick,* Acta Crystallogr., in press.

[36] *A. Jenouvier, B. Pascat,* Can. J. Phys. *51*, 2143 (1973).

[37] *R. Faggiani, R. J. Gillespie, C. J. L. Lock, J. D. Tyrer,* Inorg. Chem. *17*, 2975 (1978).

[38] *J. M. Dyke, A. Morris, I. R. Trickle,* J. Chem. Soc. Faraday Trans. II *73*, 147 (1977).

[39] *A. Karpfen, P. Schuster, J. Petkov, H. Lischka,* J. Chem. Phys. *68*, 3884 (1978).

[40] *C. Zirz, R. Ahlrichs,* private communication.

[41] *A. J. Banister, H. G. Clarke,* J. Chem. Soc. Dalton Trans. *1972*, 2661.

[42] *H. W. Roesky, W. Grosse-Böwing, I. Rayment, H. M. M. Shearer,* J. Chem. Soc. Chem. Commun. *1975*, 735; *A. J. Banister, J. A. Durant, I. Rayment, H. M. M. Shearer,* J. Chem. Soc. Dalton Trans. *1976*, 928. The first given heart-shaped structure for $S_5N_5^{\oplus}$ can presumably be explained by a disordering of the azulene structure in the solid state: *A. J. Banister, J. A. Durant,* J. Chem. Res. (M) *1978*, 1931.

[43] *O. Glemser, B. Krebs, J. Wegener, E. Kindler,* Angew. Chem. *81*, 568 (1969); Angew. Chem. Int. Ed. Engl. *8*, 598 (1969). Furthur syntheses from SCl_2, $(NSCl)_3$ and MCl_3 (M = Fe, Al): *O. Glemser, J. Wegener,* Inorg. Nucl. Chem. Lett. *7*, 623 (1971); *G. G. Alange, A. J. Banister, P. J. Dainty, ibid. 15*, 175 (1979).

[44] The S—N distance and S—N—S angles in sulfur-nitrogen compounds should follow a linear function (*A. J. Banister, J. A. Durant,* J. Chem. Res. (M) *1978*, 1912). However, the values found for the cation $[N(SCl)_2]^{\oplus}$ do not fulfill a linear relationship. To conclude from this (like *Banister et al.*) that the structure determination is incorrect is unjustified, since on the one hand a strong deviation from linearity has been observed with other species, especially cations, and on the other an X-ray structural analysis of $[N(SCl)_2]^{\oplus}AlCl_4^{\ominus}$ (*O. Glemser, E. Kindler, B. Krebs, R. Mews, F. M. Schnepel, J. Wegener,* Z. Naturforsch. *B 35*, 657 (1980)) confirms the earlier reported structure [43]; cf. also *F. M. Sheppel,* Spectrochim. Acta, in press.

[45] *H. J. Emeleus, R. J. Poulet,* J. Fluorine Chem. *1*, 13 (1971/72).

[46] *R. Mews,* unpublished.

[47] *W. Bludssus, R. Mews, O. Glemser, G. G. Alange,* Isr. J. Chem. *17*, 137 (1978).

[48] *A. Waterfeld, W. Bludssus, R. Mews, O. Glemser,* Z. Anorg. Allg. Chem. *464*, 268 (1980).

[49] *W. Bludssus, R. Mews,* unpublished.

[50] *R. S. Atkinson, B. D. Judkins,* J. Chem. Soc. Chem. Commun. *1979*, 832, 833.

[51] *W. Bludssus, R. Mews,* Chem. Ber., in press.

[52] *H. W. Roesky, O. Glemser, A. Hoff,* Chem. Ber. *101*, 1215 (1968).

[53] HNSO leads to numerous organic *N*-sulfinyl amines RNSO, as well as halides XNSO (X = F, Cl, Br, I), which like HNSO (*P. Cassoux, A. Serafini, G. Fong, R. L. Kuczkowski,* Inorg. Chem. *17*, 1204 (1978)) have a *cis*-configuration (*H. H. Eysel,* J. Mol. Struct. *5*, 275 (1970)).

[54] *O. Glemser, S. Gruhl,* unpublished work (1966).

[55] *O. Glemser, R. Mews, H. W. Roesky,* Chem. Commun. *1969*, 914.

[56] *J. Haase, H. Oberhammer, W. Zeil, O. Glemser, R. Mews,* Z. Naturforsch. *A 25*, 153 (1970).

[57] *R. R. Karl, Jr., S. H. Bauer,* Inorg. Chem. *14*, 1859 (1975).

[58] *A. R. Boate, K. F. Preston,* Inorg. Chem. *17*, 1669 (1978).

[59] *I. Stahl, R. Mews, O. Glemser,* Chem. Ber. *113*, 2430 (1980).

[60] *I. Stahl, R. Mews, O. Glemser,* Angew. Chem. *92*, 393 (1980); Angew. Chem. Int. Ed. Engl. *19*, 408 (1980).

[61] *M. Lustig, J. K. Ruff,* Inorg. Chem. *4*, 1444 (1965).

[62] *H. W. Roesky,* Angew. Chem. *80*, 626 (1968); Angew. Chem. Int. Ed. Engl. *7*, 630 (1968).

[63] *A. F. Clifford, G. R. Zeilenga,* Inorg. Chem. *8*, 1789 (1969).

[64] *A. Waterfeld, I. Stahl, R. Mews,* unpublished.

[65] *I. Stahl, R. Mews, O. Glemser,* J. Fluorine Chem. *7*, 55 (1976), $iC_3F_7NSF_4$ has only been synthesized once, *i.e.* nonreproducibly. With R = OCF, F_5SNCO, $F_5SOC(O)F$ and $F_5SOOC(O)F$ are formed, along with the products from Reaction (24) and other substances (*I. Stahl, R. Mews, O. Glemser,* Chem. Ber. *110*, 2398 (1977).

[66] *E. Castellano, H. J. Schumacher,* Z. Phys. Chem. (Frankfurt) *40*, 51 (1964).

[67] *J. Haase, H. Oberhammer, W. Zeil, O. Glemser, R. Mews,* Z. Naturforsch. *A 26*, 1333 (1971).

[68] *I. Stahl, C. Lensch, R. Mews, O. Glemser,* unpublished.

[69] *F. Königer, A. Müller, O. Glemser,* J. Mol. Struct. *46*, 29 (1978).

[70] *A. Müller, A. Ruoff, B. Krebs, O. Glemser, W. Koch,* Spectrochim. Acta *A 25*, 199 (1969).

[71] *W. H. Kirchhoff, E. B. Wilson, Jr.,* J. Am. Chem. Soc. *84*, 334 (1962).

[72] *K. Ramaswamy, K. Sathianandan, F. F. Cleveland,* J. Mol. Spectrosc. *9*, 107 (1962).

[73] *P. A. G. O'Hare, W. N. Hubbard, O. Glemser, J. Wegener,* J. Chem. Thermodyn. *2*, 71 (1970).

[74] *I. Stahl, O. Glemser,* unpublished.

[75] *W. L. Jolly, M. S. Lazarus, O. Glemser,* Z. Anorg. Allg. Chem. *406*, 209 (1974).

[76] *A. Müller, O. Glemser, K. Scherf,* Chem. Ber. *99*, 3568 (1966).

[77] *R. Mews, O. Glemser,* Angew. Chem. *87*, 208 (1975); Angew. Chem. Int. Ed. Engl. *14*, 186 (1975).

[78] *R. Mews, C. S. Liu, O. Glemser,* unpublished.

[79] *R. Mews,* J. Chem. Soc. Chem. Commun. *1979*, 278.

[80] Cf. *F. M. Schnepel,* Dissertation, Universität Göttingen 1979.

[81] *F. M. Schnepel, R. Mews, O. Glemser,* J. Mol. Struct. *60*, 89 (1980).

[82] *B. Buss, M. Noltemeyer, R. Mews, O. Glemser,* unpublished.

[83] *B. Buss, W. Clegg, G. Hartmann, P. G. Jones, R. Mews, M. Noltemeyer, G. M. Sheldrick,* J. Chem. Soc. Dalton Trans., in press.

[84] Due to thermal motion, the S—N distance cannot be determined exactly. There is a comparable example in organic chemistry: In the adduct $H_3C{-}C{-}N{\cdot}BF_3$, the system C—C—N·B is linear and has shortened C—N and C—C distances (*R. A. Walton,* Q. Rev. Chem. Soc. *19*, 126 (1965)).

[85] *A. Waterfeld, R. Mews,* unpublished.

[86] *R. Mews, H. C. Braeuer,* Z. Anorg. Allg. Chem. *447*, 126 (1978).

[87] *R. Froböse, H. C. Braeuer, R. Mews, O. Glemser,* unpublished.

[88] *R. Froböse, R. Mews, O. Glemser,* Z. Naturforsch. *B 34*, 1461 (1979).

[89] *S. Bellard, A. V. Rivera, G. M. Sheldrick,* Acta Crystallogr. *B 34*, 1034 (1978).

[90] *H. C. Braeuer, R. Mews,* unpublished.

[91] *A. F. Clifford, G. C. Duncan,* Inorg. Chem. *5*, 692 (1966).

[92] *R. Mews,* Angew. Chem. *90*, 561 (1978); Angew. Chem. Int. Ed. Engl. *17*, 530 (1978).

[93] *R. Mews, R. Bartsch, A. Waterfeld,* unpublished.

[94] A C_{3v} symmetry and a linear C—N—S group was concluded from the vibration spectrum of $[H_3C{-}NSF_3]^{\oplus}$ [80].

[95] *H. Oberhammer, R. Boggs, R. Mews, I. Stahl,* unpublished.

[96] At room temperature, the ^{19}F-NMR spectrum shows a broad signal, the ^1H-NMR spectrum a quartet. Below 0 °C, complex multiplets appear, which constantly alter up to $-120\,^{\circ}C$. Below 0 °C, the transposition of the axial and equatorial atoms is difficult, and rotation around the C—N axis is hindered.

[97] *C. W. Tullock, D. D. Coffman, E. L. Muetterties,* J. Am. Chem. Soc. *86*, 357 (1964).

[97a] *D. D. DesMarteau, K. Seppelt,* Angew. Chem. *92*, 659 (1980); Angew. Chem. Int. Ed. Engl. *19*, 643 (1980).

[98] *A. Waterfeld, R. Mews,* unpublished.

[99] The radical $^{\ominus}NSF_4$ is formed by γ-radiation of the solid solution of NSF_3 in SF_6; it has a trigonal bipyramidal structure (*A. R. Boate, J. R. Morton, K. F. Preston,* J. Phys. Chem. *80*, 409 (1976)).

[100] *A. Waterfeld, R. Mews,* unpublished.

[101] *A. F. Clifford, J. W. Thompson,* Inorg. Chem. *5*, 1424 (1966).

[102] *A. F. Clifford, G. R. Zeilenga,* Inorg. Chem. *8*, 979 (1969).

[103] *A. F. Clifford, J. L. Howell, D. E. Maurer, P. N. Skoog, J. S. Thrasher,* 4th Winter Fluorine Conf., Daytona Beach, Florida 1979.

[104] *I. Stahl, R. Mews, O. Glemser,* unpublished.

[105] *A. F. Clifford, R. G. Goel,* Inorg. Chem. *8*, 2004 (1969).

[106] *R. Hofer, O. Glemser,* Z. Anorg. Allg. Chem. *416*, 263 (1975).

[107] *R. Höfer, O. Glemser,* Z. Naturforsch. *B 30*, 458 (1975).

[108] *L. C. Duncan, T. C. Rhyne, A. F. Clifford, R. E. Shaddix, J. W. Thompson,* J. Inorg. Nucl. Chem. Suppl. *1976*, 33.

[109] *A. F. Clifford, A. Shanzer,* J. Fluorine Chem. *8*, 65 (1976).

[110] *P. Kricke, I. Stahl, R. Mews,* unpublished.

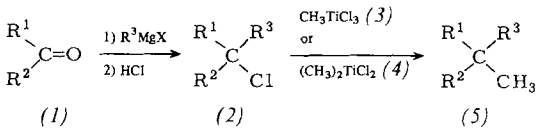
[111] *A. Waterfeld, R. Mews*, unpublished.
[112] *O. Glemser, K. Scherf*, unpublished (1966).
[113] *O. Glemser, H. Meyer, A. Haas*, Chem. Ber. *98*, 2049 (1965).
[114] *O. Glemser, W. Koch*, Z. Naturforsch. *B 23*, 745 (1968). Instead of amines, silylamines can be used to advantage.
[115] *A. F. Clifford, J. S. Harman*, J. Chem. Soc. Dalton Trans. *1974*, 571.
[116] *A. F. Clifford, J. L. Howell, D. L. Wooton*, J. Fluorine Chem. *11*, 433 (1978).
[117] *J. R. Case, J. F. Nyman*, Nature 193, 473 (1972).
[118] SF_6 is much more stable than NSF_3 against hydrolysis, probably because the S atom is coordinatively unsaturated and better protected by the F atoms than in NSF_3.
[119] *H. W. Roesky, O. Glemser, A. Hoff, W. Koch*, Inorg. Nucl. Chem. Lett. *3*, 39 (1967).
[120] *M. Feser, R. Höfer, O. Glemser*, Z. Naturforsch. *B 29*, 716 (1974).
[121] *O. Glemser, R. Mews, S. P. von Halasz*, Inorg. Nucl. Chem. Lett. *5*, 321 (1969).
[122] *K. Seppelt, W. Sundermeyer*, Angew. Chem. *82*, 931 (1970); Angew. Chem. Int. Ed. Engl. *9*, 905 (1970).
[123] *O. Glemser, H. Saran, R. Mews*, Chem. Ber. *104*, 696 (1971).
[124] *K. Seppelt, W. Sundermeyer*, Z. Naturforsch. *B 26*, 65 (1971).
[125] *C. Jäckh, A. Roland, W. Sundermeyer*, Chem. Ber. *108*, 2580 (1975).
[126] *H. Oberhammer, O. Glemser, H. Klüver*, Z. Naturforsch. *A 29*, 901 (1974).
[127] *R. Cassoux, R. L. Kuczkowski, R. A. Creswell*, Inorg. Chem. *16*, 2959 (1977).
[128] *R. Mews, O. Glemser*, Inorg. Nucl. Chem. Lett. *7*, 821 (1971).
[129] *H. Klüver, O. Glemser*, Chem. Ber. *110*, 1597 (1977).
[130] *J. Varwig, R. Mews, O. Glemser*, Chem. Ber. *107*, 2468 (1974).
[131] *W. Buckendahl, O. Glemser, H. Saran*, Z. Naturforsch. *B 28*, 222 (1973).
[132] *R. Höfer, O. Glemser*, Z. Naturforsch. *B 27*, 1106 (1972).
[133] *W. Sundermeyer, A. Roland, K. Seppelt*, Angew. Chem. *83*, 443 (1971); Angew. Chem. Int. Ed. Engl. *10*, 419 (1971).
[134] *C. Jäckh, W. Sundermeyer*, Angew. Chem. *86*, 442 (1974); Angew. Chem. Int. Ed. Engl. *13*, 401 (1974).
[135] *A. Roland, W. Sundermeyer*, Z. Naturforsch. *B 27*, 1102 (1972).
[136] *A. Roland, K. Seppelt, W. Sundermeyer*, Z. Anorg. Allg. Chem. *393*, 149 (1972).
[137] *K. Horn, H. Schachner, W. Sundermeyer*, Chem. Ber. *112*, 1189 (1979).
[138] *R. Eisenbarth, W. Sundermeyer*, Angew. Chem. *90*, 226 (1978); Angew. Chem. Int. Ed. Engl. *17*, 212 (1978).
[139] *H. J. Krannich, W. Sundermeyer*, Angew. Chem. *88*, 338 (1976); Angew. Chem. Int. Ed. Engl. *15*, 311 (1976).
[140] *R. Eisenbarth, W. Sundermeyer*, Z. Naturforsch. *B 33*, 1194 (1978).
[141] *R. Mews, O. Glemser*, J. Chem. Soc. Chem. Commun. *1973*, 823.
[142] *B. Buss, D. Altena, R. Mews, O. Glemser*, Angew. Chem. *90*, 287 (1978); Angew. Chem. Int. Ed. Engl. *17*, 280 (1978).
[143] *B. Buss, D. Altena*, Z. Anorg. Allg. Chem. *440*, 65 (1978).
[144] *B. Buss, D. Altena*, unpublished.
[145] In $[Mn(CO)_4NSOF_2]_2$, the two Mn—N bonds which are *"cis"* to the F atoms, are shorter (if only a little) than the other two.
[146] *R. Mews*, unpublished.
[147] *M. Feser, R. Mews, O. Glemser*, unpublished.
[148] *O. Glemser, J. Wegener*, Angew. Chem. *89*, 324 (1970); Angew. Chem. Int. Ed. Engl. *9*, 309 (1970).
[149] *O. Glemser, S. Pohl, F. M. Tesky, R. Mews*, Angew. Chem. *89*, 829 (1977); Angew. Chem. Int. Ed. Engl. *16*, 789 (1977).
[150] *F. M. Tesky, R. Mews, O. Glemser*, Z. Anorg. Allg. Chem. *452*, 103 (1979).
[151] *O. Glemser, M. F. Feser, S. P. von Halasz, H. Saran*, Inorg. Nucl. Chem. Lett. *8*, 321 (1972).
[152] *F. M. Tesky, R. Mews, B. Krebs, M. R. Udupa*, Angew. Chem. *90*, 722 (1978); Angew. Chem. Int. Ed. Engl. *17*, 677 (1978); *F. M. Tesky, R. Mews*, Chem. Ber. *113*, 2183 (1980).
[153] *F. M. Tesky, R. Mews*, unpublished.
[154] Sulfur is surrounded by the three ligands so forming a Y; "triene" corresponds to the three double bonds.
[155] This is the first time that this type of structure has been confirmed for the solid state. The structure of $(Me_3SiN)_3S$ was also determined (*S. Pohl, B. Krebs, U. Seyer, G. Henkel*, Chem. Ber. *112*, 1751 (1979).
[156] The formation of cyclodiazo-λ^6-thianes was first observed from the dimerization of FSO_2NSO_2 to give $(FSO_2NSO_2)_2$ (*K. D. Schmidt, R. Mews, O. Glemser*, Angew. Chem. *88*, 646 (1976); Angew. Chem. Int. Ed. Engl. *15*, 614 (1976)) and of $CF_3SO_2NSO_2$ to give $(CF_3SO_2NSO_2)_2$ (*H. W. Roesky, M. Aramaki, L. Schönfelder*, Z. Naturforsch. *B 33*, 1072 (1978)).
[157] *F. M. Tesky, R. Mews, B. Krebs*, Angew. Chem. *91*, 231 (1979); Angew. Chem. Int. Ed. Engl. *18*, 235 (1979).
[158] *J. Wegener, O. Glemser, R. Höfer*, Chem. Ber. *105*, 474 (1972).
[159] *I. Stahl, R. Mews, O. Glemser*, J. Fluorine Chem. *11*, 455 (1978).
[160] *O. Glemser, R. Höfer*, Angew. Chem. *83*, 890 (1971); Angew. Chem. Int. Ed. Engl. *10*, 815 (1971).
[161] *R. Höfer, O. Glemser*, Angew. Chem. *85*, 1105 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1000 (1973).
[162] *O. Glemser, R. Höfer*, Z. Naturforsch. *B 29*, 121 (1974).
[163] *B. Buss, D. Altena, R. Höfer, O. Glemser*, J. Chem. Soc. Chem. Commun. *1978*, 226.
[164] For example *J. K. Ruff*, Inorg. Chem. *4*, 1446 (1965); *5*, 732 (1966).
[165] *R. Mews, O. Glemser*, Z. Naturforsch. *B 28*, 362 (1973).
[166] *R. Fröböse, R. Mews, O. Glemser*, Z. Naturforsch. *B 31*, 1497 (1976).
[167] *R. D. Le Blond, D. D. DesMarteau*, J. Chem. Soc. Chem. Commun. *1974*, 555.
[168] *H. W. Roesky*, Chem.-Ztg. *98*, 121 (1974).
[169] *H. W. Roesky*, Angew. Chem. *91*, 112 (1979); Angew. Chem. Int. Ed. Engl. *18*, 91 (1979).
[170] *H. W. Roesky*, Adv. Inorg. Chem. Radiochem. *22*, 239 (1979).
[171] *O. Glemser*, Z. Naturforsch. *B 31*, 610 (1976).
[172] *L. Zborilova, P. Gebauer*, Z. Chem. *19*, 32 (1979); Z. Anorg. Allg. Chem. *448*, 5 (1979); *L. Zborilova, P. Gebauer, J. Strnad*, Z. Chem. *19*, 255 (1979).
[173] $(NSF)_4$, NSF, $(NSF)_3$ and NSF_3 among other products, can be isolated from the reaction mixture of the fluorination of S_4N_4 by AgF_2 in CCl_4 [10]. $(NSF)_4$ and $(NSF)_3$ are also produced by low temperature fluorination of S_4N_4 with F_2 and He in a nickel tube (*N. J. Maraschin, R. L. Lagow*, J. Am. Chem. Soc. *94*, 8601 (1972)). $(NSF)_4$ is the primary product, then decomposes to give NSF, which gives the other fluorides.
[174] *H. Schröder, O. Glemser*, Z. Anorg. Allg. Chem. *298*, 78 (1959).
[175] *G. A. Wiegers, A. Vos*, Acta Crystallogr. *14*, 562 (1961); *16*, 152 (1963).
[176] *B. Krebs, S. Pohl, O. Glemser*, J. Chem. Soc. Chem. Commun. *1972*, 548; *B. Krebs, S. Pohl*, Chem. Ber. *106*, 1069 (1973).
[177] *A. J. Banister, A. C. Hazell*, Proc. Chem. Soc. *1962*, 282; *G. A. Wiegers, A. Vos, ibid. 1962*, 387; *A. C. Hazell, G. A. Wiegers, A. Vos*, Acta Crystallogr. *20*, 186 (1966).
[178] The structures of $(NSF)_3$ and $(NSCl)_3$ are also practically the same [171].
[179] *W. A. Jolly*, Adv. Chem. Ser. *110*, 92 (1972).
[180] *M. J. S. Dewar, E. A. C. Lucken, M. A. Whitehead*, J. Chem. Soc. *1960*, 2423.
[181] *P. Cassoux, O. Glemser, J. F. Labarre*, Z. Naturforsch. *B 32*, 41 (1977).
[182] *H. Wagner, O. Glemser*, unpublished; *H. Wagner*, Dissertation, Universität Göttingen 1976. The reaction was followed by using the ^{19}F-NMR spectrum. *cis*-Fluorine gives a singlet, *trans*-fluorine an A_2B spectrum (cf. [187]).
[183] *R. Mews, D. L. Wagner, O. Glemser*, Z. Anorg. Allg. Chem. *412*, 148 (1975).
[184] This is valid, although in a limited way, for $(NSOCl)_3$, which reacts with weak nucleophiles, with retention of the ring, see *e.g. T. J. Maricich, M. H. Khalil*, J. Chem. Soc. Chem. Commun. *1977*, 195; Inorg. Chem. *18*, 912 (1979).
[185] *T. P. Lin, U. Klingebiel, O. Glemser*, Angew. Chem. *84*, 1149 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1095 (1972).
[186] *H. Klüver, O. Glemser*, Z. Naturforsch. *B 32*, 1209 (1977).
[187] *F. Seel, G. Simon*, Z. Naturforsch. *B 19*, 354 (1964).
[188] *D. L. Wagner, H. Wagner, O. Glemser*, Chem. Ber. *108*, 2469 (1975).
[189] An analogous anion has not yet been observed with the isoelectronic hexahalocyclotriphosphazenes.
[190] *D. L. Wagner, H. Wagner, O. Glemser*, Z. Naturforsch. *B 30*, 279 (1975).
[191] $\delta(^{19}F) = -64.2$ (d, F_α), -62.7 (dq, F_β), $J_{F-F} = 3.75$ Hz. The two F atoms are *cis*.
[192] *D. L. Wagner, H. Wagner, O. Glemser*, Z. Naturforsch. *B 33*, 300 (1978).
[193] *D. L. Wagner, H. Wagner, O. Glemser*, Chem. Ber. *109*, 1424 (1976).
[194] *H. Thamm, T. P. Lin, O. Glemser, E. Niecke*, Z. Naturforsch. *B 27*, 1431 (1972).
[195] *T. P. Lin, O. Glemser*, Chem. Ber. *109*, 3537 (1976).
[196] *H. Wagner, R. Mews, T. P. Lin, O. Glemser*, Chem. Ber. *107*, 584 (1974).
[197] *H. Wagner, D. L. Wagner, O. Glemser*, Chem. Ber. *110*, 683 (1977).
[198] *D. Schäfer, M. Becke-Goehring*, Z. Anorg. Allg. Chem. *362*, 1 (1968).
[199] *J. Weiss, R. Mews, O. Glemser*, J. Inorg. Nucl. Chem. Suppl. *1976*, 213.
[200] Cf. also *R. Bartetzko, R. Gleiter*, Chem. Ber. *113*, 1138 (1980).
[201] $(NSOF)_3$ has proven to be effective against Fasciola (liver fluke) *in vitro*, but the compound appears to be toxic; Bayer AG, unpublished.

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

Geminal Dialkylation of Ketones with Grignard Compounds and Methyltitanium(IV) Chlorides[**]

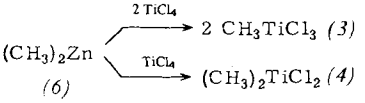
By *Manfred T. Reetz, Jürgen Westermann,* and *Rainer Steinbach*[*]

While alkyltitanium(IV) compounds are used in combination with alkylaluminum compounds as Ziegler-Natta polymerization catalysts, practically nothing is known concerning their utility as reagents in preparative organic chemistry[1a]. We describe here their use for the geminal dialkylation of ketones. Reaction of *tert*-alkyl chlorides *(2)*, which are readily accessible from the ketones *(1)*, with methyltitanium trichloride *(3)* or dimethyltitanium dichloride *(4)* at $-30\,^{\circ}C$ to room temperature leads to replacement of chlorine by the methyl group with formation of the desired product *(5)* containing a quaternary C-atom.



(1) *(2)* *(5)*

In order to optimize the decisive *tert*-alkylation *(2)*→*(5)* we have developed three methods (A, B, C). Although alkyltitanium(IV) compounds are accessible from titanium tetrachloride and the usual organometallic precursors such as alkyl-lithium and -magnesium compounds, we found it more



(6)

economical to use dimethylzinc *(6)*, which is readily obtainable from methyl iodide and zinc, and which reacts quantitatively with titanium tetrachloride to give *(3)* or *(4)*[1a]. The results of the reactions of *(2)* with *(3)* (method A), with *(4)* (method B), and with *(6)* in the presence of *catalytic* amounts of titanium tetrachloride (method C) are collected in Table 1.

Table 1. Geminal alkylation of ketones *(1)* via *tert*-alkyl chlorides *(2)* [a].

	(1)	R^3	Method [b]		*(5)*	Yield [%] [c]
(1a)	Cyclopentanone	Methyl	C	*(5a)*	1,1-Dimethylcyclopentane	88
(1b)	Cyclohexanone	Methyl	A	*(5b)*	1,1-Dimethylcyclohexane	80
(1b)	Cyclohexanone	Methyl	B	*(5b)*	1,1-Dimethylcyclohexane	85
(1b)	Cyclohexanone	Methyl	C	*(5b)*	1,1-Dimethylcyclohexane	93
(1b)	Cyclohexanone	*n*-Butyl	C	*(5c)*	1-Butyl-1-methylcyclohexane	95
(1b)	Cyclohexanone	Ethyl	C	*(5d)*	1-Ethyl-1-methylcyclohexane	90
(1b)	Cyclohexanone	Cyclohexyl	C	*(5e)*	1-Cyclohexyl-1-methylcyclohexane	66
(1c)	4-*tert*-Butylcyclohexanone	Methyl	C	*(5f)*	4-*tert*-Butyl-1,1-dimethylcyclohexane	86
(1d)	Cycloheptanone	Methyl	A	*(5g)*	1,1-Dimethylcycloheptane	70
(1e)	Cyclooctanone	Methyl	A	*(5h)*	1,1-Dimethylcyclooctane	72
(1f)	Cyclododecanone	Methyl	C	*(5i)*	1,1-Dimethylcyclododecane	90
(1g)	Acetone	*n*-Propyl	C	*(5j)*	2,2-Dimethylpentane	74
(1h)	3-Methyl-2-butanone	Methyl	C	*(5k)*	2,2,3-Trimethylbutane	63
(1i)	3-Pentanone	Ethyl	C	*(5l)*	3-Ethyl-3-methylpentane	78
(1j)	2-Hexanone	Methyl	C	*(5m)*	2,2-Dimethylhexane	77
(1k)	3-Hexanone	Methyl	C	*(5n)*	3,3-Dimethylhexane	79
(1l)	2-Heptanone	*n*-Butyl	C	*(5o)*	5,5-Dimethyldecane	95
(1l)	2-Heptanone	Methyl	B	*(5p)*	2,2-Dimethylheptane	83
(1m)	4-Heptanone	Methyl	C	*(5q)*	4,4-Dimethylheptane	85
(1n)	1-Adamantyl methyl ketone	Methyl	C	*(5r)*	1-*tert*-Butyladamantane	97
(1o)	*cis*- + *trans*-2-Decalone	Methyl	C	*(5s)*	*cis*- + *trans*-2,2-Dimethyldecalin	73
(1p)	3-Cholestanone	Methyl	C	*(5t)*	3,3-Dimethylcholestane	92
(1q)	2-Adamantanone	Methyl	C	*(5u)*	2,2-Dimethyladamantane	92

[a] The ketones *(1)* were conventionally converted by Grignardation and subsequent chlorination with HCl or PCl_5 into the *tert*-alkyl chlorides *(2)*. [b] Method A: with CH_3TiCl_3 *(3)*, B: with $(CH_3)_2TiCl_2$, C: with $(CH_3)_2Zn$ *(6)* + catalytic amounts of $TiCl_4$. Solvent: dichloromethane; 1,2-dichloromethane is also suitable. [c] Yield of isolated *(5)* based on *(2)*.

Table 1 clearly demonstrates that numerous ketones can be geminally dialkylated, methods B and C being more suitable than method A. Thus, 1,1-dialkylcycloalkanes as well as the derivatives of bi- and polycyclic ketones such as 2-decalone, 3-cholestanone, and 2-adamantanone are readily accessible for the first time. In case of open-chain branched *tert*-alkyl chlorides *(2)* the C—C coupling takes place exclusively

[*] Prof. Dr. M. T. Reetz, Dipl.-Chem. J. Westermann,
Dipl.-Chem. R. Steinbach
Institut für Organische Chemie und Biochemie
der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)
Present address: Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0900 $02.50/0

at the tertiary C-atom; this is not the case in Friedel-Crafts reactions with these compounds[2].

The advantage of the method is also evidenced by further examples[3]. In contrast, the few known reactions of *tert*-alkyl halides with alkyl-sodium[1b], -magnesium[1b] or -zinc compounds[1b] and with cuprates[4a] proceed, generally, only with preparatively poor yields (10—50%). A reaction of simple *tert*-alkyl halides with trimethylaluminum was not carried out on a preparative scale[4b]. Reaction of 2-chloro-2-methylheptane with triethylaluminum affords 3,3-dimethyloctane, which was isolated in 21% yield[5]. Related reactions with trialkynylaluminum compounds proceed in good yields, but have the disadvantage that only *one* organic group is transferred[6]. Noteworthy is also the exhaustive methylation of carbonyl compounds according to *Meisters* and *Mole,* which requires a large excess of trimethylaluminum under pyrolytic conditions (120—180 °C) and leads to moderate yields of product[7]. Other synthetic strategies are less productive or have only been tested on a few simple examples[8].

In generalizing our method we make use of the working hypothesis that the metal must be *an effective Lewis acid* and the organic group a *weak Lewis base.* The conventional alkyl-lithium, -sodium, or -magnesium compounds are unsuitable, since in the case of *tert*-alkyl halides they induce undesired olefin-forming HX elimination owing to their weak Lewis acid or strong Lewis base centers.

Procedure

(5i) according to Method C *via* 1-chloro-1-methylcyclododecane: A mixture of 1-methyl-1-cyclododecanol (23.8 g, 120 mmol) (obtained in 88% yield from cyclododecanone *(1f)*[9]) and zinc chloride (700 mg) in dry ether (50 ml) is saturated with HCl gas at 0 °C[10]. After one hours' stirring at 0 °C the mixture is treated with ice-cold water, neutralized with sodium carbonate, the aqueous phase extracted twice with ether, the combined organic phases dried over sodium sulfate, the solvent removed by evaporation and the residue recrystallized from ethyl acetate: 22.0 g (87%) 1-chloro-1-methylcyclododecane, m.p. 76 °C.

(6), obtained from methyl iodide and zinc[1c], is diluted to about 5 mol/l with dry CH_2Cl_2 at 0 °C in a flask fitted with a serum cap; this solution can be stored in a refrigerator for weeks[11].—To a solution of *(6)* (12 mmol) in CH_2Cl_2 at −30 °C is added 0.44 ml (4 mmol) of $TiCl_4$ and the mixture treated dropwise and slowly with a cold solution of 1-chloro-1-methylcyclododecane (4.34 g, 20 mmol) in CH_2Cl_2. After about 30 minutes' stirring the reaction mixture is poured into ice-water, the organic phase separated off, and the aqueous phase extracted twice with CH_2Cl_2. The combined organic phases are washed with sodium carbonate solution and dried over sodium sulfate. Distillation (136 °C/11 torr) affords 3.5 g (90%) *(5i)*; ^{1}H-NMR (CCl_4): $\delta = 0.81$ (s, 6H), 1.33 (m, 22H).

Received: April 24, 1980 [Z 592a IE]
Publication delayed at authors' request
German version: Angew. Chem. 92, 931 (1980)

CAS Registry numbers:
(1a), 120-92-3; *(1b)*, 108-94-1; *(1c)*, 98-53-3; *(1d)*, 502-42-1; *(1e)*, 502-49-8; *(1f)*, 830-13-7; *(1g)*, 67-64-1; *(1h)*, 563-80-4; *(1i)*, 96-22-0; *(1j)*, 591-78-6; *(1k)*, 589-38-8; *(1l)*, 110-43-0; *(1m)*, 123-19-3; *(1n)*, 1660-04-4; *cis-(1o)*, 1579-21-1; *trans-(1o)*, 16021-08-2; *(1p)*, 601-53-6; *(1g)*, 700-58-3; *(2a)*, 6196-85-6; *(2b)*, 931-78-2; *(2c)*, 28320-90-3; *(2d)*, 1445-98-3; *(2e)*, 36610-27-2; *(2f)*, 19311-30-9; *(2g)*, 66344-68-1; *(2h)*, 66344-69-2; *(2i)*, 75458-20-7; *(2j)*, 4398-65-6; *(2k)*, 594-57-0; *(2l)*, 994-25-2; *(2m)*, 4398-65-6; *(2n)*, 43197-78-0; *(2o)*, 75458-21-8; *(2p)*, 4325-49-9; *(2q)*, 61764-94-1; *(2r)*, 33932-93-3; *(2s)*, 36610-26-1; *(2t)*, 75520-34-2; *(2u)*, 37723-65-2; *(3)*, 2747-38-8; *(4)*, 35739-70-9; *(5a)*, 1638-26-2; *(5b)*, 590-66-9; *(5c)*, 5009-92-7; *(5d)*, 4926-90-3; *(5e)*, 1130-24-1; *(5f)*, 27042-32-6; *(5g)*, 13151-49-0; *(5h)*, 23070-52-2; *(5i)*, 22748-25-0; *(5j)*, 590-35-2; *(5k)*, 464-06-2; *(5l)*, 1067-08-9; *(5m)*, 590-73-8; *(5n)*, 563-16-6; *(5o)*, 17453-92-8; *(5p)*, 1071-26-7; *(5q)*, 1068-19-5; *(5r)*, 20440-81-7; *cis-(5s)*, 66552-66-7; *trans-(5s)*, 55982-55-3; *(5t)*, 75520-35-3; *(5u)*, 19740-34-2; *(6)*, 544-97-8

[1] *Houben-Weyl-Müller:* Methoden der Organischen Chemie. 4th Edit. Thieme, Stuttgart; a) *A. Segnitz* in Vol. 13/7, p. 366 ff. (1975); b) *F. Asinger, H. H. Vogel* in Vol. 5/1a, p. 347 ff. (1970); c) *K. Nützel* in Vol. 13/2a, p. 570 ff. (1973).
[2] *A. A. Khalaft, R. M. Roberts,* J. Org. Chem. *35,* 3717 (1970), and references cited therein.
[3] *M. T. Reetz, J. Westermann, R. Steinbach,* Angew. Chem. *92,* 933 (1980); Angew. Chem. Int. Ed. Engl. *19,* 901 (1980).
[4] a) *G. M. Whitesides,* J. Am. Chem. Soc. *91,* 4871 (1969); b) *J. P. Kennedy, U. V. Desai, S. Sivaram, ibid. 95,* 6386 (1973); see however, *H. D. Beckhaus, G. Hellmann, C. Rüchardt,* Chem. Ber. *111,* 72 (1978).
[5] *D. B. Miller,* J. Org. Chem. *31,* 908 (1966).
[6] *E. Negishi, S. Baba,* J. Am. Chem. Soc. *97,* 7385 (1975).
[7] *A. Meisters, T. Mole,* Aust. J. Chem. *27,* 1665 (1974).
[8] *G. H. Posner, D. Brunelle,* Tetrahedron Lett. *1973,* 935; *Z. Majerski, P. von R. Schleyer, ibid. 1968,* 6195; *W. Oppolzer, T. Godel,* J. Am. Chem. Soc. *100,* 2583 (1978).
[9] *J. Casanova, B. Waegell,* Bull. Soc. Chim. Fr. *1971,* 1289.
[10] In the case of sensitive systems milder reagents such as PCl_5/Na_2CO_3 are used: *R. M. Carman, I. M. Shaw,* Aust. J. Chem. *79,* 133 (1976).
[11] *J. Westermann,* Diplomarbeit, Universität Bonn 1980; *R. Steinbach,* Diplomarbeit, Universität Bonn 1980.

Chemoselective and Position Specific Methylation of *tert*-Alkyl Halides with Methyltitanium(IV) Chlorides[**]

By *Manfred T. Reetz, Jürgen Westermann,* and *Rainer Steinbach*[*]

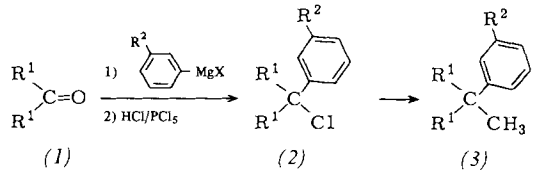
tert-Alkyl chlorides obtainable from ketones are smoothly alkylated by methyltitanium(IV) chlorides[1]. We report here on continuing investigations being carried out, *inter alia,* on especially sensitive compounds. First, the chemoselectivity of the reactions of α,α-dialkylbenzyl chlorides [*(2)*→*(3)*] was investigated in which competing Friedel-Crafts self-alkylations as well as HCl-eliminations are to be expected. The conversion of *(2)* into *(3)* was carried out with methyltitanium trichloride (method A), dimethyltitanium dichloride (method B), or dimethylzinc in the presence of catalytic amounts of titanium tetrachloride (method C)[1] (Table 1).

Whereas method A at −30 °C to room temperature favors a reaction course leading to the aforementioned undesired reactions[2], at −78 °C the yields of the desired products are good to very good (Table 1). The reaction sequence *(1)*→*(2)*→*(3)* not only makes the geminal dialkylation of ketones possible, but also provides an easy access to the *meta*-substituted derivatives previously not obtainable by Friedel-Crafts alkylation.

Also worth noting is the chemoselectivity in case of alkyl chlorides which contain an additional *primary* or *secondary* alkyl chloride unit. Thus *(4a), (4b),* and *(6)* react according to method B *only* at the tertiary C-atom with formation of *(5a), (5b)* and *(7)* in 81, 74, and 61% yield, respectively.

[*] Prof. Dr. M. T. Reetz, Dipl.-Chem. J. Westermann, Dipl.-Chem. R. Steinbach
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)
Present address: Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and by the Deutsche Forschungsgemeinschaft.



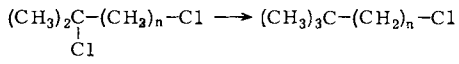
(1) (2) (3)

Table 1. Methylation of α,α-dialkylbenzyl chlorides *(2)* to *(3)* at −78 °C.

R^1	R^2	Method [a]	*t* [min]		Yield [%] [b]
CH_3	H	A	30	*(3a)*	70
CH_3	H	C	15	*(3a)*	91
CH_3	CH_3	A	20	*(3b)*	90
[c]	CH_3	C	20	*(3c)*	85
C_2H_5	H	A	20	*(3d)*	62
C_6H_5	H	C [d]	20	*(3e)*	95

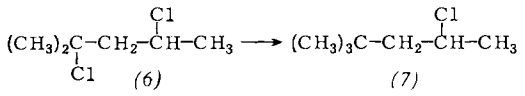
[a] Methods A, B, C, see text. [b] Yield of *(3)* isolated. [c] $-R^1-R^1-=-(CH_2)_5-$. [d] At 0 °C.

In order to check whether olefinic double bonds are also tolerated, the ester *(8)* was first converted by conventional methods into *(9)*. At −30 °C, method C (5 mol% $TiCl_4$) yields



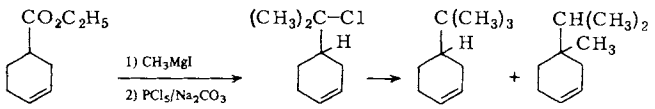
(4) *(5)*

(a), n = 2; *(b)*, n = 3



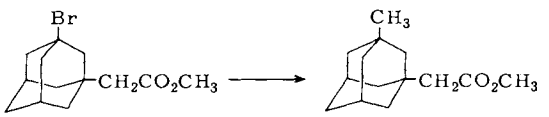
(6) *(7)*

1:1 mixtures of *(10)* and *(11)*. Although the double bond is not attacked, an undesired 1,2-hydride shift occurs. In contrast, at −78 °C a position specificity of 90% and a yield of *(10)* + *(11)* of 73% are realized. Hence, low temperatures and smallest possible amounts of effective Lewis acid ($TiCl_4$) suppress the 1,2-hydride shift almost completely.



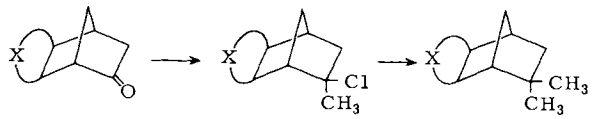
(8) *(9)* *(10)* *(11)*

Alkylations are also possible in the presence of ester functions. However an additional equivalent of titanium tetrachloride is required to ensure that maximum yields are achieved, since otherwise methyltitanium trichloride is partially complexed or deactivated by the ester groups. Thus, *(12)* reacts with a 1:1 mixture of CH_3TiCl_3 and $TiCl_4$ chemoselectively to give *(13)* with a conversion of 95% (87% isolated), whereas without $TiCl_4$ only 10% of *(13)* is formed[2].



(12) *(13)*

Finally, we investigated the position specificity in the case of two further rearrangeable systems. The *tert*-alkyl chloride *(15a)*, readily obtainable from 2-norbornanone *(14a)*[3], reacts smoothly according to method B to give *(16a)* in 89% yield. Position specificity is also observed in the methylation *(15b)*→*(16b)* (87%); skeletal rearrangements to adamantyl derivatives[4] do not occur.



(14) *(15)* *(16)*

(a), X = 2 H; *(b)*, X = $-(CH_2)_3-$

Thus, the titanium-induced methylation of *tert*-alkyl halides constitutes a mild and general C—C coupling method. Not only ketones and carboxylates are suitable starting compounds, but also olefins which form *tert*-alkyl chlorides by HCl-addition.

Received: April 24, 1980 [Z 592b IE]
Publication delayed at authors' request
German version: Angew. Chem. *92*, 933 (1980)

[1] *M. T. Reetz, J. Westermann, R. Steinbach*, Angew. Chem. *92*, 931 (1980); Angew. Chem. Int. Ed. Engl. *19*, 900 (1980).
[2] *J. Westermann*, Diplomarbeit, Universität Bonn 1980.
[3] *H. C. Brown, M. H. Rei*, J. Org. Chem. *31*, 1090 (1966).
[4] *P. von R. Schleyer, M. M. Donalson*, J. Am. Chem. Soc. *82*, 4645 (1960).

Synthesis of the Pentasaccharide Chain of the Forssman Antigen[**]

By *Hans Paulsen* und *Almuth Bünsch*[*]

The Forssman antigen[1] consists of a pentasaccharide chain and a ceramide moiety, which is anchored in the cell membrane[2]. It is assumed that, as a surface antigen, it regulates cell growth in mammals[3a]. For example, a deficiency of Forssman antigen was observed in uninhibited cell growth in hamsters[3b]. It also occurs on viruses[3c] and can therefore stimulate the formation of Forssman antibodies in infections in humans[3d]. The synthesis of the immunologically effective pentasaccharide chain *(12)* is therefore also of interest, because segments contained in it occur in many glycosphingolipids, *e.g.* globoside (P-antigen)[4], which are therefore likewise accessible[5].

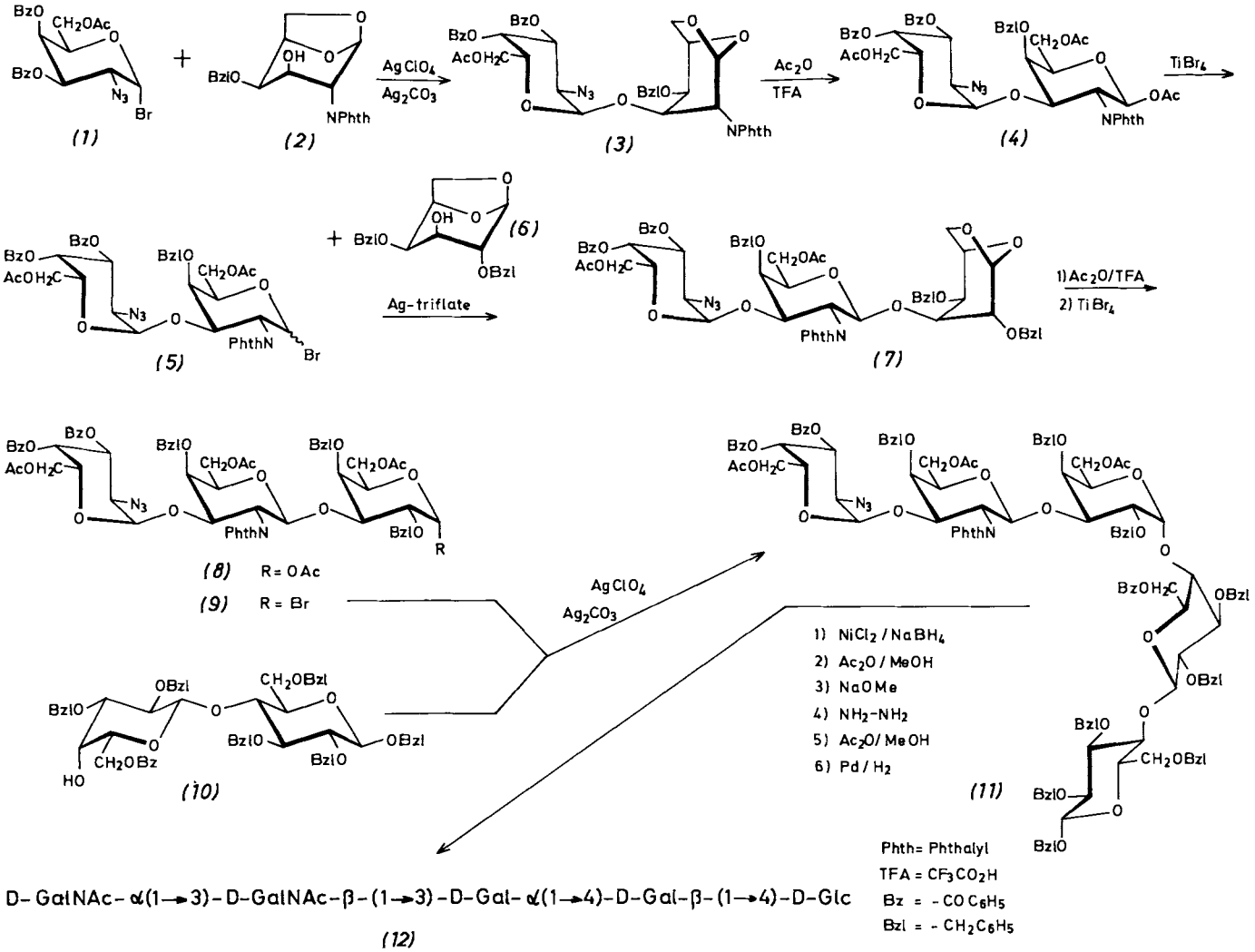
We chose a novel block synthesis method, since we have now succeeded in satisfactorily converting also oligosaccharides with titanium tetrabromide into linkable pyranosyl bromides. The reaction was carried out in absolute methylene chloride/ethyl acetate and, after completion, the products were diluted with four volumes of toluene. It is important that the excess titanium tetrabromide is destroyed with anhydrous, powdered sodium acetate in order that the toluene-insoluble sodium bromide and titanium tetraacetate can be removed by filtration. Subsequently the pyranosyl bromide was obtained by removal of solvents under strictly anhydrous conditions. For the coupling of the two blocks a bonding site was chosen at which an α-glycosidic bond must be coupled, since high reactivity of the bromide and good stereoselectivity are then guaranteed. In the case of *(12)* this is the bond between the central galactose and the lactose unit, so a brominated trisaccharide has to be coupled with the disaccharide.

[*] Prof. Dr. H. Paulsen, Dr. A. Bünsch
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] Building Blocks of Oligosaccharides, Part 24.—Part 23: *H. Paulsen, H. Bünsch*, Tetrahedron Lett., in press.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1111-0902 $02.50/0*

For the synthesis of the trisaccharide block *(7)*, *(1)*[6] was coupled in the first step with *(2)* under the conditions of the α-glycoside synthesis. The phthalimido sugar *(2)* can be synthesized by selective ring opening of 1,6:2,3-dianhydro-4-*O*-benzyl-β-D-talopyranose[7] with potassium phthalimide. The



coupled pentasaccharide *(11)* (28% based on *(9)*, $[\alpha]_D^{20} = +74.2$). The deblocking of *(11)* is carried out stepwise as follows: reduction of the azide group with $NiCl_2/NaBH_4$ and *N*-acetylation, deacylation with sodium methoxide, cleavage of the phthalimide group with hydrazine and *N*-acetalation, disaccharide *(3)* obtained (66%, $[\alpha]_D^{20} = +179.5$) is acetolyzed with acetic anhydride/trifluoroacetic acid to the β-acetate *(4)*, which on reaction with titanium tetrabromide[8] affords the linkable bromide *(5)* in 90% yield. This is immediately coupled in the presence of silver trifluoromethanesulfonate (silver triflate)/collidine and complete absence of moisture with *(6)* with formation of the β-glycosidic bond[9] to give the trisaccharide *(7)* (68% based on *(5)*, $[\alpha]_D^{20} = +87.6$).

For functionalization, *(7)* is acetolyzed with acetic anhydride/trifluoroacetic acid to the α-acetate *(8)* (98%, $[\alpha]_D^{20} = +77.7$). Reaction of *(8)* with titanium tetrabromide affords the α-bromide *(9)* in 92% yield. As coupling component for *(9)* we used the selectively blocked lactose derivative *(10)*, obtainable from benzyl-2,3,6-tri-*O*-benzyl-4-*O*-(2,3-di-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside[10] by selective benzoylation with benzoyl cyanide.

The two synthesis blocks *(9)* and *(10)* can be selectively converted under the conditions of the α-glycoside synthesis in the presence of $Ag_2CO_3/AgClO_4$ into the α-glycosidically and finally hydrogenolytic cleavage of all benzyl groups. In this way the completely deblocked pentasaccharide *(12)* is obtained ($[\alpha]_D^{20} = +134$).

Received: July 4, 1980 [Z 591a IE]
German version: Angew. Chem. 92, 929 (1980)

[1] *J. Forssman*, Biochem. Z. *37*, 78 (1911).
[2] *S. I. Hakomori, B. Siddiqui*, J. Biol. Chem. *246*, 2271 (1971).
[3] a) *S. Roth*, Q. Rev. Biol. *48*, 541 (1973); *P. Hanfland, G. Uhlenbruck*, J. Clin. Chem. Clin. Biochem. *16*, 85 (1978); b) *H. Sakiyama, T. Terasima*, Cancer Res. *35*, 1723 (1960); c) *C. Ronda-Lain, R. Lopez, A. Tapia, A. Tomasz*, J. Virol. *21*, 366 (1977); d) *J. R. Paul, W. W. Bunnel*, Am. J. Med. Sci. *183*, 90 (1932).
[4] *M. Naiki, J. Fond, R. Ledeen, D. M. Marcus*, Biochemistry *14*, 4831 (1975).
[5] *H. Paulsen*, Xth International Symposium on Carbohydrate Chemistry, Sydney 1980.
[6] *H. Paulsen, W. Stenzel*, Chem. Ber. *111*, 2334, 2348 (1978).
[7] *T. Trnka, M. Černy*, Collect. Czech. Chem. Commun. *36*, 2216 (1971).
[8] *H. Paulsen, A. Richter, V. Sinnwell, W. Stenzel*, Carbohydr. Res. *64*, 339 (1978).
[9] *R. U. Lemieux, T. Takeda, B. Y. Chung* in *H. S. El Khadem*: Synthetic Methods for Carbohydrates. ACS Symp. Ser. *39*, 90 (1976).
[10] *A. Liptak, I. Jodal, P. Nanasi*, Carbohydr. Res. *52*, 17 (1976).

Synthesis of Chiral Valienamine[**]

By *Hans Paulsen* and *Fred R. Heiker*[*]

Valienamine *(22)*, an unsaturated amino-cyclitol derivative with side chain, is a component of the aminoglycoside antibiotics of the validamycin type[1], distinguished for its fungicidal action with low toxicity. Above all, however, valienamine is the cardinal building block of the oligosaccharide Acarbose®, in which it is coupled to a 6-deoxy-D-glucose unit, which in turn is bound to two glucose building blocks[2]. With Acarbose®, a highly effective inhibitor of the α-glucosidases in the human digestive tract, it is possible to delay the breakdown of ingested carbohydrates (sucrose, starch) and consequently to control the resorption of glucose from the intestines. Clinical studies of Acarbose® have been able to prove the usefulness of this new therapeutic principle through the treatment of diabetes mellitus[3]. We have now succeeded in carrying out the first synthesis of valienamine *(22)*, as the chiral compound.

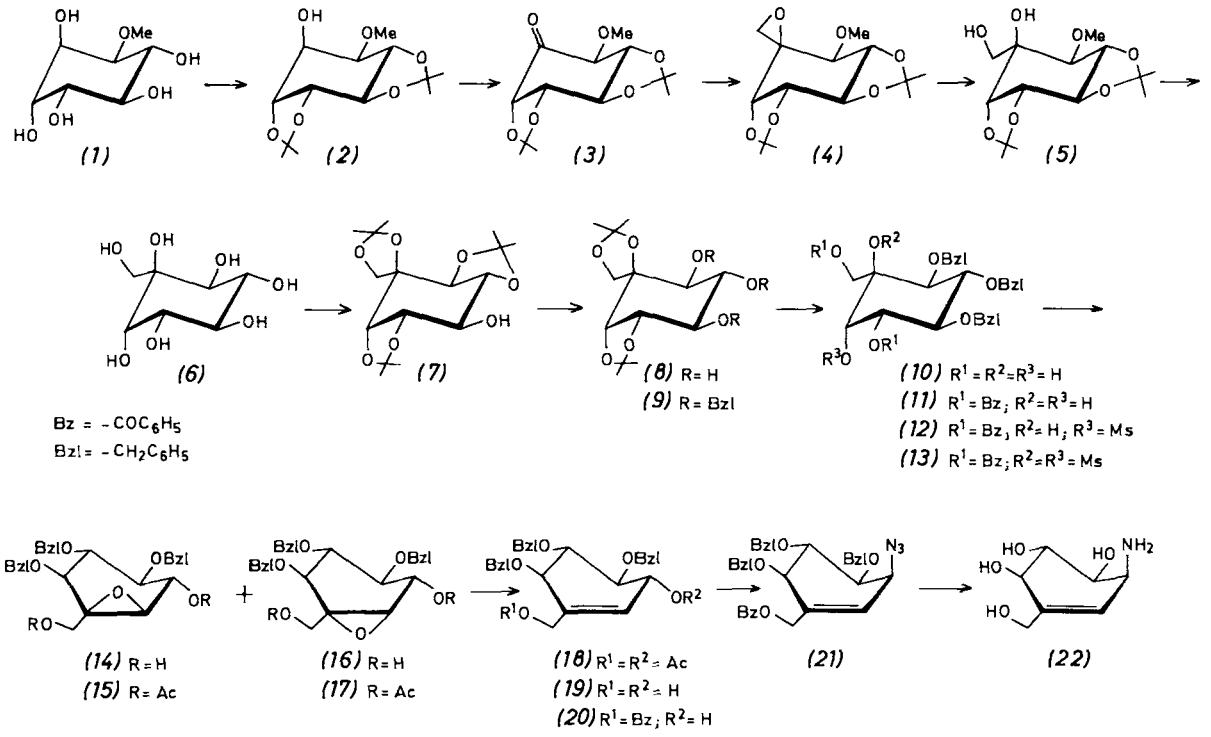
As starting material we used quebrachitol *(1)* (2-*O*-methyl-L-chiroinositol), which is formed as byproduct in the production of natural rubber[4]. For incorporation of the side chain, *(1)* is converted with dimethoxypropane into the diisopropylidene compound *(2)*, which can be catalytically oxidized with ruthenium tetroxide/sodium periodate to the ketone *(3)* (63%, m.p. 86 °C, $[\alpha]_D^{20} = +1.6$). On reaction with dimethyloxosulfonium methylide[5], *(3)* stereoselectively forms the epoxide *(4)* (57%, m.p. 92 °C, $[\alpha]_D^{20} = 41.5$). Reaction of *(3)* with the anion of the dithiane analogue *N*-methylthioformaldine (5-methylperhydro-1,3,5-dithiazine)[6] affords—likewise stereoselectively—the product with the other (undesired) stereochemistry at the branching site. The ring-opening product *(5)* (89%, m.p. 86 °C, $[\alpha]_D^{20} = -4.1$) can be obtained by hydrolysis of *(4)* with aqueous alkali.

Since the stereochemistry of the side chain in *(5)* is fixed, the methyl ether can now be cleaved; on reaction with boron tribromide the completely deblocked product *(6)* is formed. Reaction of *(6)* with dimethoxypropane yields the triisopropylidene compound *(7)*. Selective hydrolysis of the *trans*-isopropylidene group leads to formation of *(8)*, from which the tribenzyl ether *(9)* (75%, $[\alpha]_D^{20} = -42.2$) can be obtained.

The benzoylation of the tetrol *(10)*, obtainable from *(9)* by acid hydrolysis, can be so steered that it selectively furnishes the dibenzoate *(11)* (82%, m.p. 162 °C, $[\alpha]_D^{20} = -18.5$). The OH group at the branching site and the 6-OH group are considerably less reactive. On mesylation of *(11)* one obtains an inseparable mixture of monomesylate *(12)* and dimesylate *(13)* (Ms = CH_3SO_3). Treatment of this mixture with sodium ethoxide affords a mixture of the epoxides *(14)* and *(16)*, which are isolated as the acetates *(15)* + *(17)*. The double bond is incorporated by reaction of *(15)* + *(17)* with sodium iodide followed by elimination with phosphorus oxide trichloride; this leads uniformly to the olefin *(18)* (69%, $[\alpha]_D^{20} = -85.9$).

For introduction of the amino group the side chain, after hydrolysis of *(18)* to *(19)*, is protected by selective benzoylation to *(20)*. It is now possible to convert the free hydroxy group at the allyl position into an azido group with hydrazoic acid/triphenylphosphane/azodicarboxylate[7] to give *(21)* (72%, $[\alpha]_D^{20} = +53.5$), which has the stereochemistry of valienamine. The azido group in *(21)* is converted with triphenylphosphane into the phosphinimide[8], which can be hydrolyzed to the amino group. Cleavage of the benzyl ether protecting groups is achieved with sodium in liquid ammonia: Valienamine *(22)* is isolated as the hydrochloride; its optical rotation is +48.6.

Received: July 4, 1980 [Z 591 b IE]
German version: Angew. Chem. *92*, 930 (1980)



[*] Prof. Dr. H. Paulsen, Dr. F. R. Heiker
Institut für Organische Chemie und Biochemie
der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] Cyclitol Reactions, Part 3. We thank Bayer AG, Wuppertal-Elberfeld (Germany), for help with these investigations.—Part 2: *H. Paulsen, U. Maasz*, Chem. Ber., in press.

[1] *Y. Kameda, S. Horii*, J. Chem. Soc. Chem. Commun. *1972*, 746, 747; *T. Suami*, J. Antibiot. *32*, S-91 (1979).
[2] *D. D. Schmidt, W. Frommer, B. Junge, L. Müller, W. Wingender, E. Truscheit*, Naturwissenschaften *64*, 535 (1977).
[3] *W. Puls, U. Keup, H. P. Krause, G. Thomas, F. Hoffmeister*, Naturwissenschaften *64*, 536 (1977); *W. Puls*, Habilitationsschrift, Universität Düsseldorf 1980.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0904 $02.50/0

[4] *J. van Alphen*, Ind. Eng. Chem. *43*, 141 (1951).
[5] *E. J. Corey, M. Chaykovsky*, J. Am. Chem. Soc. *87*, 1353 (1965).
[6] *R. D. Balanson, V. M. Kobal, R. R. Schumaker*, J. Org. Chem. *42*, 393 (1977).
[7] *H. Loibner, E. Zbiral*, Helv. Chim. Acta *59*, 2100 (1976).
[8] *H.-J. Altenbach, H. Stegelmeier, M. Wilhelm, B. Voss, J. Lex, E. Vogel*, Angew. Chem. *91*, 1028 (1979); Angew. Chem. Int. Ed. Engl. *18*, 962 (1979).

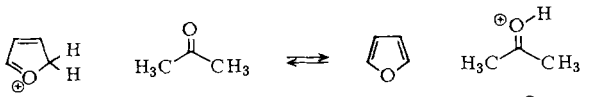
Proton and Hydrogen Affinity of Furan and the Site of Protonation in the Gas Phase[**]

By *Raymond Houriet, Helmut Schwarz,* and *Waltraud Zummack*[*]

The determination of molecular parameters such as adiabatic ionization energy (IE) or proton (PA) and hydrogen affinity (HA) provides direct information on some important *inherent* properties of molecules (*B*) when the experiments are carried out in the gas phase[1]. Thus, the ionization energy describes the nature of the bonding of an electron in B, while the proton affinity allows conclusions to be drawn about the readiness of *B* to share its electron density with a proton $H^{\oplus}$. The hydrogen affinity is a measure of the interaction of a $H^{\odot}$ atom with the radical cation $B^{\oplus\odot}$. Common to all parameters is the fact that they reflect the electronic properties of B under various experimental conditions. While IE and PA values [defined by eq. (a), (b)] are easily accessible by photoelectron (PE) and ion cyclotron resonance spectroscopy (ICR), respectively, the HA values [defined by eq. (c)] are most conveniently determined by a thermochemical cyclic process according to eq. (d).

$$B \rightarrow B^{\oplus\odot} + e^{\ominus} \quad \Delta H_1 = IE(B) \qquad (a)$$
$$BH^{\oplus} \rightarrow B + H^{\oplus} \quad \Delta H_2 = PA(B) \qquad (b)$$
$$BH^{\oplus} \rightarrow B^{\oplus\odot} + H^{\odot} \quad \Delta H_3 = HA(B^{\oplus\odot}) \qquad (c)$$
$$HA(B^{\oplus\odot}) = PA(B) + IE(B) - IE(H) \qquad (d)$$

We report here our investigations on furan *(1)*, whose electrophilic substitution constitutes a fundamental type of reaction in organic chemistry. From ion cyclotron resonance (ICR) measurements[2] on the pair furan *(1)*/acetone *(2)*



(e)

(1-H)$^{\oplus}$ *(2)* *(1)* *(2-H)*$^{\oplus}$
m/e = 69 *m/e* = 59

(Fig. 1) we obtained $\Delta\Delta G = -0.59$ kcal mol^{-1} for the reaction (e)[3]. From this, and the entropy term $T \cdot R \ln 2$ [in contrast to *(2)*, *(1)* has *two* potential centers for protonation, *vide infra*] we calculated the proton affinity of *(1)* at 323 K to be PA *(1)* = 195.5 kcal mol^{-1}[4a]. Combination of this value with the adiabatic ionization energy of *(1)* (IE = 205.2 kcal mol^{-1}[5]) and that of the $H^{\odot}$ atom (IE = 313.6 kcal mol^{-1}) yields for $(1)^{\oplus\odot}$ a hydrogen affinity HA = 87 kcal mol^{-1}. The corresponding HA values for the radical cations of benzene and pyrrole are 84[4b] and 83.4 kcal mol^{-1}[1a], respectively. This means that the radical cation of furan is 3 kcal mol^{-1} *destabilized* compared to that of benzene, while the pyrrole radical cation experiences a stabilization of about 0.6 kcal mol^{-1}.

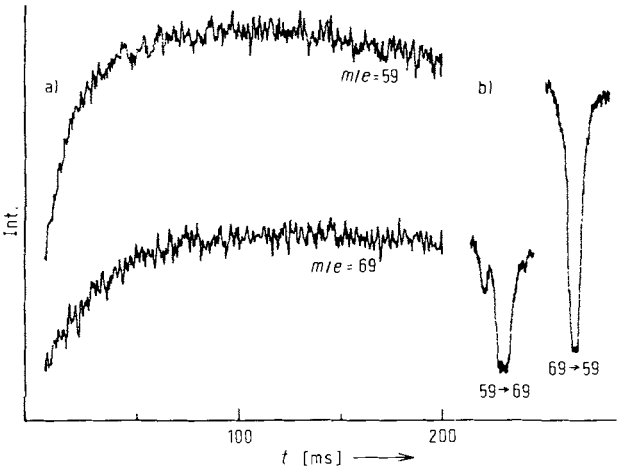
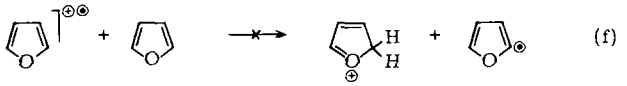


Fig. 1. a) Ion intensity as a function of time in a 1:1 mixture of furan *(1)* and acetone *(2)* (6×10^6 torr; 2.5 ms-pulse of 20 eV electrons); b) double resonance pulse at 200 ms.

The relatively small HA value of 87 kcal mol^{-1} for $(1)^{\oplus\odot}$ explains why reaction (f) is not observed. If one assumes that the (C—H) bonding energy of *(1)* is of the same order of magnitude as that of benzene (110 kcal mol^{-1}[6]), then the reaction (f) would be 23 kcal mol^{-1} *endothermic* and should therefore not take place. In fact, there is also no experimental evidence that $(1)^{\oplus\odot}$ reacts according to eq. (f). On the contrary: the concentration of $(1)^{\oplus\odot}$ remains virtually unchanged as a function of reaction time.



(f)

(1)$^{\oplus\odot}$ *(1)* *(1-H)*$^{\oplus}$ *(3)*

That the gas-phase protonation of furan—an electrophilic substitution *par excellence*—takes place exclusively at the α- and not at the β-position of the heterocycle is confirmed by investigations on the specifically [α-D]- and [β-D]-labeled furans *(1a)* and *(1b)*, respectively[7]. We find that a mixture of *(1b)* with *(2)* gives no signal at *m/e* = 60 (acetone-$D^{\oplus}$) alongside that at *m/e* = 59 under ICR conditions, even after



(1a) *(1b)*

200 ms, as must be the case if the β-position of the furan ring were to participate in the reversible H/D exchange between furan and acetone. Conversely, we find for mixtures of *(1a)* with *(2)* a signal ratio (*m/e* = 59)/(*m/e* = 60) of 47:53 after 200 ms[8]; *i.e.* the α-position[9] participates in proton exchange. Conclusion: in the prototype electrophilic reaction—the protonation—furan reacts as a typical arene and not as an enol ether, both in the gas phase as well as in the condensed phase[10].

Received: May 14, 1980 [Z 593 IE]
supplemented: July 7, 1980
German version: Angew. Chem. 92, 934 (1980)

[*] Prof. Dr. H. Schwarz, W. Zummack
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Dr. R. Houriet
Physikalisch-chemisches Laboratorium der Eidgenössischen Technischen Hochschule
CH-1015 Lausanne (Switzerland)

[**] This work was supported by the Fonds der Chemischen Industrie, the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung, and the Gesellschaft von Freunden der TU Berlin. We thank Prof. Dr. *H. Bornowski*, Berlin, for supplying us with β-bromofuran.

[1] a) *M. T. Bowers:* Gas Phase Ion Chemistry. Vol. 1, 2. Academic Press, New York 1979; b) *P. Kebarle, W. R. Davidson, J. Sunner, S. Meza-Höjer,* Pure Appl. Chem. *51*, 63 (1979); c) *E. M. Arnett,* Acc. Chem. Res. *6*, 404 (1973).

[2] The ICR spectrometer used for the measurements, which was built at the ETH Lausanne, contains a Varian-V-7300 magnet; the experiments were carried out in a flat four-section cell under "trapped ion" conditions; *T. B. MacMahon, J. L. Beauchamps,* Rev. Sci. Instrum. *43*, 509 (1972).

[3] Double resonance experiments confirm that 1) $H^{\oplus}$ is transferred in *both* directions according to eq. (e), *i.e.* an equilibrium is set up, and 2) only the ions depicted in eq. (e) participate in the proton transfer (see also the change in signal for the double resonance pulse in Fig. 1b).

[4] a) Reference basis is PA (NH_3) = 205 kcal mol^{-1} (see [1]); b) *R. V. Hodges, J. L. Beauchamp, A. J. Ashe III:* J. Am. Chem. Soc., in press.

[5] a) *J. H. D. Eland,* Int. J. Mass Spectrom. Ion Phys. *2*, 471 (1969); b) *A. D. Baker, D. Betteridge, N. R. Kemp, R. E. Kirby,* Anal. Chem. *42*, 1064 (1970); c) *P. J. Derrick, L. Asbrink, Q. Edqvist, B.-Ö. Jonsson, E. Lindholm,* Int. J. Mass Spectrom. Ion Phys. *6*, 161 (1971). In the case of *(1)* the first ionization potential is assigned to the $1a_2$ orbital, which is of the π-type.

[6] *S. W. Benson:* Thermochemical Kinetics. Wiley, New York 1976, p. 309. To our knowledge no dissociation energies are known for *(1)*.

[7] *(1a)* was obtained by low-temperature metalation of *(1)*, followed by hydrolysis with D_2O/CH_3OD, while *(1b)* is accessible by metalation of β-bromofuran and decomposition with D_2O/CH_3OD at −78 °C. The amount of D and the position of labeling were determined by 270-MHz ^{1}H-NMR spectroscopy.

[8] This value indicates that 1) H/D isotope effects play either no role or only a slight one, and 2) at least four exchange cycles [eq. (e)] have taken place.

[9] See also *P. Politzer, H. Weinstein,* Tetrahedron *31*, 915 (1975).

[10] *U. E. Wiersum, H. Wynberg,* Tetrahedron Lett. *1967*, 2951.

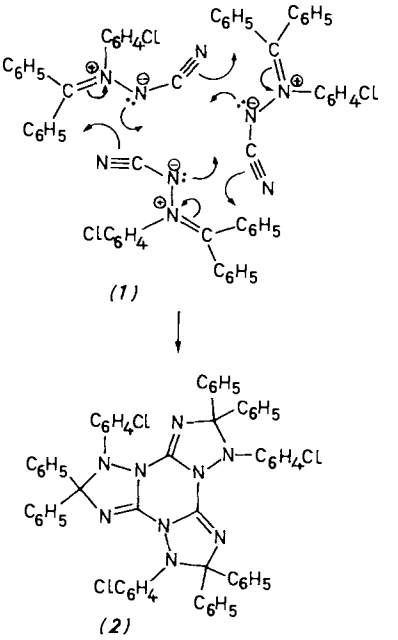
Trimerization of an Azomethine Imine by Three Successive 1,3-Dipolar Cycloaddition Reactions[**]

By *Judith L. Flippen-Anderson, Isabella Karle, Rolf Huisgen,* and *Hans-Ulrich Reissig*[*]

The reaction of the electrophilic aryldiazocyanides and the nucleophilic diaryldiazoalkanes afforded the first class of stable, crystalline azomethine imines, *e.g., (1)* from *p*-chlorobenzene-*anti*-diazocyanide and diphenyldiazomethane[1]. Reactions of azomethine imines of this type served as an early test[2] for the synthetic potential of 1,3-dipolar cycloaddition; the reactions with olefinic[3] and acetylenic[4] dipolarophiles gave rise to pyrazolidines and 3-pyrazolines, respectively. The orange-yellow C,C,N^{α}-triaryl-N^{β}-cyanoazomethine imines of type *(1)* are stable in the crystal, but are converted in hot solution to colorless high-melting trimers[5]. Vapor pressure osmometry and the mass spectrum (300 °C) secured the molecular weight of the trimer of *(1)* (m.p. 288—289 °C). The monomer *(1)* incorporates the 1,3-dipolar azomethine imine system as well as the dipolarophilic cyano group. Conceivably, the trimerization consists of a succession of three 1,3-dipolar cycloadditions of which the concluding one takes place intramolecularly and produces *(2)*.

The structure *(2)* for the trimer has now been established by X-ray structure analysis on solvent-free single crystals, which were obtained from acetone/methanol in 6 weeks (Fig. 1).

The central ring of *(2)* is approximately planar with the three carbon atoms shifted slightly below this plane and the three nitrogen atoms shifted slightly above the plane. It is only the skeleton of the tetracyclic heterosystem in *(2)* which shows approximate three-fold symmetry. The symmetry vanishes, if one takes the aryl substituents into account. The iminium nitrogen of *(1)* becomes pyramidal in the cycloadduct



(1)

(2)

(2). Two of the *p*-chlorophenyl groups are located on one side of the average plane of the tetracyclic system, whereas the third projects out from the opposite side (Fig. 1). Some variations in the rotations of the remaining six phenyl groups can probably be accounted for by intra- and intermolecular forces. The bond length of 1.26 Å for the CN double bonds is shorter than "normal"[9], although one expects a bond order below 2 for the amidinohydrazine moiety in *(2)*.

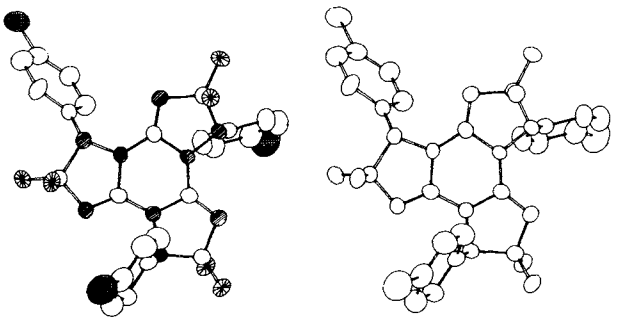


Fig. 1. Stereodrawing of the molecular structure of 1,5,9-tris(*p*-chlorophenyl)-1,2,5,6,9,10-hexahydro-2,2,6,6,10,10-hexaphenyl-tris[1,2,4]triazolo[1,5-*a*: 1′,5′-*c*: 1″, 5″-*e*][1,3,5]triazine *(2)*. The compound crystallizes in the body centered triclinic system with $a = 16.102$, $b = 24.894$, $c = 13.241$ Å, $\alpha = 96.7$, $\beta = 102.1$, $\gamma = 106.8°$ and $Z = 4$; the reduced cell dimensions are $a = 13.242$, $b = 13.558$, $c = 16.103$ Å, $\alpha = 108.5$, $\beta = 91.2$, $\gamma = 111.6°$ and $Z = 2$. The structure was solved by direct methods [6] and refined by a restrained least-square procedure [7] to a *R*-factor of 6.5% for 6053 independently measured intensities [8].—For ease of viewing the phenyl groups have been left out and their positions are indicated by ⊛. Chlorine atoms: ●, nitrogen atoms: ●.

The direction of addition revealed in *(2)* was also observed for the 1,3-dipolar cycloadditions of azomethine imines of type *(1)* to ethyl cyanoformate[10], whereas benzonitrile and acetonitrile fail to react.

Received: June 20, 1980 [Z 595 IE]
German version: Angew. Chem. *92*, 936 (1980)

[*] Dr. J. L. Flippen-Anderson, Dr. I. Karle
Laboratory for the Structure of Matter, Naval Research Laboratory
Washington, D. C. 20375 (USA)
Prof. R. Huisgen
Institut für Organische Chemie der Universität München
Karlstr. 23, 8000 München 2 (Germany)
Dr. H.-U. Reissig
Institut für Organische Chemie der Universität Würzburg
Am Hubland, 8700 Würzburg (Germany)

[**] 1,3-Dipolar Cycloadditions, Part 86.—Part 85: *R. Huisgen, T. Schmidt,* Justus Liebigs Ann. Chem. *1978*, 29.

[1] *R. Huisgen, R. Fleischmann, A. Eckell,* Tetrahedron Lett. *1960*, No. 12, p. 1; Chem. Ber. *110*, 500 (1977).
[2] *R. Huisgen, A. Eckell,* Tetrahedron Lett. *1960*, No. 12, p. 5.
[3] *R. Huisgen, A. Eckell,* Chem. Ber. *110*, 522, 540 (1977).
[4] *A. Eckell, R. Huisgen,* Chem. Ber. *110*, 559 (1977).
[5] *R. Huisgen, R. Fleischmann, A. Eckell,* Chem. Ber. *110*, 514 (1977).
[6] *J. Karle, I. L. Karle,* Acta Crystallogr. *21*, 849 (1966).
[7] *J. Konnert,* Acta Crystallogr. *A 32*, 614 (1976); *J. Konnert, W. Hendrickson, ibid. A 36*, 344 (1980).
[8] For further details of the solution and refinement see *J. L. Flippen-Anderson, J. Konnert, R. D. Gilardi,* Acta Crystallogr. *B*, in press.
[9] *E. M. Layton, R. D. Kross, V. A. Fassel,* J. Chem. Phys. *25*, 135 (1956).
[10] *A. Eckell, R. Huisgen,* Chem. Ber. *110*, 571 (1977).

Alkali Metal-Induced Transformations of *cis*-1,2-Dibenzoylalkenes: Transformation of 11,12-Dibenzoyl-9,10-dihydro-9,10-ethenoanthracene

By *Bipin Pandey, M. P. Mahajan,* and *Manapurathu V. George*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

Alkali metals add to 1,2-dibenzoylalkenes to give radical anion intermediates, which subsequently undergo different transformations, depending on the nature of the starting material and reaction conditions[1]. The reaction of *o*-dibenzoylbenzene with potassium, for example, has been reported to give a mixture of products consisting of 1,3-diphenylisobenzofuran, 10-hydroxy-10-phenyl-9-anthrone, 9-phenyl-9,10-dihydroanthracene-9,10-diol, anthraquinone and a dimeric reduction product[2,3]. In the present studies we have examined the reaction of 11,12-dibenzoyl-9,10-dihydro-9,10-ethenoanthracene *(1)* with potassium to determine the nature of products formed and to explore the synthetic utility of such reactions.

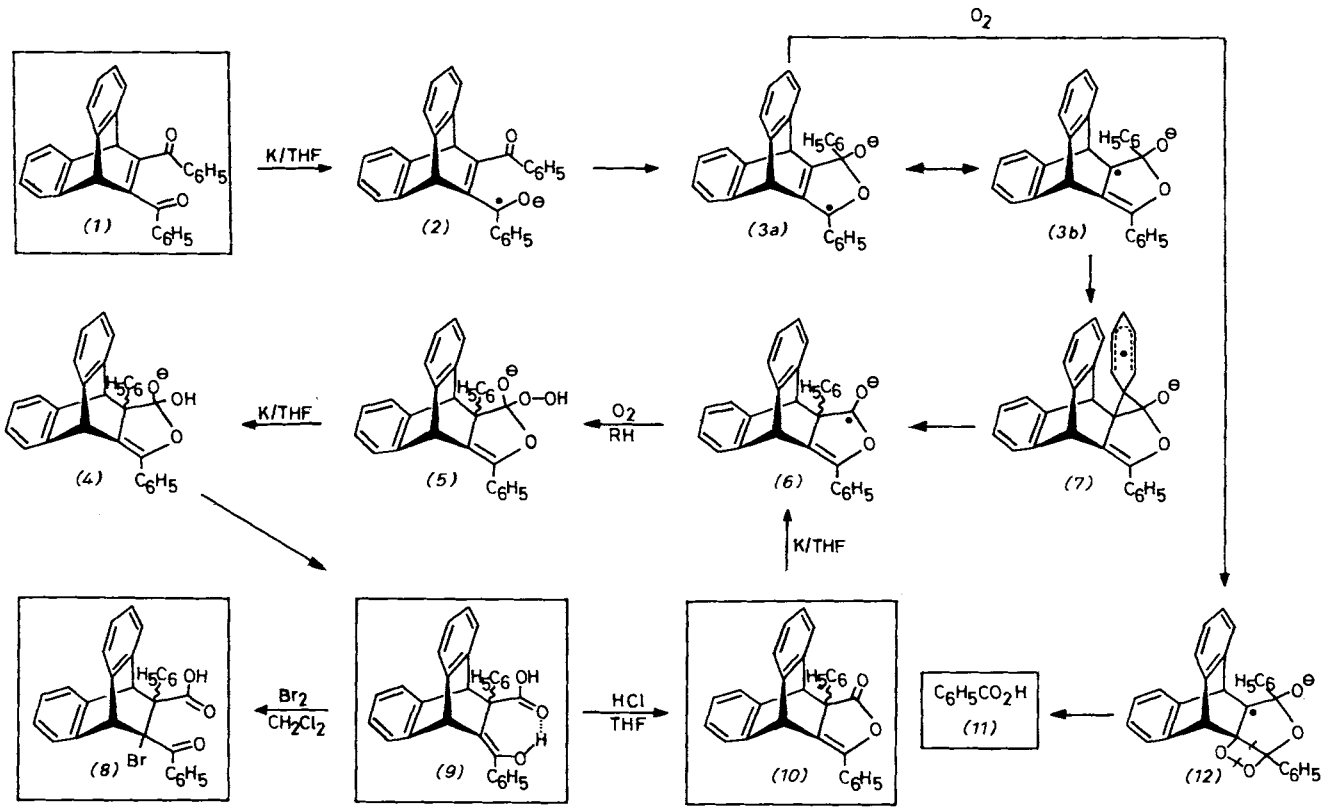
Treatment of a solution of *(1)* in tetrahydrofuran (THF) with potassium in a Schlenk tube for 10 h and subsequent work-up of the mixture by exposure to air, removal of the solvent under vacuum and chromatography over silica gel gave a mixture of products consisting of benzoic acid *(11)* (3%), anthracene (7%), and 12-(α-hydroxybenzylidene)-11-phenyl-9,10-dihydro-9,10-ethanoanthracene-11-phenyl-11-carboxylic acid *(9)* (35%) (see Table 1).

Passage of dry HCl gas through a solution of *(9)* in THF gave the lactone *(10)* in 59% yield (Table 1); treatment of *(9)* with bromine in dichloromethane gave a 42% yield of 12-benzoyl-12-bromo-11-phenyl-9,10-dihydro-9,10-ethanoanthracene-11-carboxylic acid *(8)*.

Table 1. Some physical data of the products *(8)*, *(9)*, and *(10)*.

(8) m.p. 153 °C; UV (ethanol): $\lambda_{max} = 240$ nm ($\varepsilon = 20600$), 278 (2200); IR: 3665 (COO*H*), 1780 (C=O, α-bromoketone), 1725 cm^{-1} (C=O)
(9) m.p. 171—172 °C; UV (methanol): $\lambda_{max} = 250$ nm ($\varepsilon = 7500$), 278 (3750), 330 (7300); IR: 3554 (CO*OH*), 3046, 3013, 1625 cm^{-1} (C=O); ^{1}H-NMR: $\delta = 3.45$ (s, 1H, COOH) [a], 4.3 (s, 1H [b]), 4.9 (s, 1H, [b]), 6.45—7.70 (m, 18H, aromatic), 16.4 (s, 1H, =CH*OH* [a]); MS: $m/e = 430$ ($10 = M^+$)
(10) m.p. 135 °C; UV (ethanol): $\lambda_{max} = 225$ nm ($\varepsilon = 5100$), 278 (2400); IR: 1795 cm^{-1} (C=O); ^{1}H-NMR: $\delta = 5.42$ (s, 2H [b]), 6.82—7.4 (m, 18H, aromatic); MS: $m/e = 412$ (20%, M^+)

[a] D_2O-exchangeable. [b] Bridgehead proton.



Scheme 1.

The formation of *(9)* on reaction of *(1)* with potassium may be rationalized in terms of the mechanism shown in Scheme 1. We assume that the dibenzoylalkene *(1)* accepts an electron from potassium to give initially the radical anion intermediate *(2)*, which then rearranges to a new radical anion intermediate *(3)*. Similar radical anion intermediates have been postulated in the reaction of *o*-dibenzoylben-

[*] Prof. M. V. George [**], B. Pandey, Dr. M. P. Mahajan
Department of Chemistry
Indian Institute of Technology
Kanpur 208016 (India)
[**] Present address: Institut für Strahlenchemie
Max-Planck-Institut für Kohlenforschung
Stiftstrasse 34—36, D-4330 Mülheim a. d. Ruhr 1 (Germany)

zene[3] and *o*-dimesitoylbenzene[4] with alkali metals in aprotic solvents. Subsequent rearrangement of *(3)*, involving a 1,2-phenyl migration leads to a new radical anion intermediate *(6)*, which on reaction with atmospheric oxygen gives the hydroperoxide intermediate *(5)*. Reduction of *(5)* with further potassium leads to the intermediate *(4)*, whose hydrolysis affords the final products *(9)*.

If a radical anion such as *(6)* is involved in the transformation of *(1)* to *(9)*, then it would be reasonable to assume that the lactone *(10)* which can generate the same intermediate *(6)*, by reaction with potassium, should also give rise to the same product *(9)*, under similar conditions. Reaction of *(10)* with potassium in THF, under conditions similar to those employed in the case of *(1)*, did indeed give *(9)* in 30% yield, thereby supporting the possible participation of *(6)*.

The formation of benzoic acid *(11)* in the reaction of *(1)* with potassium may be rationalized in terms of the dioxetane intermediate *(12)*, formed through the reaction of *(3a)* with oxygen; the formation of anthracene could be possible by retro-Diels-Alder fragmentation of one of the radical anions. Preliminary investigations have shown that *cis*-1,2-dibenzoylstyrene, 2,3-dibenzoylbicyclo[2.2.1]hepta-2,5-diene, and 2,3-dibenzoylbicyclo[2.2.2]octa-2,5-diene undergo similar transformations, on treatment with potassium.

Received: April 10, 1980 [Z 594 IE]
German version: Angew. Chem. 92, 939 (1980)

CAS Registry numbers:
(1), 13391-20-3; *(8)*, 75476-33-4; *(9)*, 75476-34-5; *(10)*, 75476-35-6; *(11)*, 65-85-0; anthracene, 120-12-7

[1] For a comprehensive review on the addition of alkali metals to unsaturated systems, see: *V. Kalyanaraman, M. V. George*, J. Organometal. Chem. *47*, 225 (1973).

[2] *A. G. Brook, H. L. Cohen, G. F. Wright*, J. Org. Chem. *18*, 447 (1953); *J. W. B. Reesor, J. G. Smith, G. F. Wright, ibid. 19*, 940 (1954); *B. J. Herold*, Rev. Fac. Cienc. Univ. Lisboa, B 7, 155 (1959—60); Chem. Abstr. *55*, 19877 (1961); Rev. Port. Quim. *3*, 101 (1961); Chem. Abstr. *60*, 13204 (1964).

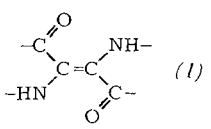
[3] *B. J. Herold*, Tetrahedron Lett. *1962*, 75; *J. A. Campbell, R. W. Koch, J. V. Hay, M. A. Ogliaruso, J. F. Wolfe*, J. Org. Chem. *39*, 146 (1974).

[4] *B. J. Herold, A. F. N. Correia, J. S. Veiga*, J. Am. Chem. Soc. *87*, 2661 (1965); *B. J. Herold, M. Celina, R. L. R. Lazana, H. M. Novais*, Tetrahedron *33*, 517 (1977).

Captodative Substituent Effects and the Chromophoric System of Indigo

By *Martin Klessinger*[*]

The principle of radical stabilization by captodative substitution recently discussed by *Viehe et al.*[1] is not only of importance regarding syntheses with radicals and radicophiles but proves to be a fundamental model for understanding many properties of organic compounds. This is demonstrated using as example the chromophoric system of indigo *(1)*, whose unusual color[2] can readily be explained in terms of the principle of captodative substitution. At the same time this example shows that the effect of captodative substitution can be very easily assessed with the simple HMO model.



(1)

The π-electron system of the chromophoric system of indigo can be formally constructed from two identical subsystems (Fig. 1), whereby the coupling of two radical centers affords one bonding and one antibonding π-MO of the central CC double bond which is substituted by two donor as well as by two acceptor groups. If the energetic splitting of these two MOs is sufficiently small they form the HOMO and the LUMO of the combined system, and the difference Δε of their orbital energies is responsible for the absorption of light of longest wavelength.

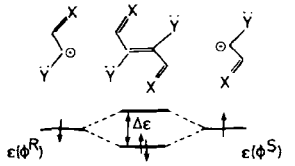


Fig. 1. Construction of the chromophoric system of indigo from two captodative stabilized radicals; interaction of the singly occupied π-MOs.

In the HMO approximation, according to the 1st order perturbation theory[3] the following applies:

$$\Delta\varepsilon = 2\, c_\rho^R\, c_\sigma^S\, \beta_{\rho\sigma}$$

Thus the orbital energy difference Δε is smaller, the smaller are the absolute values of the LCAO-MO coefficients c_ρ^R and c_σ^S of the singly occupied MOs ϕ^R and ϕ^S of the subsystems R and S at the coupling sites ρ and σ. The coefficients can also be estimated with the aid of perturbation theory as a function of the HMO parameters h_X and h_Y for the Coulomb integrals $\alpha_X = \alpha + h_X\beta$ an $\alpha_Y = \alpha + h_Y\beta$ of the heteroatoms X and Y[4]; starting from the butadienide ion as isoselectronic hydrocarbon we find

$$c_\rho^R = -0.372 + 0.184\, h_X - 0.304\, h_Y$$

Thus, c_σ^R is smaller the more electronegative X is, and the less electronegative Y is, *i. e.* the more pronounced are the acceptor and donor properties of the substituents —C=X and —Ÿ at the radical center. These are exactly the conditions corresponding to the greatest possible delocalization of the unpaired electron.

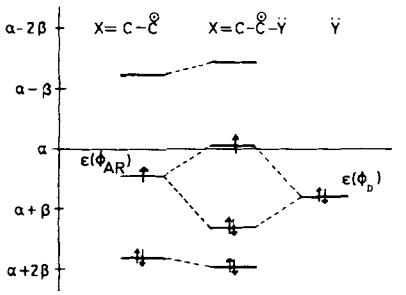


Fig. 2. Orbital energy correlation diagram for the captodative stabilization of a radical center by the substituents —C=X and —Ÿ (the data were obtained from a HMO calculation with $h_X = 1.0$ and $h_Y = 0.8$).

From the orbital energy correlation diagram (Fig. 2) it is clear that the intuitive condition of maximum delocalization of the radical electron agrees with the energetic criteria for an optimum captodative radical stabilization: As a 2nd order perturbation effect, the interaction between the radical center substituted by the acceptor group —C=X and the donor group —Ÿ is all the greater the smaller is the difference of the corresponding orbital energies[3], *i. e.* the closer are the singly occupied π-MO ϕ_{AR} of the radical X=C—Ċ and the doubly occupied donor MO ϕ_D. Starting from the allyl radical, 1st order perturbation theory yields the energy ε_{AR} of the singly occupied radical MO as $\varepsilon_{AR} = 1/2\, h_X\beta$, while the energy ε_D of the donor orbital is given by $\varepsilon_D = h_y\beta$; thus optimum

[*] Prof. Dr. M. Klessinger
Organisch-chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0908 $02.50/0

stabilization is reached for $h_Y = 1/2\,h_X$. A glance at the usual parameter values[5] shows that this situation cannot be reached with the the common heteroatoms (N, O, S, *etc.*) but is more nearly approached the greater h_X and the smaller h_Y, *i.e.* the more pronounced the donor and acceptor properties of the substituents.

Figure 2 shows, furthermore, that the stabilization of the system substituted by captodative groups is greater than the sum of the substituent effects: on using the given parameter values, the interaction of the radical center with the acceptor group —C≡X or with the donor group —Ÿ results in a stabilization of the π-system by 0.81β or 0.68β, respectively; the overall captodative stabilization is 1.67β, *i.e.* 0.18β greater than the sum of the individual effects.

A quantitative determination of the optimum radical stabilization on the basis of the donor and acceptor properties of the substituents taking into consideration electron-interaction effects is possible[7] with the LCFO model[6].

Received: June 2, 1980 [Z 597 IE]
German version: Angew. Chem. *92*, 937 (1980)

[1] *H. G. Viehe, R. Merényi, L. Stella, Z. Janousek,* Angew. Chem. *91*, 982 (1979); Angew. Chem. Int. Ed. Engl. *18*, 917 (1979).—I thank Prof. *Viehe* for a stimulating discussion of the principle of captodative substitution.
[2] *M. Klessinger, W. Lüttke,* Tetrahedron *19*, Suppl. 2, 315 (1963).
[3] *M. J. S. Dewar, R. C. Dougherty:* The PMO Theory of Organic Chemistry. Plenum Press, New York 1975.
[4] *E. Heilbronner, H. Bock:* Das HMO-Modell und seine Anwendung. Vol. 1. Verlag Chemie, Weinheim 1968, p. 179. The HMO Model and its Application. Wiley, London, and Verlag Chemie, Weinheim 1976, p. 179.
[5] *A. Streitwieser:* Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961.
[6] *M. Klessinger,* Theor. Chim. Acta *49*, 77 (1978).
[7] *M. Klessinger, W. Merker,* unpublished; cf. *W. Merker,* Diplomarbeit, Universität Münster 1980.

droperoxides, peracids, or iodosylbenzene[1]. Evidence has been presented for involvement of a high valency iron-oxo species as the active oxygen transfer agent[1,2]. Very few chemical systems are known to efficiently catalyze alkane hydroxylation under such mild conditions[1a]. Very recently, iron-porphyrins have been shown to catalyze iodosylarene-supported hydroxylations of nonactivated C—H bonds[3,4]. As a part of our effort to understand the mechanisms of the reactions between hemoproteins or metalloporphyrins and two-electron oxidizing agents[5], and to define good catalysts for hydroxylation of alkanes by readily available single oxygen donors, we have compared, in the present study, the abilities of various metalloporphyrins to catalyze cyclohexane hydroxylation by alkyl hydroperoxides[6].

Cumyl hydroperoxide, $C_6H_5C(CH_3)_2OOH$, is stable for days in benzene-cyclohexane (1:1) at 20 °C. Addition of a catalytic amount of *meso*-tetraphenylporphyrin-iron(III) chloride, Fe(TPP)Cl, to this mixture leads to fast decomposition of the hydroperoxide ($t_{1/2} \approx 1$ min) with formation of a nearly stoichiometric amount of cumenol, $C_6H_5C(CH_3)_2OH$, (95%) and acetophenone in minor quantities (≈2—4%). Study of the reaction mixture by HPLC and GLC also shows a concomitant formation of cyclohexanol and cyclohexanone with final yields (reached after about 10 min) of 40 and 20% based on starting hydroperoxide[7]. These products were also identified by IR and ^{1}H-NMR after distillation or silica gel chromatography of the reaction mixture. Visible spectroscopy shows that Fe(TPP)Cl is unchanged at the end of the reaction and therefore behaves as a true catalyst. Very similar yields of cyclohexanol and cyclohexanone are obtained under anaerobic conditions (argon), the reaction being only slightly faster than in the presence of O_2. Taking into account that two moles of oxidant are necessary for cyclohexa-

Table 1. Cyclohexane oxidation by cumyl hydroperoxide [a] with various catalysts (molar ratio 120:1:0.05) [b].

Catalyst		Fe(TPP)Cl	$TPPH_2$ or $FeCl_3$ or $FeCl_2$	Co^{II}(TPP) [d]	M^{II}(TPP) M = Cu, Ni, Zn, or Mg	M^{IV}(TPP)O M = Ti, V	Mn^{III}(TPP)Cl	Os(TPP)(CO)(py) [d]
Yield [%] [c]	Cyclo-hexanol	40	0 [e]	45	0 [e]	0	1 (25 after 10 d)	5%
after 15 min	Cyclo-hexanone	20	0	23	0 [e]	0	0.5 (12% after 10 d)	2.5%
$t_{1/2}$ of $C_6H_5C(CH_3)_2$—OOH		1—2 min	[e]	0.3 min	[f]	[f]	3 d	3.5 h

[a] Commercial (Fluka) samples containing 30% cumene; same results obtained with pure hydroperoxide with Fe(TPP)Cl. [b] Addition of 50 mM hydroperoxide to 6 ml of a benzene/cyclohexane mixture (1:1) containing 2.5 mmol l^{-1} catalyst. $FeCl_2$ and $FeCl_3$ were first dissolved in the minimum amount of CH_3CN. [c] Based on starting hydroperoxide. [d] The visible spectrum of the porphyrin (in benzene for Os(TPP)(CO)(py) and in pyridine for Co(TPP)) is greatly modified at the end of the reaction. [e] 5% cyclohexanol after 20 d. [f] No significant decomposition of the hydroperoxide after 2 d.

Metalloporphyrin-Catalyzed Hydroxylation of Cyclohexane by Alkyl Hydroperoxides: Pronounced Efficiency of Iron-Porphyrins[**]

By *Daniel Mansuy, Jean-François Bartoli, Jean-Claude Chottard,* and *Marc Lange*[*]

Cytochromes P450 are able to catalyze the hydroxylation of nonactivated alkanes, either by O_2 in the presence of a reducing agent, or by two-electron oxidants such as alkyl hydroperoxides, peracids, or iodosylbenzene[1]. Evidence has been presented for involvement of a high valency iron-oxo species as the active oxygen transfer agent[1,2]. Very few chemical systems are known to efficiently catalyze alkane hydroxylation under such mild conditions[1a]. Very recently, iron-porphyrins have been shown to catalyze iodosylarene-supported hydroxylations of nonactivated C—H bonds[3,4]. As a part of our effort to understand the mechanisms of the reactions between hemoproteins or metalloporphyrins and two-electron oxidizing agents[5], and to define good catalysts for hydroxylation of alkanes by readily available single oxygen donors, we have compared, in the present study, the abilities of various metalloporphyrins to catalyze cyclohexane hydroxylation by alkyl hydroperoxides[6].

Cumyl hydroperoxide, $C_6H_5C(CH_3)_2OOH$, is stable for days in benzene-cyclohexane (1:1) at 20 °C. Addition of a catalytic amount of *meso*-tetraphenylporphyrin-iron(III) chloride, Fe(TPP)Cl, to this mixture leads to fast decomposition of the hydroperoxide ($t_{1/2} \approx 1$ min) with formation of a nearly stoichiometric amount of cumenol, $C_6H_5C(CH_3)_2OH$, (95%) and acetophenone in minor quantities (≈2—4%). Study of the reaction mixture by HPLC and GLC also shows a concomitant formation of cyclohexanol and cyclohexanone with final yields (reached after about 10 min) of 40 and 20% based on starting hydroperoxide[7]. These products were also identified by IR and ^{1}H-NMR after distillation or silica gel chromatography of the reaction mixture. Visible spectroscopy shows that Fe(TPP)Cl is unchanged at the end of the reaction and therefore behaves as a true catalyst. Very similar yields of cyclohexanol and cyclohexanone are obtained under anaerobic conditions (argon), the reaction being only slightly faster than in the presence of O_2. Taking into account that two moles of oxidant are necessary for cyclohexanone formation from cyclohexane, 80% of the oxidizing equivalents of the hydroperoxide are used for cyclohexane oxidation. Neither ferric or ferrous chloride nor the free porphyrin ($TPPH_2$) gives any cyclohexane oxidation in the reaction conditions (Table 1) indicating that both the metal ion and its porphyrin ligand are necessary for the catalysis to take place.

Table 1 compares various metalloporphyrins[8] as catalysts for cyclohexane oxidation.

From these results, the metalloporphyrins studied can be divided into three classes. (i) The Cu^{II}-, Ni^{II}-, Zn^{II}-, Mg^{II}-, V^{IV}-, and Ti^{IV}-porphyrins are completely inactive in our conditions. (ii) Co(TPP) and Os(TPP)(CO)(py) are able to catalyze cyclohexane oxidation, the former even giving a slightly faster reaction and better yields than Fe(TPP)(Cl),

[*] Dr. D. Mansuy, Dr. J. F. Bartoli, Prof. Dr. J. C. Chottard, Dr. M. Lange
Laboratoire de Chimie de l'Ecole Normale Supérieure,
Associé au CNRS
24, rue Lhomond, F-75231 Paris Cedex 05 (France)

[**] We are indebted to Dr. *P. Battioni* for supplying Os(TPP)(CO)(py) and Ti(TPP)(O).

but appear greatly modified at the end of the reaction, exhibiting a decreased activity upon further hydroperoxide addition to the reaction mixture. (iii) Fe- and Mn(TPP)Cl are true catalysts found unchanged at the end of the reaction and exhibiting a constant activity upon new addition of hydroperoxide.

In reactions catalyzed by Fe(TPP)Cl, cumyl- and *tert*-butyl hydroperoxide give similar results but with better yields for the former; iodosylbenzene gives lower yields of oxidation products with a very different cyclohexanol/cyclohexanone ratio with an almost exclusive formation of the alcohol as reported previously[3] (Table 2). Moreover, an important irreversible oxidation of the porphyrin ring takes place with the latter oxidant[4] under our conditions.

Table 2. Cyclohexane oxidation by single oxygen donors catalyzed by Fe(TPP)Cl [a].

Oxidant	Yield [%] after 15 min		$t_{1/2}$ for reaction [min]
	$C_6H_{11}OH$	$C_6H_{10}O$	
$C_6H_5C(CH_3)_2O_2H$	40	20	1—2
t-BuO_2H	20	12	5
C_6H_5IO [b]	12	1	15

[a] Same conditions as Table 1. [b] Not completely soluble in the medium at the beginning of the reaction.

In biological systems, hydroperoxide reactions are generally catalyzed by iron-porphyrins; it is noteworthy that we also found an iron-porphyrin to be the best catalyst in our system[9].

Received: March 21, 1980;
revised: September 15, 1980 [Z 598 IE]
German version: Angew. Chem. *92*, 938 (1980)

CAS Registry numbers:
Cyclohexane, 110-82-7; cyclohexanol, 108-93-0; cyclohexanone, 108-94-1; cumyl hydroperoxide, 80-15-9

[1] a) *V. Ullrich*, Top. Curr. Chem. *83*, 68 (1979); b) *A. D. Rahimtula, P. J. O'Brien, E. G. Hrycay, J. A. Peterson, R. W. Estabrook*, Biochem. Biophys. Res. Commun. *60*, 695 (1974); c) *F. Lichtenberger, W. Nastainczyk, V. Ullrich, ibid. 70*, 939 (1976); d) *G. D. Nordblom, R. E. White, M. J. Coon*, Arch. Biochem. Biophys. *175*, 524 (1976).

[2] *J. T. Groves, G. A. McClusky, R. E. White, M. J. Coon*, Biochem. Biophys. Res. Commun. *81*, 154 (1978).

[3] *J. T. Groves, T. E. Nemo, R. S. Myers*, J. Am. Chem. Soc. *101*, 1032 (1979).

[4] *C. K. Chang, M. S. Kuo*, J. Am. Chem. Soc. *101*, 3413 (1979).

[5] a) *D. Mansuy, J. P. Battioni, J. C. Chottard, V. Ullrich*, J. Am. Chem. Soc. *101*, 3971 (1979); b) *D. Mansuy, J. C. Chottard, M. Lange, J. P. Battioni*, J. Mol. Catal. *7*, 215 (1980).

[6] Preliminary results concerning *t*BuOOH supported hydroxylation of cyclohexane catalyzed by an iron-porphyrin have been recently mentioned: *J. T. Groves*, Symposium on Microsomes and Drug Oxidation, Ann Arbor 1979.

[7] Treatment of 50 mmol of cyclohexanol (in benzene) by 50 mmol of cumyl hydroperoxide in the presence of 2.5 mmol of Fe(TPP)Cl at 20 °C leads to cyclohexanone in 10—15% yield.

[8] a) *J. H. Fuhrhop, K. M. Smith* in *K. M. Smith:* Porphyrins and Metalloporphyrins. Elsevier, Amsterdam 1975, p. 757; b) *J. W. Buchler* in *D. Dolphin:* The Porphyrins. Vol. 1. Academic Press, New York 1978.

[9] Preliminary results show that $Ru(TPP)(PEt_3)_2$ is also an active catalyst leading to 35% cyclohexanol and 12% cyclohexanone within a few minutes at 20 °C under the conditions of Table 1, but appears partially modified at the end of the reaction.

Separation of the Enantiomers of 2-Hydroxycarboxylic Acids on Optically Active Stationary Phases

By *Wilfried A. König, Susanne Sievers,* and *Uwe Schulze*[*]

The direct gas chromatographic separation of optical antipodes on chiral stationary phases has already been achieved in the case of amino acids, amino alcohols, amines and 2-alkylcarboxamides[1,2]. In these cases the separation was attributed exclusively to selective hydrogen bonding interactions[2,3]. We have shown with several model species that *e.g.* also dipole-dipole interactions effect an enantiomer separation[4].

Stationary phases developed for the separation of amino acids[1,2], however, are not suitable for the separation of enantiomers of nitrogen-free compounds. We have now succeeded for the first time in separating also the trifluoroacetylated esters of 2-hydroxycarboxylic acids on some novel stationary phases. Acids of this type are metabolic products of higher organisms[5] and constituents of important brain glycolipids[6].

As stationary phases we used the L-(*S*)-mandelic acid derivatives *(1)—(4)* (Table 1), coated on the inner surface of glass capillary columns (borosilicate glass, 40 m, 0.2 mm internal diameter). The separation factors for the trifluoroacetylated compounds investigated are presented in Table 1. As expected, the respective (*S*)-enantiomers are always retarded on phases *(1)—(4)* which contain the (*S*)-mandelic acid as structural unit. The elution sequence was checked in the case of the enantiomers of mandelic acid, alanine, valine, valinol, 2-aminopentane, and α-phenylethylamine.

The amino acid enantiomers are eluted in the reverse order on the phase diastereomeric to *(1)*, with (*R*)-α-phenylethylamine. The separation factors are expectedly smaller than in the case of *(1)* (*e.g.* DL-mandelic acid: $\alpha = 1.007$ at 70 °C; DL-alanine: $\alpha = 1.012$ at 80 °C; DL-valinol: $\alpha = 1.013$ at 80 °C). It can be concluded from this behavior that both chiral centers of the stationary phase influence the separation. As shown by the results with phase *(3)*, a single asymmetic center can also suffice for "chiral recognition" (cf. Table 1).

Interestingly, phases *(1)* and *(4)* show a noticeable selectivity for the enantiomers of mandelic acid, while the homologous racemic 3-phenyllactic acid is separated only on phases *(2)* and *(3)*. This is an indication that "chiral recognition" is favored by a close structural relationship between the interacting chiral partners. Also on cyclohexyl *O*-benzyloxycarbonyl-(*S*)-mandelate as stationary phase, of the hydroxy acids only DL-mandelic acid is separated. Remarkably, in this case "chiral recognition" is even observed in a nitrogen-free system.

The phases *(2)* and *(3)*, on which also aliphatic hydroxy acids are separated, behave less specifically. Hydrogen bonding interactions are in any case of secondary importance for the selectivity of the phases *(2)* and *(3)* for hydroxy acids, since at most *one* hydrogen bridge can be formed between the phase and the substrate. This argument is further supported by the observation that the phases *(1)* and *(4)*, *i.e.* in the cases where *two* hydrogen bridge bonds are possible, show rather less selectivity towards hydroxy acids than the other two phases. On the other hand, an essential contribution of hydrogen bonding interactions cannot be ruled out for the separation of the amines on phase *(4)*.

The possibility of separating enantiomeric hydroxy acids on phases such as *(2)* and *(3)* or similar compounds extends the scope of gas chromatography as a rapid method for configurational analysis. The partial separation of the enantiomers of trifluoroacetylated 1-phenylethanol on *O*-benzyloxycarbonyl-(*S*)-3-phenyllactic acid *tert*-butylamide indicates that diastereomeric interactions can be exploited for the separation of enantiomers also in the case of other nitrogen-free compounds.

Preliminary results with polymer-based phases of this type for enantiomer separation indicate that this method of analysis will undoubtedly gain practical importance.

[*] Prof. Dr. W. A. König, Dipl.-Chem. S. Sievers, U. Schulze
Institut für Organische Chemie und Biochemie
der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0910 $02.50/0

Table 1. Gas chromatographic separation of enantiomers on the stationary phases *(1)*—*(4)*.
Phase *(1)*: (*S*)-mandelic acid-(*S*)-α-phenylethylamide
Phase *(2)*: *O*-benzyloxycarbonyl-(*S*)-mandelic acid (*S*)-α-phenylethylamide
Phase *(3)*: *O*-benzyloxycarbonyl-(*S*)-mandelic acid *tert*-butylamide
Phase *(4)*: *N*-[(*S*)-mandeloyl]-(*S*)-valine cyclohexyl ester

Racemate	Separation factor α/Column temperature [°C]			
	Phase *(1)*	Phase *(2)*	Phase *(3)*	Phase *(4)*
DL-Mandelic acid [a]	1.032/90	1.019/118	1.018/110	1.018/90
DL-3-Phenyllactic acid [a]	—	1.010/113	1.008/110	—
DL-2-Hydroxy-4-methylpentanoic acid [a]	—	1.008/89	1.014/80	—
DL-2-Hydroxyhexanoic acid [a]	—	1.010/89	1.011/80	—
DL-2-Hydroxyoctanoic acid [a]	—	1.014/89	1.015/80	—
DL-2-Hydroxydodecanoic acid [a]	—	1.014/120	[e]	—
DL-Alanine [b]	1.053/70	1.016/100	1.020/90	1.020/90
DL-Valine [b]	1.075/70	1.017/100	1.020/90	1.025/90
DL-Alaninol [c]	1.029/90	1.010/123	—	1.017/90
DL-Valinol [c]	1.025/90	—	1.005/110	1.012/90
DL-2-Aminopentane [d]	—	—	1.010/100	1.014/90
DL-2-Aminoheptane [d]	[e]	—	1.015/100	1.022/90
DL-2-Amino-6-methylheptane [d]	[e]	—	1.015/100	1.024/90
DL-2-Aminooctane [d]	1.048/80	—	1.014/100	1.024/90
DL-α-Phenylethylamine [d]	1.090/90	—	1.033/110	1.055/110

[a] Separated as 2-(trifluoroacetoxy)carboxylic acid isopropyl ester. [b] Separated as 2-(trifluoroacetylamino)carboxylic acid isopropyl ester. [c] Separated as 2-(trifluoroacetylamino)alkyl trifluoroacetate. [d] Separated as *N*-(2-methylalkyl)trifluoroacetamide. [e] Not tested.

Received: May 2, 1980 [Z 596 IE]
German version: Angew. Chem. *92*, 935 (1980)

CAS Registry numbers:
(1), 75475-77-3; *(2)*, 75475-78-4; *(3)*, 75475-79-5; *(4)*, 75475-80-8; isopropyl (±)-α-(trifluoroacetoxy)benzeneacetate, 75475-81-9; isopropyl (±)-α-(trifluoroacetoxy)benzenepropanoate, 75475-82-0; isopropyl (±)-4-methyl-2-(trifluoroacetoxy)pentanoate, 75475-83-1; isopropyl (±)-2-(trifluoroacetoxy)hexanoate, 75475-84-2; isopropyl (±)-2-(trifluoroacetoxy)octanoate, 75475-85-3; isopropyl (±)-2-(trifluoroacetoxy)dodecanoate, 75475-86-4; (DL)-*N*-(trifluoroacetyl)alanine isopropyl ester, 6823-43-4; (DL)-*N*-(trifluoroacetyl)valine isopropyl ester, 37516-92-0; (±)-*N*-(trifluoroacetyl)alaninol trifluoroacetate, 75475-87-5; (±)-*N*-(trifluoroacetyl)valinol trifluoroacetate, 75475-88-6; (±)-*N*-(trifluoroacetyl)-2-aminopentane, 75475-89-7; (±)-*N*-(trifluoroacetyl)-2-aminoheptane, 28382-70-9; (±)-*N*-(trifluoroacetyl)-2-amino-6-methylheptane, 75475-90-0; (±)-*N*-(trifluoroacetyl)-2-aminooctane, 51241-64-6; (±)-*N*-(trifluoroacetyl)-α-phenylethylamine, 28332-81-2

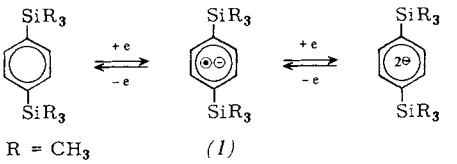
[1] *E. Gil-Av, B. Feibush, R. Charles-Sigler* in *A. B. Littlewood:* Gas-Chromatography 1966. Institute of Petroleum, London 1967, p. 227; *W. A. König, G. J. Nicholson*, Anal. Chem. *47*, 951 (1975).
[2] *U. Beitler, B. Feibush*, J. Chromatogr. *123*, 149 (1976); *S. Weinstein, B. Feibush, E. Gil-Av, ibid. 126*, 97 (1976); *H. Frank, G. J. Nicholson, E. Bayer*, Angew. Chem. *90*, 396 (1978); Angew. Chem. Int. Ed. Engl. *17*, 363 (1978).
[3] *B. Feibush, A. Balan, B. Altman, E. Gil-Av*, J. Chem. Soc. Perkin Trans. II *1979*, 1230.
[4] *K. Stölting, W. A. König*, Chromatographia *9*, 331 (1976); *W. A. König, K. Stölting, K. Kruse, ibid. 10*, 444 (1977).
[5] *Y. Kishimoto, N. S. Radin*, J. Lipid Res. *4*, 139 (1963).
[6] *Y. Kishimoto, N. S. Radin*, Lipids *1*, 47 (1966).

Isoelectronic Radical Ions and Redox Systems[**]

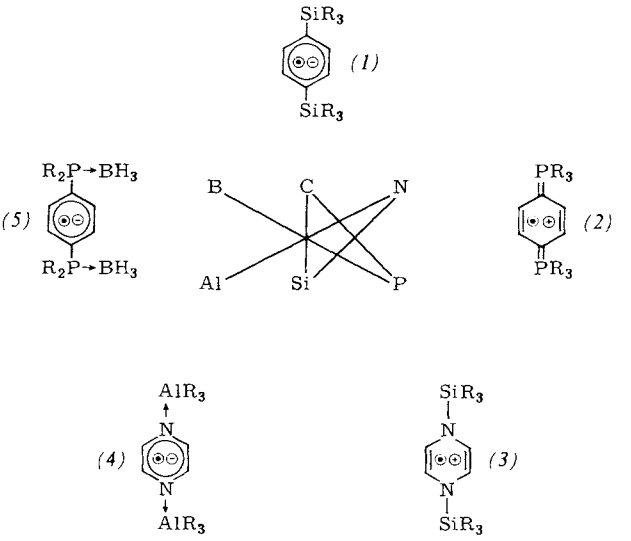
By *Wolfgang Kaim*[*]

Several systematic concepts have been developed regarding the stability and persistency of radicals and radical ions[1]. In this communication an additional route to stable open-shell systems is presented: The directed synthesis of isoelectronic radical ions[2] and redox systems.

The starting compound for the present isoelectronic series is 1,4-bis(trimethylsilyl)benzene, which, despite its low reduction potential of only −2.35 V[3], forms a stable anion *(1)*[3] and—on reaction with potassium at low temperature—also a dianion[4].



By combination of elements of the first (B, C, N) and second (Al, Si, P) periods of the periodic system four further redox systems isoelectronic to *(1)*[5] were devised; Scheme 1 shows the respective paramagnetic intermediates.



Scheme 1. Construction principle for five isoelectronic radical ions (R = CH_3). The radical ions were generated as follows: *(1)*, by reaction of 1,4-bis(trimethylsilyl)benzene with K in DME, *(2)* by cathodic reduction of 1,4-phenylenebis(trimethylphosphonium) diiodide in DMF, *(3)* by reaction of 1,4-dihydro-1,4-bis(trimethylsilyl)pyrazine with $AlCl_3$ in CH_2Cl_2 [4], *(4)* by reaction of pyrazine and $Al(CH_3)_3$ with K in benzene and *(5)* by alkali-metal reduction of 1,4-bis(dimethylphosphino)benzene in BH_3/THF.

All the radical ions *(1)*—*(5)* are persistent at room temperature and can be identified by ESR spectroscopy (Table 1). As representative example Figure 1 shows the spectrum of the N—Al compound[6] *(4)*.

[*] Dr. W. Kaim
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

[**] This work was supported by a Liebig Grant from the Verband der Chemischen Industrie.

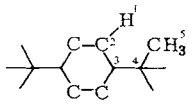


Table 1. ESR coupling constants [mT] and g-factors of the radical ions *(1)*—*(5)*.

	(1)	*(2)*	*(3)*	*(4)*	*(5)*
a_1	0.179	0.195	0.313	0.262	0.188
a_2	[a]	[a]	[a]	0.22	[a]
a_3	0.9	[a]	0.664	0.677	0.92
a_4	0.535	1.310	0.279	0.221	0.908
a_5	0.027	0.030	<0.005	<0.005	[b]
g	2.0029	2.0028	2.0033	2.0035	2.0028

[a] Not observed. [b] Superposition of borane and methyl coupling constants.

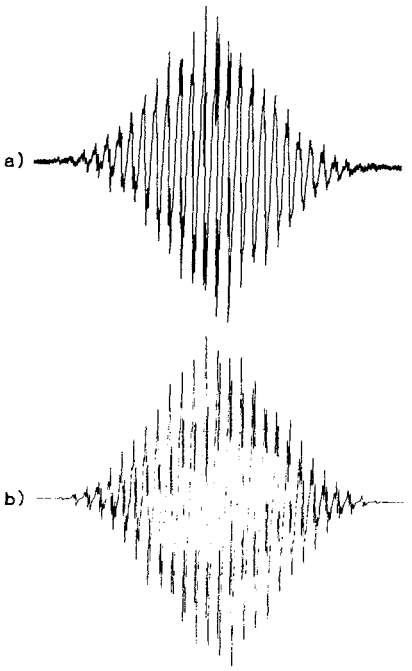


Fig. 1. a) ESR spectrum of the radical anion *(4)*; b) computer simulation.

The ESR parameters (Table 1) of the five isoelectronic radical ions reflect the structural differences: the pyrazine derivatives *(3)* and *(4)* have larger ring-proton and smaller methyl-proton coupling constants as well as higher g-factors than the benzene derivatives *(1)*, *(2)* and *(5)*.

The cations *(2)* and *(3)* are to be regarded as one-electron oxidation products of extremely electron-rich neutral compounds[8], but they can also be generated by reduction of the corresponding dications. The anions *(4)* and *(5)*, on the other hand, are the first examples of a new type of paramagnetic donor-acceptor complexes[9]; the strength of the complex bond is considerably influenced by the electron distribution.

Received: May 8, 1980 [Z 599 IE]
German version: Angew. Chem. 92, 940 (1980)

[1] a) *D. Griller, K. U. Ingold*, Acc. Chem. Res. *9*, 13 (1976); b) *H. Bock, W. Kaim*, Tetrahedron Lett. *1977*, 2343; J. Organomet. Chem. *135*, C14 (1977); c) *K. Deuchert, S. Hünig*, Angew. Chem. *90*, 927 (1978); Angew. Chem. Int. Ed. Engl. *17*, 875 (1978); d) *H. G. Viehe, R. Merényi, L. Stella, Z. Janousek*, Angew. Chem. *91*, 982 (1979); Angew. Chem. Int. Ed. Engl. *18*, 917 (1979).

[2] Pairs of isoelectronic radicals or radical ions have already been investigated in some cases; cf., *e.g., J. E. Leffler, G. B. Watts, T. Tanigaki, E. Dolan, D. S. Miller*, J. Am. Chem. Soc. *92*, 6825 (1970); *H. Bock, W. Kaim, P. L. Timms, P. Hawker*, Chem. Ber. *113*, 3196 (1980).

[3] a) *H. Alt, H. Bock, F. Gerson, J. Heinzer*, Angew. Chem. *79*, 933 (1967); Angew. Chem. Int. Ed. Engl. *6*, 941 (1967); b) *A. L. Allred, L. W. Bush*, J. Am. Chem. Soc. *90*, 3352 (1968).

[4] *H. Bock, W. Kaim*, J. Am. Chem. Soc. *102*, 4429 (1980).

[5] The $-P(CH_3)_2 \cdot BH_3$ group isoelectronic to $-Si(CH_3)_3$ has recently been reported: *H. Schmidbauer, E. Weiss*, Angew. Chem. *91*, 847 (1979); Angew. Chem. Int. Ed. Engl. *18*, 781 (1979).

[6] Organoaluminum radicals have been discussed in the literature [7] but have not been unequivocally characterized ESR spectroscopically; a recently introduced "$KAl(C_2H_5)_3$" radical ion can most likely be identified as the biphenyl radical anion: *H. Hoberg, S. Krause, E. Ziegler*, J. Organomet. Chem. *184*, 1 (1980).

[7] *R. Köster, P. Binger*, Adv. Inorg. Chem. Radiochem. *7*, 263 (1965), and references cited therein; see also *E. Ziegler, G. Fuchs, H. Lehmkuhl*, Z. Anorg. Allg. Chem. *355*, 145 (1967).

[8] *W. Kaim*, unpublished results.

[9] Complexes of free radicals with Lewis acids: *B. M. Hoffmann, T. B. Eames*, J. Am. Chem. Soc. *91*, 5169 (1969).

Radical Cation Salts of Simple Arenes—A New Family of "Organic Metals"[**]

By *Christoph Kröhnke, Volker Enkelmann*, and *Gerhard Wegner*[*]

The charge transfer complexes of tetracyanoquinonedimethane (TCNQ) and tetrathiofulvalene (TTF) have been used as examples to formulate general principles which correlate the occurrence of metallic conductivity with structural parameters[1a,b]. The common structural principle of electrically conductive molecular crystals is the crystallization of the donor and acceptor in separated stacks with equal distance between the molecules within each stack[1c] but with only a partial transfer of charge[1a]. For synthesis of most of the previously known "organic metals" the charges are generated by a redox reaction between dissolved reaction partners, followed by crystallization[1d]. The low stability of the intermediary radical ions occurring in solution has hitherto limited the number of possible structures to pairs of heterocycles (*e.g.* TTF, phthalocyanine[1e]) and compounds containing heteroatoms (*e.g.* TCNQ).

Stable radical cations of arenes can be generated by anodic oxidation and can be separated at the anode in the presence of suitable anions as radical cation salts $[aryl_2]^{\odot\oplus}X^{\ominus}$ in the form of shiny black crystals, as has been shown by *Fritz et al.* for the example of $[naphthalene_2]^{\odot\oplus}PF_6^{\ominus}$ *(1a)*[2]. Crystals of this type represent a new class of organic metals.

We have synthesized the corresponding complexes of the radical cations of triphenylene, pyrene, perylene, fluoroanthene *etc.* with the anions BF_4^-, ClO_4^-, PF_6^-, AsF_6^- and SbF_6^- and investigated their conductivity (see also Table 1).

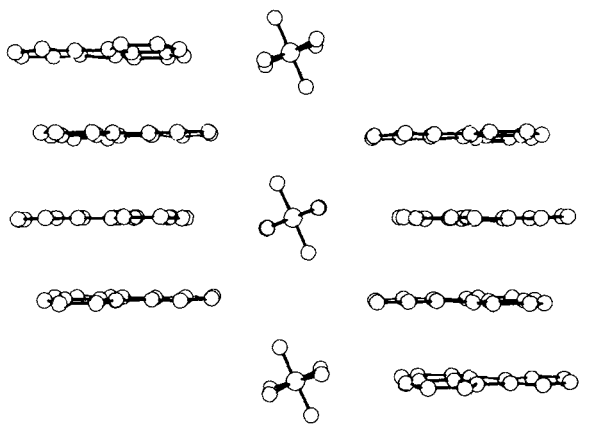


Fig. 1. Crystal structure of $[fluoroanthene_2]^{\odot\oplus}PF_6^{\ominus}$ *(2a)*.

[*] Prof. Dr. G. Wegner, Dr. C. Kröhnke, Dr. V. Enkelmann
Institut für Makromolekulare Chemie der Universität
Stefan-Meier-Str. 31, D-7800 Freiburg (Germany)

[**] This work was supported by Stiftung Volkswagenwerk.

All these complexes show a common structural principle. The arenes are packed in stacks with short distances of 320—325 pm between the molecular planes. The anions are located in the channels between the stacks. Anions of various sizes can be incorporated without essentially altering the structure. All organic molecules within a stack are crystallographically identical, *i.e.* the radical cation is not localized.

The extremely anisotropic ESR signals with linewidths of, in part, only 20 mG[3] also indicate strong interaction and a rapid charge transfer between the molecules within a stack. Figure 1 shows as example the structure of the complex $[\text{fluoroanthene}_2]^{\oplus}PF_6^{\ominus}$ *(2a)*, prepared by us for the first time. The isotropic conductivity σ measured on polycrystalline samples has a magnitude of *ca.* 0.1—0.001 $\Omega^{-1}\,\text{cm}^{-1}$ for all complexes at room temperature. The temperature dependence of σ for fluoroanthene with various anions is presented in Figure 2. The solid line was calculated according to an expression given by *Epstein* and *Conwell*[4]

$$\sigma_n = \sigma_T/\sigma_{295} = A \cdot T^{-\alpha} \exp\left(\frac{-E}{RT}\right) \qquad \text{(a)}$$

with $\alpha = 2.5$ and $E = 0$. The term $T^{-\alpha}$ describes the temperature dependence of the carrier mobility, E is the activation energy for generation of the charge carriers, A is a preexponential factor. In all cases the fitting of the measured curves gives $E = 0$. The counterion has only a small influence on the value of α. We are consequently dealing with organic metals in which the mobility of the charge carriers is strongly temperature-dependent.

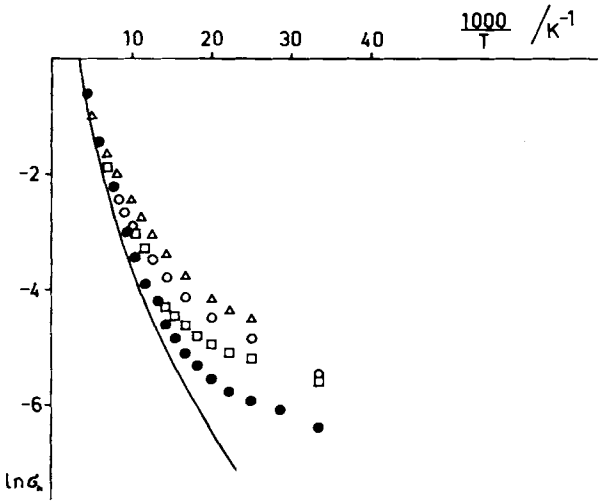


Fig. 2. Dependence of conductivity σ_n on T^{-1} for fluoroanthene radical cation salts *(2)* with various anions. The unbroken curve is calculated according to eq. (a). ●: $(FA)_2PF_6$ *(2a)*, □: $(FA)_2AsF_6$ *(2b)*, △: $(FA)_2SbF_6$ *(2c)* (FA = fluoroanthene), ○: $[\text{triphenylene}_2]^{\oplus}PF_6^{\ominus}$.

Below 150 K, phase transitions occur which imply the deviation of the measured values from the curve determined by eq. (a). Table 1 lists some of the distances between the molecular planes determined crystallographically by us, together with some conductivity values at room temperature.

A similar conductivity behavior is also observed in the case of polymers doped with strong oxidizing agents in the solid state; for example, polyacetylene[5] and poly-*p*-phenylene sulfide[6]. We assume that the transport of charge carriers also proceeds in these cases *via* complexes between individual segments of the polymers having the structure of radical cations. It is known that at least the radical cations of arenes can be obtained as unstable solids by reaction with typical "doping agents" such as $SbCl_5$[7].

Table 1. Distance *d* between the ring planes and isotropically measured specific conductivity σ_{295} in the salts $[\text{aryl}_2]^{\oplus}X^{\ominus}$.

	Aryl	X	*d*/pm	$\sigma_{295}/\Omega^{-1}\,\text{cm}^{-1}$
(1a)	Naphthalene	PF_6	320 [6]	0.12 [6]
(2a)	Fluoroanthene	PF_6	328	0.05
(2b)		AsF_6	330	0.02
(2c)		SbF_6	330	0.01
(3d)	Perylene	BF_4		$4\cdot10^{-4}$
(3a)		PF_6	335	0.04
(3b)		AsF_6		0.04
(3c)		SbF_6		$4\cdot10^{-3}$
(4a)	Pyrene	PF_6	320	
(4b)		AsF_6		$1\cdot10^{-3}$
(4c)		SbF_6		$1\cdot10^{-3}$
(5a)	Triphenylene	PF_6		$7\cdot10^{-3}$
(5b)		AsF_6		$3\cdot10^{-3}$

The salt $(TMTSF)_2PF_6$[8], which is superconductive at $T < 1$ K and pressures of $p > 12$ kbar, also has a packing related to that in the salts *(1)*—*(5)*.

Procedure

Crystals of $[\text{fluoroanthene}_2]^{\oplus}PF_6^{\ominus}$ *(2a)*: A solution of fluoroanthene (10 mmol) in CH_2Cl_2 (200 ml) is treated with tetrabutylammonium hexafluorophosphate (20 mmol). The solution is cooled to −30 °C and electrolyzed between Ni electrodes with a spacing of 1 cm and a current of 2 mA (20 V potential). Shiny black crystals of *(2a)* begin to grow on the anodes within a few minutes.

Received: August 4, 1980 [Z 600 IE]
German version: Angew. Chem. *92*, 941 (1980)

CAS Registry numbers:
(1a), 67063-23-4; *(2a)*, 75506-25-1; *(2b)*, 75506-27-3; *(2c)*, 75506-29-5; *(3a)*, 75506-31-9; *(3b)*, 75506-33-1; *(3c)*, 75506-35-3; *(3d)*, 75506-37-5; *(4a)*, 75506-39-7; *(4b)*, 75506-41-1; *(4c)*, 75506-43-3; *(5a)*, 75506-45-5; *(5b)*, 75506-47-7

[1] a) *J. B. Torrance*, Acc. Chem. Res. *12*, 79 (1979); b) *W. E. Hatfield:* Molecular Metals. Plenum Press, New York 1979; c) survey of crystal structures: *S. Flandrois, D. Chasseau*, Acta Crystallogr. *B 33*, 2744 (1977); d) *D. J. Sandman*, Mol. Cryst. Liqu. Cryst. *50*, 235 (1979); e) *T. E. Phillips, R. P. Scaringe, B. M. Hoffman, J. A. Ibers*, J. Am. Chem. Soc. *102*, 3435 (1980).
[2] *H. P. Fritz, H. Gebauer, P. Friedrich, P. Ecker, R. Artes, U. Schubert*, Z. Naturforsch. *B 33*, 498 (1978).
[3] *H. Eichele, M. Schwoerer*, Universität Bayreuth, private communication.
[4] *A. J. Epstein, E. M. Conwell*, Solid State Commun. *24*, 627 (1977).
[5] *A. G. MacDiarmid, A. J. Heeger* in [1b], p. 161 f.
[6] *R. R. Chance, L. W. Shacklette, G. G. Miller, D. M. Ivory, J. M. Sowa, R. L. Elsenbaumer, R. H. Baughman*, J. Chem. Soc. Chem. Commun. *1980*, 348.
[7] *I. C. Lewis, L. S. Singer*, J. Chem. Phys. *43*, 2712 (1965).
[8] $(TMTSF)_2PF_6$: bis(tetramethyltetraselenafulvalene) hexafluorophosphate; *D. Jerome, M. Ribault, K. Beechgaard*, New Sci. *1980*, 104.

Geometrically Induced Loss of Aromaticity in Bridged [14]Annulenes: *syn*-1,6-Ethano-8,13-methano[14]annulene

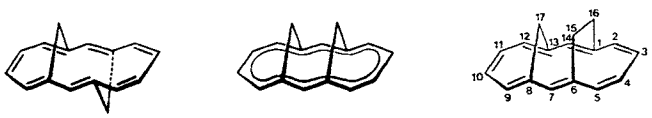
By *Emanuel Vogel, Hans M. Deger, Peter Hebel,* and *Johann Lex*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The rigid bridged [14]annulenes with acene perimeters are ideal substrates for investigations on the interrelation between aromaticity and molecular geometry, since the choice

[*] Prof. Dr. E. Vogel, Dr. H. M. Deger, Dipl.-Chem. P. Hebel, Dr. J. Lex
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

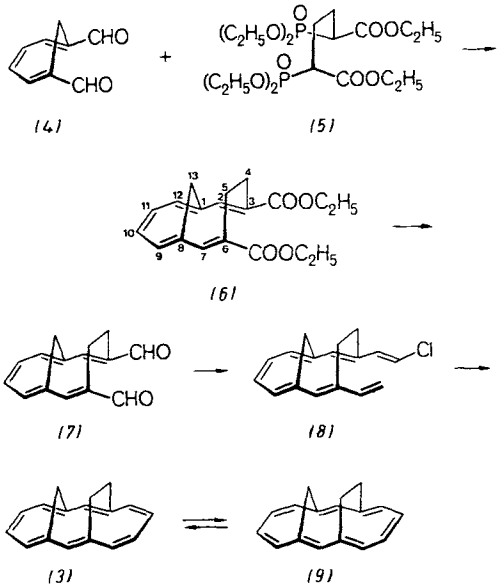
of bridge type and steric arrangement of the bridges (*syn*- or *anti*-configuration) enables variation of the conformation of the annulene ring within relatively wide limits[1].



(1) (2) (3)

The influence of ring conformation on the π-electron structure of a bridged [14]annulene manifests itself most impressively in the case of the *syn*- and *anti*-1,6:8,13-bismethano[14]annulenes [*(2)* and *(1)*, respectively]. While *(2)* is aromatic, even though it contains a noticeably bent annulene ring[2a], *(1)* with its strongly puckered ring is an olefinic molecule with fluctional π-bonds[2b]. The absence of a geometrically induced loss of aromaticity in the case of *(2)* is consistent with knowledge gained from other bridged [14]annulenes, according to which a [4*n*+2]annulene tolerates considerable deformation of the ring skeleton without substantial weakening of the π-electron delocalization, provided that the torsional angles of the C_{sp^2}—C_{sp^2} bonds in the ring are not greater than *ca.* 45—55°[1a,3]. The maximum value of these torsional angles in the case of *(2)* is 34°, and in the case of *(1)* *ca.* 70°!

We have now found that the title compound, *syn*-1,6-ethano-8,13-methano[14]annulene, for which greater torsions in the annulene ring can be anticipated than in *(2)*[4], is, like *(1)*, an olefinic [14]annulene [*(3)* and/or *(9)*]. The preparation of the compound was accomplished using the recently developed building-block approach for the synthesis of bridged annulenes[5].



(4) (5) (6) (7) (8) (3) (9)

Reaction of *(4)*[5] with *(5)*[6] (for conditions see [5]) smoothly afforded the diester *(6)* (yield 69%, see Table 1), which by successive treatment with diisobutylaluminum hydride and manganese dioxide[5] could be transformed into the dialdehyde *(7)* [yield of diol and *(7)* 83 and 80%, respectively; dark yellow rhombs (ethyl acetate), m.p. 150—151 °C].

Table 1. Physical data of the diester *(6)* and of the *syn*-1,6-ethano-8,13-methano[14]annulene [*(3)*⇄*(9)*].

(6), M.p. = 88 °C (methanol); yellow needles; ^{1}H-NMR ($CDCl_3$): δ = 1.53 and 3.15 (AX system, *J* = 13.5 Hz, 2H, H-13), 2.17—2.78 (AA'BB' system, 4H, H-4,5), 6.45—6.85 (AA'XX' system, 4H, H-9,10,11,12), 7.77 (s, 2H, H-2,7), 1.33 and 4.23 (t and q, 10H, $2C_2H_5$); UV (dioxane): λ_{max} = 275 nm (ε = 41400), 356 (7650); IR (KBr): 1700 cm^{-1} (C=O); MS: *m/e* = 314 (M^+, 11%)

[*(3)*⇄*(9)*], dec. >250 °C (hexane); red, oblong-shaped crystals; ^{1}H-NMR (CCl_4): δ = 1.53 and 4.28 (AX system, *J* = 12.5 Hz, 2H, H-17), 1.90—2.82 (AA'BB' system, 4H, H-15,16), 5.98—6.55 (m, 10H, 10 perimeter-H); ^{13}C-NMR (CD_2Cl_2): δ = 141.7, 133.9, 133.7, 132.0, 128.4, 126.4, 123.6, 32.1, 29.9; UV (cyclohexane): λ_{max} = 287 nm (ε = 28000), 381 (3500); IR (CsI): 1599 cm^{-1} (C=C); MS: *m/e* = 220 (M^+, 30%), 205 (38), 191 (76), 178 (67), 165 (95), 152 (41), 142 (100), 128 (85), 115 (72), 91 (56)

For conversion into *(8)* (for procedure see [7]), *(7)* was allowed to react with methylene(triphenyl)phosphorane (molar ratio 1:1.3) to give the vinylaldehyde (6-vinylbicyclo[6.4.1]trideca-1(12),2,6,8,10-pentaene-3-carbaldehyde) [deep-yellow crystals (from ethyl acetate), m.p. 85 °C; yield 45%], which on treatment with chloromethylene(triphenyl)phosphorane afforded *(8)*. Owing to its strong tendency to polymerize, the chromatographically (silica gel, dichloromethane/hexane) separated *(8)* was "cyclodehydrochlorinated" by thermolysis (1 h) in boiling dimethylformamide without further purification. *syn*-1,6-Ethano-8,13-methano[14]annulene was formed stereoselectively as an easily isolable compound (yield 23% referred to the vinylaldehyde), which polymerizes relatively rapidly on exposure to air, but can be stored under an inert gas at low temperature.

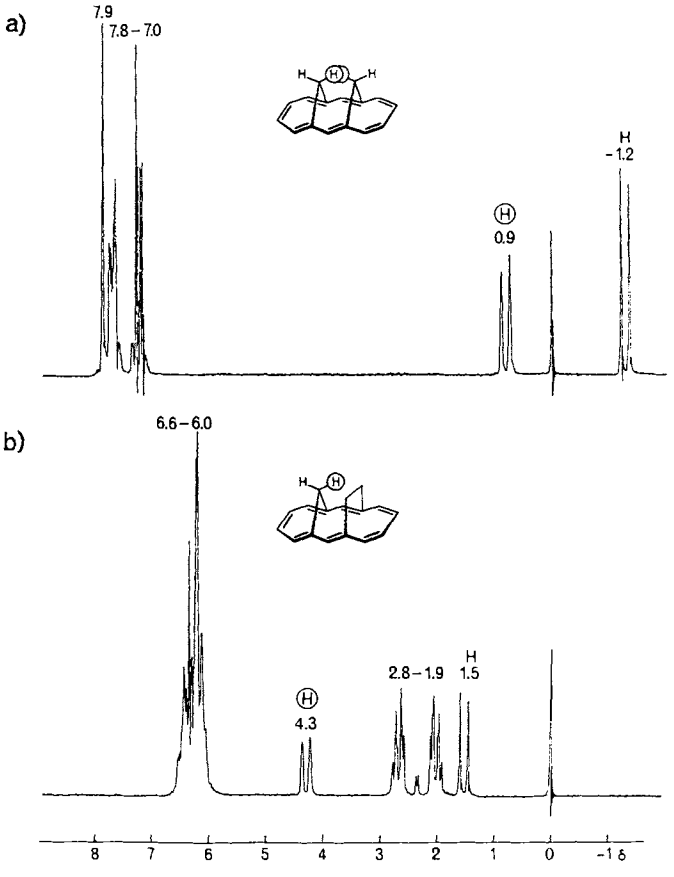


Fig. 1. 90-MHz ^{1}H-NMR spectra of a) *syn*-1,6:8,13-bismethano[14]annulene *(2)* and b) *syn*-1,6-ethano-8,13-methano[14]annulene [*(3)*⇄*(9)*] (in each case in CCl_4, TMS as internal standard).

© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/1111-0920 $02.50/0

Proof of structure was chiefly secured by a combination of its ^{1}H- and ^{13}C-NMR spectra (see Table 1). The 90-MHz ^{1}H-NMR spectrum immediately reveals the olefinic nature, for in comparison to the spectrum of *(2)* the resonances of the annulene protons are shifted upfield by *ca.* 1.2 ppm and those of the CH_2-bridge protons downfield by 2.7 (H_{exo}) and 3.4 (H_{endo}) ppm (see Fig. 1). The unusual deshielding of H_{endo} [by 1.7 ppm compared to the corresponding protons of *(1)*], together with a positive nuclear Overhauser effect can only be explained by the assumption that H_{endo} is sterically strongly compressed. It follows that the title compound must have *syn*-configuration. Since the ^{1}H-NMR spectrum does not completely rule out the valence isomer of *(9)* having a cyclobutane ring—the norcaradiene valence isomer of *(3)* is ruled out on the basis of the geminal coupling of the CH_2 protons—the ^{13}C-NMR spectrum was measured. Consistent with the annulene structure, a total of nine resonances is observed, of which seven belong to sp^2- and two to sp^3-hybridized carbon atoms. It was only by detailed analysis of the high resolution NMR spectra that the presence of *(3)* and *(9)* in rapid valence tautomeric equilibrium could be established (see [8]).

The title compound is characterized as an olefin also by its electronic spectrum. While *(2)* shows a spectrum consisting of three main bands[9], the ethano compound exhibits a two-band spectrum without vibrational fine structure.

The X-ray structure analysis of the new bridged [14]annulene gave a result which was surprising in view of the agreement between the NMR and electron spectral data. Though the analysis confirmed the *syn*-1,6-ethano-8,13-methano[14]annulene structure (transannular distances C1—C6 and C8—C13: 2.744 and 2.392 Å, respectively), C—C bond lengths (1.368—1.417 Å) were found for the annulene ring which would indicate the presence of an aromatic molecule. This contradiction is resolved if one assumes that *(3)* and *(9)* exist alongside each other at room temperature. A low-temperature X-ray structure analysis is planned.

Received: May 29, 1980 [Z 601a IE]
revised: August 21, 1980
German version: Angew. Chem. *92*, 943 (1980)

CAS Registry numbers:
(1), 7068-22-6; *(2)*, 55821-04-0; *(3)*, 75476-60-7; *(4)*, 28172-94-3; *(5)*, 68539-80-0; *(6)*, 75476-61-8; *(7)*, 75476-62-9; *(8)*, 75476-63-0

[1] a) Summaries: *E. Vogel*, Pure Appl. Chem. *28*, 355 (1971); Isr. J. Chem. *20*, 215 (1980); b) for the deformation of benzenoid rings in cyclophanes see: *D. J. Cram, J. M. Cram*, Acc. Chem. Res. *4*, 204 (1971); *H. Iwamura, H. Kihara, S. Misumi, Y. Sakata, T. Umemoto*, Tetrahedron *34*, 3427 (1978); *Y. Sekine, M. Brown, V. Boekelheide*, J. Am. Chem. Soc. *101*, 3126 (1979); *H. Iwamura, M. Katoh, H. Kihara*, Tetrahedron Lett. *1980*, 1757; cf. geometrically induced loss of aromaticity in [10]annulenes *S. Masamune, N. Darby*, Acc. Chem. Res. *5*, 272 (1972).

[2] a) *E. Vogel, J. Sombroek, W. Wagemann*, Angew. Chem. *87*, 591 (1975); Angew. Chem. Int. Ed. Engl. *14*, 564 (1975); *R. Destro, T. Pilati, M. Simonetta*, Acta Crystallogr. *B 33*, 940 (1977); b) *E. Vogel, U. Haberland, H. Günther*, Angew. Chem. *82*, 510 (1970); Angew. Chem. Int. Ed. Engl. *9*, 513 (1970); *C. M. Gramaccioli, A. S. Mimun, A. Mugnoli, M. Simonetta*, J. Am. Chem. Soc. *95*, 3149 (1973); the X-ray structure analysis was carried out on the 7-methoxycarbonyl derivative of *(1)*.

[3] Summaries: *M. Simonetta*, Pure Appl. Chem., in press; *A. Gavezzotti, M. Simonetta*, Helv. Chim. Acta *59*, 2984 (1976); in the case of 1,5-methano[10]annulene force-field calculations gave torsional angles of up to 54° for the C_{sp^2}—C_{sp^2} bonds of the annulene ring, thus suggesting bond alternation; *N. L. Allinger, J. T. Sprague*, J. Am. Chem. Soc. *95*, 3893 (1973). The 1,5-methano[10]annulene synthesized in 1976 by *Masamune*, for which there is still no X-ray structure analysis available, has however a delocalized 10π-electron system: *S. Masamune, D. W. Brooks, K. Morio, R. L. Sobczak*, J. Am. Chem. Soc. *98*, 8277 (1976); *S. Masamune, D. W. Brooks*, Tetrahedron Lett. *1977*, 3239; *L. T. Scott, W. R. Brunsvold*, J. Am. Chem. Soc. *100*, 4320 (1978).

[4] Cf. the transition from the 1,6-methano- to the 1,6-ethano[10]annulene, which is associated with a [10]annulene/*cis*-9,10-dihydronaphthalene valence isomerization due to diminished $2p_z$ orbital overlap in the annulene ring. *E. Vogel, W. Maier, J. Eimer*, Tetrahedron Lett. *1966*, 655; *J. J. Bloomfield, J. R. Smiley Irelan, ibid. 1966*, 2971.

[5] *E. Vogel, H. M. Deger, J. Sombroek, J. Palm, A. Wagner, J. Lex*, Angew. Chem. *92*, 43 (1980); Angew. Chem. Int. Ed. Engl. *19*, 41 (1980).

[6] For the synthesis of *(5)*, molten diethyl α,α'-dibromoadipate (*meso* and racemic form) (1 mol) was added slowly to triethyl phosphite (4 mol) at 160 °C and the mixture kept at this temperature for 6 h; distillation over a 30-cm Vigreux column gave *(5)* in a purity of *ca.* 98%, satisfactory for preparative purposes [b.p. 198—205 °C/5 × 10^5 torr; yield 49%; *m/e* 474 (M^+)]. The ^{31}P-NMR spectrum indicated the presence of a mixture of stereoisomers.

[7] *W. Wagemann, M. Iyoda, H. M. Deger, J. Sombroek, E. Vogel*, Angew. Chem. *90*, 988 (1978); Angew. Chem. Int. Ed. Engl. *17*, 956 (1978).

[8] *H. Günther, H. von Puttkamer, H. M. Deger, P. Hebel, E. Vogel*, Angew. Chem. *92*, 944 (1980); Angew. Chem. Int. Ed. Engl. *19*, 921 (1980).

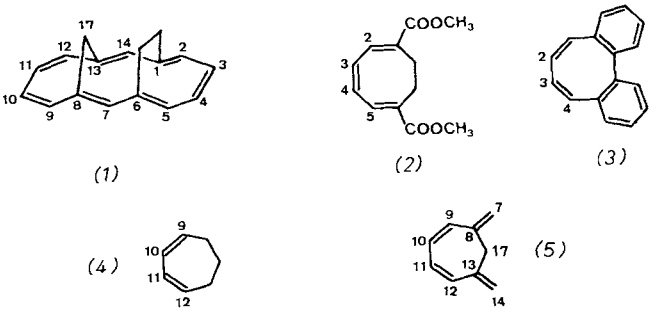
[9] *J. Kolc, J. Michl, E. Vogel*, J. Am. Chem. Soc. *98*, 3935 (1976); *H.-R. Blattmann, W. A. Böll, E. Heilbronner, G. Hohlneicher, E. Vogel, J.-P. Weber*, Helv. Chim. Acta *49*, 2017 (1966).

Structure and Dynamic Behavior of *syn*-1,6-Ethano-8,13-methano[14]annulene[**]

By *Harald Günther, Henning von Puttkamer, Hans M. Deger, Peter Hebel*, and *Emanuel Vogel*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The bond length and bond order relationships of vicinal H,H-coupling constants[1] for cyclic π-systems have been so well investigated[2] that detailed structural information on unsaturated ring systems is accessible *via* ^3J(H,H) values. Whereas the chemical shifts generally only permit differentiation between diatropic, paratropic, or olefinic character, the ^3J(H,H) data provide additional information about the relative bond lengths and the conformation. We have now exploited this fact in structural investigations on the new 1,6-ethano-8,13-methano[14]annulene *(1)*[3]. Of particular interest here was a complete analysis of the ^{1}H-NMR spectrum, because the position of the proton resonances in the 90-MHz spectrum clearly indicated olefinic character, while the X-ray



[*] Prof. Dr. H. Günther [+], Dipl.-Chem. H. von Puttkamer
Universität-Gesamthochschule Siegen, FB 8, OC II
Postfach 210209, D-5900 Siegen 21 (Germany)
Prof. Dr. E. Vogel, Dr. H. M. Deger, Dipl.-Chem. P. Hebel
Institut für Organische Chemie der Universität Köln (Germany)
[+] Author to whom correspondence should be addressed.

[**] Proton Resonance Spectroscopy of Unsaturated Ring Systems, Part 28. This work was supported by the Fonds der Chemischen Industrie.—Part 27: *H. Günther, M. E. Günther, D. Mondeshka, H. Schmickler, F. Sondheimer, N. Darby, T. M. Cresp*, Chem. Ber. *112*, 71 (1979).

structural data pointed to similar bond lengths and thus to a bond equalization due to delocalization—*i.e.* to aromatic character[3].

The strongly coupled spin system of the ring protons of *(1)* at 90 MHz is well resolved at 400 MHz and, besides the singlet for H(7, 14), shows two AA'BB' systems in the olefinic region (Table 1). The signals of the CH_2-bridge are observed as an AB system at higher field, those of the CH_2—CH_2-bridge as an AA'BB' system. Analysis of the ring-proton signals at 34 °C yielded the data given in Table 1, which on the whole are consistent with structure *(1)*, especially as a nuclear Overhauser effect of 20 and 28%, respectively, between the *endo*-methylene protons evidences the *syn*-position of the two bridges. *(1)* can therefore be regarded as a cyclic olefin with alternating double and single bonds.

The possible dynamic processes which must lead to an averaging of the NMR data.

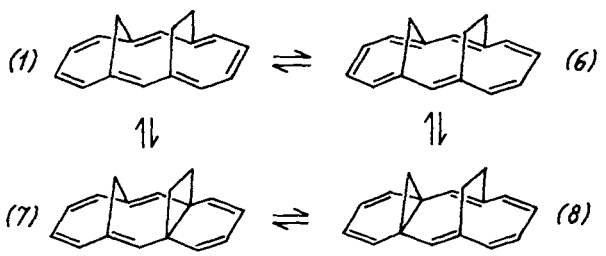
The valence-tautomeric equilibria which are likely in the case of *(1)* are given in Scheme 1. It should be possible to demonstrate experimentally an interchange *(1)*⇌*(6)*, in particular *via* the temperature dependence of the H,H-coupling constants, and an interchange of the type *(1)*⇌*(7)* or *(1)*⇌*(6)*⇌*(8)* *via* the temperature dependence of the ^{13}C-NMR shifts of the quaternary C-atoms[5]. As the ^{13}C-NMR data show (Table 1), the influence of temperature here is only slight so that any mentionable participation of the valence tautomeric structures *(7)* and/or *(8)* can be ruled out. On the other hand, analysis of the ^{1}H-NMR spectrum at various temperatures gave changes in the H,H-coupling constants (Table 1) which clearly indicate a double bond shift of

Table 1. ^{1}H- and ^{13}C-NMR data of *(1)* and the model systems *(2)*—*(5)* [a]. Chemical shifts δ (ppm); coupling constants in Hz.

^{1}H-NMR; solvent CS_2/CD_2Cl_2 (2:1)										
Cpd.	T [°C]	δ(2,5)	δ(3,4)	δ(7,14)	δ(9,12)	δ(10,11)	δ(15_{ex})	δ(15_{en})	δ(17_{ex})	δ(17_{en})
(1)	34	6.110	6.293	6.213	6.474	6.305	2.062	2.690	1.621	4.359
Cpd.	T [°C]	J(2,3)	J(2,4)	J(2,5)	J(3,4)	J(9,10)	J(9,11)	J(9,12)	J(10,11)	J(17_{ex}, 17_{en})
(1)	34	7.12	−0.81	2.24	10.45	9.22	0.20	1.40	9.03	(−) 12.70
	−73	5.82	−1.54	2.44	10.83	9.89	0.47	0.86	8.60	(−) 12.70
(2)	[b]	5.75	−0.66	1.17	12.30	—	—	—	—	—
(3)	[b]	3.62	−0.87	—	11.65	—	—	—	—	—
(4)	[b]	—	—	—	—	11.55	0.67	0.72	6.89	—
(5)	[b]	—	—	—	—	11.73	0.70	1.23	7.97	—
^{13}C-NMR; solvent CD_2Cl_2										
Cpd.	T [°C]	δ(1,6)	δ(8,13)	δ(2,5)	δ(9,12)	δ(3,4)	δ(10,11)	δ(7,14)	δ(15,16)	δ(17)
(1)	34	142.1	124.0	134.3	134.2	128.9	126.6	132.2	32.0	29.7
	−123	141.0	123.3	134.7	133.2	130.4	124.9	129.3	30.6	29.5
(5)	[b]	—	144.9	—	134.7	—	125.1	118.9	—	43.0

[a] PFT high-field spectrometer WH 400 (Bruker Analytische Messtechnik, Karlsruhe). The chemical shifts are referred to TMS. [b] Room temperature.

The data of compounds *(2)*—*(5)*[4] can be taken as model values for the coupling constants of the cyclooctatriene and cycloheptadiene partial structures of *(1)* (Table 1). However, *(4)* and *(5)* are only of limited value for comparison, since they have C_2 symmetry and thus a twisted diene system, whereas a nearly coplanar arrangement of the C-9 to C-12



Scheme 1

fragment must be assumed for *(1)*. The J(H,H) values in the cyclooctatriene fragment of *(1)* are in good agreement with those of model compounds. Observation of practically the same ^3J(H,H) values in the cycloheptadiene fragment could, of course, be explained in terms of the aforementioned coplanarity, but at the same time motivated an investigation of the type *(1)*⇌*(6)*. In particular, the N-parameter of the two AA'BB' systems[6] of the ring protons is sensitive to the associated diene-triene isomerism[7] (Fig. 1). According to these results the equilibrium *(1)*⇌*(6)* shifts further to the side of

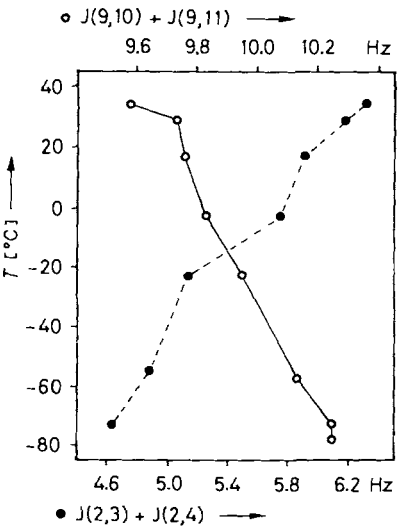


Fig. 1. Temperature dependence of the N-parameter [6] in the two AA'BB' systems of the ring protons H(2)—H(5) and H(9)—H(12) in *(1)*.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0922 $02.50/0

the stable *(1)* at lower temperatures. A rough estimate on the basis of the vicinal coupling $J(3,4)$ yields an equilibrium constant of $K \approx 2$ and thus a ΔG^0 of *ca.* 2 kJ/mol in favor of *(1)* at room temperature[8].

From the negative allylic coupling $J(2,4)$ and the relatively large homoallylic coupling $J(2,5)$ we conclude that a much greater dihedral angle C-1,2,5,6/C-2,3,4,5 exists for *(1)* than is suggested by the X-ray structure analysis for the solid[3,9]. On the other hand, the positive allylic coupling $J(9,11)$ and the decrease in the homoallylic coupling $J(9,12)$ on lowering the temperature are consistent with an essentially coplanar arrangement of the diene system, and the alternance of the vicinal coupling constants observed at $-73\,^{\circ}C$ is now in line with the overall picture.

Received: May 2, 1980 [Z 601 b IE]
German version: Angew. Chem. *92*, 944 (1980)

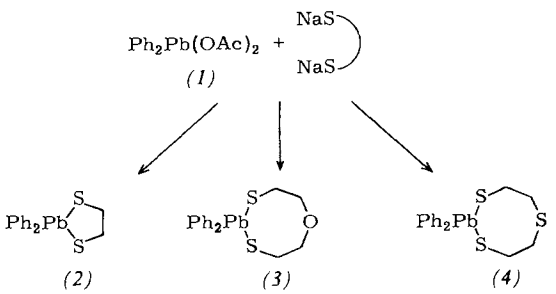
[1] a) *M. Karplus*, J. Chem. Phys. *30*, 11 (1959); b) *N. Jonathan, S. Gordon, B. P. Dailey, ibid. 36*, 2443 (1962).
[2] *H. Günther, H. Schmickler, M.-E. Günther, D. Cremer*, Org. Magn. Reson. *9*, 420 (1977).
[3] *E. Vogel, H. M. Deger, P. Hebel, J. Lex*, Angew. Chem. *92*, 943 (1980); Angew. Chem. Int. Ed. Engl. *19*, 913 (1980).
[4] *(2): H. Günther, H.-H. Hinrichs*, Justus Liebigs Ann. Chem. *706*, 1 (1967); *(3): H. Günther, M.-E. Günther, D. Mondeshka, H. Schmickler, ibid. 1978*, 165; *(4): P. Crews*, J. Am. Chem. Soc. *95*, 636 (1973); *(5):* this work. *(2)—(5)* are numbered analogously to *(1)*.
[5] *H. Günther, T. Keller*, Chem. Ber. *103*, 3231 (1970).
[6] $N = J(2,3) + ((2,4)$ or $J(9,10) + J(9,11)$; cf. *H. Günther*, Angew. Chem. *84*, 907 (1972); Angew. Chem. Int. Ed. Engl. *11*, 861 (1972).
[7] *H. Günther, H.-H. Hinrichs*, Tetrahedron Lett. *1966*, 787.
[8] A direct demonstration of the valence tautomerism *(1)*⇌*(6)* by low temperature NMR measurements (down to $-140\,^{\circ}C$) has so far not been possible.
[9] A dihedral angle C-1,2,5,6/C-2,3,4,5 of 152.2° was found (*J. Lex*, private communication).

1,3,2-Dithiaplumbocanes—Heterocycles with Lead(IV)—Sulfur Bonds[**]

By *Martin Dräger* and *Norbert Kleiner*[*]

Knowledge of the biochemical mode of action of lead compounds is essentially confined to the strong coordination of lead to sulfur and nitrogen, through which it can displace other metals from some enzymes[1]. This is true both for lead(II) ions as well as for organolead(IV) compounds which constitute the primary ecological burden[2], and which, moreover, can be bioalkylated by bacteria in sulfidic media[3]. This implication of the lead(IV)-sulfur bond in the biocycle of lead induced us to carry out structural investigations on compounds containing the $R_2Pb(S—)_2$ group; it was found that lead(IV) can form an astonishingly wide variety of coordinations with S, both in the solid state and in solution.

From diphenyllead diacetate *(1)*[4], which reacts more rapidly and smoothly than the dihalides[5] with disodium dithiolates, we obtained the five-membered 2,2-diphenyl-1,3,2-dithiaplumbolane *(2)* prepared previously[5] and the new eight-membered heterocycles 5,5-diphenyl-1,4,6,5-oxadithiaplumbocane *(3)* and 2,2-diphenyl-1,3,6,2-trithiaplumbocane *(4)*.



All three compounds are hydrolytically stable, but light-sensitive; *(3)*, and particularly *(4)* are thermally stable only below the temperature of dry-ice. *(2)* crystallizes from ethanol or methanol as colorless, very thin orthorhombic needles. *(3)* crystallizes dimorphically: from ether/ethanol (20:1) as pale yellow orthorhombic *(3a)*, from ether/methanol (20:1) as pale yellow triclinic parallelepipeds [*(3b)*]; *(3a)* and *(3b)* are colorless below $-25\,^{\circ}C$. No single crystals of the colorless *(4)* could be prepared because of its thermal lability. All decomposition products are intensely yellow.

The X-ray structure analyses (at $-160\,^{\circ}C$) of *(2)*, *(3a)* and *(3b)*[6] gave for the five-membered ring of *(2)* an envelope conformation, for the eight-membered ring of *(3)* in *(3a)* twice chair-chair conformation and in *(3b)* both a chair-chair conformation for one molecule and a boat-chair conformation for the other (Fig. 1). *(3b)* is the first example exhibiting both conformations of the eight-membered ring (chair-chair and boat-chair) in the same structure[7]. The occurrence of both conformations in *(3b)* supports the assumption based on NMR spectra that an equilibrium exists between both conformations in solution[8].

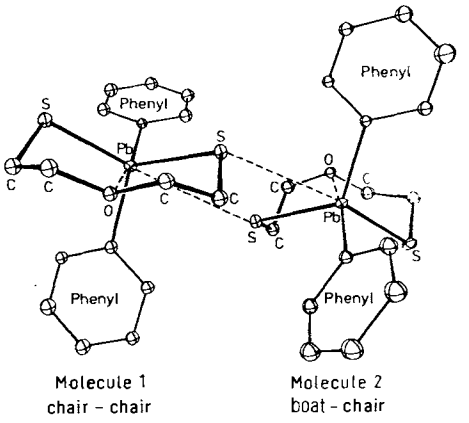


Fig. 1. Dimer pair of *(3)* in the triclinic modification *(3b)* with inter- and intramolecular coordinative bonds (broken lines).

In the crystal, *(2)* forms infinite chains *via* intermolecular Pb...S interactions; lead(IV) is coordinated trigonal-bipyramidally with one long and two short Pb—S distances (Table 1). *(3a)* contains isolated *(3)*-molecules in the crystal, but there is a clear 1,5-transannular Pb...O interaction within the eight-membered ring, so that lead(IV) in *(3a)* is penta-

[*] Prof. Dr. M. Dräger, Dipl.-Chem. N. Kleiner
Institut für Anorganische Chemie und Analytische Chemie
der Universität
Johann-Joachim-Becher-Weg 24, D-6500 Mainz (Germany)

[**] Lead-containing Heterocycles, Part 1. Presented in part in a lecture at the 9th International Conference on Organometallic Chemistry, Dijon, Sept. 7, 1979. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Table 1. Pb^{IV}—S and Pb^{IV}—O bond lengths in *(2)*, *(3a)* and *(3b)* [pm] [a] and ^{207}Pb-NMR data of *(2)*, *(3)* and *(4)* [b].

Cpd.	Pb—S intramolecular		Pb···S intermolecular	Pb···O transannular
(2)	252(2)	249(1)	355(2)	—
(3a)	250.0(3)	249.9(2)	547.5(3)	285.5(5)
	250.2(2)	248.2(3)		288.8(6)
(3b)	251.4(5)	251.9(6)	411(1)	292(1)
	251.8(5)	249.1(5)	375(1)	308(1)

Cpd.	$\delta(^{207}Pb)$	$^2J(^{207}Pb\text{-}^{13}C)$	$^3J(^{207}Pb\text{-}^1H)$
(2)	324	6.6	74.2
(3)	125	27.9	81.7
(4)	173	27.9	100.0

[a] Pb^{IV}—C bond lengths 218—222 pm. [b] In $CDCl_3$ referred to $PbMe_4$, J in Hz.

coordinated (monocapped tetrahedra). There are also 1,5-transannular Pb...O interactions in *(3b)*; moreover, the two independent molecules of the asymmetric moiety are coupled *via* two intermolecular Pb...S bridges to form a dimer (Fig. 1). Lead(IV) is thus hexacoordinated (bicapped tetrahedra). The Pb^{IV}—S single bond in *(2)*, *(3a)* and *(3b)* has an average length of 250(2) pm.

In solution ($CDCl_3$), *(2)*, *(3)* and *(4)* were characterized by their ^{1}H-, ^{13}C- and ^{207}Pb-NMR spectra (Table 1). The strong downfield shift in the case of *(2)* and the smaller coupling constants show that *(2)* is monomeric in solution and contains tetrahedrally coordinated lead(IV). In the case of *(3)* and *(4)*, on the other hand, the pentacoordination observed in the crystal is retained (high-field shift of the Pb^{IV} signals[9] and stronger coupling).

Procedure

A solution of sodium (0.5 g, 22 mmol) in methanol (100 ml) is added to a solution of the dithiolate (10.4 mmol) in methanol (50 ml) and the mixture boiled for a few minutes. After cooling to 0 °C, a suspension of *(1)* (5.0 g, 10.4 mmol) in methanol (100 ml) is added with stirring. *(1)* is completely dissolved within a few minutes, while at the same time the product is partly precipitated. The solvent is removed *in vacuo* in a rotary evaporator and the residue is taken up in 150 ml of boiling ether. The filtered solution is evaporated in a vacuum until crystals separate. Yields: 3.2 g (68%) of *(2)*, 3.2 g (64%) of *(3)* and 2.6 g (51%) of *(4)*. Immediate work-up is necessary; on evaporation and recrystallization heating should be kept to a minimum and should be as brief as possible.

Received: March 27, 1980 [Z 602 IE]
German version: Angew. Chem. *92*, 950 (1980)

CAS Registry numbers:
(1), 6928-68-3; *(2)*, 1083-82-5; *(3)*, 75522-43-9; *(4)*, 75522-44-0

[1] *R. A. Bailey, H. M. Clarke, J. P. Ferris, S. Krause, R. L. Strong:* Chemistry of the Environment. Academic Press, New York 1978, p. 395; *M. Friedman:* Protein-Metal Interactions. Plenum Press, New York 1974.
[2] *R. A. Henry, K. H. Byington,* Biochem. Pharmacol. *25*, 2291 (1976).
[3] *P. T. S. Wong, Y. K. Chau, P. L. Luxon,* Nature *253*, 263 (1975); *A. W. P. Jarvie, R. N. Markall, H. R. Potter, ibid. 255*, 217 (1975).
[4] *L. C. Willemsens:* Investigations in the Field of Organolead Chemistry. Internat. Lead-Zinc Res. Org., New York 1965.
[5] *W. E. Davidsson, K. Hills, M. C. Henry,* J. Organomet. Chem. *3*, 285 (1965); *M. Wieber, U. Baudis, ibid. 125*, 199 (1977).
[6] CAD4 diffractometer. *(2):* space group $P2_12_12_1$, $Z=4$, 2357 reflections, refinement to $R=0.048$; 1 Pb-, 2 S- and 1 C-atom plane, 1 C-atom 79 pm above this plane. *(3a):* space group Pbca, $Z=16$, 5249 reflections, refinement to $R=0.027$. *(3b):* space group $P\bar{1}$, $Z=4$, 6938 reflections, refinement to $R=0.071$. Both modifications *(3a)* and *(3b)* contain two independent molecules of *(3)* in the asymmetric unit.
[7] *F. A. L. Anet,* Top. Curr. Chem. *45*, 139 (1974); *M. Dräger,* Z. Anorg. Allg. Chem. *428*, 243 (1977).
[8] *M. Dräger, L. Ross,* Chem. Ber. *108*, 1712 (1975).
[9] *D. C. van Beelen, H. O. van der Kooi, J. Wolters,* J. Organomet. Chem. *179*, 37 (1979).

^{15}N-NMR Spectroscopic Detection of the Tetrazolo[1,5-*a*]pyrimidine/2-Azidopyrimidine Equilibrium[**]

By *William E. Hull, Michael Künstlinger,* and *Eberhard Breitmaier*[*]

The tetrazole-azide valence isomerism has hitherto been investigated by ^{1}H-NMR and by 1,3-dipolar cycloaddition[1]. A direct and very informative probe for the tetrazole-azide equilibrium is provided by ^{15}N nuclear resonance. However, its previous application was thwarted by the very low natural concentration of ^{15}N and the lack of sufficiently concentrated samples.

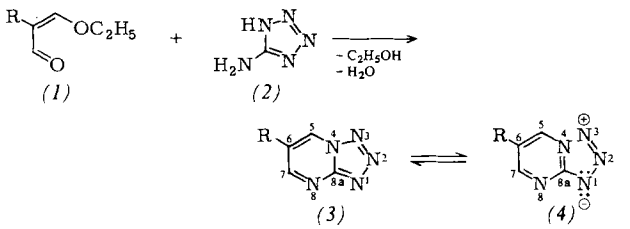


Table 1. Yields and characterization data of the heterocycles *(3)*⇄*(4)*.

Cpd.	R	Yield [%]	M.p. [°C]	B.p. [°C/torr]	Tetrazole *(3)*/Azide *(4)* in $CDCl_3$	in $(CD_3)_2SO$	without solvent
a	H	72	123	—	17/83	95/5	—
b	CH_3	66	118	—	27/73	94/6	—
c	C_2H_5	60	31	60/0.05	63/37	94/6	90/10
d	nC_3H_7	56	—	78/0.3	64/36	93/7	81/19
e	iC_3H_7	62	50	67/0.05	80/20	95/5	—
f	nC_4H_9	77	—	83/0.05	54/46	93/7	84/16

By cyclization of 2-alkyl-3-ethoxyacroleins *(1)* with 5-aminotetrazole *(2)* we have now been able to prepare tetrazo-

[*] Prof. Dr. E. Breitmaier, Dipl.-Chem. M. Künstlinger
Institut für Organische Chemie und Biochemie
der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn 1 (Germany)
Dr. W. E. Hull
Bruker Analytische Meßtechnik
Silberstreifen, D-7512 Karlsruhe-Forchheim (Germany)

[**] This work was supported by the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen.

lo[1,5-*a*]pyrimidines *(3)*, whose equilibrium with the 2-azidopyrimidines *(4)* (Table 1) can be detected particularly well in reasonable measuring time by high-field ^{15}N nuclear resonance (40.55 MHz).

Figure 1 shows the ^{15}N-NMR spectrum of the equilibrium mixture *(3f)* ⇄ *(4f)*, R = nC_4H_9, recorded without proton decoupling. The more intense signals of the tetrazolo[1,5-*a*]pyrimidine *(3f)* (85%) and the weaker ones of the 2-azidopyridine *(4f)* (15%) are easily recognizable. Table 2 lists the assignment of all the ^{15}N-, ^{13}C- and ^{1}H-signals. The assignment of the ^{15}N-signals is based on the known sequence of the signals of tetrazoles, pyridines and azides[2] and on the $^{2}J_{NH}$ coupling constants, which are larger (11—12 Hz) for nitrogen atoms of the pyridine type [N-8 in *(3)* and N-4,8 in *(4)*] than for nitrogen atoms of the pyrrole type [N-4 in *(3)*, not resolved][2].

Procedure

A solution of equimolar amounts of *(2)* and *(1)*[3] or malondialdehyde tetraethylacetal[3] in glacial acetic acid (10 equiv.) is heated under reflux for 1 h. After removal of the

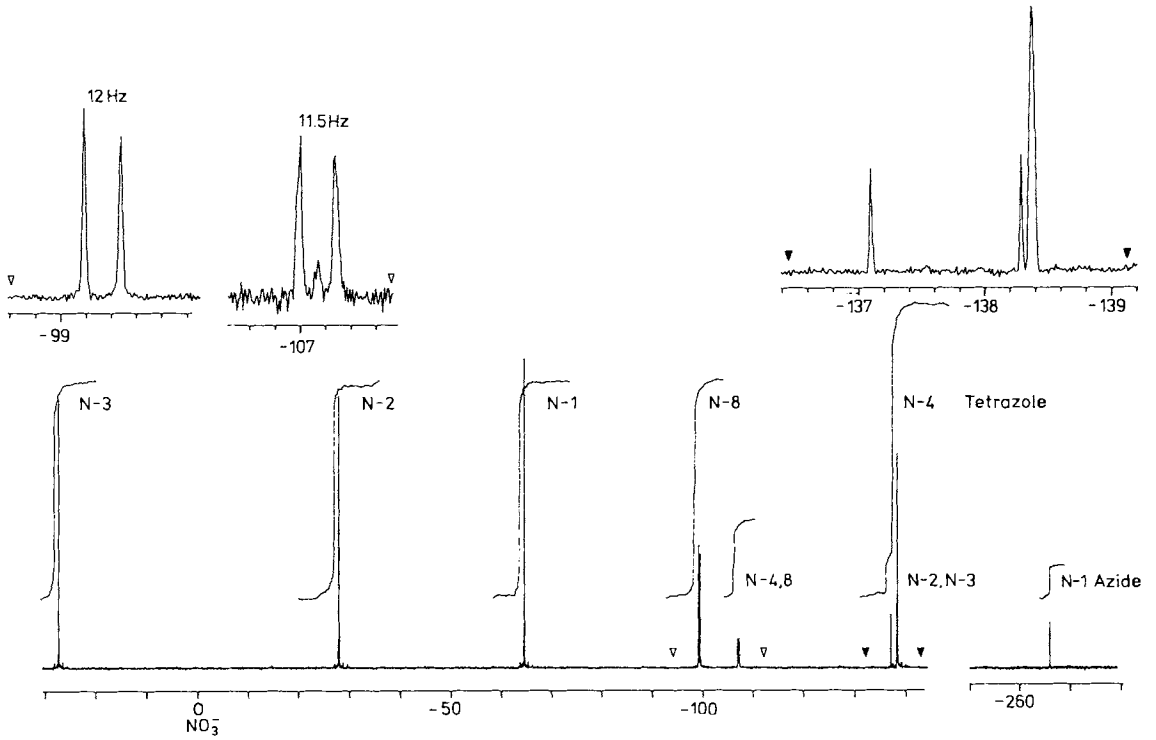


Fig. 1. ^{15}N-NMR spectrum of 6-*n*-butyltetrazolo[1,5-*a*]pyrimidine *(3f)* in equilibrium with 2-azido-5-*n*-butylpyrimidine *(4f)* without solvent. Recording conditions: 40.55 Hz, PFT technique, 45° pulses, delay time 30 s, 2500 scans; standard: $^{15}NH_4{}^{15}NO_3$ in D_2O (external); 15 mm-(∅) sample; spectrometer: WH-400 (Bruker).

Table 2. ^{1}H-, ^{13}C- and ^{15}N-shifts (δ values), multiplicities [a], coupling constants in Hz and coupling partners of *(3f)* and *(4f)* at 30 °C without solvent (^{1}H and ^{15}N) and in hexadeuterioacetone (^{13}C), respectively.

Cpd.	Pos. [b]	^{1}H (TMS, 90 MHz)	^{13}C (TMS, 20.115 MHz)	^{15}N [e] (NO_3^-, 40.55 MHz)
(3f)	1	—	—	− 65.0
	2	—	—	− 28.0
	3	—	—	27.3
	4	—	—	−138.4
	5	9.37; d: 2.5 (7-H)	131.9; Ddt: 193.1 (5-H), 6.3 (7-H), 5.9 (10-H_2)	—
	6	—	129.0; ttt: 9.2 (10-H_2), 3.4 (5-H, 7-H), 2.4 (9-H_2)	—
	7	9.72; d: 3.0 (5-H)	161.9; Dq: 185.5 (7-H), 5.4 (5-H, 9-H_2)	—
	8	—	—	− 99.4; d: 12.0 (7-H)
	8a	—	154.4; dd: 14.9 (7-H), 3.4 (5-H)	—
	9	3.22; t: 7.0 (10-H_2)	32.7; Tm: 126.0 (9-H_2)	—
	10	1.93; qui: 7.0 (9-H_2, 11-H_2)	29.6; Tm: 127.0 (10-H_2)	—
	11	1.55; sext.: 7.0 (10-H_2, 12-H_3)	22.5; Tm: 127.0 (11-H_2)	—
	12	0.95; t: 7.0 (11-H_2)	13.9; Qm: 127.0 (12-H_3)	—
(4f)	1	—	—	−266.0
[d]	2	—	—	−137.1 [c]
	3	—	—	−138.3 [c]
	4, 8	—	—	−107.1; d: 11.5 (5-H, 7-H)
	5, 7	8.67	159.4; Dq: 180.2 (5-H, 7-H), 5.4 (7-H, 5-H, 9-H_2)	—
	6	—	132.2; m	—
	8a	—	160.2; t: 12.2 (5-H, 7-H)	—
	9	2.78; t: 7.0 (10-H_2)	33.3; Tm: 126.0 (9-H_2)	—

[a] D, T, Q: doublet, triplet, quartet from coupling *via* one bond; d, t, q, qui, sext, m: doublet, triplet, quartet, quintet, sextet, multiplet from coupling *via* two or three bonds. [b] Position 9—12: *n*-butyl (C-9 is attached to C-6). [c] Assignment interchangeable. [d] 10, 11, 12 as *(3f)*. [e] For conversion to liquid ammonia as reference [2b] add 375 (± 1) ppm to the given values.

solvent *in vacuo* the heterocycles *(3)*⇄*(4)* can be obtained from the residue by recrystallization *(a, b)* or distillation *(c—f)*.

Received: April 24, 1980 [Z 603 IE]
German version: Angew. Chem. *92*, 957 (1980)

CAS Registry numbers:
(1a), 19060-08-3; *(1b)*, 42588-57-8; *(1c)*, 30989-75-4; *(1d)*, 21037-71-8; *(1e)*, 30989-77-6; *(1f)*, 21037-73-0; *(2)*, 4418-61-5; *(3a)*, 275-03-6; *(3b)*, 75495-11-3; *(3c)*, 75495-12-4; *(3d)*, 75495-13-5; *(3e)*, 75495-14-6; *(3f)*, 75495-15-7; *(4a)*, 3960-55-2; *(4b)*, 35762-89-1; *(4c)*, 75495-16-8; *(4d)*, 75495-17-9; *(4e)*, 75495-18-0; *(4f)*, 75495-19-1

[1] *C. Temple, J. A. Montgomery*, J. Org. Chem. *30*, 826 (1969); *R. Huisgen, K. von Framberg, H. J. Sturm*, Tetrahedron Lett. *1969*, 2589; *C. Wentrup*, Tetrahedron *26*, 4969 (1970); *A. Könnecke, R. Dörre, E. Kleinpeter, E. Lippmann, ibid. 35*, 1957 (1979).

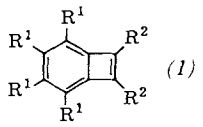
[2] a) *M. Witanowski, G. A. Webb:* Nitrogen NMR. Plenum Press, London 1973; b) *G. C. Levy, R. L. Lichter:* Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy. J. Wiley, Chichester 1979.

[3] Cf. *e.g. E. Breitmaier, S. Gassenmann*, Chem. Ber. *104*, 665 (1971).

Complexation of a Benzodicyclobutadiene with $Fe_2(CO)_9$[**]

By *Thomas Butters, Fumio Toda,* and *Werner Winter*[*]

Up to now, only a few derivatives of monobenzoannelated [4]annulene (benzocyclobutadiene) have been isolated[1]. According to the results of three X-ray structure analyses, the best representation of the benzocyclobutadiene-framework is the valence-bond formula *(1)*[2].

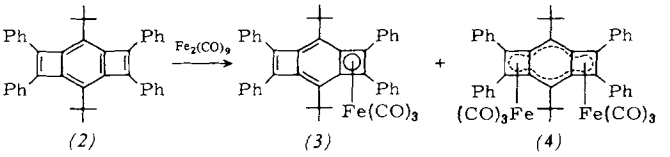


(1)

Using *(1)*, with $R_1 = CH_3$ and $R_2 = tC_4H_9$, as example, we have already shown[3] that reaction with $Fe_2(CO)_9$ leads to a η^4-coordination of the four-membered ring. In this case, however, the outer double-bond of the four-membered ring is much more strongly coordinated to iron. Obviously, complexed *(1)* represents a compromise between an aromatic six-membered ring and an aromatic cyclobutadiene-$Fe(CO)_3$ unit.

Assuming this to be so, we have investigated the only benzodicyclobutadiene *(2)*[4] so far known in order to ascertain whether it likewise yields cyclobutadiene complexes, or whether it behaves more like a benzene derivative, the annelated double bonds of which undergo η^2-coordination.

When equimolar amounts of *(2)* and $Fe_2(CO)_9$ are heated for 4 h in xylene under reflux (N_2), subsequent work-up of the reaction mixture affords red crystals of the 1:1 complex *(3)* (yield 85%, m.p. 222—223 °C) and black-red crystals of the 1:2 complex *(4)* (yield 5%, m.p. 214—216 °C).



(2) *(3)* *(4)*

In order to establish the bonding properties, we have carried out X-ray structure analyses[5] on both *(3)* and *(4)*. It was established that the most suitable representation of the 1:1-complex is the valence-bond formula *(3)*: it is a 'real' cyclobutadiene complex with a square four-membered ring (C—C = 1.464(3) Å), and the iron atom is situated almost exactly above the middle of this ring. As a consequence of this strong coordination to the cyclobutadienic unit, the other C—C bonds in the whole ring system alternate between 1.354 and 1.509(3) Å.

The structure of complex *(4)* is surprising. The iron atoms are coordinated more strongly to the 'outer' double bonds, analogously to those in the iron complex of *(1)* (Fig. 1). The arrangement of both $Fe(CO)_3$ groups on the same side of the ligand is also surprising.

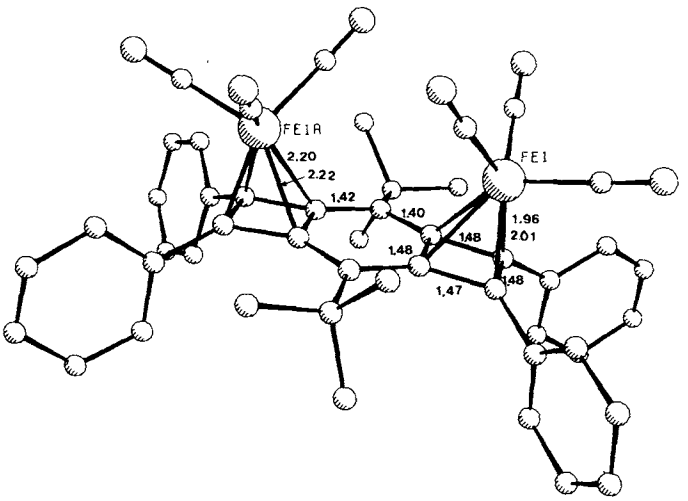


Fig. 1. Molecular structure of complex *(4)* (mean standard deviations of the bond lengths: 0.013 Å); since the molecule lies on a twofold crystallographic axis, it shows exact C_2 point symmetry.

The complexes *(3)* and *(4)* show, on the one hand, that the $Fe(CO)_3$-unit prefers a η^4-cyclobutadiene coordination and, on the other, that it is in fact possible to regard *(2)* as a benzo-*dicyclobutadiene* (at least from the point of view of the transition-metal).

Received: April 28, 1980 [Z 604 IE]
German version: Angew. Chem. *92*, 952 (1980)

[*] Doz. Dr. W. Winter [+], Dipl.-Chem. Th. Butters
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
Prof. Dr. F. Toda
Ehime University, Department of Chemistry
Faculty of Engineering
Matsuyama (Japan)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft.

[1] a) *H. Straub*, Angew. Chem. *86*, 412 (1974); Angew. Chem. Int. Ed. Engl. *13*, 405 (1974); b) Tetrahedron Lett. *1976*, 3513; Justus Liebigs Ann. Chem. *1978*, 1675; c) *F. Toda, N. Dan*, J. Chem. Soc. Chem. Commun. *1976*, 30; *F. Toda, K. Tanaka, ibid. 1976*, 1010; *K. P. C. Vollhardt, L. S. Yee*, J. Am. Chem. Soc. *99*, 2010 (1977).

[2] *W. Winter, H. Straub*, Angew. Chem. *90*, 142 (1978); Angew. Chem. Int. Ed. Engl. *17*, 127 (1978); *H. Tsukada, H. Shimanouchi, Y. Sasada*, Acta Crystallogr. *B 33*, 2951 (1977); Bull. Chem. Soc. Jpn. *51*, 985 (1978).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0926 $02.50/0

[3] *H. Straub, G. Döring, W. Winter*, Z. Naturforsch. *B 34*, 125 (1978); see also *R. E. Davis, R. Pettit*, J. Am. Chem. Soc. *92*, 716 (1970).

[4] *F. Toda, M. Ohi*, J. Chem. Soc. Chem. Commun. *1975*, 506.

[5] *(3)*: Triclinic, $P\bar{1}$ ($Z=2$); $a=10.267(4)$, $b=12.466(1)$, $c=14.756(2)$ Å, $\alpha=91.618(9)$, $\beta=99.84(2)$, $\gamma=76.05(2)°$; 5824 reflections ($I>2\sigma(I)$), $Mo_{K\alpha}$-graphite monochromator, Nonius CAD4, solution: heavy-atom method; refinement: $R=0.038$, $R_G=0.038$; *(4)*: monoclinic, C2/c ($Z=4$); $a=16.307(5)$, $b=17.749(3)$, $c=16.95(1)$ Å, $\beta=102.93(4)°$; 1559 reflections ($F>2\sigma(F)$), $Mo_{K\alpha}$-graphite monochromator, Nonius CAD4, solution: heavy-atom method; refinement: $R=0.063$, $R_G=0.076$ (disordered dichloromethane and pentane solvent molecules).

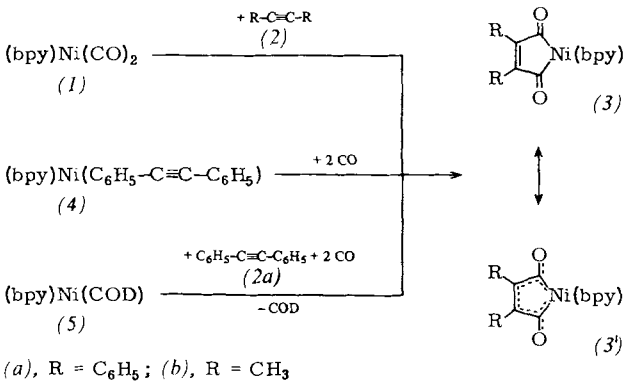
Nickelacyclopentene Derivatives from Nickel(0), Carbon Monoxide and Alkyne

By *Heinz Hoberg* and *Antonio Herrera*[*]

Alkynes and carbon monoxide are known to be activated by complexation with transition metals in such a way that they react to give open-chain or cyclic products *via* C—C linkage[1]. Unsaturated nickelacycles have been discussed as intermediates of the cyclization when $Ni(CO)_4$ is used as catalyst[1b,2], but to our knowledge they have so far not been isolated[3].

We describe here the synthesis and isolation of the nickelacyclopentene complex *(3)* stabilized by α,α'-bipyridine (bpy). Reaction of (bpy)Ni(CO)$_2$ with tolan *(2a)* and with butyne *(2b)* in tetrahydrofuran (THF) at 20 °C affords the nickelacyclopentenediones *(3a)*, R = C_6H_5, and *(3b)*, R = CH_3, in 60 and 25% yields, respectively.

(3a) can also be obtained without prior fixation of CO to nickel, *e.g.* by reaction of (bpy)Ni(tolan) *(4)* with CO (40% yield) or of (bpy)Ni(COD) *(5)* (COD = 1,5-cyclooctadiene) with CO and tolan *(2a)* (25% yield) (Scheme 1).

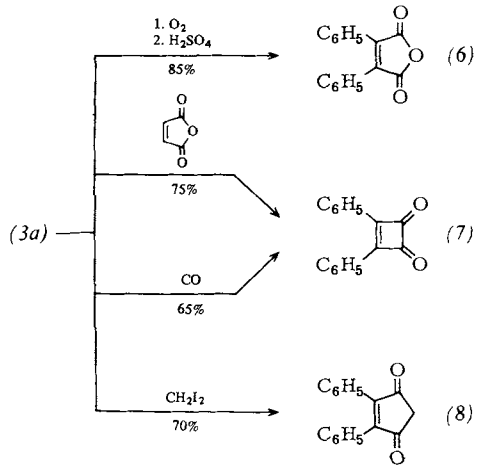


Scheme 1. Possible syntheses of *(3)*.

The compounds *(3a)* and *(3b)*, which crystallize as dark red lamellae[4], are diamagnetic and are thermally very stable in the absence of air [*(3a)*, m.p. 234 °C (dec.); *(3b)*, m.p. 224 °C (dec.)]. They are only sparingly soluble in the common solvents such as toluene, THF or diethyl ether.

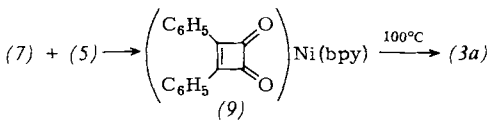
The mass spectrum of *(3a)* shows only the fragment ions $m/e = 178$ ($(C_6H_5)_2C_2$), 156 (bpy) and 28 (CO). The IR spectrum (KBr) shows no characteristic bands above 1600 cm^{-1} (C=O region). The long-wave shift of the C=O vibration corresponds to a pronounced delocalization to *(3')*, which is also reflected in a lower chemical reactivity.

Thus, *(3a)* is hydrolyzed neither by water nor by 2 N H_2SO_4 (40 °C, THF, 12 h); protonolysis to the anhydride *(6)* only takes place after oxidation with atmospheric oxygen (20 °C, toluene). *(3a)* does not react with tolan *(2a)* (110 °C, toluene, 7 d), but maleic anhydride already effects a reductive elimination at 20 °C in THF after 2 h, giving the cyclobutenedione *(7)*, which with carbon monoxide at 80 °C and 1 bar is only complete after 10 h. Reaction of *(3a)* with diiodomethane affords the cyclopentenedione *(8)* (Scheme 2).



Scheme 2. Reactions of *(3a)*. The structure of the products *(6)*, *(7)* and *(8)* were determined spectroscopically (IR, MS, ^{1}H- and ^{13}C-NMR) and compared with the data of authentic samples [*(6)* [5], *(7)* [5], *(8)* [6]].

The reductive elimination of the C_4-ring in *(3a)* to give *(7)* is reversible: reaction of the cyclobutenedione *(7)* with (bpy)Ni(COD) *(5)* in THF (20 °C, 3 h) leads to the nickel(0) complex *(9)*, which already gives *(3a)* again within 1 h at 100 °C in toluene in the sense of an oxidative addition.



Procedure

A solution of tolan *(2a)* (7.42 g, 41.7 mmol) in THF (50 ml) is added dropwise to a solution of *(1)*[7] (11.0 g, 40.8 mmol) in THF (150 ml) at room temperature. The dark-red crystals which separates out after 24 h are filtered, washed with 30 ml THF, and dried; yield 10.9 g (59%) *(3a)*.

Received: May 2, 1980 [Z 605 IE]
German version: Angew. Chem. *92*, 951 (1980)

CAS Registry numbers:
(1), 14917-14-7; *(2a)*, 501-65-5; *(2b)*, 503-17-3; *(3a)*, 75507-29-8; *(3b)*, 75507-30-1; *(4)*, 75507-31-2; *(5)*, 55425-72-4; *(6)*, 4808-48-4; *(7)*, 24234-76-2; *(8)*, 51306-98-0; *(9)*, 75507-32-3; CH_2I_2, 75-11-6

[*] Prof. Dr. H. Hoberg, Dr. A. Herrera
Max-Planck-Institut für Kohlenforschung
Postfach 011325, D-4330 Mülheim a. d. Ruhr 1 (Germany)

[1] a) *I. Wender, P. Pino*: Organic Syntheses via Metal Carbonyls. Vol. 1. Wiley, New York 1968; Vol. 2, 1977; b) *P. W. Jolly, G. Wilke*: The Organic Chemistry of Nickel. Vol. 2. Academic Press, New York 1975, Chap. 6; *R. Eisenberg, D. E. Hedriksen*, Adv. Catal. *28*, 79 (1979).

[2] *K. Kinugasa, T. Agawa*, Organomet. Chem. Synth. *1*, 427 (1972).

[3] For details on the synthesis of nickelacyclopentanes from alkenes and nickel(0) compounds cf. *P. Binger, M. J. Doyle*, J. Organomet. Chem. *162*, 195 (1978); *R. H. Grubbs, A. Miyashita*, J. Am. Chem. Soc. *100*, 7417 (1978).

[4] An X-ray structure analysis has been carried out on the complex *(3b)* prepared from *(1)* and *(2b)* (*C. Krüger, G. Wolmershäuser*, unpublished).

[5] *A. T. Blomquist, E. A. Lalancette*, J. Am. Chem. Soc. *83*, 1387 (1961).

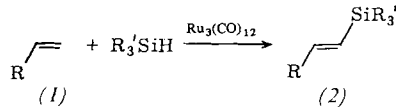
[6] *M. Giaunella, F. Gualfieri, C. Melchiorre, M. Pigini*, Farmaco, Ed. Sci. *28*, 597 (1973).

[7] *E. Zahn*, Dissertation, Technische Hochschule München 1959.

$Ru_3(CO)_{12}$-Catalyzed Synthesis of Vinylsilanes from Olefins and Hydrosilanes[**]

By *Yoshio Seki, Kenji Takeshita, Kazuaki Kawamoto, Shinji Murai,* and *Noboru Sonoda*[*]

Vinylsilanes have recently been shown to be versatile intermediates in organic synthesis[1], and they have usually been prepared from alkynes by hydroalumination of alkynylsilanes[2] or directly by hydrosilylation[3]. During the course of our investigations of catalytic reactions with hydrosilanes and carbon monoxide[4], we have now found a new method for the synthesis of vinylsilanes. The reaction of a fivefold excess of styrene *(1a)* with triethylsilane in the presence of catalytic amounts of $Ru_3(CO)_{12}$[5] affords (*E*)-β-triethylsilylstyrene *(2a)* in 93% yield (cf. [8]). The vinylsilanes *(2b)*—*(2i)* were obtained in high yields *via* the same route.



(1) *(2)*

Table 1. Yields, boiling points and some spectroscopic data of the vinylsilanes *(2)* [a].

	R	SiR_3'	^{1}H-NMR δ [b]	IR (film) [cm^{-1}] [c]	Yield [%] [d]	B.p. [°C/torr]
a	C_6H_5	$SiEt_3$	6.28, 6.83	1603	93	152—154/20
b	C_6H_5	$SiMe_3$	6.27, 6.80	1610	86 [e]	125—135/53
c	C_6H_5	$SiEt_2Me$	6.28, 6.87	1605	93	140—145/28
d	C_6H_5	$SiMe_2Ph$	6.40, 6.92	1605	96	150—160/26
e	*p*-CH_3—C_6H_4	$SiEt_3$	6.20, 6.80	1610	100	175—179/30
f	*p*-CH_3O—C_6H_4	$SiEt_3$	6.07, 6.70	1610	83	115—120/0.03
g	*p*-Cl—C_6H_4	$SiEt_3$	6.25, 6.77	1610	94	180—185/23
h	2-Naphthyl	$SiEt_3$	6.40, 7.02	1620	88	140—150/0.05
i	$C_6H_5OCH_2$	$SiEt_3$	5.88, 6.20 [f]	1600	80 [g]	165—170/20

[a] Reaction conditions: 50 mmol olefin, 10 mmol silane, 0.05 mmol $Ru_3(CO)_{12}$, 10 ml benzene, 80 °C, 5 h. [b] In CCl_4, signals of the olefinic protons $^3J = 19$ Hz. [c] $\nu_{C=C}$. [d] Determined gas-chromatographically. [e] 100 °C, 5 h, stainless steel autoclave. [f] $J = 19$ Hz, 4 Hz. [g] Without benzene, 50 °C, 12 h.

In the case of 3-phenoxy-1-propene, only traces (less than 3%) of the isomeric product, 1-phenoxy-3-triethylsilyl-1-propene, could be detected by GLC.

A large number of catalysts are known for the synthesis of alkylsilanes by hydrosilylation[6], but there are only few for the "dehydrogenative silylation" of olefins[6b,7]; the examples described in this connection are not suitable for the preparation of vinylsilanes.

Experimental:

(2a): A stirred mixture of *(1a)* (5.75 ml, 50 mmol), triethylsilane (1.16 g, 10 mmol) and $Ru_3(CO)_{12}$ (0.034 g, 0.05 mmol) in benzene (10 ml) was heated at 80 °C for 5 h under nitrogen. Analysis of the reaction mixture by GLC (Silicone OV-1, 5%, on Uniport KS, 3 m, 160 °C, internal standard: *n*-heptadecane) showed it to contain *(2a)* in 93% yield. Analytically pure *(1a)* was obtained by fractional distillation.

[*] Prof. Dr. Y. Seki [+], K. Takeshita, Prof. Dr. K. Kawamoto
Faculty of Economics, Kagawa University
Takamatsu, Kagawa 760 (Japan)
Prof. Dr. Murai [+], Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering,
Osaka University
Suita, Osaka 565 (Japan)
[+] Authors to whom correspondence should be addressed.

[**] Transition Metal Reactions of Silanes, Part 7.—Part 6: *S. Murai, T. Kato, N. Sonoda, Y. Seki, K. Kawamoto,* Angew. Chem. *91*, 421 (1979); Angew. Chem. Int. Ed. Engl. *18*, 393 (1979).

Received: May 23, 1980 [Z 606 IE]
German version: Angew. Chem. *92*, 974 (1980)
CAS Registry numbers:
(1a), 100-42-5; *(1e)*, 622-97-9; *(1f)*, 637-69-4; *(1g)*, 1073-67-2; *(1h)*, 827-54-3; *(1i)*, 1746-13-0; *(2a)*, 21209-32-5; *(2b)*, 19372-00-0; *(2c)*, 62621-34-5; *(2d)*, 64788-85-8; *(2e)*, 75476-54-9; *(2f)*, 75476-55-0; *(2g)*, 75476-56-1; *(2h)*, 75476-57-2; *(2i)*, 75476-58-3; 1-phenoxy-3-trimethylsilyl-1-propene, 75476-59-4; $SiEt_3H$, 617-86-7; $SiMe_3H$, 993-07-7; $SiEt_2MeH$, 760-32-7; $SiMe_2PhH$, 766-77-8

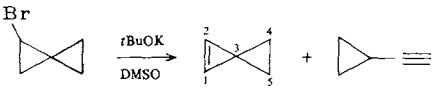
[1] *T. H. Chan,* Acc. Chem. Res. *10*, 442 (1977); *P. F. Hudrlik* in *D. Seyferth:* New Applications of Organometallic Reagents in Organic Synthesis, Elsevier, Amsterdam, 1976, p. 127; *T. H. Chan, I. Fleming,* Synthesis *1979*, 761; for intensive literature survey: *F. Cook, R. Moerck, J. Schwindeman, P. Magnus,* J. Org. Chem. *45*, 1046 (1980).
[2] *R. B. Miller, G. McGarvey,* J. Org. Chem. *43*, 4424 (1978) and references cited therein.
[3] *R. A. Benkeser, R. A. Hickner,* J. Am. Chem. Soc. *80*, 5298 (1958); *R. A. Benkeser, M. L. Burrous, L. E. Nelson, J. V. Swisher,* J. Am. Chem. Soc. *83*, 4385 (1961); *I. Ojima, M. Kumagai,* J. Organomet. Chem. *66*, C14 (1974).
[4] For a review, see: *S. Murai, N. Sonoda,* Angew. Chem. *91*, 896 (1979); Angew. Chem. Int. Ed. Engl. *18*, 837 (1979).
[5] The reaction involving catalytic activation of R_3SiH by $Ru_3(CO)_{12}$ is important regarding our recent study on the catalytic reaction using hydrosilane and carbon monoxide; see footnote [20] in ref. [4].
[6] a) *J. F. Harrod, A. J. Chalk* in *I. Wender, P. Pino:* Organic Syntheses *via* Metal Carbonyls, Vol. 2, Wiley, New York, 1977, p. 673; b) *J. L. Sperier* in *F. G. A. Stone, R. West:* Adv. Organomet. Chem. *17*, 407 (1979).
[7] *M. A. Schroeder, M. S. Wrighton,* J. Organomet. Chem. *128*, 345 (1977); *R. G. Austin, R. S. Paonessa, P. J. Griordano, M. S. Wrighton,* Adv. Chem. Ser. *168*, 189 (1978); *A. N. Nesmeyanov, R. K. Freidlina,* Tetrahedron *17*, 61 (1962); *S. A. Shchepinov, M. L. Khidekel, G. V. Lagodzinskaya,* Izv. Akad. Nauk SSSR, Ser. Khim. *1968*, 2165; Chem. Abstr. *70*, 20154b (1969).
[8] A preliminary experiment shows that the dehydrogenative silylation of styrene *(1a)* gives almost quantitative yields (referred to silane) of ethylbenzene in addition to the vinylsilane *(2a)* (see Table 1).

Spiropentene

By *Robert Bloch* and *Jean-Marc Denis*[*]

Spiropentene *(1)*, comprising a cyclopropane and a cyclopropene unit linked through a spiro carbon atom, was hitherto unknown. Its high strain (≈90 kcal mol^{-1}) probably accounts for the difficulties encountered in its synthesis[1]. Thus only two highly substituted derivatives of spiropentene *(1)* have been described so far[2]. In this communication we wish to report the synthesis of the parent compound and some of its properties.

4-Bromo-1,1-dimethylspiropentane reacts with an excess of potassium *tert*-butoxide in dimethyl sulfoxide (DMSO) at 25 °C to give 1,1-dimethyl-2-ethynylcyclopropane in 30% yield[3]. We have also observed the formation of ethynylcyclopropane *(2)* by reaction of gaseous bromospiropentane with solid KO*t*Bu supported on silica[4] [traces of spiropentene *(1)* are detected by NMR spectroscopy]. However, the slow addition of a solution of KO*t*Bu in DMSO to a hot solution (90 °C) of bromospiropentane in DMSO, under vacuum (80 torr) leads in 60—70% yield to spiropentene *(1)* together with 2—4% of *(2)*. Under these conditions, *(1)* is immediately extracted from the reaction mixture upon formation and can be dissolved in a solvent kept in a cold trap. Compound *(1)* is



(1) > 95% *(2)* < 5%

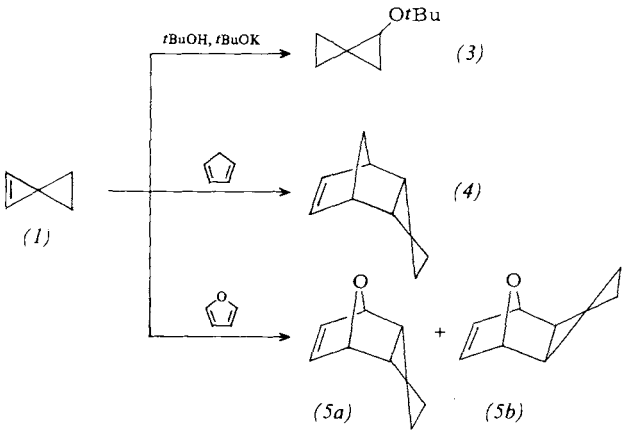
[*] Dr. R. Bloch
Laboratoire des Carbocycles—E.R.A. 316
Bât. 420—Université de Paris XI
91405 Orsay (France)
Dr. J. M. Denis
Laboratoire de Chimie Organique Physique—E.R.A. 827
Université des Sciences et Techniques de Lille I
59655 Villeneuve d'Ascq (France)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0928 $02.50/0

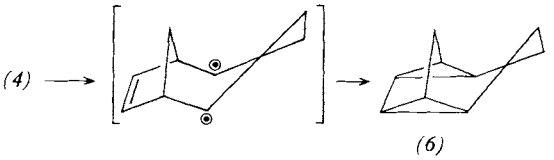
thus obtainable only as a chloroform solution with 2—4% of *(2)* and 10—15% of *tert*-butyl alcohol.

Although the hydrocarbon *(1)* is a highly reactive compound, which polymerizes in condensed phase even at −78 °C, its solution in chloroform containing a small amount of hydroquinone can be kept several days at −30 °C. Its spectroscopic data[5] resemble those of cyclopropane and cyclopropene. In particular the ^{13}C-H spin-spin coupling constants (158 and 225 Hz) compared to the coupling constants observed for cyclopropane and 3,3-dimethylcyclopropene (respectively 161 and 220 Hz)[6], suggest no difference in the states of hybridization of the corresponding C—H bonds. This would indicate that *(1)* is a normal spiro compound, and that the interaction between the cyclopropane Walsh orbitals and the cyclopropene π orbitals (pseudoconjugation)[7], if at all present, is not important. Confirmation by UV and PE spectroscopy has so far been precluded by the impurities present in *(1)*.

The high strain of *(1)* is revealed by its unusual chemical reactivity compared with that of 3,3-disubstituted cyclopropenes. As expected, the cyclopropene double bond is very



reactive toward nucleophiles; for example, *(1)* adds readily *tert*-butanol in the presence of *tert*-BuOK to give the spiro compound *(3)*[5]. Unlike 3,3-dimethylcyclopropene[8], spiropentene reacts rapidly and quantitatively, even at 0 °C, with cyclopentadiene and furan, respectively giving almost exclusively[9] the *endo* adduct *(4)*[5] and two adducts *(5a)*[5] and *(5b)* (1:3)[10]. Assignment of the configurations is based on the ^{1}H-NMR spectra. In particular, the bridgehead protons show neat coupling to the vicinal cyclopropyl hydrogens only for the *endo* configuration[10]. It appears also to be general that the olefinic protons of the endo-adducts are more shielded than the vinyl protons of the *exo* adducts.



Heating of the compounds *(4)* or *(5)* does not regenerate *(1)* (retro Diels-Alder rupture). *(5)* leads to several unidentified products, while *(4)* affords a unique compound *(6)* both in the vapor phase at 500 °C and in the condensed phase at 180 °C. The mass spectral data show that *(6)* is an isomer of the starting material *(4)*. The NMR spectrum has multiplets between $\delta = 0.1$ and $\delta = 2.0$, but no more absorption in the olefinic proton region. Such rearrangements *via* stabilized 1,3-diradicals, have been already observed in analogous systems[11].

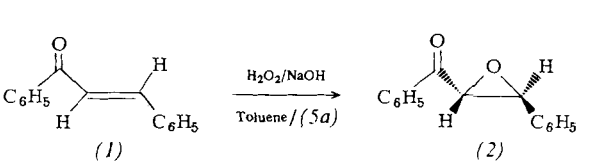
Received: January 16, 1980 [Z 607 IE]
German version: Angew. Chem. 92, 969 (1980)

[1] *J. Kao, L. Radom*, J. Am. Chem. Soc. *100*, 760 (1978).
[2] a) *W. M. Jones, M. E. Stowe, E. E. Wells, Jr., E. W. Lester*, J. Am. Chem. Soc. *90*, 1849 (1968); b) *J. P. Zahra, B. Waegell*, Tetrahedron Lett. *1970*, 2537.
[3] *A. A. Formanovskii, I. G. Bolesov*, Zh. Org. Khim. *14*, 884 (1978).
[4] *J. M. Denis, R. Niamayaua, M. Vata, A. Lablache-Combier*, Tetrahedron Lett. *1980*, 515.
[5] Spectroscopic data of the new compounds: *(1)*: IR ($CDCl_3$) 3060, 1635, 1010 cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 7.10$ (br. q, 2H, $J = 1.5$ Hz), 0.58 (br. t, 4H, $J = 1.5$ Hz); ^{13}C-NMR ($CDCl_3$): $\delta = 114.7$ (C2, C1), 16.8 (C3), 4.1 (C4, C5). *(3)*: ^{1}H-NMR (CCl_4): $\delta = 3.32$ (m, 1H); 1.18 (s, 9H); 0.72—1.05 (m, 6H). *(4)*: ^{1}H-NMR (CCl_4): $\delta = 5.83$ (t, 2H), 2.78 (m, 2H), 1.6—1.9 (m, 4H), 0.1—0.9 (m, 4H). *(5a)*: ^{1}H-NMR (CCl_4): $\delta = 6.05$ (br. s, 2H), 4.76 (m, 2H), 2.12 (m, 2H), 0.35—1.05 (m, 4H). *(5b)*: ^{1}H-NMR (CCl_4): $\delta = 6.46$ (br. s, 2H), 4.58 (br. s, 2H), 1.38 (s, 2H), 0.35—1.05 (m, 4H).
[6] *J. B. Stothers*: Carbon-13 NMR Spectroscopy. Academic Press, New York 1972, p. 336.
[7] *W. A. Bernett*, J. Chem. Educ. *45*, 17 (1967).
[8] *G. L. Closs*, Adv. Alicyclic Chem. *1*, 77 (1966).
[9] Less than 5% of a second adduct was present but could not be separated. However, the chemical shift of the olefinic protons ($\delta = 6.35$) is in good agreement with the shift expected for the *exo* adduct.
[10] Cyclopropene itself gives two adducts with furan in the ration of 1:1, see *R. W. La Rochelle, B. M. Trost*, J. Chem. Soc. Chem. Commun. *1970*, 1353.
[11] *R. Bloch, F. Leyendecker, N. Toshima*, Tetrahedron Lett. *1973*, 1025.

"Synthetic Enzymes". Highly Stereoselective Epoxidation of Chalcone in a Triphasic Toluene-Water-Poly[(S)-alanine] System[**]

By *Sebastián Juliá, Jaume Masana*, and *Juan Carlos Vega*[*]

The use of synthetic peptides as stereoselective catalysts in organic reactions is an attractive alternative to the use of enzymes[1]. However, many of the examples reported[2] have considerable disadvantages: optical yields may be too low[2a]; reaction times too long[2b], or the amounts of protein required too large[2c,d]. To our knowledge we report here the first example of a nearly stereospecific reaction by means of a triphase catalysis using readily available synthetic chiral polypeptides, which does not suffer from any of the drawbacks of the methods just mentioned. Thus, we have achieved the epoxidation of chalcone *(1)* to levorotatory *(2)* in optical yields higher than 90% and satisfactory chemical yields with poly[(*S*)-alanine] *(5a)*, poly[5-benzyl-(*S*)-glutamate] *(5b)*, and poly[5-butyl-(*S*)-glutamate] *(5c)* as catalysts.

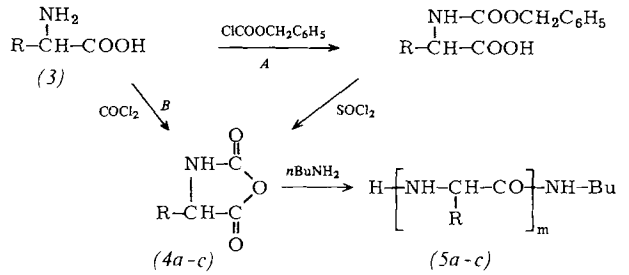


Previously, epoxychalcone *(2)* was obtained in 34% optical yield by a phase-transfer method using benzylquininium chloride as catalyst[3]. Its absolute configuration has been recently determined[3]. The polypeptides were synthesized according to Scheme 1, method *A* being used for the preparation of polyalanine, and method *B* being preferred for the synthesis of polyglutamates[4].

[*] Prof. Dr. S. Juliá, Chem. Eng. J. Masana
Departamento de Química Orgánica
Instituto Químico de Sarriá
Barcelona 17 (Spain)
Dr. J. C. Vega
Pontificia Universidad Católica de Chile
Santiago (Chile)

[**] *J. M.* and *J. C. V.* acknowledge a grant from INAPE, and financial support from the Ministerio de Universidades e Investigación of Spain, respectively.

The polymerization of the *N*-carboxy anhydrides *(4)*, was performed with *n*-butylamine (molar ratio 10:1). This assumes that the polymers contain an avarage of ten amino acids. IR data show both extended and helicoidal conformations to be present[5].



a, R = CH_3; *b*, R = $(CH_2)_2COOCH_2C_6H_5$;
c, R = $(CH_2)_2COO(CH_2)_3CH_3$
m = 10

Scheme 1

Experimental

Poly[(*S*)-alanine] *(5a)*: (*S*)-Alanine *N*-carboxyanhydride[4b] (11.39 g, 0.1 mol) is dissolved in acetonitrile (400 ml) (dried over P_2O_5). *n*-Butylamine (0.728 g, 0.01 mol) is added and the mixture is stirred for 4 d at room temperature. A white solid appears. The solvent is removed *in vacuo*, and the polymer is washed with diethyl ether. The polymer is dried *in vacuo*. Yield 7.5 g; m.p. >300 °C; IR (KBr): 3370, 3060, 1655, 1630, 1540 cm^{-1}; ^{1}H-NMR (CF_3COOH): $\delta = 7.3$ (—N*H*), 4.2 (—NH—C*H*—CO), 3.0 (—CH_2—R), 1.1 (CH_2—CH_2—CH_2—CH_3, and NH—CH(CH_3)CO), 0.5 $(CH_2)_3$—CH_3); $[\alpha]_{589}^{20} = -120.5$ ($c = 0.996$, CF_3COOH).

(−)-1,3-Diphenyl-2(*R*),3(*S*)-epoxypropan-1-one *(2)* (Table 1, exp. 3): To a solution of *(1)* (1.00 g, 4.8 mmol) in toluene (6.00 g) is added poly[(*S*)-alanine] (400 mg, 0.5 mmol; approx. mol. weight 783). The mixture is stirred for 30 min and a solution of NaOH in 30% H_2O_2 (0.08 g/ml) is slowly added dropwise. The mixture is stirred at room temperature for 48 h. The catalyst is filtered and washed with CH_2Cl_2 (50 ml). The organic phase is washed three times with water, dried over $MgSO_4$, and the solvent evaporated. The residue is purified by column chromatography, using 100 g of silica gel (Merck 0.2—3.0, 200 mm) and toluene as eluant. Yield 0.754 g (70%); $[\alpha]_{578}^{20} = -184$ ($c = 2.717$ in Cl_2CH_2), m.p. 59—61 °C. Spectroscopic data: IR, ^{1}H-NMR were satisfactory and in agreement with the literature[7]. Crystallization of this epoxide from *n*-hexane gave a product with $[\alpha]_{578}^{20} = -214$ °C, m.p. 63—65 °C. The m.p. and rotation remained unchanged after a second crystallization. The crude extract obtained in experiment 6 is divided into two parts before chromatography. One of them was chromatographed as described, yielding an epoxide of 93% o.p. The other one was directly crystallized from *n*-hexane yielding a product of 96% o.p. and m.p. 63—65 °C.

Table 1. Epoxidation of chalcone *(1)* in the presence of polypeptides *(5)*. Levorotatory epoxide *(2)* was formed in all cases *(2)* [a].

Exp.	Poly-peptide	*(1)* [g]	$NaOH/H_2O_2$ [b] [ml]	Toluene [g]	*(5)* [g]	*(5)*:*(1)*	*t* [h]	Chem. yield [c] [%]	Opt. yield [d] [%]
1		1	4.4	6	—	—	48	0	—
2	*(5a)*	1	4.4	6	0.2	0.2:1	48	76	86
3	*(5a)*	1	4.4	6	0.4	0.4:1	48	70	86
4	*(5a)*	1	4.4	6	0.8	0.8:1	48	26	97
5	*(5a)*	0.5	4.4	6	0.4	0.8:1	24	85	93
6	*(5a)*	0.5	8.8	6	0.4	0.8:1	48	80	93
7 [e]	*(5a)*	0.5	4.4	6	0.4	0.8:1	48	36	72
8	*(5b)*	1	4.4	6	1.3	1.3:1	48	6	57
9	*(5b)*	1	8.8	13	0.65	0.65:1	144	12	11
10	*(5b)*	1	8.8	26	1.3	1.3:1	144	8	11
11	*(5c)*	1	4.4	6	0.98	0.98:1	48	10	28

[a] For conditions of the reaction, see *Experimental*. [b] Solid NaOH in H_2O_2 30% (0.08 g/ml). [c] Product isolated by silica-gel chromatography. [d] $100 \times [\alpha]_{578}^{20}$ 214; maximum value $[\alpha]_{578}^{20} = -214$ ($c = 1.6$ in CCl_2H_2). [e] Polymer recovered after one experiment.

Our experiments are summarized in Table 1. From the results, the following inferences can be made:

a) Use of polyglutamates *(5b)* and *(5c)* instead of polyalanine *(5a)* lowers both the optical and the chemical yield significantly (exp. 8—11).

b) The polyalanine *(5a)* is necessary both for reaction to occur as well as for stereoselectivity to be observed. This implies that reaction takes place at the chiral interface (exp. 1).

c) The change in weight ratio chalcone *(1)*:polymer *(5)* does not seem to influence significantly the stereoselectivity (exp. 2, 3, 5 and 9,10), even though, optical yields higher than 90% were only obtained at a weight ratio of 1:0.8 (exp. 4—6, but not 7).

d) Polyalanine *(5a)* recovered from the reaction can be recycled[6] (exp. 7), giving rise to a decrease in chemical yield and optical purity, although the latter is still substantial.

e) The relative proportions in the liquid/solid/liquid phases seems to be important. For example, exp. 4 which gave a much lower chemical yield than exp. 3, used the same weight of aqueous phase and toluene while the weight of polymer was double. An increase in the proportion of toluene (compare exps. 8 and 10) resulted in a decrease in optical purity. The amount of aqueous solution does not appear to be crucial.

These results show that the use of simple polypeptides as "synthetic enzymes" may be a valuable tool for performing stereoselective organic reactions.

Received: April 2, 1980 [Z 608 IE]
German version: Angew. Chem. *92*, 968 (1980)

[1] *S. Inoue*, Adv. Polym. Sci. *21*, 78 (1976).
[2] a) *J. Oku, N. Ito, S. Inoue*, Makromol. Chem. *180*, 1089 (1979); b) *K. Ueyanagi, S. Inoue, ibid. 178*, 235 (1977); c) *T. Sugimoto, Y. Matsumura, S. Tanimoto, M. Okano*, J. Chem. Soc. Chem. Commun. *1978*, 926; *N. Baba, Y. Matsumura, T. Sugimoto*, Tetrahedron Lett. *1978*, 4281; *T. Sugimoto, T. Kokubo, J. Miyazaki, S. Tanimoto, M. Okano*, J. Chem. Soc. Chem. Commun. *1979*, 402; d) *ibid. 1979*, 1052.
[3] *B. Marsman, H. Wynberg*, J. Org. Chem. *44*, 2312 (1979).
[4] a) *H. Fukushima, S. Inoue*, Makromol. Chem. *177*, 2617 (1976); b) *L. A. A. Sluyterman, B. Labruyère*, Rec. Trav. Chim. Pays-Bas *73*, 347 (1954); c) *Y. Iwakura, K. Uni, M. Oya*, J. Polym. Sci. *A-1*, *6*, 2165 (1968).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0930 $02.50/0

[5] *D. W. Jones:* Introduction to the Spectroscopy of Biological Polymers, Academic Press, New York 1976.
[6] The polymer is washed with water, acetone, and ether, and dried.
[7] *S. Mitsui, Y. Senda, T. Shimodaira, H. Ichikawa,* Bull. Chem. Soc. Jpn. *38*, 1897 (1965).

Upright Unsymmetrical Coordination in a Cyclopropenylnickel Complex: Synthesis and Structure of $[(C_3Ph_3)Ni(PPh_3)_2]PF_6$

By *Carlo Mealli, Stefano Midollini, Simonetta Moneti,* and *Luigi Sacconi*[*]

Unsymmetrical coordination of the cyclopropenylium ion has been found only in the complex $[(C_3Ph_3)Pt(PPh_3)_2]PF_6$[1]. Here the $C_3Ph_3^{\oplus}$ triangle has an isosceles shape with one large (1.58 Å) and two short (1.39 Å) sides. The PtP_2 fragment is displaced towards the base which lies approximately in the plane of the PtP_2 unit ("in-plane" conformation).

We have succeeded in preparing the analogous nickel complex $[(C_3Ph_3)Ni(PPh_3)_2]PF_6$ *(1)*, whose X-ray structure analysis shows that the $C_3Ph_3^{\oplus}$ unit is coordinated to the metal in an unprecedented unsymmetrical fashion (Fig. 1)[2].

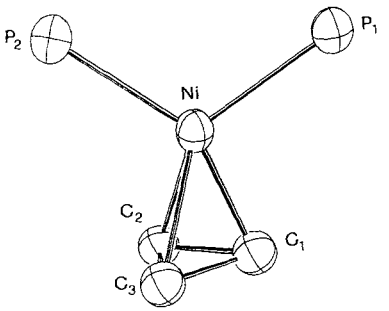
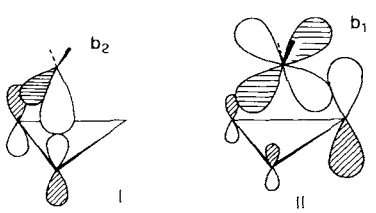


Fig. 1. ORTEP diagram of the skeleton of the complex cation in *(1)*. Important distances [Å] and angles [°] are: Ni—P1 = 2.242(4), Ni—P2 = 2.234(4), Ni—C1 = 1.91(1), Ni—C2 = 2.02(1), Ni—C3 = 2.07(1), C1—C2 = 1.46(2), C1—C3 = 1.44(2), C2—C3 = 1.34(2), P1—Ni—P2 = 107.4(2), C1—Ni—C2 = 43.7(5), C1—Ni—C3 = 42.1(5), C2—Ni—C3 = 38.4(4), C1—C2—C3 = 61.4(8), C1—C3—C2 = 63.4(9), C2—C1—C3 = 55.2(8).

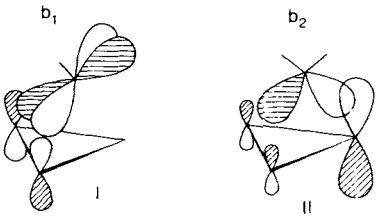
Also in this complex the cyclopropenylium ion has an isosceles shape but the base (1.35 Å) is shorter than the two other sides (1.43 Å). The nickel atom is located at 2.01 and 2.07 Å respectively from the two carbon atoms of the base and at 1.89 Å from the apical carbon atom. The plane of the NiP_2 moiety is almost perpendicular to the base of the triangle (84.09°). This can be named *upright* conformation and is just opposite to that of the platinum complex.

The bonding in both the metal complexes can be fairly well elucidated by considering the interactions of the b_1 and the b_2 orbitals of the MP_2 fragment (mainly metal d_{xz} and d_{yz} orbitals in nature) with the two π-set orbitals of the cyclopropenylium ion being the major bonding interactions in this complex[3].

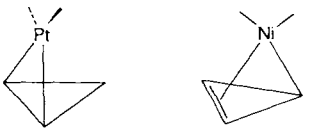


[*] Prof. Dr. L. Sacconi [+], Dr. C. Mealli, Dr. S. Midollini, Dr. S. Moneti
Istituto di Chimica Generale e Inorganica dell'Università,
Laboratorio CNR,
39 Via J. Nardi, I-50132 Firenze (Italy)
[+] Author to whom correspondence should be addressed.

In the case of the platinum complex the b_2 orbital is favorably oriented for bonding interaction with the antibonding π^* orbital I of the cyclopropenylium ion, while overlap of b_1 with II falls to a very low value.



A reversed situation is observed in the nickel complex. The 90° rotation of the NiP_2 fragment with respect to the $C_3Ph_3^{\oplus}$ ring as well as the very short Ni—C(apical) distance favors a large overlap of b_2 with II and a lower overlap of b_1 with I. Also the very short distance (1.35 Å) between the two basal carbon atoms in the $C_3Ph_3^{\oplus}$ ring, which is only a bit larger than the C—C double bond in the free ethylene molecule (1.337(2) Å)[4], suggests that their engagement in bonding with nickel is strongly reduced. (For a discussion see also ref.[5].)



Experimental

All operations were performed under nitrogen and with oxygen-free solvents. Triphenylcyclopropenylium perchlorate (366 mg, 1 mmol) in methanol (20 ml) was added to a solution of $(C_2H_4)Ni(PPh_3)_2$ (611 mg, 1 mmol) in benzene (20 ml). On addition of $(n\text{-}Bu)_4NPF_6$ (386 mg, 1 mmol) in butanol (20 ml) and slow evaporation of the solvent, red crystals were formed: yield 75%.

Received: April 24, 1980 [Z 609 IE]
German version: Angew. Chem. *92*, 967 (1980)

CAS Registry numbers:
(1), 75507-34-5; $(C_2H_4)Ni(PPh_3)_2$, 23777-40-4

[1] *M. D. McClure, D. L. Weaver,* J. Organomet. Chem. *54*, C59 (1973).
[2] Philips PW 1100 automated diffractometer. $a = 15.815(4)$, $b = 13.781(4)$, $c = 12.764(4)$ Å, $\alpha = 114.06(9)$, $\beta = 95.92(9)$, $\gamma = 97.74(9)$ space group $P\bar{1}$, $Z = 2$; $R = 0.079$ for 2919 reflections with $I < 3\sigma(I)$.
[3] *T. A. Albright, R. Hoffmann, Yuk-Ching Tse, T. D'Ottavio,* J. Am. Chem. Soc. *101*, 3812 (1979).
[4] *L. S. Bartell, E. A. Roth, C. D. Hollowell, K. Kuchitsu, J. E. Young,* J. Chem. Phys. *42*, 2683 (1965).
[5] *T. A. Albright, R. Hoffmann, J. C. Thibeault, L. Thorn,* J. Am. Chem. Soc. *101*, 3801 (1979).

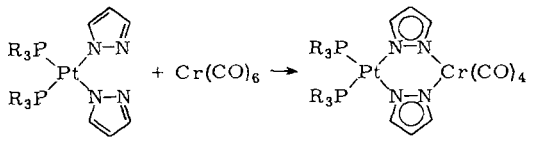
Transition-Metal Complexes with Pyrazolyl Bridging Ligands between Very Different Metal Centers

By *Stephen R. Stobart, Keith R. Dixon, Donald T. Eadie, Jerry L. Atwood,* and *Michael D. Zaworotko*[*]

The structural characterization of transition-metal complexes with bridging pyrazolyl ligands[1] has thus far only

[*] Prof. Dr. S. R. Stobart [+], Prof. Dr. K. R. Dixon, D. T. Eadie
Department of Chemistry, University of Victoria
Victoria, British Columbia (Canada) V8W 2Y2
Prof. Dr. J. L. Atwood, M. D. Zaworotko
Department of Chemistry, The University of Alabama
University, Alabama 35486 (USA)
[+] To whom correspondence should be addressed.

embraced systems incorporating homometallic bridged frameworks[2]. We wish to report the synthesis of some novel heterometallic analogues and the X-ray crystal structure of one of them.



(1) *(2)*

(a), $PR_3 = PEt_3$; *(b)*, $PR_3 = PMe_2Ph$

On UV irradiation (tetrahydrofuran, inert atmosphere) of the *cis*-bis(pyrazolyl)platinum(II) complexes *(1a)* and *(1b)* in the presence of $Cr(CO)_6$, the yellow compounds *(2a)* and *(2b)* were isolated. Molybdenum and tungsten analogues and the corresponding 3,5-dimethylpyrazolyl-bridged derivatives can be synthesized similarly[3]. The ^{1}H-NMR spectrum of *(2a)* (30 °C, CD_2Cl_2 solution) revealed that the methyl groups in the phosphane ligands are not magnetically equivalent; this is consistent only with a nonplanar conformation for the cyclic unit, and establishes that ring inversion for the latter is not rapid at ambient temperature. We subsequently determined the X-ray crystal structure of *(2a)*[4] (Fig. 1) and found a boat conformation for the central six-membered ring.

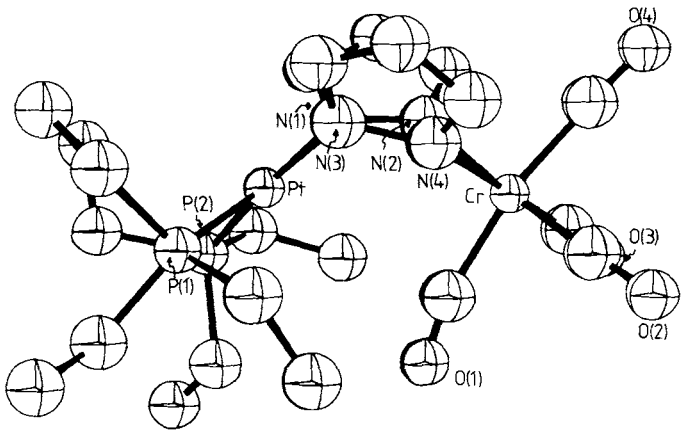


Fig. 1. ORTEP drawing of *(2a)* in crystal. Principal bond lengths [Å] and angles [°]:

Pt—N(1)	2.07(2)	N(1)—N(2)	1.39(3)
N(2)—Cr	2.14(2)	Cr—N(4)	2.16(2)
N(3)—N(4)	1.38(2)	Pt—N(3)	2.05(2)
Pt—N(1)—N(2)	121(1)	N(1)—N(2)—Cr	125(1)
N(2)—Cr—N(4)	85.6(7)	Cr—N(4)—N(3)	124(1)
N(4)—N(3)—Pt	120(1)	N(3)—Pt—N(1)	84.2(7)

These observations are of considerable current interest, in that structural data for related pyrazolyl-bridged complexes refer exclusively to homometallic molecules in which each metal atom has an identical environment. Such species exhibit a remarkable range of geometries from the chair conformation of $[(\eta^5\text{-}C_5H_5)_2Ti(\mu\text{-}C_3N_2H_3)]_2$[2a] through planar for $[Ni(NO)(\mu\text{-}C_3N_2HMe_2)]_2$[2b], to boat-shaped in a cobalt(I) analogue[2c]. In compound *(2a)*, whose pyrazolyl bridges link two dissimilar metal atoms in very different coordination environments and formal oxidation states, the central ring adopts a steep boat conformation in which the Pt—Cr distance is only 3.69 Å. This ability of the exobidentate pyrazolyl ligand to accommodate widely differing bridging configurations may be of considerable significance in relation to electrical or catalytic cooperativity effects between adjacent metal centers.

Received: February 15, 1980 [Z 610 IE]
German version: Angew. Chem. 92, 964 (1980)

CAS Registry numbers:
(1a), 75476-71-0; *(1b)*, 75476-72-1; *(2a)*, 75476-73-2; *(2b)*, 75476-74-3; $Cr(CO)_6$, 13007-92-6

[1] *S. Trofimenko*, Inorg. Chem. *10*, 1372 (1971); *G. Minghetti, G. Banditelli, F. Bonati*, Chem. Ind. (London) *1977*, 123; J. Chem. Soc. Dalton Trans. *1979*, 1851.

[2] a) *B. F. Fieselmann, G. D. Stucky*, Inorg. Chem. *17*, 2074 (1978); b) *K. S. Chong, S. J. Rettig, A. Storr, J. Trotter*, Can. J. Chem. *57*, 3090 (1979); c) *ibid.* 57, 3119 (1979).

[3] Satisfactory C, H, and N analysis and complementary spectroscopic data were obtained for all complexes reported herein.

[4] *(2a)* forms, triclinic crystals, space group $P\bar{1}$, $a = 9.564(5)$, $b = 11.164(6)$, $c = 14.980(8)$ Å, $\alpha = 78.66(5)$, $\beta = 87.61(5)$, $\gamma = 65.35(4)°$, $U = 1424$ Å^3, $\rho_{calc.} = 1.70$ g cm^{-3}, $Z = 2$, $\mu(Mo_{K\alpha}) = 56.9$ cm^{-1}. 4406 independent observed reflections with $I\theta \geq 3\sigma(I)$ were collected using graphite crystal monochromated radiation ($2\theta \leq 50°$) on an Enraf-Nonius CAD-4 diffractometer. Utilization of the direct methods program MULTAN facilitated location of the coordinates of the platinum and chromium atoms. Full-matrix least-squares refinement of the model obtained from the subsequent difference Fourier phased on these atoms led to an R value of 0.088.

Synthesis of Alternating Depsipeptides with the 4-Methylthiophenoxycarbonyl Group as Protecting and Activating Group for the Amino Function[**]

By *Horst Kunz* and *Klaus Lorenz*[*]

Depsipeptides made up of alternating hydroxy and amino acids are of interest owing to their antibiotic properties and their ability to selectively complex ions. Methods from peptide chemistry[1] are employed to synthesize these compounds, although the ester bonds of the chain cause characteristic differences of reactivity relative to peptides.

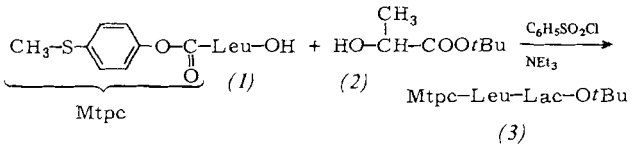
In the case of depsipeptides having α-hydroxycarboxylic acid units, these ester groups not only lead to undesired hydrolyses but also react readily with free amino groups of the linkage partner or of the compounds own amino end group and thus cause error sequences and self-cyclization. In order to counter these effects, the drastic acyl chloride method is often used for chain-lengthening amide formation in depsipeptide synthesis[2]. In addition amino groups have to be liberated from the hydro salts during the condensation step.

During our studies on protecting groups[3] for peptide synthesis, we have found the 4-methylthiophenoxycarbonyl (Mtpc) group to combine protective and activation properties for the amino function which specifically meet the needs of depsipeptide synthesis. This group provides a means of avoiding the presence of free amino groups during the synthesis, of circumventing the extreme activation of the carboxy groups *via* the acyl chloride, and of combining carboxyl activation and condensation in a single step.

The Mtpc group is introduced by 4-methylthiophenyl chloroformate on reaction according to conventional methods with the amino acids in aqueous alkaline solution. This affords *e.g.* 4-methylthiophenoxycarbonyl-L-leucine *(1)* in 92% yield. Compound *(1)* is then coupled with *tert*-butyl L-lactate *(2)*[5] by the benzenesulfonyl chloride method[4] to give the Mtpc depsidipeptide ester *(3)* in 90% yield.

[*] Prof. Dr. H. Kunz, Dipl.-Chem. K. Lorenz
Institut für Organische Chemie der Universität
Johann-Joachim-Becher-Weg 18—20, D-6500 Mainz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

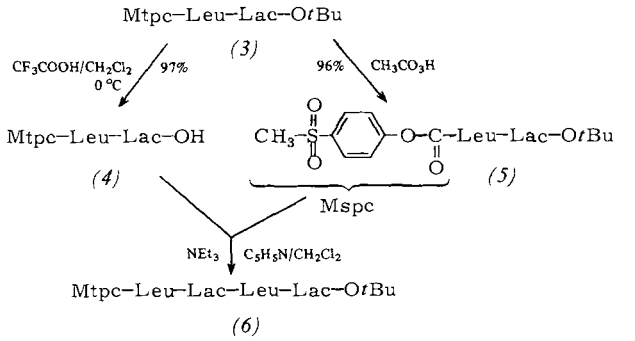


Mtpc (1) (2) Mtpc–Leu–Lac–OtBu (3)

The valuable properties of the Mtpc group for depsipeptide synthesis can be illustrated with the model compound *(3)*.

1) Mtpc protection is unaffected by trifluoroacetic acid, so that the C-terminal *tert*-butyl ester can be selectively removed.

2) The Mtpc group, which proved to be stable towards weak bases (pH = 12) under the conditions of its incorporation, can be easily oxidized by peracetic acid almost quantitatively to the base-labile 4-methylsulfonylphenoxycarbonyl (Mspc) group.



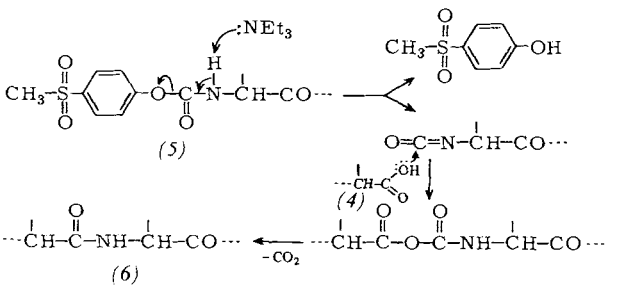
Mtpc–Leu–Lac–OtBu (3) → Mtpc–Leu–Lac–OH (4) + Mspc–Leu–Lac–OtBu (5) → Mtpc–Leu–Lac–Leu–Lac–OtBu (6)

Both reactions afford synthons useful for chain elongation. Coupled removal of the N-terminal protecting group and condensation with the next carboxylic component is accomplished by reaction of the N-terminal protected depsipeptide *(4)* with the N-terminally activated depsipeptide ester *(5)* in dichloromethane/pyridine/triethylamine. The N- and C-terminally protected tetradepsipeptide *(6)* is formed in a crude yield of 91%[6].

As with *(3)* the tetradepsipeptide *(6)* can be smoothly deprotected at the C-terminus (85% yield) and activated to the Mspc derivative at the N-terminal by treatment with peracetic acid (92% yield). Condensation of these derivatives under the same conditions as used for *(4)* and *(5)* furnishes a 93% crude yield of the octadepsipeptide Mtpc-(Leu-Lac)$_4$-OtBu. Purification by column chromatography gave an analytically pure yellowish oil (56%)[6].

Scheme 1 shows our concept of the reaction course. An analogous reaction sequence had already been utilized by *Gante*[7] for C-terminal chain elongation of peptides with *N*-(2,4-dinitrophenoxycarbonyl)amino acid esters.

The finding that the phenol is eliminated only from the Mspc form under the conditions employed is of decisive importance for depsipeptide synthesis by the Mtpc/Mspc principle.



(5) (4) (6) $-CO_2$

Scheme 1

Procedure

tert-Butyl *O*-(4-methylthiophenoxycarbonyl-L-leucyl-L-lactyl-L-leucyl)-L-lactate *(6)*: Compound *(4)* [10.26 g, 27.7 mmol; $[\alpha]_D^{22} = -36.3$ ($c = 2.4$, dichlormethane)], and *(5)* [13.14 g, 28.6 mmol; $[\alpha]_D^{22} = -32.8$ ($c = 0.95$, dichloromethane)] are stirred in a mixture of anhydrous dichloromethane (50 ml), anhydrous pyridine (170 ml), and anhydrous triethylamine (10 ml) for 72 h at 40 °C in the presence of a 4-Å molecular sieve. The mixture is diluted with dichloromethane and washed with citric acid solution (pH = 2), 5% $NaHCO_3$ solution, and water, and then dried over sodium sulfate. Removal of the solvent leaves a dark oil (15.5 g, 91%) which is chromatographed on a silica gel 60 column with ethyl acetate/benzene (1 : 1); yield 12.0 g (71%), yellowish oil, $[\alpha]_D^{22} = -39.4$ ($c = 2.4$, dichloromethane).

Received: June 11, 1980 [Z 611 IE]
German version: Angew. Chem. *92*, 953 (1980)

CAS-Registry numbers:
(1), 75521-95-8; *(2)*, 13650-70-9; *(3)*, 75521-96-9; *(4)*, 75521-97-0; *(5)*, 75521-98-1; *(6)*, 75521-99-2; 4-methylthiophenyl chloroformate, 52177-63-6; *(L)*-leucine, 61-90-5

[1] Review: *Yu. A. Ovchinnikov, V. T. Ivanov* in *H. N. Rydon:* International Review of Science. Ser. 2, Vol. 6. Butterworth, London 1976, p. 219.
[2] Cf., *e.g., M. M. Shemyakin, Yu. A. Ovchinnikov, V. T. Ivanov, A. V. Evstratov, I. I. Mikhaleva, I. D. Ryabova*, Zh. Obshch. Khim. *42*, 2320 (1972).
[3] *H. Kunz*, Chem. Ber. *109*, 3693 (1976); Justus Liebigs Ann. Chem. *1976*, 1674; *H. Kunz, M. Buchholz*, Chem. Ber. *112*, 2145 (1979); *R. Barthels, H. Kunz*, Z. Naturforsch. *B 34*, 1121 (1979).
[4] *P. A. Plattner, K. Vogler, R. O. Studer, P. Quitt, W. Keller-Schierlein*, Helv. Chim. Acta *46*, 927 (1963).
[5] *M. M. Shemyakin, N. A. Aldanova, E. I. Vinogradova, M. Y. Feigina*, Bull. Acad. Sci. USSR, Chem. Div. *1966*, 2074.
[6] The structure was secured by ^{1}H-NMR and field desorption mass spectrometry; *(6)*: $M^+ = 610$.
[7] *J. Gante*, Angew. Chem. *77*, 813 (1965); Angew. Chem. Int. Ed. Engl. *4*, 790 (1965); Chem. Ber. *99*, 1576 (1966).

Cyclic Oligomers of Propellanes and Bridged Annulenes with Bis(triazolinediones) Studied by ^{252}Cf-Plasma Desorption Mass Spectrometry[**]

By *P. Ashkenazi, R. D. Macfarlane, W. A. Oertling, Heinrich Wamhoff, K. M. Wald*, and *David Ginsburg*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

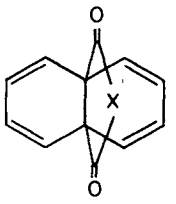
For several years we have been studying the reaction of various polyenic propellanes of type *(1)* and bridged [10]annulenes with 1,2,4-triazoline-3,5-diones and have put forth rather convincing evidence that *syn*-attack (with reference to the hetero-ring) by the dienophile *(2)* occurs because of sec-

[*] Dr. P. Ashkenazi, Prof. Dr. D. Ginsburg [*]
Department of Chemistry, Israel Institute of Technology
Haifa (Israel)
Prof. Dr. R. D. Macfarlane, Dr. W. A. Oertling
Department of Chemistry, Texas A & M University
College Station, Texas 77843 (USA)
Prof. Dr. H. Wamhoff, Dr. K. M. Wald
Institut für Org. Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)
[*] To whom correspondence should be addressed.

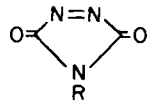
[**] Propellanes, Part 60. We are grateful to the National Science Foundation and the Robert A. Welch Foundation for support of the mass spectral work *(R. D. M.* and *W. A. O.)*, without which publication of these results would not have been possible. Support by the Deutsche Forschungsgemeinschaft and by Bayer AG is gratefully acknowledged *(H. W.* and *K. M. W.)*. We thank Prof. Dr. *A. Mandelbaum* for drawing our attention to ^{252}Cf plasma desorption mass spectrometry and Prof. Dr. *E. Vogel* for samples of bridged annulenes and his interest in this work. — Part 59: *I. M. Landheer, D. Ginsburg*, Heterocycles, in press.

ondary orbital interactions between the π^* carbonyl orbitals in *(1)* (LUMO) and the n_--antisymmetric combination of nitrogen lone pair orbitals in *(2)* (HOMO)[1].

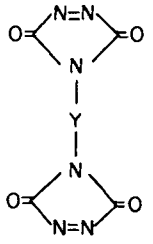
Perhaps our most exciting additional support for this thesis arose from the idea (suggested by *H. W.*) that we react our propellane substrates with bis(triazolinediones) *(3)*[2] in the hope that [2+2] cyclic oligomers be obtained. This hope was realized in the case of several 1,6-bridged [10]annulenes. Just as in the simpler reactions with *(2)*, exclusive *anti* attack occurs due to steric hindrance caused by the bridge, and the bis(triazolinedione) is able to form a [2+2] oligomer with an elliptical cavity *(4)*.

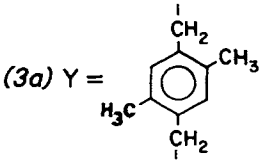


(1) *a* X = O
b X = NH
c X = NMe
d X = NPh



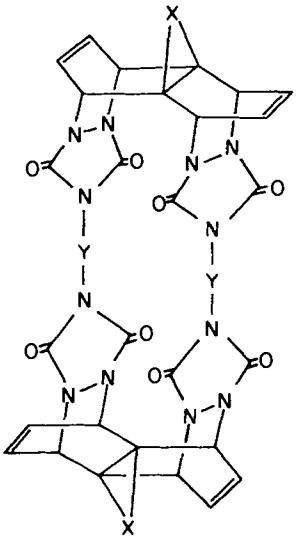
(2) R = Me, Ph





(3a) Y =

(3b) Y = $-(CH_2)_6-$



(4) X = CH_2, O
Y as in *(3)*

However, in the case of *(1)*, no [2+2] oligomers could be observed. The cavity in such a product is evidently not large enough to accommodate the peripheral structure. However, our hope was also realized in principle for *(1)*. We could easily demonstrate that certain substrates gave oligomers in the range [3+3] to [6+6] (Table 1). We exemplify this by structure *(5)*. When this as well as the analogous products obtained from substrates in Table 1 were irradiated in solution, all of the double bonds disappeared and the vinylic protons of *(5)* were replaced by the cyclobutane protons in *(6)*. We must however confess that the conformation exhibited by *(5)* and *(6)* has not been unequivocally proven as we have thus far not succeeded in obtaining crystals suitable for X-ray crystallography.

Although in one or two cases of 2:1 adducts (Table 1) a Rast molecular weight determination could be carried out (*e.g.* in camphor, borneol, or bornylamine), in all other cases temperature and solubility of the product did not permit this.

Table 2. Reaction of dienes obtained by 2:1 addition (see Table 1) with dienophiles in a molar ratio of 1:1.

Diene	Dienophile	Product	M.p. [°C]	M. wt. calc.	M. wt. exp.
[2 *(1c)* + *(3a)*]	*(3b)*	[4+4] [a]	273	2070	2091 (+Na)
[2 *(1c)* + *(3b)*]	*(3a)*	[4+4] [a]	273—275	2070	2072
[2 *(1c)* + *(3b)*]	*(3b)*	[4+4] [a]	263—265	1974	1975
		[6+6] [a]		2961	2963
[2 *(1d)* + *(3b)*]	*(3a)*	[4+4]	255 (dec.)	2318	2320

[a] Photocyclization to cyclobutane derivatives.

The only method permitting interpretation of our findings was Cf-252 plasma desorption mass spectrometry[3]. Other mass spectral methods including field desorption could at most afford fragment peaks resulting from retro-Diels-Alder reactions, due to the low thermal stability of these molecules.

The chemical result we wish to emphasize is the photocyclization of compounds such as *(5)* → *(6)* in which a [4+4] oligomer was formed clearly stepwise, yet in the rapid reaction leading to it (instantaneous at RT) the bis-compound *(3)* is discerning enough to attack (on eight occasions!) *syn* to the imide ring. In *(3a)* + *(1d)*, this occurs on 12 occasions but six to eight is impressive enough. Calculations by *Gleiter* indicate that the attraction in the relevant secondary orbital in-

Table 1. Reactions of dienes and dienophiles in molar ratios 1:1 and 2:1.

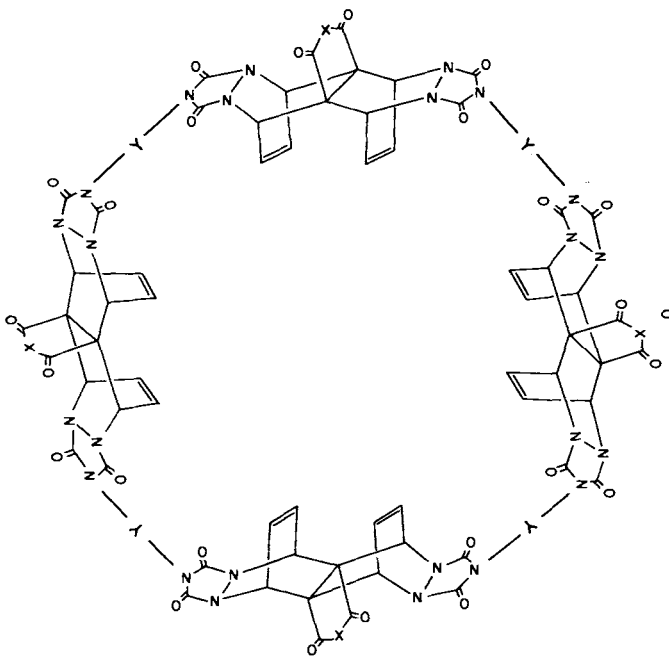
Diene	Dienophile	Ratio 1:1 Product	M.p. [°C]	M. wt. calc.	M. wt. exp.	Ratio 2:1 Product	M.p. [°C]	M. wt. calc.	M. wt. found
(1a)	*(3a)*					[2+1]	150—160 200 (dec.)	729	729
(1b)	*(3a)*	[3+3]	>290	1582	1582	[2+1]	245—247	727	726
(1c)	*(3a)*	[3+3] [a, d]	250 (dec.)	1624	1624	[2+1]	238—240	755	755
(1d)	*(3a)*	[3+3] [d]	268—270	1812	1812	[2+1]	212—214	879	881
(1c)	*(3b)*	[3+3] [d]	250	1480	1482	[2+1]	235—236	707	708
		[4+4] [d]		1973	1974				
(1d)	*(3b)*					[2+1]	220 (dec.)	829	833, 834
1,6-Oxa-[10]annulene	*(3a)*	[2+2]	180	945	944				
		[3+3]		1417	1417				
1,6-Methano-[10]annulene	*(3a)*	[2+2] [b]	187—190	941	941				
1,6-Methano-[10]annulene	*(3b)*	[2+2]	268—270	845	844				
		[4+4] [c]		1689	1689				

[a] On examination at a later time [4+4]-, [5+5]-, and [6+6] peaks were also found. [b] Trace of [3+3] product. [c] No [3+3] signal. [d] Photocyclization to cyclobutane derivatives.

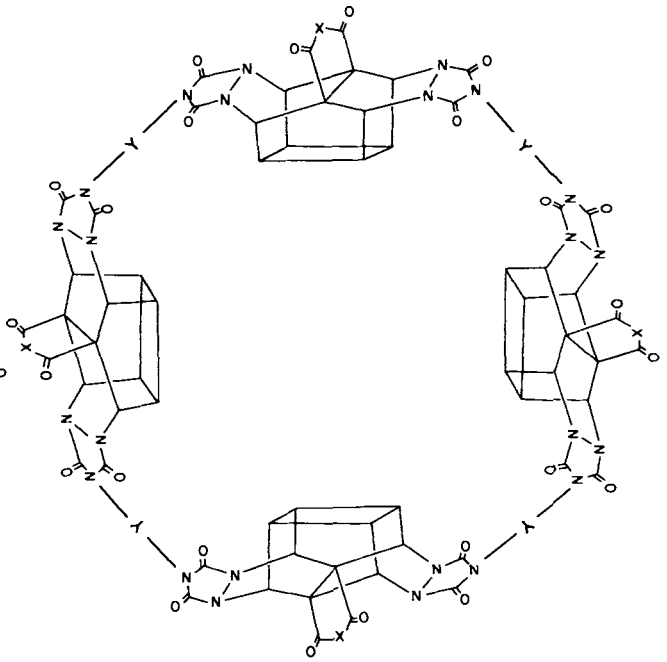
© Verlag Chemie, GmbH, 6940 Weinheim, 1980
0570-0833/80/1111-0934 $02.50/0

teraction is *ca.* 4—6 kcal/mol[4], of the order of a hydrogen bond. But the experimental results of the photocyclization (cf. [5]) are overwhelming support for secondary orbital interactions as the controlling factor in this *syn* attack.

obtain products of type *(9)*, of which *(5)* is an example. This means that in the reaction between P—T_a—P and T_a (or T_b) or P—T_b—P and T_b (or T_a) the reactants must necessarily interact head (P) to tail (T) throughout, even when as many as

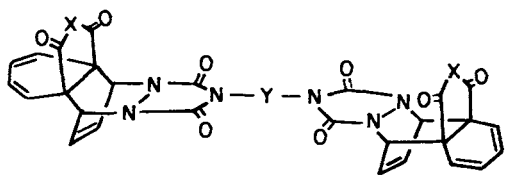


(5) X as in *(1)*
Y as in *(3)*



(6) X as in *(1)*
Y as in *(3)*

Perhaps the most interesting deduction from Table 2 is that the cavity in a [2+2] oligomer [from *(1)*] is evidently not big enough to sustain the structure and therefore the reactants prefer to react further, to the [4+4] stage or higher. The general structure of a [2+1] adduct obtainable from propellanes but not from bridged [10]annulenes (cf. also simpler cases in [5,6]) is given by formula *(7)*.

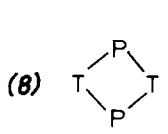


(7) X as in *(1)*
Y as in *(3)*

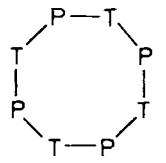
The central portion of formula *(7)* stems from the bis(triazolinedione) *(3a)* or *(3b)* (symbolized by T_a or T_b and its two side moities stem from the appropriate tetraenic propellane (symbolized by P); thus *(7)* may be abbreviated as, *e.g.* P—T_a—P or P—T_b—P (each P still has a cyclohexadiene ring capable of reacting with one end of T_a or T_b).

The course of reaction of P—T—P with T might be expected to lead to cyclic oligomers of type *(8)*, *i.e.* a [2+2] oligomer, but as we have seen in Table 2, it is more usual to

three P—T—P molecules are reacting with three molecules to give the dodecamers listed in Tables 1 and 2. Furthermore, the photoreaction [exemplified by *(5)*→*(6)*] indicates that these molecules are also aware of secondary orbital interaction, as exclusive *syn*-attack occurs throughout.



(8)



(9)

Because they react with dienophiles of type T in *anti-anti* sense with reference to the bridge, the Köln bridged annulenes are the only substrates able to form a [2+2] adduct with an elliptical cavity [type *(4)*], but Table 1 shows that they too may form [3+3] and [4+4] oligomers.

Received: June 2, 1980 [Z 612a IE]
German version: Angew. Chem. *92*, 970 (1980)

[1] *R. Gleiter, D. Ginsburg*, Pure Appl. Chem. *51*, 1301 (1979), and references cited therein.
[2] *K. Wald, H. Wamhoff*, Chem. Ber. *111*, 3519 (1978); *K. B. Wagener, S. R. Turner, G. B. Butler*, J. Polym. Sci. Polym. Lett. *10*, 805 (1972).
[3] *R. D. Macfarlane, D. F. Torgerson*, Int. J. Mass Spectrom. Ion Phys. *21*, 81 (1976); Science *191*, 920 (1976).
[4] *M. C. Böhm, R. Gleiter*, personal communication; Tetrahedron, in press.
[5] *M. Korat, D. Tatarsky, D. Ginsburg*, Tetrahedron *28*, 2315 (1972).
[6] *P. Ashkenazi, E. Vogel, D. Ginsburg*, Tetrahedron *33*, 1169 (1977).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1111-0935 $02.50/0*

Mixed Oligomers of Propellanes and Bridged Annulenes with Bis(maleimides) and Bis(triazolinediones) Studied by ^{252}Cf-Plasma Desorption Mass Spectrometry[**]

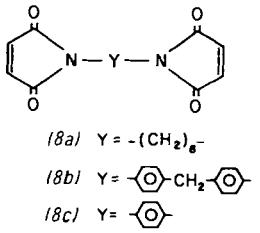
By *P. Ashkenazi, R. D. Macfarlane, W. A. Oertling, Heinrich Wamhoff, K. M. Wald,* and *David Ginsburg*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

On using propellanes as stereochemical models in various types of reactions, we discovered that for steric reasons simple substituted maleimides attack tetraenic propellanes from the side *anti*- to the heteroring[1]. In contradistinction to maleimides, substituted triazolinediones contain nitrogen atoms whose antisymmetric n_- combination of lone pair orbitals (HOMO) can undergo secondary orbital interactions with the CO π^* orbitals (LUMO) of the propellane hetero ring causing *syn*-attack with reference to the carbonyl-containing rings[2].

Before we began our work we knew that a tetraenic propellane mono-Diels-Alder adduct with a substituted maleimide, *e.g. (2),* will react with a simple triazolinedione such as *(3)* to give *(4)* and with another mole of a maleimide also to give the same type of *anti-syn*-bisadduct *(4)*. On the other hand, the monoadduct *(6)* with the substituted maleimide *(7)* does not afford a bisadduct even under forcing conditions[6].

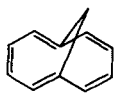
In view of the results described in the preceding paper[3] and in view of the existence of bis(maleimides)[4] we decided to study mixed oligomers of tetraenic propellanes and bridged annulenes with both the bis(triazolinedione) type of dienophile *(12)*[3,5] and with the bis(maleimide) type *(8)*.



(8a) Y = $-(CH_2)_6-$

(8b) Y =

(8c) Y =

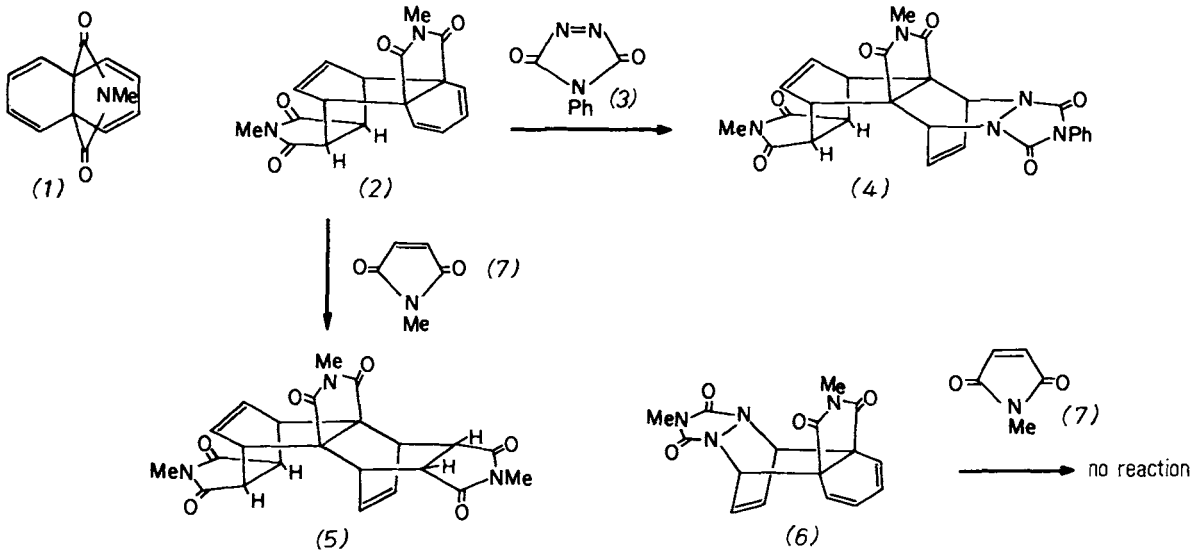


(9)

Table 1. Reaction of dienes *(1)* and *(9)* with *(8)* in a molar ratio of 2:1.

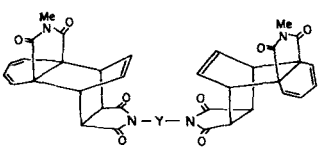
Diene	Dienophile	Product	M.p. [°C]	M.wt. calc.	M.wt. exp.
(1)	*(8a)*	*(10a)*	195	703	704
(1)	*(8b)*	*(10b)*	200	785	786
(1)	*(8c)*	*(10c)*	216	695	696
(9)	*(8b)*	*(11)*	232	643	644

Table 1 lists 2:1 compounds *(10)* prepared from tetraenic propellane *(1)* and three different bismaleimides *(8a—c)* as well as the 2:1 adduct *(11)* of 1,6-methano[10]annulene *(9)*

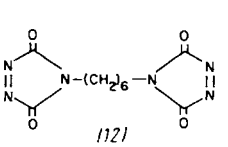


We assume in our subsequent argument, albeit without iron-clad proof, that the bisdienophiles behave analogously to the monofunctional dienophiles.

with *(8b)*. When *(10a)* and *(10b)* (Table 1) were treated with *(12)*, the compounds *(13a)* and *(13b)*, respectively, were obtained (Table 2). Compound *(13a)* was accompanied by the



(10a-c) Y as in *(8)*



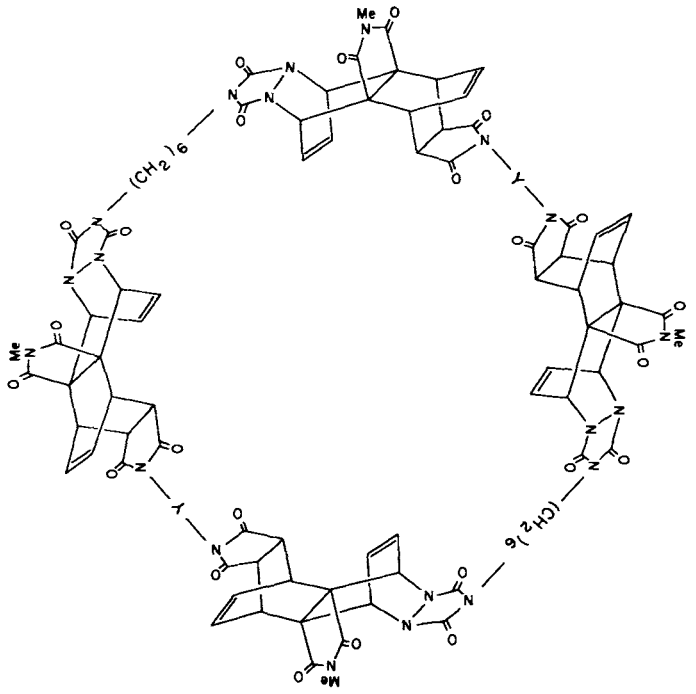
(12)

Table 2. Reaction of dienes *(10)* with dienophile *(12)* in a molar ratio of 1:1.

Diene	Dienophile	Product	M.p. [°C]	M.wt. calc.	M.wt. exp.
(10a)	*(12)*	*(13a)*	258—259	1966	1967
(10b)	*(12)*	*(13b)*	277—278	2130	2135

[*] Dr. P. Ashkenazi, Prof. Dr. D. Ginsburg [+]
Department of Chemistry, Israel Institute of Technology
Haifa (Israel)
Prof. Dr. R. D. Macfarlane, Dr. W. A. Oertling
Department of Chemistry, Texas A & M University
College Station, Texas 77843 (USA)
Prof. Dr. H. Wamhoff, Dr. K. M. Wald
Institut für Org. Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)
[+] To whom correspondence should be addressed.

[**] Propellanes, Part 61. We are grateful to the National Science Foundation and the Robert A. Welch Foundation for support of the mass spectral work *(R. D. M.* and *W. A. O.)* without which publication of these results would not have been possible. Support by the Deutsche Forschungsgemeinschaft and by Bayer AG is gratefully acknowledged *(H. W.* and *K. M. W.)*. We thank Prof. Dr. *A. Mandelbaum* for drawing our attention to ^{252}Cf plasma desorption mass spectrometry, and Prof. Dr. *E. Vogel* for samples of bridged annulenes and for his interest in this work.—Part 60: [3].



(13a,b) Y as in *(8)*

1:1 adduct of *(10a)* with *(12)* [M.wt. 983 (calc.); 984 (found)], whilst *(13b)* showed no such analogue in the mass spectrum, but was rather accompanied by the product containing eight equiv. of *(1)*, 4 equiv. of *(8b)*, and 4 equiv. of *(12)* [M.wt. 4260 (calc.); 4269 (found)]. The molecular weights were determined by ^{252}Cf plasma desorption mass spectrometry (cf. [3]); all other analytical methods of structural elucidation failed.

Received: June 2, 1980 [Z 612b IE]
German version: Angew. Chem. *92*, 972 (1980)

CAS Registry numbers:
(1), 16609-30-6; *(8a)*, 4856-87-5; *(8b)*, 13676-54-5; *(8c)*, 3278-31-7; *(9)*, 2443-46-1; *(10a)*, 75495-29-3; *(10b)*, 75495-30-6; *(10c)*, 75495-31-7; *(11)*, 75506-22-8; *(12)*, 38727-98-9; *(13a)*, 75506-23-9; *(13b)*, 75495-32-8

[1] *M. Kaftory, M. Peled, D. Ginsburg*, Helv. Chim. Acta *62*, 1326 (1979).
[2] *R. Gleiter, D. Ginsburg*, Pure Appl. Chem. *51*, 1301 (1979), and reference cited therein.
[3] *P. Ashkenazi, R. D. Macfarlane, W. A. Oertling, H. Wamhoff, K. M. Wald, D. Ginsburg*, Angew. Chem. *92*, 970 (1980); Angew. Chem. Int. Ed. Engl. *19*, 933 (1980).
[4] *R. J. Cotter, C. K. Sauers, J. M. Whelan*, J. Org. Chem. *26*, 10 (1961); *P. Kovacic, R. W. Hein*, J. Am. Chem. Soc. *81*, 1187 (1959).
[5] *K. Wald, H. Wamhoff*, Chem. Ber. *111*, 3519 (1978); *K. B. Wagener, S. R. Turner, G. B. Butler*, J. Polym. Sci. Polym. Lett. *10*, 805 (1972).
[6] *M. Peled, D. Ginsburg*, unpublished results.

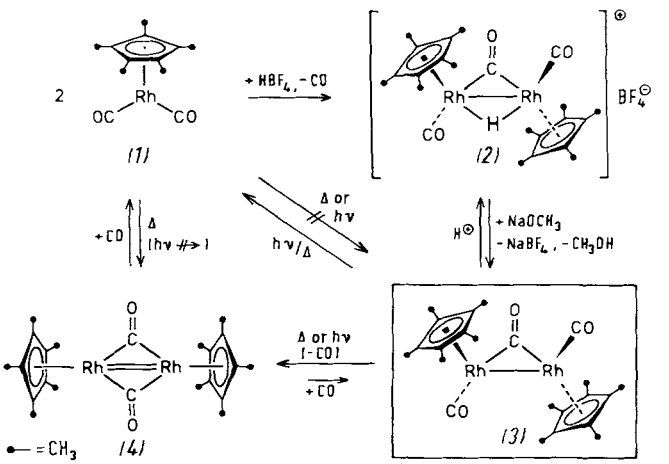
A Simple Method of Forming Metal-to-Metal Bonds[**]

By *Johann Plank, Doris Riedel*, and *Wolfgang A. Herrmann*[*]

Our studies on the acid-induced formation of trinuclear methylidynerhodium clusters from the methylene complex μ-$CH_2[(\eta^5\text{-}C_5H_5)Rh(CO)]_2$[1] and the smooth spontaneous formation of $(\eta^5\text{-}C_5H_5)_3Rh_3(\mu\text{-}CO)_3$ from the μ-hydrido complex $[(\eta^5\text{-}C_5H_5)_2Rh_2(CO)_3H]BF_4$ have demonstrated the activation of basic molecular centers to constitute a powerful alternative method of metal-metal bond making[2]. We now report the synthesis of a simple dinuclear rhodium compound which is accessible from its mononuclear precursor neither by thermal nor by light-induced reactions.

The action of tetrafluoroboric acid on diethyl ether solutions of dicarbonyl(η^5-pentamethylcyclopentadienyl)rhodium *(1)* effects fast and complete precipitation of an ionic, exceptionally base-sensitive dark brown complex *(2)*, which is thermally stable up to about 85 °C and is shown by its properties (Table 1) to be a cationic μ-hydrido complex (Scheme 1). The intermediacy of the primary protonation product $[(\eta^5\text{-}C_5Me_5)Rh(CO)_2H]BF_4$ in the formation of *(2)* is evidenced by independent protonation experiments carried out in *n*-pentane[9] and similar reactions of the cobalt complex $(\eta^5\text{-}C_5H_5)Co(PMe_3)_2$, related to *(1)* for which *Werner et al.* have observed a variety of surprising secondary reactions of the mononuclear hydrido complex $[(\eta^5\text{-}C_5H_5)Co(PMe_3)_2H]BF_4$[3].

The most striking property of the nitromethane-soluble compound *(2)* is its proclivity to undergo deprotonation, which is slow with basic solvents (dimethylformamide, dimethyl sulfoxide, acetonitrile) but *fast* and *quantitative* with sodium methoxide/methanol (Scheme 1); the violet-red neutral complex *(3)* is isolated which, strangely enough, was hitherto unknown (Table 1).



Scheme 1

Table 1. Physical and spectroscopic properties of the new rhodium complexes *(2)* and *(3)*.

(2): dark brown powder, can be stored indefinitely with rigorous exclusion of light and moisture, decomposes above *ca.* 85 °C (m.p. >240 °C, sealed capillary). Readily soluble and stable in nitromethane. Equivalent conductivity (CH_3NO_2, 21.6 °C, $c = 3.0 \times 10^{-4}$ mol/l): $\Lambda = 137$ cm^2 mol^{-1} Ω^{-1}. IR (νCO; cm^{-1}): 2010 vs, 1836 s (KBr) [a]; 2022 vs, 1834 vs (CH_3NO_2); 2026 vs, 1839 vs (CH_2Cl_2). ^{1}H-NMR (90 MHz; CD_3NO_2, −25 °C): $\delta = 2.03$ (s, 30H), −10.40 (t, 1H; $^1J_{Rh,H} = 19.2$ Hz)

(3): carmine red powder or violet-red, light-sensitive needles; stable in air for several days at room temperature in the dark. Sinters at 141—143 °C (sealed capillary) with weak evolution of gas and formation of the deep blue derivative *(4)*. Readily soluble in THF, CH_2Cl_2, and benzene; equivalent conductivity (THF, 21.6 °C, $c = 2.8 \times 10^{-4}$ mol/l): $\Lambda = 1.1$ cm^2 mol^{-1} Ω^{-1} (non-electrolyte). IR (νCO; cm^{-1}): 1947 vs, 1794 vs (KBr); 1952 vs, 1791 vs (THF); 1951 vs, 1778 vs (CH_2Cl_2). ^{1}H-NMR (90 MHz; [D$_8$]-THF, −10 °C): $\delta = 1.91$ ("s"); MS (12 eV); T_Q 140 °C, T_E 110 °C): $m/e = 560$ (M^+, 11%); 532 ([M−CO]$^+$, 100), 504 ([M−2CO]$^+$, 4), 476 ([M−3CO]$^+$, 1), 373 ($(C_5Me_5)_2Rh^+$, 82)

[a] IR spectra of KBr disks prepared in air already show the CO bands of product *(3)* alongside the νCO absorptions of *(2)*.

[*] Prof. Dr. W. A. Herrmann, Dr. J. Plank, D. Riedel
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)

[**] Syntheses of Metal Carbonyls, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, Degussa Hanau and Hoechst AG.—Part 5: W. A. Herrmann, H. Biersack, J. Organometal. Chem. *191*, 397 (1980).

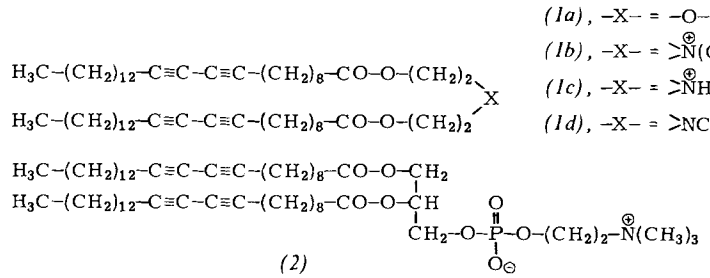
According to the data shown in Table 1, *(3)* has the same structure as the analogous cyclopentadienyl compound[4, 10] having no substituent in the five-membered ring. Complex *(3)* decomposes both thermally (150 °C, 1 h) and photochemically (tetrahydrofuran, Hg high-pressure lamp, $\lambda > 300$ nm) *via* carbonyl elimination to form *(1)* and the twofold carbonyl-bridged derivative *(4)*. *Maitlis et al.* obtained *(4)* by heating *(1)* (80—85 °C/10—20 torr)[5]; however, *(4)* does not form photochemically. Carbonylation of *(4)* under normal pressure essentially affords the starting material *(1)* along with very small amounts of *(3)*.

The carbonylrhodium compound *(3)* which in fact is inaccessible by thermal or photochemical (dimerizing) decarbonylation of *(1)* can readily be obtained by the protonation/deprotonation sequence presented in this communication. Owing to the basic character of *(1)* and analogous metal-carbonyl systems, their acid activation constitutes a clear-cut method for the facile construction of polynuclear complexes which can be obtained only with difficulty, in only low yields, or not at all by conventional methods[6].

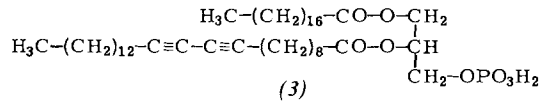
Procedure[7]

(2): To a vigorously stirred solution of *(1)*[8] (294 mg, 1.0 mmol) in diethyl ether (20 ml) is added dropwise 54% HBF_4 (*ca.* 0.2 ml) in the same solvent. Towards the end of acid addition, compound *(2)* deposits as a dark brown floccular precipitate which is quickly filtered off on a D3 frit, washed with ether (4 × 6 ml), and dried for 3 h in a high vacuum; yield 298 mg (92%).

(3): Compound *(2)* (298 mg, 0.46 mmol) is treated with a saturated $NaOCH_3/CH_3OH$ solution (6 ml) in the dark at +20 °C, whereupon microcrystalline, carmine-red *(3)* (sparingly soluble in CH_3OH) is formed instantaneously. Compound *(3)* is *immediately* (!) filtered off on a D3 frit, quickly washed with methanol (3 × 6 ml) and dried in a high vacuum; yield 248 mg (97%). This product is already analytically pure but can be recrystallized from THF/ether (10: 1; −25 °C) *in the dark* (!).



(2)



(3)

Received: May 22, 1980 [Z 613 IE]
German version: Angew. Chem. *92*, 961 (1980)
Publication delayed at authors' request

[1] *W. A. Herrmann, J. Plank, E. Guggolz, M. L. Ziegler*, Angew. Chem. *92*, 660 (1980); Angew. Chem. Int. Ed. Engl. *19*, 653 (1980); *W. A. Herrmann, J. Plank, M. L. Ziegler, B. Balbach*, J. Am. Chem. Soc. *102*, 5906 (1980); *W. A. Herrmann, J. Plank, D. Riedel, M. L. Ziegler, K. Weidenhammer, E. Guggolz, B. Balbach, ibid.*, in press.

[2] *W. A. Herrmann, J. Plank, D. Riedel*, J. Organomet. Chem. *190*, C47 (1980).

[3] *H. Werner, W. Hofmann*, Chem. Ber. *110*, 3481 (1977); cf. also Angew. Chem. *90*, 496 (1978); Angew. Chem. Int. Ed. Engl. *17*, 464 (1978); *H. Werner, R. Feser, W. Buchner*, Chem. Ber. *112*, 834 (1979), and references cited therein; *H. Werner, H. Neukomm, W. Kläui*, Helv. Chim. Acta *60*, 326 (1977).

[4] *E. O. Fischer, K. Bittler*, Z. Naturforsch. *B 16*, 835 (1961); *O. S. Mills, J. P. Nice*, J. Organomet. Chem. *10*, 337 (1967).

[5] *A. Nutton, P. M. Maitlis*, J. Organomet. Chem. *166*, C21 (1979).

[6] *H. Vahrenkamp*, Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978).

[7] All operations must be performed with rigorous exclusion of O_2, H_2O, and light (Schlenk technique).

[8] *J. W. Kang, P. M. Maitlis*, J. Organomet. Chem. *26*, 393 (1971).

[9] Reaction of $[\eta^5\text{-}C_5(CH_3)_5]Ir(CO)_2$ with HBF_4 (diethyl ether, 0 °C) affords the salt-like complex $[\{\eta^5\text{-}C_5(CH_3)_5\}Ir(CO)_2H]BF_4$ in a quantitative yield: IR(CH_3NO_2): 2111 vs, 2070 vs (νCO); ^{1}H-NMR (CD_3NO_2, int. TMS, −20 °C): $\delta = 2.43$ (s, 15H), −13.82 (m, 1H); equivalent conductivity: $\Lambda = 94.6$ cm^2 mol^{-1} Ω^{-1} (CH_3NO_2, 23.4 °C, $c = 10^{-4}$ mol/l). The complex can be reversibly deprotonated with $NaOCH_3/CH_3OH$. These findings support the assumption that the reaction *(1)*→*(2)* proceeds *via* the analogous mononuclear hydrido complex *(1)*-$H^{\oplus}BF_4^{\ominus}$. — Compound *(3)* is also protonated by CF_3SO_3H to form *(2)*, $CF_3SO_3^{\ominus}$ in place of $BF_4^{\ominus}$. The thermal and the photochemical disproportionation of *(3)* both follow the equation

$3\,(3) \rightarrow 2\,(1) + 2\,(4) + CO$

[10] *Note added in proof:* Meanwhile, an X-ray diffraction study of *(3)* has been carried out which confirmed the suggested structure; see Scheme 1 (*M. L. Ziegler, W. A. Herrmann, et al.*, unpublished results, 1980).

Polymerizable Phospholipid Analogues—New Stable Biomembrane and Cell Models[**]

By *Hans-Henning Hub, Bernd Hupfer, Horst Koch,* and *Helmut Ringsdorf*[*]

Biological membranes consist of phospholipids, proteins, and other compounds. Liposomes (vesicles)—artificially built up spherical particles with bimolecular membranes and aqueous cores—are particularly appropriate cell and membrane models[1]. One of the disadvantages of liposomes consisting of natural phospholipids is their short lifetime and especially their low stability in the interaction with natural cell systems. This hinders their application as models for cell-cell interactions as well as their use as carriers for drugs and other biologically active substances.

Initial attempts to work with model systems not composed of natural phospholipids have recently been described. These

(1a), –X– = –O–$(CH_2)_2$–O–$(CH_2)_2$–O–

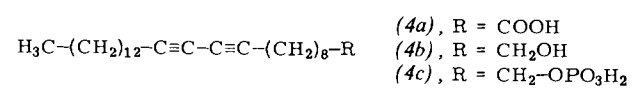
(1b), –X– = $\geq\overset{\oplus}{N}(CH_3)_2$ $Br^{\ominus}$

(1c), –X– = $\geq\overset{\oplus}{N}H$–$(CH_2)_2$–$SO_3^{\ominus}$

(1d), –X– = $\geq NCH_3$

(2)

(3)



(4a), R = COOH
(4b), R = CH_2OH
(4c), R = CH_2–OPO_3H_2

synthetic liposomes consist either of long chain fatty acids[2a] ("ufasomes"), of fatty acid/lysophospholipid mixtures[2b], or of lipid analogous dialkyl compounds[2c]. Single-chain ammonium amphiphiles bearing two charged end groups and a rigid segment are able to form membrane-like assemblies as well[2d]. Yet all these models exhibit a limited lifetime.

[*] Prof. Dr. H. Ringsdorf, Dipl.-Chem. H.-H. Hub, Dipl.-Chem. B. Hupfer, Dipl.-Chem. H. Koch
Institut für Organische Chemie der Universität Mainz
J.-J.-Becher-Weg 18—20, D-6500 Mainz 1 (Germany)

[**] Polyreactions in Ordered Systems, Part 20. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.—Part 19: [5b].

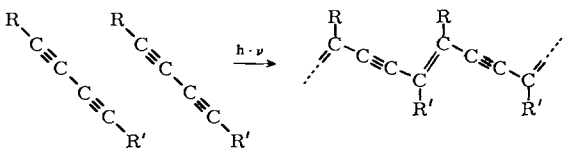
Novel, stable liposomes that are more suited as cell membrane models can be obtained *via* polymerization of the lipid bilayers of vesicles with retention of their structure. For this purpose lipid-analogous [*(1)—(3)*] and lysolipid analogous monomers *(4)* were synthesized containing polymerizable diacetylene moieties in the side chains (Table 1).

Table 1. Polymerizable lipid and lysolipid analogues; yields and melting points.

Compound	Yield [%]	M.p. [°C]	
(1a)	32 [a]	49.0—49.5	(ethanol)
(1b)	76 [a]	93.5—94.5	(acetone)
(1c)	80 [a]	109	(chloroform)
(1d)	85 [a]	47.5—48.5	[4a]
(2)	20 [a]	— [b]	
(3)	24 [a]	37—38	(acetone)
(4a)	55	68—69	(hexane)
(4b)	64	59—60	(hexane)
(4c)	86 [c]	79—82	(hexane)

[a] Based on *(4a)*. [b] Uncharacteristic m.p., in analogy to other synthetic lecithins [10]. [c] Based on *(4b)*.

Diacetylenes are known to be polymerizable topochemically by UV irradiation in the solid state[3a] and in oriented mono-[3b] and multilayers[3c,d]. The resulting polymers have a red color due to their conjugated enyne structure.



Prior to the investigation of the polymerization of compounds *(1)—(4)* in liposomes, we examined their surface pressure-area and polymerization behavior in monolayers at the gas-water interface[4] according to earlier investigations[3b,c]. In order to obtain vesicles, the lipid analogues *(1)—(3)* as well as the single chain lysolipid analogues *(4)* were sonicated as aqueous suspensions at 50 °C under nitrogen. Electron microscopy of the resulting clear, colorless solutions proves the formation of spherical vesicles of different diameters (up to several μm). Only after sonication for longer than 30 min the formation of small unilamellar liposomes occurs (diameter: approximately 100 nm, wall thickness: approximately 10 nm, Fig. 1).

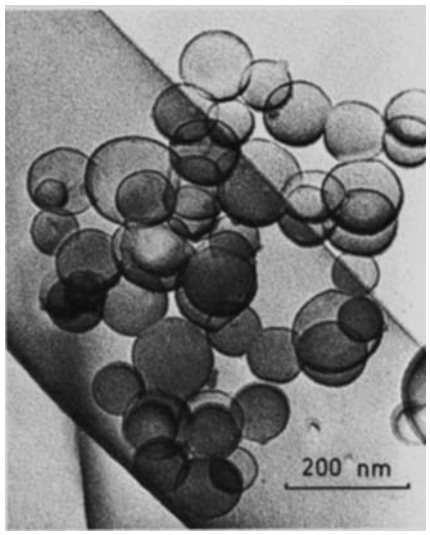


Fig. 1. Small unilamellar monomer vesicles of lipid analogue *(1a)* after 30 min of sonication, negatively stained with uranyl acetate. Philips EM 300 electron microscope, acceleration voltage: 80 kV.

On UV irradiation, the vesicle solutions of the lipid analogues *(1a)—(1c)*, *(3)*, and of the lysolipid analogues *(4a)—(4c)* exhibit a color change from colorless *via* blue to red, which had already been observed in the solid state and in multilayers[5a]. The lecithin analogue *(2)* turns red without going through the blue intermediate. The absorption spectra of the polymer vesicles are qualitatively identical to those of the polymer monolayers[5b] (Fig. 2).

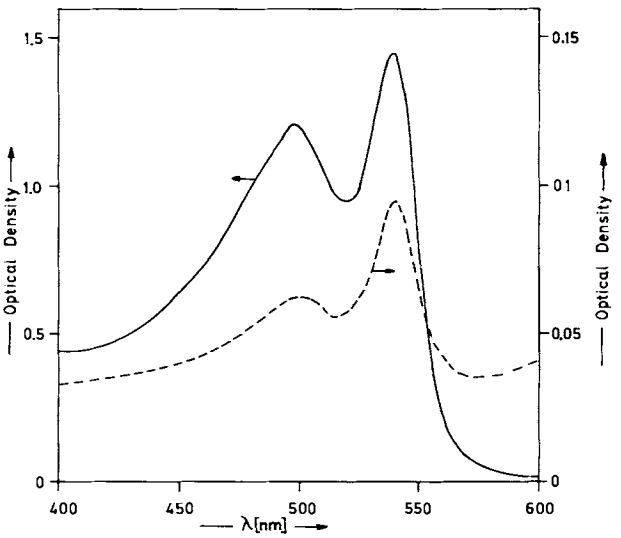
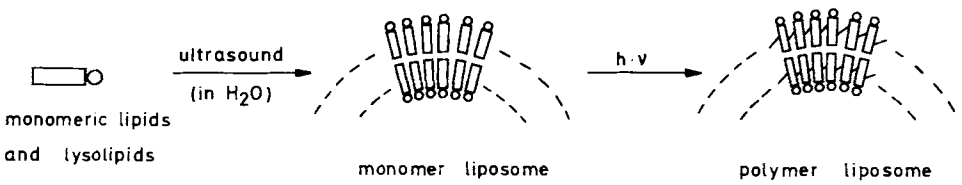


Fig. 2. UV spectrum of *(1b)* polymer liposomes after 15 min of UV irradiation (multichromatic light) (——), $c = 0.5$ mg ml^{-1}; reference spectrum of a polymer monolayer of *(1b)* after 60 min of irradiation [4b] (– – – –).

It can be shown by electron microscopy that the shape of the monomer vesicles is retained during the polymerization. Obviously a topochemical polymerization of diacetylenes is even possible in spherical liposomes. As far as we know, this is the first example of a transformation of defined monomer into defined polymer vesicles under complete retention of the orientation of the monomers and the structure of the vesicles (Scheme 1).

The polymeric character of these vesicles is also documented by their enhanced stability. In contrast to their monomeric analogues, aqueous dispersions of the polymeric liposomes are completely stable. Moreover, they cannot be destroyed by organic solvents: the dilution of a vesicle dispersion with 50% of ethanol does not lead to a precipitation. The spherical structure remains unchanged. A precipitation can be achieved by the addition of salts (KCl), but again it



Scheme 1. Formation of polymer liposomes from polymerizable lipid analogues.

has to be pointed out that the liposomes are not destroyed by the osmotic shock. Electron miscoscopy proved that the precipitate consisted of spherical vesicles.

In addition, the possibility of obtaining scanning electron micrographs of the polymer liposomes (Fig. 3) also hints at their great stability. In contrast, the monomer vesicles are destroyed during sample preparation.

These stable lipid bilayer vesicles could be of use as models for the study of cell-cell interactions or as carriers for biologically active substances. Preliminary experiments have already shown that mixed membranes consisting of polymerizable and natural lipids and proteins, respectively, can be realized at the gas-water interface. These mixed systems are of special interest for the investigation of interactions with natural cell systems. Synthetic lipids with different polymerizable groups[6] (vinyl and butadiene derivatives) can also be used for these experiments instead of the excessively rigid polydiacetylenes.

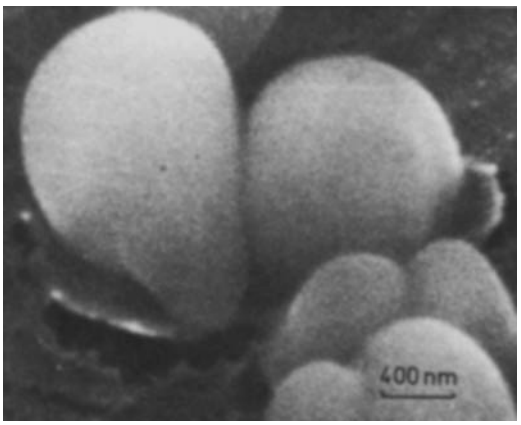


Fig. 3. Scanning electron micrograph of large, multilamellar *(1b)* polymer vesicles. ISI-40 scanning electron microscope, acceleration voltage 15 kV.

Experimental[7]

(4c): (4b)[3d] (10 mmol) is added to $POCl_3$ (15 mmol) dissolved in anhydrous CCl_4 (25 ml). After standing stoppered overnight the mixture is refluxed for 6 h. The solvent and excess $POCl_3$ are evaporated *in vacuo*, and the residue is heated with water (50 ml) for 30 min. The mixture is extracted with ether and the product recrystallized.

(1a): (4a)[3d] is reacted with oxalyl chloride to obtain the acid chloride[8]. The acid chloride (10 mmol) dissolved in anhydrous chloroform (10 ml) are added dropwise at 0 °C to a mixture of tetraethyleneglycol (5 mmol) and anhydrous pyridine (15 mmol) dissolved in anhydrous chloroform (20 ml). The mixture is stirred overnight at room temperature and worked up with ether.

(1b): (1d) is obtained from *N*-methyliminodiethanol and the acid chloride of *(4a)* as described for *(1a)*. *(1d)* is quaternized with CH_3Br in anhydrous acetone at 0 °C.

(1c): A mixture of the acid chloride of *(4a)* and *N,N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid in anhydrous chloroform/pyridine is refluxed overnight. *(1c)* crystallizes on chilling.

(2): 1,2-Bis(10,12-hexacosadiynoyl)glycerol, m.p. 65—66 °C (from light petroleum), was obtained using a general procedure described in ref. [9]. This product was acylated with β-bromoethylphosphoric dichloride according to *Eibl et al.*[10], hydrolyzed, and reacted with $N(CH_3)_3$ and Ag_2CO_3.

(3): 2-(10,12-Hexacosadiynoyl)-3-stearoylglycerol iodohydrin, m.p. 34—36 °C (ether/methanol), was obtained by stepwise acylation of racemic glycerol iodohydrin[11]. This product is phosphorylated with silver di-*tert*-butyl phosphate[12]. The *tert*-butyl protecting groups are removed by gaseous HCl in anhydrous $CHCl_3$[12].

Received: July 23, 1980 [Z 614 IE]
German version: Angew. Chem. *92*, 962 (1980)

CAS Registry numbers:
(1a), 75495-20-4; *(1b)*, 75495-21-5; *(1c)*, 75495-22-6; *(1d)*, 73510-24-4; *(2)*, 75495-23-7; *(3)*, 75495-24-8; *(4a)*, 73510-21-1; *(4a)* acid choride, 75495-25-9; *(4b)*, 75495-26-0; *(4c)*, 75495-27-1; tetraethyleneglycol, 112-60-7; *N*-methyliminodiethanol, 105-59-9; *N,N*-bis(z-hydroxyethyl)-2-aminoethanesulfonic acid, 10191-18-1; 1,2-bis(hexacosa-10,12-diynoyl)glycerol, 75495-28-2; 3-bromethylphosphoric dichloride, 4167-02-6; 2-(hexacosa-10,12-diynoyl)-3-stearoylglycerol iodohydrin, 75506-21-7; silver di-*tert*-butyl phosphate, 18281-42-0

[1] *H. T. Tien:* Bilayer Lipid Membranes. Marcel Dekker, New York 1974; *A. D. Bangham, M. W. Hill, N. G. Hill,* Methods Membr. Biol. *11*, 38 (1974).
[2] a) *J. M. Gebicki, M. Hicks,* Chem. Phys. Lipids *16*, 142 (1976); *W. R. Hargreaves, D. W. Daemer,* Biochemistry *17*, 3759 (1978); b) *M. K. Jain, C. J. A. van Echteld, F. Ramirez, J. de Gier, G. H. de Haas, L. L. M. van Deenen,* Nature *284*, 486 (1980); c) *T. Kunitake,* J. Macromol. Sci.-Chem. *A 13*, 587 (1979); *J. H. Fendler,* Acc. Chem. Res. *13*, 7 (1980); *K. Deguchi, J. Mino,* J. Colloid Interface Sci. *65*, 155 (1978); *R. A. Mortara, F. H. Quina, H. Chaimovich,* Biochem. Biophys. Res. Commun. *81*, 1080 (1978); d) *Y. Okahata, T. Kunitake,* J. Am. Chem. Soc. *101*, 5231 (1979); *E. Baumgartner, J.-H. Fuhrhop,* Angew. Chem. *92*, 564 (1980); Angew. Chem. Int. Ed. Engl. *19*, 550 (1980).
[3] a) *G. Wegner,* Makromol. Chem. *154*, 35 (1972); *R. H. Baughman,* Contemp. Top. Polym. Sci. *2*, 205 (1977); b) *D. Day, H. Ringsdorf,* J. Polym. Sci. Polym. Lett. Ed. *16*, 205 (1978); c) *B. Tieke, G. Lieser, G. Wegner,* J. Polym. Sci. Polym. Chem. Ed. *17*, 1631 (1979); d) *B. Tieke, G. Wegner, D. Naegele, H. Ringsdorf,* Angew. Chem. *88*, 805 (1976); Angew. Chem. Int. Ed. Engl. *15*, 764 (1976); e) *D. Naegele, H. Ringsdorf,* J. Polym. Sci. Polym. Chem. Ed. *15*, 2821 (1977).
[4] a) *D. Day, H.-H. Hub, H. Ringsdorf,* Isr. J. Chem. *18*, 325 (1979); b) *H.-H. Hub, B. Hupfer, H. Ringsdorf,* Am. Chem. Soc., Org. Coatings Plastics Chem. Div. Prepr. *42*, 2 (1980); c) *H. Koch,* Diploma thesis, Universität Mainz 1980; *B. Hupfer,* Ph. D. thesis, Universität Mainz, scheduled for 1981.
[5] a) *G. N. Patel, J. D. Witt, Y. P. Khanna,* J. Polym. Sci. Polym. Phys. Ed. *18*, 1383 (1980); b) *D. R. Day, H. Ringsdorf,* Makromol. Chem. *180*, 1059 (1979).
[6] *K. Dorn, H. Schupp,* Ph. D. thesis, Universität Mainz, scheduled for 1981.
[7] All reactions were carried out with exclusion of moisture. All new compounds yielded correct elemental analyses, as well as appropriate IR, ^{1}H- and ^{13}C-NMR, and FD mass spectra.
[8] *F. H. Matson, R. A. Volpenheim,* J. Lipid Res. *3*, 281 (1962).
[9] *F. R. Pfeiffer, C. K. Miao, J. A. Weisbach,* J. Org. Chem. *35*, 221 (1970).
[10] *H. Eibl, D. Arnold, H. U. Weltzien, O. Westphal,* Justus Liebigs Ann. Chem. *709*, 226 (1967).
[11] *G. H. de Haas, L. L. M. van Deenen,* Rec. Trav. Chim. Pays-Bas *80*, 951 (1961).
[12] *P. P. M. Bonsen, G. H. de Haas,* Chem. Phys. Lipids *1*, 100 (1967).

Conversion of an Iodomethyl(phosphane)- into a Methylenephosphorane-Complex: Example of a Nucleophile-Catalyzed Isomerization Reaction[1]

By *Rainer Feser* and *Helmut Werner*[*]

Dedicated to Professor Fritz Seel on the occasion of his 65th birthday

The pronounced Lewis-base behavior of $C_5H_5Rh(PMe_3)_2$ *(1)* can be exploited for the synthesis of cationic hydrido-, alkyl-, and halo-complexes of the type $[C_5H_5RhR(PMe_3)_2]^+$ (R = H, Me, Et, MeCO, PhCO, Cl, I, *etc.*)[2]. We have now also attempted the preparation of a cationic iodomethyl complex. Such a compound containing a carbenoid ligand should be readily convertible into cations of the type $[C_5H_5Rh(CH_2L)(PMe_3)_2]^{2+}$ (L = PR_3, NR_3) and $[C_5H_5Rh(CH_2X)(PMe_3)_2]^+$ (X = halogen, OCH_3, *etc.*). Ylide complexes were hitherto prepared either by reaction of a

[*] Prof. Dr. H. Werner, Dipl.-Chem. R. Feser
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

suitable substrate with a free ylide[3] or of a methylene complex with a nucleophile[4].

The synthesis of the iodomethylbis(phosphane)-complex *(2)* was accomplished by the rapid, smooth reaction of *(1)* with diiodomethane.

$$C_5H_5Rh(PMe_3)_2 + CH_2I_2 \rightarrow [C_5H_5Rh(CH_2I)(PMe_3)_2]I$$
(1) *(2)*

The product is a colorless solid which is moderately soluble in polar organic solvents. *(2)* is stable for several days in CH_3NO_2 and CH_3OH, whereas in dimethyl sulfoxide a rapid reaction takes place, giving $[C_5H_5RhI(PMe_3)_2]I$.

The lability of the carbon-iodine bond in *(2)* is confirmed by the reactions with various nucleophiles. Reaction with trimethylphosphane in nitromethane at room temperature leads after 30 h to almost quantitative formation of the dicationic methylenephosphorane complex $[C_5H_5Rh(CH_2PMe_3)(PMe_3)_2]^{2+}$:

$$(2) + PMe_3 \rightarrow [C_5H_5Rh(CH_2PMe_3)(PMe_3)_2]I_2$$
(3)

No reaction is observed with triphenylphosphane under the same conditions. With triethylamine the nitrogen-ylide complex corresponding to *(3)* is not formed, but surprisingly the compound *(4)* isomeric with *(2)*.

$$(2) \xrightarrow{(NEt_3)} [C_5H_5Rh(CH_2PMe_3)(PMe_3)I]I$$
(4)

The anion is apparently of no significance for this conversion: The complex $[C_5H_5Rh(CH_2I)(PMe_3)_2]BF_4$, obtained from *(2)* and $[CPh_3]BF_4$, likewise reacts smoothly with NEt_3, to give the ylide complex $[C_5H_5Rh(CH_2PMe_3)(PMe_3)I]BF_4$.

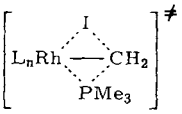
That not only neutral, but also anionic nucleophiles catalyze the isomerization *(2)*→*(4)*, is shown by the reaction of *(2)* with NaOMe in methanol. Instead of the expected product $[C_5H_5Rh(CH_2OMe)(PMe_3)_2]I$ (which is readily accessible *via* another route[5]), *(4)* is formed quantitatively. With the weaker base SMe^- a mixture of $[C_5H_5Rh(CH_2SMe)(PMe_3)_2]I$ *(5)* and $[C_5H_5Rh(SMe)(CH_2PMe_3)PMe_3]I$ *(6)* is formed; the latter mentioned compound is—as shown in an independent experiment—the product of a rapid secondary reaction of *(4)* with NaSMe.

The synthesis of the methylenephosphorane-metal complex from a phosphane-metal complex and dihalomethane is not new. Thus the reaction of $Co(PMe_3)_4$ with CH_2Cl_2 leads to $(Me_3PCH_2)_2CoCl_2$[6], and that of $Pt(PPh_3)_4$ with CH_2ClI to *cis*-$[(Ph_3P)_2Pt(CH_2PPh_3)Cl]I$[7]. As an important step in their one-pot synthesis of $(Me_3PCH_2)_2CoCl_2$, *Klein* and *Hammer*[6] postulated the formation of a halomethyl(phosphane)-complex which reacts very rapidly *via* $[Co(CH_2PMe_3)(PMe_3)_3Cl]$ as a further non-isolated intermediate to give the product.

Our investigations demonstrate for the first time the sequence

$$[L_nM(CH_2X)(PMe_3)]^+ \rightarrow [L_nM(CH_2PMe_3)X]^+$$

A remarkable feature of the conversion *(2)*→*(4)* is the migration of one of the two trimethylphosphane groups from rhodium to the carbon of the carbenoid ligand. In no case have we previously been able to demonstrate the dissociation of a Rh—PMe_3 bond in reactions of the cations $[C_5H_5RhR(PMe_3)_2]^+$ (R = H, Me, MeCO, *etc.*) either with nucleophiles or with electrophiles[2,5]. The possibility thus arises that the isomerization *(2)*→*(4)* proceeds intramolecularly, and formation of a four-center transition state



(with participatation of the catalyst) would be plausible.

Table 1. ^1H- and ^{31}P-NMR data of *(2)*—*(6)*, in CD_3NO_2 [δ values, TMS int. (^1H) and 85% H_3PO_4 ext. (^{31}P); J in Hz].

Complex	C_5H_5	$RhPMe_3$	CH_2	$CPMe_3$	SMe	$RhPMe_3$	$CPMe_3$
(2)	5.67 d × t J_{RhH} = 0.4, J_{PH} = 1.2	1.75 d × vt J_{RhH} = 0.9	3.13 d × t J_{RhH} = 3.5, J_{PH} = 5.3				
(3)	5.90 t J_{PH} = 1.1	1.73 d × vt J_{RhH} = 0.8	1.10 d × d × t J_{RhH} = 2.0, $^2J_{PH}$ = 12.0, $^3J_{PH}$ = 4.8	1.90 d J_{PH} = 13.2		5.9 d × d J_{RhH} = 129.5, J_{PP} = 7.4	36.5 d × t J_{RhP} = 4.5, J_{PP} = 7.4
(4)	5.63 d × d J_{RhH} = 0.4, J_{PH} = 1.5	1.80 d × d J_{RhH} = 0.8, J_{PH} = 11.2	[a]	1.90 d J_{PH} = 13.2		9.6 d × d J_{RhP} = 132.5, J_{PP} = 10.4	38.5 d × d J = 6.0, J' = 10.4 [b]
(5)	5.63 d × t J_{RhH} = 0.4, J_{PH} = 1.2	1.72 d × vt J_{RhH} = 1.0	2.37 d × t J_{RhH} = 2.4, J_{PH} = 5.0		2.13 s		
(6)	5.47 d J_{PH} = 1.6	1.60 d × d J_{RhH} = 0.8, J_{PH} = 11.2	[a]	1.80 d J_{PH} = 13.2	1.92 d × d J_{RhH} = 1.6, J_{PH} = 0.5	15.3 d × d J_{RhP} = 140.6, J_{PP} = 8.5	34.5 "t" $J_{RhP} \approx J_{PP}$ = 8.5

[a] The signal for the CH_2 protons disappears owing to several couplings in the background noise. [b] Assignment of coupling constants to J_{RhP} and J_{PP} is not possible.

Received: June 9, 1980 [Z 615 IE]
German version: Angew. Chem. *92*, 960 (1980)

CAS Registry numbers:
(1), 69178-15-0; *(2)*, 75522-37-1; *(3)*, 75522-38-2; *(4)*, 75522-39-3; *(5)*, 75522-40-6; *(6)*, 75522-41-7; $[C_5H_5Rh(CH_2OMe)(PMe_3)_2]I$, 75522-42-8; CH_2I_2, 75-11-6

[1] Basic Metals, Part 25. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by gifts of chemical from BASF AG, Ludwigshafen, and DEGUSSA, Hanau. We thank *A. Höhn* for valuable assistence with the experiments.—Part 24: *H. Werner, B. Juthani*, Z. Anorg. Allg. Chem., in press.
[2] *H. Werner, R. Feser, W. Buchner*, Chem. Ber. *112*, 834 (1979).
[3] *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1976).
[4] *W. K. Wong, W. Tam, J. A. Gladysz*, J. Am. Chem. Soc. *101*, 5440 (1979); and references cited therein.
[5] *R. Feser*, unpublished.
[6] *H. F. Klein, R. Hammer*, Angew. Chem. *88*, 61 (1976); Angew. Chem. Int. Ed. Engl. *15*, 42 (1976).
[7] *J. R. Moss, J. C. Spiers*, J. Organomet. Chem. *182*, C20 (1979).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1111-0941 $02.50/0*

Tris(fluorosulfonyl)methane, $HC(SO_2F)_3$[**]

By *Gerhard Klöter, Hans Pritzkow,* and *Konrad Seppelt*[*]

Dedicated to Professor Fritz Seel on the occasion of his 65th birthday

In the course of a search for simple hydrocarbon derivatives bearing electronegative substituents we succeeded in preparing the title compound. Thus acetanilide reacts in oleum to form a species that can be precipitated as $HC(SO_3^-K^+)_3 \cdot H_2O$[1] on addition of potassium carbonate. The sulfonic acid $HC(SO_3H)_3$ can be liberated *via* the barium salt, and converted into the sulfonyl fluoride *(1)* by treatment with sulfur tetrafluoride.

$$H_3C{-}CO{-}NHPh \xrightarrow[2)\ K_2CO_3]{1)\ SO_3/H_2SO_4} HC(SO_3^-K^+)_3 \xrightarrow{Ba^{2+}}$$

$$HC(SO_3^-Ba^{+}_{1/2})_3 \xrightarrow{H_2SO_4} HC(SO_3H)_3 \xrightarrow{SF_4} HC(SO_2F)_3 \qquad (1)$$

The new compound *(1)* is a colorless, evil-smelling, crystalline solid (m.p. 44.5—45.5 °C, subl. 25 °C/10^{-2} mbar) with a considerable vapor pressure. Its structure is derived from its NMR spectra (^{1}H: quartet, $\delta = 6.85$; ^{19}F: doublet, $\delta = 67.6$, $J_{HF} = 1.8$ Hz).

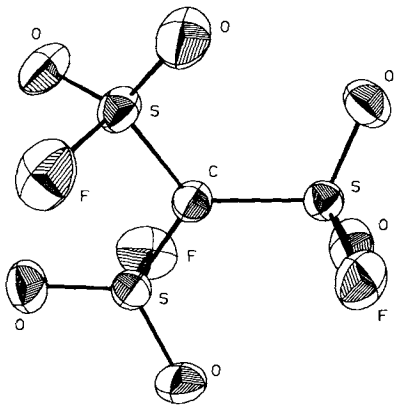


Fig. 1. Structure of the anion $C(SO_2F)_3^-$ in crystals of the salts with K^+ and Rb^+. The CS_3 skeleton is planar, the C—S distances (1.70 Å) indicate double bonding components. K salt: $P2_1/c$, $a = 7.899(1)$, $b = 11.729(2)$, $c = 18.557(3)$ Å, $\beta = 92.48(2)°$, $V = 1717.54$ Å^3, $Z = 8$, $\rho_{calc} = 2.323$, $\rho_{exp} = 2.32$ g/cm^3; 4637 reflections, $R = 0.039$. Rb salt: $R\bar{3}$, $a = 7.910(2)$, $c = 25.825(5)$ Å, $V = 1399.34$ Å^3, $Z = 3$; 557 reflections, $R = 0.043$.

The most striking property of *(1)* is its extreme acid character. Combination of this highly hygroscopic compound with water is extremely exothermic, with no hydrolysis of a fluorosulfonyl group being observed in a short period of time; after several weeks' standing a hydrate $HC(SO_2F)_2SO_3H \cdot nH_2O$ can be isolated. The aqueous solution of *(1)* proves to be a strong monobasic acid on titration with caustic alkali. Raman spectra of the equilibria

$$HC(SO_3F)_3 + K^+SO_3F^- \rightleftharpoons K^+C(SO_2F)_3^- + HSO_3F$$
$$HC(SO_3F)_3 + K^+NO_3^- \rightleftharpoons K^+C(SO_2F)_3^- + HNO_3$$

showed the acid strength to lie between the values for fluorosulfuric acid and nitric acid[2]. This remarkable finding is probably due to the mesomeric distribution of the negative charge in the anion.

Salts with K^+, Rb^+, and Cs^+ as counterions crystallize from water in order of decreasing solubility. Crystal structure analysis shows the CS_3 skeleton to be planar.

In order to determine the electronegativity of the $-C(SO_2F)_3$ group we prepared the methyl compound *(2)* (m.p. 145—146 °C, subl. −20 °C/10^{-2} mbar):

$$Ag^+C(SO_2F)_3^- + CH_3I \rightarrow AgI + CH_3{-}C(SO_2F)_3 \qquad (2)$$

The chemical shift of the methyl protons ($\delta = 3.125$) can be correlated with the electronegativity of the ligands[3], yielding a value of *ca.* 3.2.

The halogen derivatives $XC(SO_2)F_3$ were also synthesized:

$$HC(SO_2F)_3 \xrightarrow[CF_2Cl_2,\ -10\,°C]{XeF_2} Xe + HF + FC(SO_2F)_3 \qquad (3a)$$

$$Ag^+C(SO_2F)_3^- \xrightarrow[CH_2Cl_2]{X_2} AgX + C(SO_2F)_3$$

(3b), X = Cl
(3c), X = Br
(3d), X = I

The fluorine compound *(3a)* is a stable colorless liquid (b.p. 117—118 °C, m.p. −25.5 to −26.5 °C). No evidence for the existence of a compound containing a $Xe{-}C(SO_2F)_3$ link was obtained during the formation of *(3a)*. The chlorine and bromine compounds are colorless, evil-smelling solids [*(3b)*: m.p. 127—129 °C, subl. −20 °C/10^{-2} mbar; *(3c)*: m.p. 164 °C, subl. 0 °C/10^{-2} mbar]. Even the chlorine compound reacts with aqueous KI solution according to

$$(3b) + 2I^- \rightarrow C(SO_3F)_3^- + Cl^- + I_2$$

indicating the presence of a partial positive charge on chlorine. The yellow iodine compound [*(3d)*: m.p. 207—210 °C, subl. 35 °C/10^{-2} mbar] is unstable towards radiation; however, neither the $^{\bullet}C(SO_2F)_3$ radical nor its dimer could be detected during its decomposition.

All compounds were identified by complete elemental analysis and spectroscopic data (MS, IR, and Raman, ^{1}H and ^{19}F-NMR).

Received: March 4, 1980 [Z 616 IE]
German version: Angew. Chem. 92, 954 (1980)

[*] Prof. Dr. K. Seppelt [+], Dipl.-Chem. G. Klöter, Dr. H. Pritzkow
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[+] To whom correspondence should be directed. Present address: Institut für Anorganische und Analytische Chemie der Freien Universität, Fabeckstrasse 34—36, D-1000 Berlin 33 (Germany).

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *H. J. Backer*, Recl. Trav. Chim. Pays-Bas *49*, 1107 (1930); cf. crystal structure analysis: *J. R. Hall, R. A. Johnson, C. H. L. Kennard, G. Smith*, J. Chem. Soc. Dalton Trans. *1980*, 149.

[2] Attempted quantitative determination of the acid strength of *(1)* in glacial acetic acid by ^{1}H-NMR measurements according to *B. U. Rode, A. Engelbrecht, J. Schantl* [Z. Phys. Chem. (Leipzig) *253*, 17 (1972)] gave a value many orders of magnitude greater than that for HSO_3F. We therefore conclude that the method is unsuitable for such highly mesomeric systems.

[3] *A. L. Allred, E. G. Rochow*, J. Inorg. Nucl. Chem. *5*, 269 (1958); *J. Gasteiger*, Nachr. Chem. Tech. Lab. *28*, 17 (1980); *J. Gasteiger, M. Marsili*, unpublished; *K. Seppelt*, Z. Anorg. Allg. Chem., in press.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1111-0942 $02.50/0

N-(Amidosulfonyl)hydroxylamine, H_2NSO_2NHOH[**]

By *Michael Boldhaus, Klaus Brink,* and *Claus Bliefert*[*]

Dedicated to Professor Fritz Seel on the occasion of his 65th birthday

While two amides of hydrazinesulfonic acid have already been described[1], not one unsubstituted amide of any of the five different hydroxylaminesulfonic acids has as yet been reported in the literature. Only two derivatives of the amide of hydroxylamine-*N*-sulfonic acid are known, namely $H_2N—SO_2—NHOCH_3$[2a] and $(CH_3)_2N—SO_2—NHOH$[2b].

Reaction of amidosulfonyl fluoride with hydroxylamine in ethanol leads to formation of *N*-(amidosulfonyl)hydroxylamine *(1)* (hydroxysulfamide).

$$H_2N—SO_2—F + 2\,H_2NOH \rightarrow H_2N—SO_2—NHOH + [H_3NOH]F$$
(1)

(1) is a colorless crystalline solid (m.p. 86—87 °C) which can be isolated in pure form only in small yields (*ca.* 2%). The new compound was identified by elemental analysis, molecular weight determination and spectroscopic data. Under normal conditions it is stable and non-hygroscopic. Its aqueous solutions react neutral. *(1)* is readily soluble in water and dimethyl sulfoxide, moderately soluble in methanol and ethanol, and only sparingly soluble in ether. Alkaline hydrolysis leads, as in the case of other sulfohydroxamic acids $R—SO_2—NHOH$[3] to monomeric hyponitrous acid (detection as $K_2[Ni(CN)_3NO]$[4]).

$$(1) \xrightarrow[-H_2O]{+2OH^-} SO_3^{2-} + NH_3 + HNO \rightarrow \tfrac{1}{2}(N_2O + H_2O)$$

Procedure

Amidosulfonyl fluoride (33.7 g, 0.34 mol) is added dropwise within 1 h to a stirred solution of hydroxylamine (45 g, 1.36 mol) in ethanol (750 ml) such that the temperature in the reaction vessel does not exceed 0 °C. The alcoholic solution, and thus large amounts of ethyl amidosulfonate that are formed, is decanted off. The remaining cloudy oil (*ca.* 80 g) is taken up in anhydrous sodium sulfate (120 g) and extracted with ether for 3 d in a Soxhlet apparatus. An oil (*ca.* 4 g) free of hydroxylammonium fluoride is obtained, from which *(1)* can be isolated as a colorless viscous liquid by renewed extraction with ethanol. *(1)* crystallizes out (0.8 g) after several days at room temperature.

IR (cm^{-1}, rel. int.): 3350 (vs, sh), 3200 (vs, br), 2840 (m, sh), 1615 (w), 1540 (m), 1370 (vs, sh), 1340 (vs), 1170 (vs), 985 (w), 905 (w), 710 (m, br), 570 (m), 530 (w) (KBr disk).

MS (*m/e*, rel. int.): 96 (5), 82 (5), 81 (10), 80 (100), 65 (43), 64 (66), 63 (7), 49 (4), 48 (51), 47 (8), 46 (24), 33 (74), 32 (48), 31 (19), 30 (63), 28 (26), 18 (81), 17 (57), 16 (20) (70 eV, 50 °C).

Received: December 13, 1979 [Z 617 IE]
German version: Angew. Chem. 92, 957 (1980)

CAS Registry numbers:
(1), 27596-79-8; hydroxylamine 7803-49-8; amidosulfonyl fluoride 14986-54-0; hydroxylammonium fluoride 17256-78-9

[*] Prof. Dr. C. Bliefert, Ing. (grad.) M. Boldhaus, Ing. (grad.) K. Brink
Fachbereich Chemieingenieurwesen der Fachhochschule Münster
Postfach 1220, D-4430 Steinfurt 1 (Germany)

[**] Amides of Hydroxylaminesulfonic Acids, Part 2. We thank Hoechst AG, Frankfurt for supplying the chlorosulfonyl isocyanate.—Part 1: [2b].

[1] *R. Appel, G. Berger,* Chem. Ber. *91*, 1339 (1958); *R. Appel, W. Senkpiel, ibid. 92*, 1102 (1959).

[2] a) *R. Ohme, H. Preuschhof,* Justus Liebigs Ann. Chem. *713*, 74 (1968); b) *J. Oettle, K. Brink, G. Morawietz, M. Backhaus, M. Boldhaus, C. Bliefert,* Z. Naturforsch. *B 33*, 1193 (1978).

[3] Cf. *e.g. K. Brink, W. Gombler, C. Bliefert,* Z. Anorg. Allg. Chem. *429*, 255 (1977); *U. Hermann, M. Yaktapour, C. Bliefert,* Z. Naturforsch. *B 33*, 574 (1978).

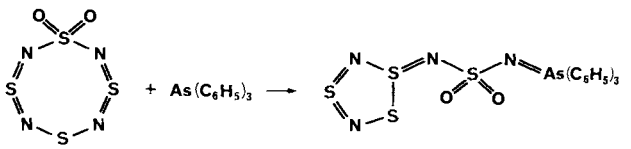
[4] *R. Nast, E. Proeschel,* Z. Anorg. Allg. Chem. *256*, 160 (1948).

(8→5) Contraction of the Eight-Membered Ring of $S_4N_4O_2$[**]

By *Herbert W. Roesky, Michael Witt, William Clegg, Wilhelm Isenberg, Mathias Noltemeyer,* and *George M. Sheldrick*[*]

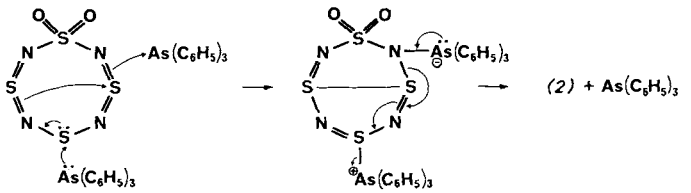
Dedicated to Professor Fritz Seel on the occasion of his 65th birthday

Degradation reactions of sulfur-nitrogen rings generally proceed in unclear fashion and sometime nonstoichiometrically[1]. We have now found that the reaction of $S_4N_4O_2$ *(1)*[2] with triphenylarsane affords the asymmetrically substituted sulfamide *(2)*.



(1) *(2)*

It was known[3] from mechanistic studies that nucleophilic reagents attack *(1)* at the S-5 atom located opposite the SO_2. The increase in electron density leads to formation of a central sulfur-sulfur bond between S-3 and S-7. Degradation of *(1)* would therefore appear to proceed *via* a transition state involving two molecules of triphenylarsane.



The molecular structure of *(2)* was determined by X-ray diffraction analysis of a single crystal[4] (Fig. 1). The five-membered ring in *(2)* is comparable with the rings in $S_3N_2{=}N—SO_2F$[5] and $S_3N_2{=}N—P_3N_3F_5$[6].

Triphenylarsoranediylaminosulfonylimino-1λ⁴,2,4λ⁴,3,5-trithiadiazole *(2)* cannot be sublimed without decomposition. The mass spectrum contains $(C_6H_5)_3AsS$, $m/e = 338$, as the highest fragment.

Procedure

A solution of $AsPh_3$ (7.6 g, 25 mmol) in benzene (50 ml) is added dropwise to *(1)* (5.4 g, 25 mmol) in benzene (100 ml).

[*] Prof. Dr. H. W. Roesky, Dipl.-Chem. M. Witt
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. G. M. Sheldrick, Dr. W. Clegg, Dipl.-Chem. W. Isenberg, Dr. M. Noltemeyer
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and Hoechst AG, Frankfurt am Main.

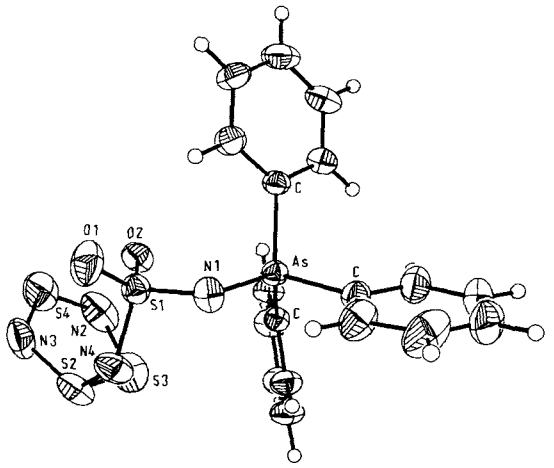


Fig. 1. Structure of the molecule of *(2)* in the crystal; vibrational ellipsoids of the atoms (except H) correspond to 50% probability. Bond lengths and angles: S2—N3 1.659(3), N3—S4 1.571(3), S4—N2 1.548(4), N2—S3 1.610(3), S3—S2 2.230(1), S2—N4 1.544(2), N4—S1 1.671(3), S1—N1 1.572(2), N1—As 1.760(2), As—C (average value) 1.915, S1—O (average value) 1.440 Å; S1—N1—As 117.2(1), S1—N4—S2 124.8(2)°.

The reaction mixture is briefly heated to boiling. After cooling, the precipitate is filtered off, dried, and extracted with acetonitrile. Blood-red crystals of *(2)*, m.p. 119—120 °C (dec.), precipitate from the extract. Yield before extraction 10.9 g (84%).

Received: March 5, 1980 [Z 618 IE]
German version: Angew. Chem. 92, 959 (1980)

[1] *H. W. Roesky, M. Witt, M. Diehl, J. W. Bats, H. Fuess*, Chem. Ber. *112*, 1372 (1979); *H. W. Roesky, M. Witt, J. W. Bats, H. Fuess*, Z. Anorg. Allg. Chem. *458*, 225 (1979).
[2] *H. W. Roesky, W. Schaper, O. Petersen, T. Müller*, Chem. Ber. *110*, 2695 (1977).
[3] *H. W. Roesky, M. Witt, B. Krebs, H. J. Korte*, Angew. Chem. *91*, 444 (1979); Angew. Chem. Int. Ed. Engl. *18*, 415 (1979).
[4] Space group $P2_1/n$, $a = 11.376(3)$, $b = 15.045(5)$, $c = 12.497(4)$ Å, $\beta = 100.81(3)$, $Z = 4$; four-circle diffractometer data, $R = 3.4\%$.
[5] *B. Krebs, G. Henkel, S. Pohl, H. W. Roesky*, Chem. Ber. *113*, 226 (1980).
[6] *A. Gieren, B. Dederer, H. W. Roesky, E. Janssen*, Angew. Chem. *88*, 853 (1976); Angew. Chem. Int. Ed. Engl. *15*, 783 (1976).

The Pentafluoropyridine Cation $C_5F_5N^+$ [**]

By *Klaus Züchner, Thomas J. Richardson, Oskar Glemser,* and *Neil Bartlett*[*]

Dedicated to Professor Fritz Seel on the occasion of his 65th birthday

Salts of the hexafluorobenzene cation $C_6F_6^+$ were obtained by one-electron oxidation of C_6F_6 with $O_2^+X^-$ ($X^- = AsF_6^-$, SbF_6^-, $Sb_2F_{11}^-$) in WF_6[1]. Although numerous aromatic radical cations had already been detected in solution by spectroscopic data, this constituted the first isolation of such a paramagnetic species. We have now also accomplished the oxidation of pentafluoropyridine, as the first heterocycle, with $O_2^+AsF_6^-$ in SO_2ClF as solvent and moderator:

$$C_5F_5N + O_2^+AsF_6^- \xrightarrow[-45\,^\circ C]{SO_2ClF} C_5F_5N^+AsF_6^- + O_2$$

The suspended product, which is deep blue in the moist state, is only slightly soluble in SO_2ClF. Its ESR spectrum in SO_2ClF shows a broad singlet at $g = 2.0032$. Removal of the solvent and unreacted C_5F_5N at $-22\,^\circ C$ leaves a pale blue powder. This decomposes at 0 °C to give a white crystalline substance whose physical properties, especially the Raman and mass spectrum, are due to a 1:1 mixture of the molecular adducts $C_5F_5N \cdot AsF_5$[2] and $C_5F_7N \cdot AsF_5$ (cf. Table 1)[3] in accord with the disproportionation

$$2C_5F_5N^+AsF_6^- \rightarrow C_5F_5N \cdot AsF_5 + C_5F_7N \cdot AsF_5$$

Table 1. Raman data [cm^{-1}] of C_5F_5N and its derivatives.

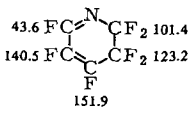
Mode [a]	C_5F_5N [a]	$C_5F_5N \cdot AsF_5$ [b]	$C_5F_5NH^+AsF_6^-$ [c]
C—F def.	174 w		
	224 w	225 w	219 (1)
	273 (2)	285 (1)	270 (1)
	310 (1)	304 (1)	
			349 (1)
	353 (6)	348 w	354 (1)
			370 (1) [d]
	428 (7)	409 (3)	410 (2)
Ring (?)	457 (7)	453 (4)	446 (3)
	476 (7)	490 (2)	478 (2)
			527 (1)
	593 (9)	596 (10)	593 (10)
	620 (3)	643 (2)	
		668 (6)	
	694 (5)	673 (1)	673 (3)
C—F def.	706 (3)	713 (3) [e]	
C—C twist	736 (2)	720 (2)	738 (3)
		754 (1) [f]	
Comb.	857 (1)		812 (3)
C—F str.	1154 (2)		
	1172 (5)		
Comb.	1243 (1)		1217 (1)
C—F str.	1285 (5)		1290 (1)
	1420 (5)		
Comb.	1473 (1)		
Ring str.	1492 (1)		
	1529 (4)		
	1650 (4)		
N—H str.			3002 (1)

[a] Assignment according to [5]; [b] solid-state spectrum; [c] produced by the method of *Chambers et al.* [6]; [d] $\nu_s(AsF_6^-)$; [e] $\nu(AsF^a)$; [f] $\nu(AsF^e)$.

The heterocyclic components can be liberated from the adduct mixture with acetonitrile:

$$C_5F_5N \cdot AsF_5 + C_5F_7N \cdot AsF_5 + 2CH_3CN \rightarrow C_5F_5N + C_5F_7N + 2CH_3CN \cdot AsF_5$$

The ^{19}F-NMR spectrum shows that C_5F_5N consists solely of heptafluoro-1-aza-1,3-cyclohexadiene[4] (δ values rel. to internal CCl_3F).



We rationalized the formation of the adduct of only the 1,3-diene C_5F_7N, and not that of the 1,4-diene, on thermoly-

[*] Prof. Dr. O. Glemser, Dr. K. Züchner
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)
Prof. Dr. N. Bartlett, Dr. T. J. Richardson
Department of Chemistry, University of California
Material and Molecular Research Division, Lawrence Berkeley Laboratory
Berkeley, Calif. 94720 (USA)

[**] This work was supported by the U. S. Department of Energy, Office of Basic Energy Sciences, *N. B.* gratefully acknowledges the award of a U. S. Senior Scientist Award by the Alexander von Humboldt Foundation. We are grateful to Prof. *R. D. Chambers* for supplying perfluoropyridine and Prof. *A. Weller* for help in recording the ESR spectrum.

sis of $C_5F_5N^+AsF_6^-$ in the following way: Since disproportionation occurs in the solid state and at relatively low temperature, only a slight activation energy will be required and the distribution of the molecules in the solid state will limit the possible reaction products. The first step is probably transfer of $F^\ominus$ from the anion to the cation, which is associated with a shift of the lone pair from the N to the As atoms:

$$C_5F_5N^\oplus AsF_6^\ominus \rightarrow C_5F_6N^\odot \cdot AsF_5$$

If this is valid, then the charge density values according to *Chambers et al.*[4a] would suggest that the $F^\ominus$ transferred to $C_5F_5N^\oplus$ is bonded to a carbon atom adjacent to the nitrogen atom. Redox reaction with the salt still present

$$C_5F_6N^\odot \cdot AsF_5 + C_5F_5N^\oplus AsF_6^\ominus \rightarrow C_5F_5N \cdot AsF_5 + C_5F_6N^\oplus AsF_6^\ominus$$

might be the next step.

The formation of C_5F_7N from $C_5F_6N^\oplus$ might similarly be initiated by a slight shift of $F^\ominus$ to $AsF_6^\ominus$, coupled with an acid/base interaction generating the $C_5F_7N \cdot AsF_5$ adduct.

Procedure

$O_2^+AsF_6^-$ (0.5 mol) is placed in a quartz- or Teflon FEP reaction vessel connected with a Monel vacuum apparatus. SO_2ClF (0.05 mol) and C_5F_5N (0.5 mol) are then condensed onto the solid at $-196\,^\circ C$. On warming to $-45\,^\circ C$, evolution of O_2 ensues. Decomposition of 1 mol of the salt at $-20\,^\circ C$ affords 0.5 mol of the original pentafluoropyridine and 0.5 mol of heptafluoro-1-aza-1,3-cyclohexadiene, both as AsF_5 adducts (1:1).

Received: July 14, 1980 [Z 619 IE]
German version: Angew. Chem. 92, 956 (1980)

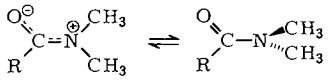
[1] *T. J. Richardson, N. Bartlett*, J. Chem. Soc. Chem. Commun. *1974*, 427.
[2] Pure $C_5F_5N \cdot AsF_5$ was produced by tensimetric titration of the components. Its Raman spectrum and its Debye-Scherrer diagram are identical with those of the disproportionation product after the more volatile $C_5F_7N \cdot AsF_5$ has been removed *in vacuo*.
[3] The reaction of $O_2^+Sb_2F_{11}^-$ with C_5F_5N gave a product resembling $C_5NF_5^+AsF_6^-$. In contrast to the corresponding $C_6F_5^+$-fluoroantimonate(v), however, the thermal stability is not greater than that of hexafluoroarsenate.
[4] a) *R. D. Chambers, D. T. Clark, T. F. Holmes, W. K. R. Musgrave, I. Ritchie*, J. Chem. Soc. Perkin Trans. I *1974*, 114; b) *I. J. Hotchkiss, R. Stephens, J. C. Tatlow*, J. Fluorine Chem. *10*, 541 (1977).
[5] *D. A. Long, R. T. Bailey*, Trans. Faraday Soc. *59*, 599 (1963).
[6] *S. L. Bell, R. D. Chambers, W. K. R. Musgrave, J. G. Thorpe*, J. Fluorine Chem. *1*, 51 (1971).

Influence of Ionic and Polar Solutes upon $\Delta G^\ddagger$ and $\Delta V^\ddagger$ of the Amide Rotation in Aqueous Solutions of Dimethylacetamide[**]

By *Gerhard Völkel, Johann Hauer*, and *Hans-Dietrich Lüdemann*[*]

Dedicated to Professor Ernst Ulrich Franck on the occasion of his 60th birthday

The free activation energy for the rotation of the dimethylamino group in dimethylamides is altered strongly by variation of the substituent at the carbonyl group. Smaller but significant effects on $\Delta G^\ddagger$ are caused by changes in the polarity of the solvent[1].



The pressure dependence of $\Delta G^\ddagger$, defined by the activation volume $\Delta V^\ddagger$

$$\left(\frac{\partial \Delta G^\ddagger}{\partial P}\right)_T = \Delta V^\ddagger$$

however does not reveal any systematic dependence on the carbonyl substituents (R = H, CH_3, C_6H_5) or the solvent polarity (CCl_4, C_6D_6, $(CD_3)_2CO$, $(CD_3)_2SO$, CD_3CN, CD_3OD)[2]. For all solvents and substituents studied hitherto the activation volume is found to $\Delta V^\ddagger \approx 10$ cm^3 mol^{-1}, the only exception being the dilute aqueous solution ($x_{D_2O} > 0.98$) of the dimethylamides. In these dilute solutions, the rotation of the dimethylamino group becomes almost pressure independent (*e.g.* dimethylacetamide in D_2O, $x_{D_2O} = 0.99$, $\Delta V^\ddagger = 0.3$ cm^3 mol^{-1})[3].

The preliminary explanation for this unexpected result is the formation of an open hydration shell around the dimethylamino group, permitting amide rotation to occur without significant rearrangements of the water molecules in the first hydration layer. This attempted explanation predicts that the addition of polar or ionic solutes to the aqueous solutions, which alters the water structure, should lead to a significant increase of the $\Delta V^\ddagger$ observed.

In the first experiments dimethylacetamide (5% w/w) in aqueous solutions of sodium bromide and urea was studied. The results are given in Figures 1 and 2. Relatively small

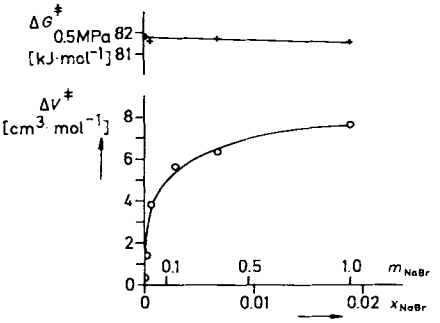


Fig. 1. $\Delta G^\ddagger$ and $\Delta V^\ddagger$ of the amide rotation in aqueous solutions of dimethylacetamide (DMA), $x_{DMA} = 0.012$ ($\approx 5\%$ w/w DMA), as function of the sodium bromide concentration. (In neat DMA, $\Delta V^\ddagger = 7.6$ cm^3 mol^{-1}.)

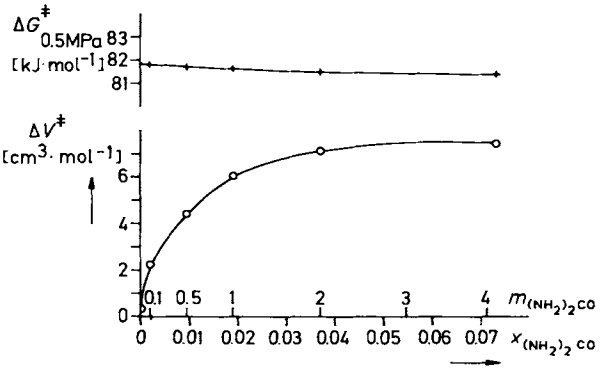


Fig. 2. $\Delta G^\ddagger$ and $\Delta V^\ddagger$ of the amide rotation in aqueous solutions of dimethylacetamide (DMA), $x_{DMA} = 0.012$ ($\approx 5\%$ w/w DMA), as function of the urea concentration. (In neat DMA, $\Delta V^\ddagger = 7.6$ cm^3 mol^{-1}.)

[*] Prof. Dr. H.-D. Lüdemann, Dr. G. Völkel, Dipl.-Phys. J. Hauer
Institut für Biophysik und Physikalische Biochemie der Universität
Universitätsstrasse 31, D-8400 Regensburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

concentrations of sodium bromide do increase ΔV^+ significantly. 5% w/w of dimethylacetamide dissolved in a 0.14 molal solution of NaBr yields an activation volume of $\Delta V^+ = 5.6$ cm^3 mol^{-1}, which is fairly close to the results found in the common solvents. It must be concluded that the average distribution of the water molecules in the immediate vicinity of the dimethylamino group is drastically altered, and that the unique features of the binary aqueous solutions are destroyed almost completely by addition of small amounts of ionic solutes. The changes in ΔV^+ caused by comparable amounts of urea are smaller than the effects observed with NaBr. This might be explained qualitatively by the different influence of the urea molecules, which are incorporated into the hydrogen bond network of water and thus cause only local disturbance of the average water structure, while the electric charges of the sodium and bromide ions will cause longer-range changes in the water structure.

Our results show that the hydrophobic solvation of the apolar moieties of the dissolved molecules is significantly influenced by relatively small additions of ions, and indicate that the determination of ΔV^+ for the rotation of the dimethylamino group is a sensitive probe for structural changes of the hydrate structure.

The steepest increase of ΔV^+ is found in sodium bromide solutions with an ion/DMA ratio smaller than 1:6. It is thus unlikely that the effects observed can be explained by a preferential solvation of the ions by the DMA molecules. This assumption is further corroborated by the variation of x_{DMA} at constant x_{NaBr}. At $x_{DMA} = 0.012$ and $x_{NaBr} = 0.0003$ a value of $\Delta V^+ = 3.8$ cm^3 mol^{-1} is found. ΔV^+ remains essentially unchanged on lowering the DMA concentration to $x_{DMA} = 0.0024$.

ΔG^+ (cf. Fig. 1 and 2) is not influenced by the addition of NaBr or urea. This shows that the determination of ΔV^+ by high pressure studies can yield information about solvent structure which could not be obtained from the ambient pressure activation parameters ΔG^+, ΔH^+, and ΔS^+.

Experimental

ΔV^+ was derived from the pressure dependence of the ^{1}H-NMR signals of the N—CH_3 groups between 0.1 and 150 MPa. The rate of rotation was determined by computer simulation of the exchange broadened spectra in the region of the coalescence temperature (T_c: 370—380 K). Observation frequency: 100.1 MHz. Details of the high pressure apparatus and the simulation procedure have been published previously[2, 3].

Received: December 4, 1979 [Z 620 IE]
German version: Angew. Chem. 92, 955 (1980)
Publication delayed at authors' request

[1] *L. M. Jackman* in *L. M. Jackman, F. A. Cotton:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975.
[2] *R. Rauchschwalbe, G. Völkel, E. Lang, H.-D. Lüdemann,* J. Chem. Res. (S) 448, (M) 5325 (1978).
[3] *G. Völkel, E. Lang, H.-D. Lüdemann,* Ber. Bunsenges. Phys. Chem. *83*, 722 (1979).

BOOK REVIEWS

Physical Chemistry of High Temperature Technology. By *E. T. Turkdogan.* Academic Press, New York 1980. xv, 447 pp., bound, $ 49.50.

The author of this book has been active in applied research in the steel industry for over 30 years and was also involved in some basic work through numerous investigations. Here he gives a comprehensive account of the fundamental relationships and ideas in the form in which they are of immediate use in applied research, *i. e.* in the solution of technical problems. Such books are rare, and are therefore particularly valuable, for in general there is a gap between fundamental monographs, usually too detailed and too specialized for the practical man, and literature devoted simply to technical processes. A discussion of learned points of dispute is generally of little practical value. The present book confines itself first to the presentation of the physicochemical principles essential for understanding the processes in the smelting of solid and liquid chalcogenides, carbonates, and silicates, after which, in the second part, it shows examples of their application (mainly in the field of ferrous metallurgy). To this extent, the phrase "high temperature technology" as used in the title is not as wide as it seems.

The thermodynamics of metals, alloys, oxides, and silicates take up much of the first part, and in addition transport phenomena in particular are treated very exhaustively. In the second part, an account of the interplay of reaction and transport phenomena forms the basis for a discussion of the kinetics of individual processes (*e.g.* calcination, the blast-furnace process, steel production). 900 references indicate original papers and compilations of data (not only American) giving further information. The book constitutes a welcome supplementation of *Darken* and *Gurry*'s monograph; it is an introduction into an industrially particularly important field of applied chemistry that goes beyond the elementary principles.

Lothar Riekert [NB 520 IE]

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar*, **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors Dr. *Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 19 · Number 12
December 1980
Pages 947–1034

1,5,-Electrocyclizations— An Important Principle of Heterocyclic Chemistry

By Rolf Huisgen[*]

Robert Burns Woodward—In Memoriam

The principle of orbital control of pericyclic reactions has deepened our understanding of reaction phenomena and provided an excellent classification of these one-step processes. The electrocyclic reaction of the *pentadienyl anion* ⇄ *cyclopentenyl anion* type is relatively unimportant in all-carbon systems and has not even been verified in the case of the parent compound. In the heterocyclic series, however, where up to five C-atoms of the pentadienyl anion are replaced by heteroatoms, a multitude of ring closures and ring openings find their ordering principle in the mentioned electrocyclic reaction. The replacement of the carbon atoms by heteroatoms can take place *isoionically, i.e.,* with retention of the anionic character, or *isoelectronically.* An isoelectronic replacement of CR_2 in position 1 by NR_2 or OR, and of CR in position 3 by NR or O leads to a charge-free resonance structure for the open-chain species; the migration of the charge during the electrocyclization results in a correlation with a cyclic zwitterion. Conversely, isoelectronic exchange of CR in position 2 by NR or O produces a conjugated 1,3-dipole, which cyclizes to a charge-free unsaturated five-membered ring. Twofold isoelectronic exchange allows the whole process to take place in a cation. Selected examples are to shed light on the classification and the thermodynamics of this electrocyclic reaction.

1. Introduction

The term "electrocyclic reaction" was coined by *Woodward* and *Hoffmann*[1]. A polyene (even-numbered) or a polyenyl (odd-numbered) system closes a ring in a process that can be described by a cyclic electron shift; its net result is the conversion of a π-bond into a σ-bond. Corresponding ring openings take place *via* the same energy profile. Electrocyclic ring closures and ring openings belong to the class of one-step "pericyclic reactions" which conform to the principle of conservation of orbital symmetry[2]. Electrocyclic reactions may benefit from the energetically favored concertedness only by taking the steric course defined by the *Woodward-Hoffmann* rules.

The fascination with the idea of orbital control led to a vigorous development of the chemistry of pericyclic reactions after 1965. At times, the mechanistic studies availed themselves of ingeniously conceived models, so inaccessible as to induce outsiders to raise the cry of "orchid chemistry". This is unjustified. On the contrary, pericyclic reactions offer an eminent classification principle[3] for a large number of well-known reactions, whose interrelation was frequently not recognized. The preparative and methodological gain tends to become effective only after the common mechanistic principle has been unveiled.

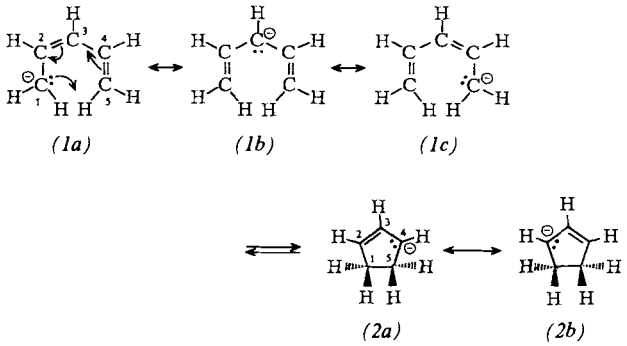
[*] Prof. R. Huisgen
Institut für Organische Chemie der Universität
Karlstrasse 23, 8000 München 2 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-947 $ 02.50/0

2. Reaction Scheme, Orbital Control, Stereochemistry

2.1. Overall Course and Charge Migration

The pentadienyl anion *(1)* has six electrons in five parallel π-orbitals. The resonance structures *(1a)—(1c)* illustrate the charge distribution over the carbon atoms 1, 3, and 5. The electrocyclic ring closure requiring a U configuration of the open-chain species is associated with a transformation of the terminal sp^2-hybridized centers into tetrahedral carbon atoms. The remaining four π-electrons emerge as an allyl anion group, *i.e.*, the lower vinylog of the pentadienyl anion, in the cyclopentenyl anion *(2)*. The reaction course is demonstrated by the cyclic shift of electrons depicted in *(1a)*.



(1a) *(1b)* *(1c)*

(2a) *(2b)*

This pattern of charge distribution can also be reproduced by the MO model, yet not in such a clear symbolism. The superiority of the MO model over the classical concept of resonance becomes evident in the *orbital control* of the steric course of electrocyclic processes.

2.2. Orbital Control of the Steric Course

The ring closure of *(1)* consists of coordinated deformation and twisting motions: two 90° rotations about the C1—C2 and C4—C5 bond axes are required, while carbon atoms 1 and 5 approach in order to create a new σ-bond from the former π-orbitals. *Woodward* and *Hoffmann*[1] found the inspection of the HOMO (highest occupied molecular orbital) symmetry to be the simplest treatment accounting for the steric course of electrocyclic reactions. According to Figure 1, phase consistent σ-overlap calls for one 90° rotation being clockwise and the second anticlockwise (disrotation). Similarly, conrotatory movements are derived from the symmetry properties of ψ_4 for the first excited singlet state of *(1)*.

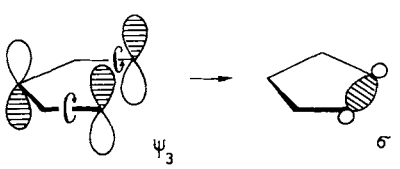


Figure 1. Derivation of disrotation for the cyclization of the pentadienyl anion from the HOMO symmetry.

The *disrotatory* mode of the reaction can be described in terms of a symmetry plane (C_s) as a molecular symmetry element, whereas in the course of *conrotation* a twofold axis of symmetry is preserved. The MO symmetry correlation diagram[2] can be constructed on the basis of the transformation properties of the involved MO's (symmetric or antisymmetric) in relation to the above-mentioned symmetry element. Accordingly, for the disrotatory ring closure the occupied orbitals of the ground state of *(1)* are connected to those of *(2)* without encroaching on the antibonding side.

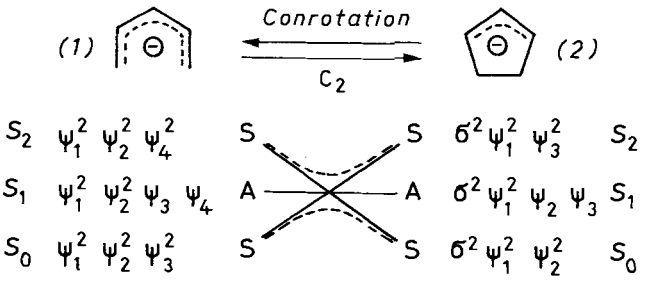
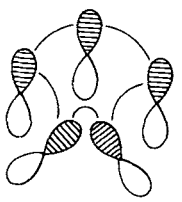


Fig. 2. Symmetry correlation diagram of molecular states for the conrotatory cyclization of the pentadienyl anion.

The *symmetry correlation of the molecular states*[4] furnishes a superior picture of the nature and energy requirement of the symmetry-forbidden reaction, as shown in Figure 2 for conrotation. The electronic configuration of the ground state of *(1)* is symmetry-connected with a higher excited state, S_2, of the cyclopentenyl anion; two electrons from ψ_2 of the allyl anion are promoted to ψ_3. Correspondingly, the ground state of *(2)* is correlated with a higher singlet excited state (S_2) of *(1)*. All the electronic configurations mentioned are symmetric with respect to a twofold axis of symmetry which dominates the conrotatory ring closure. Therefore, S_0 and S_2 of *(1)* and S_0 and S_2 of *(2)* enter into "configuration interaction" which with decreasing energy separation leads to an increasing admixture of S_2 in S_0 and *vice versa*. This interaction is the reason for the "non-crossing rule" which forbids the crossover of correlation lines between electronic configurations of the same symmetry. Thus, the cyclization of *(1)* in the ground state follows the dashed line and reaches S_0 of *(2)*, *i.e.*, the ground state; the forbiddenness of the thermal conrotation rests on the energy hill between the S_0 states of educt and product. Hence it is clear that "forbidden" does not mean that the reaction cannot take place, but rather that a higher activation energy is imposed on the process.



(3)

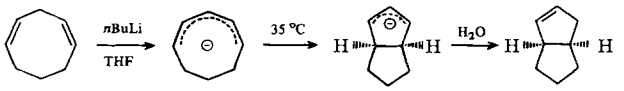
As an alternative treatment of orbital control, the *Evans-Zimmerman-Dewar* principle[5,6] shows the topology of the basis set of the atomic orbitals in the transition state to exhibit no phase dislocation; with 6 electrons, *(3)* characterizes an "aromatic" transition state for the disrotatory ring closure of *(1)*→*(2)*, symmetry not playing any part here.

This is noteworthy, since any substitution of the parent compound affects not only the symmetry of the molecule,

but *via* a change in the atomic orbital coefficients also that of the MO's involved in the reaction. The same applies to the replacement of carbon atoms by heteroatoms. Nevertheless, orbital control is retained qualitatively; the height of the symmetry-inflicted energy barrier of the forbidden reaction, however, can be strongly influenced by the substitution pattern.

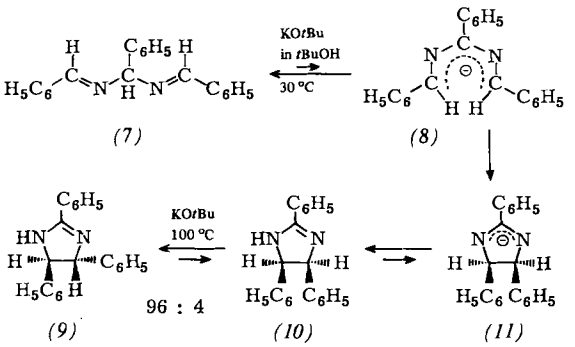
2.3. Steric Course of the Reaction

According to *Bates* and *McCombs*[7], the deprotonation of 1,4-cyclooctadiene with butyllithium in tetrahydrofuran (THF)-hexane takes place at −78 °C. NMR observations show that the cyclization of the cyclooctadienyl anion *(4)* to the bicyclic allyl anion *(5)* proceeds with a half-life of 80 min at 35 °C. The uptake of a proton leads to bicyclo[3.3.0]oct-2-ene *(6)* with *cis*-linkage of the rings[8]. It is true that this is the disrotation permitted by orbital symmetry, but the fact that the *cis*-form *(6)* is the thermodynamically more stable configuration diminishes the evidential value for orbital control.



(4) *(5)* *(6)*

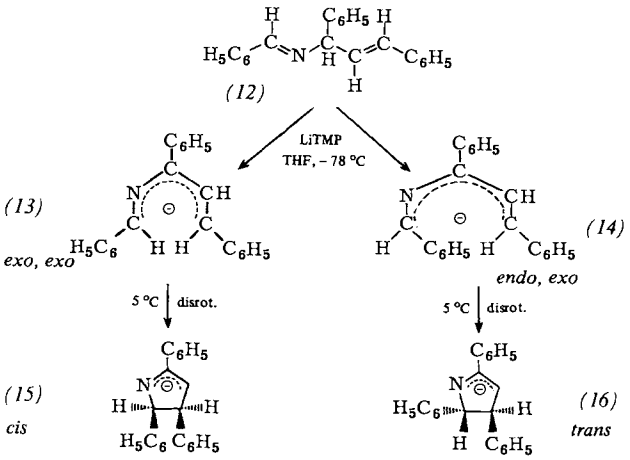
A diaza derivative permits further-reaching conclusions. As early as 1844, by heating hydrobenzamide *(7)* *Laurent*[9] obtained "amarine", later recognized as *cis*-2,4,5-triphenyl-1-imidazoline *(10)*. In an elegant study, *Hunter* and *Sim*[10] found the ring closure to be base-catalyzed; under the assumption that *(8)* with its *exo*-located terminal phenyls represents the most favorable U configuration of the heteropentadienyl anion, they deduced a disrotatory cyclization, *(8)*→*(11)*. Amarine *(10)* is the labile *cis*-4,5-diphenyl isomer. The rapid ring closure with potassium *tert*-butoxide (KO*t*Bu) at 30 °C was followed at 100 °C by a slow equilibration with isomarine *(9)* the *trans*-isomer.



(7) *(8)* *(9)* *(10)* *(11)*

Reaction of lithium tetramethylpiperidide (LiTMP) with *(7)* in methyltetrahydrofuran at −130 °C afforded the purple anion *(8)*, whose cyclization to *(11)*—even at −130 °C too fast to be followed by NMR—occurred with better than 99.7% stereospecificity[11].

The persuasive power behind this finding for the orbital control is diminished by the lack of stereoselectivity in the ring closure of the monoaza compound *(12)*. The deprotonation of *(12)* with LiTMP in THF furnished a blue solution; under conditions of kinetic control the anions *(13)* and *(14)* cyclized to *(15)* and *(16)*, respectively, whose hydrolysis



(12)

(13) *exo, exo*

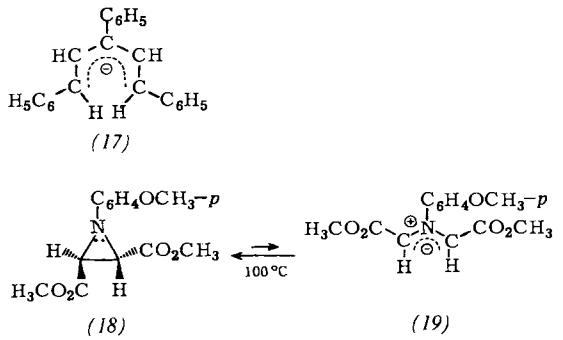
(14) *endo, exo*

(15) *cis*

(16) *trans*

yielded the *cis*- and *trans*-isomers of 2,4,5-triphenyl-1-pyrroline in a ratio of 1:1[12].

The key to an understanding of the difference in behavior of the diaza-anion *(8)* and the monoaza-anion of *(12)* is provided by the fact that cyclization of the former takes place approximately 10^6 times faster. The early transition state of the highly exothermic ring closure of *(8)* is structurally still in close relation to *(8)*. For reasons discussed in Section 3, a smaller reaction enthalpy is expected for the cyclization of the anion from *(12)*. If the reaction is almost thermoneutral, the later transition state at a higher energy level—cyclization takes place only above 0 °C—should receive contributions from the educt and the product. On the educt side the anion *(13)* will be more stable than *(14)*, since in the latter the *endo*-1-phenyl group disturbs the coplanarity. On the product side, however, the *trans*-anion *(16)* is preferred to the *cis*-anion *(15)*. It is conceivable that the transition states of the *two disrotations*, *(13)*→*(15)* and *(14)*→*(16)*, have the same energy level. The formation of *(15) and (16)*, therefore, does not necessarily involve an infringement of orbital control. In the case of the 1,3,5-triphenylpentadienyl anion *(17)*, cyclization is no longer observable; according to *Hunter et al.*[11], it might possibly be endothermic.



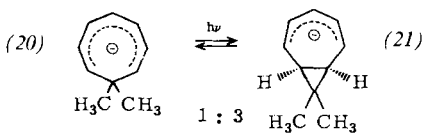
(17)

(18) *(19)*

Do the electrocyclic reactions of the lower and higher vinylogs of the pentadienyl anion—conrotation is expected for both in the ground state—follow the *Woodward-Hoffmann* rules? The steric course of the ring opening of substituted cyclopropyl anions to form allyl anions could not yet be observed directly, since equilibrium of the configurations was established by rapid subsequent rotation[13].

Symmetry-allowed conrotation has, however, been verified for the electrocyclic equilibration of the aziridine *(18)* with a small concentration of the azomethine ylide *(19)*[14,15];

these species are isoelectronic with the cyclopropyl anion and the allyl anion, respectively.



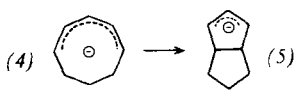
The heptatrienyl anion as the higher vinylog of *(1)* is incorporated in the 8-membered ring of *(20)*. Geometric constraints allow an intraannular ring closure only by disrotation which is symmetry-forbidden for the thermal electrocyclic reaction. Therefore, the equilibrium *(20)* $\rightleftharpoons$ *(21)* is not established thermally, but merely photochemically[16].

3. Thermodynamic and Kinetic Considerations

The different positions of the electrocyclic reaction equilibria have already been referred to. In the transformation of the cyclopropyl anion into the allyl anion a σ-bond is converted into a π-bond (+20 kcal mol^{-1}) and the ring strain (−28 kcal mol^{-1}) as well as the delocalization energy (−28 kcal mol^{-1}) are released, thus making the ring opening highly exergonic. No experimental value is available for the delocalization energy; it should be identical with the rotational barrier of the allyl anion for which an *ab initio* calculation (4-31 G) furnished 28 kcal mol^{-1} [13,17]. In addition, solvation and ion pairing will modify the energy balance. The reverse process has never been observed.

In the case of the higher vinylog, the heptatrienyl anion, the ring closure to form the low-strain cycloheptadienyl anion acquires driving force, since the energy gain in the transformation of a π-bond into a σ-bond (−20 kcal mol^{-1}) certainly exceeds the loss of delocalization energy. The cyclization of the unsubstituted heptatrienyl anion proceeds to completion in THF-hexane at −30 °C with a half-life of 13 min[18].

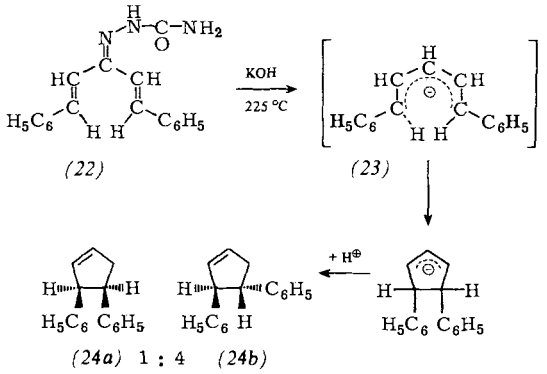
From a consideration of the above examples it can be assumed that the position of the electrocyclic equilibrium of pentadienyl anion $\rightleftharpoons$ cyclopentenyl anion depends on the substitution pattern. Let us first discuss the energy balance of the intraannular cyclization *(4)*→*(5)*.



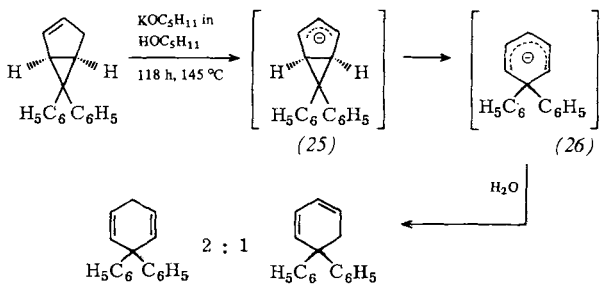
π-bond→σ-bond	−20 kcal mol^{-1}
Increase in ring strain (estimated)	+ 4 kcal mol^{-1}
Decrease in delocalization energy	≤ +14 kcal mol^{-1}

By attributing ≥2 kcal mol^{-1} to the exergonic cyclization[7], there is a decrease of ≤14 kcal mol^{-1} for the delocalization energy in going from the pentadienyl to the allyl anion.

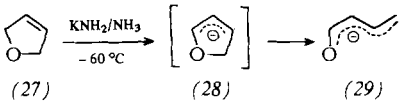
In the cyclization of the *open-chain* pentadienyl anion a ring strain of approx. 7 kcal mol^{-1} [19] is built up. Furthermore, the conversion to the rigid cyclopentenyl anion causes a decrease of entropy during the cyclization. Indeed, no cyclization of open-chain pentadienyl anions has been observed so far, and it is still unclear whether this failure is due to thermodynamic or kinetic reasons. A single unexplained exception will be briefly discussed here.



Shoppee and *Henderson*[20] achieved the conversion of the semicarbazone *(22)* into the cyclopentenes *(24)* with 12% yield by heating it with powdered potassium hydroxide or potassium *tert*-butoxide. The concepts of the mechanism of the Wolff-Kishner reduction suggest the intermediacy of the anion *(23)*. The equilibration of *(24a)* and *(24b)* under these conditions together with the conversion into the conjugated diphenylcyclopentenes prevents any conclusion about the steric course of the process. A cyclization of *(23)* was even less predictable due to the concomitant loss of phenyl conjugation energy. Moreover, the attempted cyclization was unsuccessful, when 1,5-diphenyl-1,4-pentadiene was heated with butyllithium to 190 °C. The ring closure *(22)*→*(24)* may possibly be ascribed to the changed solvation and protonation conditions on the surface of the solid potassium hydroxide or *tert*-butoxide at 225 °C.



In contrast, the anionic ring opening *(25)*→*(26)* which profits from the release of the cyclopropane ring strain is obvious[21].



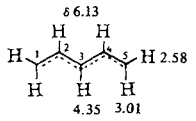
No less apparent is the influence of heteroatoms on the electrocyclic equilibrium which is of prime importance here. Shortly after deprotonation of 2,5-dihydrofuran *(27)* with potassium amide in liquid ammonia, *Kloosterziel et al.*[22] observed the NMR spectrum of *(29)* in which the negative charge is mainly located on the oxygen. The butadienolate *(29)* is a weaker base than the pentadienyl anion *(1)* by about 20 pK units, which favors the ring opening *(27)*→*(29)* at −60 °C by about 20 kcal mol^{-1}. The resonance structures of *(1)* reveal that the replacement of carbon by heteroatoms of

higher electronegativity in positions 1, 3, and 5 should provide the driving force for ring opening.

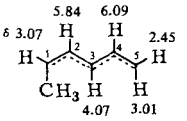
Replacement in position 2 or 4 acts in the opposite direction; by taking over the negative charge, heteroatoms in these positions effect stabilization not in the open-chain, but rather in the cyclic species. Transfer of the negative charge to the two nitrogen atoms of the 2,4-diazapentadienyl anion *(8)* makes the ring closure to *(11)* fast even at $-130\,^{\circ}C$. Amide anions are favored over carbanions. However, the monoaza substitution in *(13)* and *(14)* reduces the thermodynamic drive of the cyclization which is observed only above $0\,^{\circ}C$. This coupling of thermodynamic and kinetic reasoning is based on the *Hammond* postulate: in a family of mechanistically related reactions the transition state will resemble the educt structure all the more and require all the less activation enthalpy, the higher is the liberated reaction enthalpy.

4. Charge Distribution and Configuration of the Pentadienyl Anion

Pentadienyl anions are conceivable in three idealized planar configurations, described as the W, S, and U forms. All three configurations can be established in cyclic derivatives. A comparison of the coupling constants in the ^{1}H-NMR spectra of the open-chain pentadienyl anions *(30)* and *(31)* with those of cyclic models permits the conclusion that *(30)* and *(31)* exist in the W form.

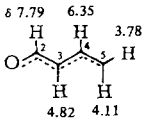


(30)



(31)

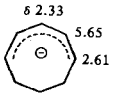
This conclusion is also supported by the symmetry of the parent system *(30)*, which can be generated by reaction of 1,4-pentadiene with potassium amide in liquid ammonia. According to *Kloosterziel et al.*[23], the chemical shift of the 2-H and 4-H of *(30)* shows the normal δ value for vinyl protons. The higher electron density on the carbon atoms 1, 3, and 5 is responsible for the shielding by several ppm, which is greater for 1- and 5-H than for 3-H. The δ values of the *cis*-1-methyl compound *(31)* bear witness to the electron-repelling effect of the methyl group.



(32)

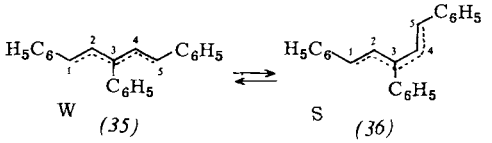


(33)



(34)

The replacement of a terminal CH_2 in the pentadienyl anion by oxygen in *(32)* is accompanied by an increase in the δ-values of 3-H and 5-H by 0.5—1.2 ppm, corresponding to a reduction in the respective electron densities[23]. If *one* resonance structure is to be chosen for *(32)*, this should be the dienolate formula. In the anions *(33)* and *(34)*[23] the U configuration due to the ring structure exhibits a similar pattern of charge distribution as the W form of *(30)*. An even more sensitive probe for the charge distribution is provided by the ^{13}C-NMR shifts[24,25].



(35) *(36)*

The configurational equilibrium of 1,3,5-triphenylpentadienyllithium in THF contains comparable amounts of the W and S forms: $\Delta G^{+} = 12$ kcal mol^{-1} for the transformation *(35)*⇌*(36)* was explained by *Hunter et al.*[26] in terms of a rotational barrier.

Whereas electrostatic considerations favor extended forms of the pentadienyl anion, the synphasic terminal atomic orbitals in two of the three occupied MO's were suggested as a factor which stabilizes the U configuration by bonding overlap[27]. Although the U form has not yet been detected experimentally, we nevertheless regard it as the *precursor of cyclization*. Only a simultaneous 180° rotation about the C2—C3 bond and 90° rotation about the C1—C2 bond in the S form *(36)* could yield a transition state of the ring closure reaction without passing through the sterically hindered planar U configuration.

5. Heterosubstitution and Charge Migration

The great importance of 1,5-electrocyclization becomes manifest in the hetero series. A distinction is made between *isoionic* and *isoelectronic* replacement by a heterofunction, which may be explained with nitrogen and oxygen as examples and applies *mutatis mutandis* to other heteroatoms.

5.1. Isoionic Replacement

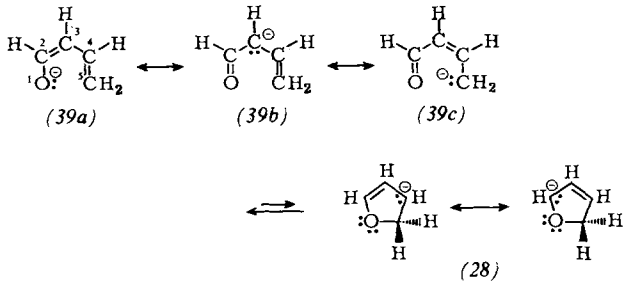
The *isoionic* replacement of the carbanionic C-atom in the pentadienyl species *(1)* by an amide anion or an olate function according to *(37)* does in fact change the extent to which



(37) *(38)*

the individual resonance structures participate in the electron distribution of the ground state; however, the formal pattern of distribution of the negative charge is retained. The same applies to the replacement of the charge-free olefinic C-atom in the resonance structures of *(1)* according to *(38)* by imine nitrogen or carbonyl oxygen, which likewise bear no formal charge. Exchange of CRR′ by NR or O in positions 1 and 5 of the pentadienyl anion is conceivable, whereas in positions 2, 3, and 4 only the nitrogen atom can function as an exchange partner. The isoionic replacement can occur repeatedly without loss of the monoanionic character of the species.

The base-catalyzed ring opening of dihydrofuran *(27)* may again serve as an illustration. Only the oxapentadienyl anion profits from the isoionic replacement of CH_2 by O in position 1; the high electronegativity of oxygen stabilizes *(39a)*, but not the cyclic species *(28)*, and thus determines the electrocyclic equilibrium in the sense of *ring opening*.



(39a) (39b) (39c) (28)

Are *two* 90° rotations about the terminal bond axes essential for electrocyclic processes? The availability of free electron pairs on the terminal olate oxygen or amide nitrogen enables *the rotations, e.g.,* in the ring opening reaction *(28)→(39), to be limited to one.* Presumably it is not the electron pair of the C—O σ-bond of *(28)* which enters into the pentadienyl π-system of *(39).* Instead, the dihydrofuran anion *(28)* contains a quasi-6π-system which is merely reorganized during ring opening. The stereoelectronics of the cyclization of the parent substance *(1)* is therefore drastically modified by the introduction of the heteroatom.

This also acts kinetically by lowering the activation barrier, since in the transition state a smaller amount of the bond energy of the reactants need be sacrificed. The ring opening *(28)→(39)* at as low a temperature as −60 °C may be ascribed to the highly exothermic character of the reaction as discussed in Section 3. However, we shall become acquainted in Section 8 with examples of thermoneutral cyclizations in which the equilibrium is established rapidly even at room temperature. In all these cases at least one sp^3-carbon of the cyclopentenyl anion *(2)* is replaced by a heteroatom with an unshared electron pair.

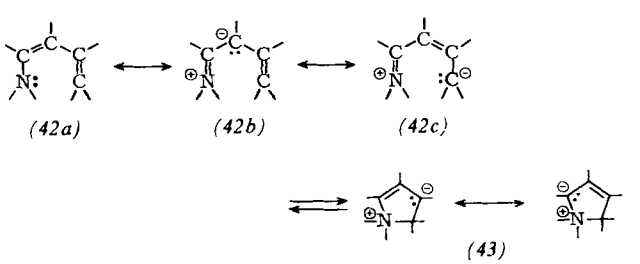
5.2. Isoelectronic Exchange

Amino nitrogen and ether oxygen have free electron pairs and, as per *(40),* are isoelectronic with the carbanion without harboring its negative charge. In accord with *(41),* the imin-



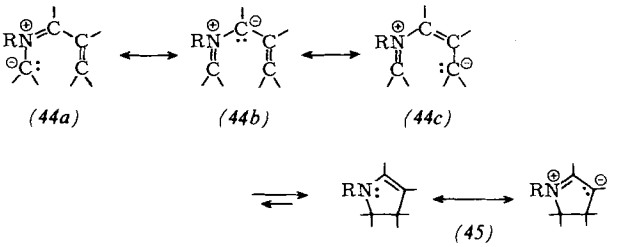
(40) (41)

ium ion and the oxonium ion permit the ethylenic carbon atom in the resonance structures of *(1)* to be replaced isoelectronically. This exchange can occur in all positions of *(1),* although the consequences are very different.



(42a) (42b) (42c) (43)

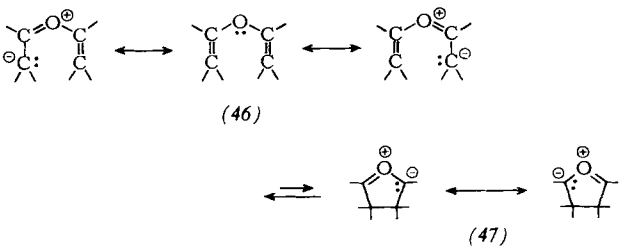
Replacement of CH_2 in position 1 by an amino function permits us to expect the *charge-free* resonance structure *(42a)* along with the less important zwitterionic formulas *(42b)* and *(42c).* The charge migration associated with ring closure leads to the cyclic ammonium ion *(43),* which contains a normal allyl anion system. Stabilizing reactions may follow cyclization.



(44a) (44b) (44c) (45)

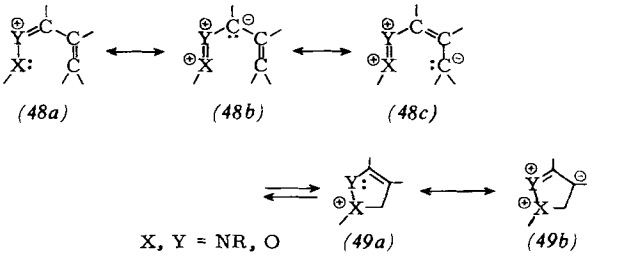
Isoelectronic replacement by NR in position 2 gives an iminium zwitterion *(44),* which delocalizes the carbanionic charge in its three all-octet structures *(44a)—(44c).* The ring closure is accompanied by charge compensation; a cyclic enamine *(45)* arises, the neutral and zwitterionic forms of which reveal the allyl anion structure.

The formulas *(44a)* and *(44b)* characterize a vinyl-substituted azomethine ylide. *(44)* acts as a representative for the large class of 1,3-dipoles of the allyl type conjugated with a CC or hetero double bond[28]. In Section 9 it will be shown that the cyclizations of conjugated 1,3-dipoles of the propargyl-allenyl type can be similarly treated. Here we are faced with the largest group of heteropentadienyl anion ring closures, whose range was recognized in *Reimlinger's* pioneering paper[29] in 1970 and which was called "1,5-dipolar cyclization". Recently, *Taylor* and *Turchi*[30] discussed this group in a review paper. The possibility of the stepwise replacement of all the carbons of the pentadienyl anion by heteroatoms—the exchange in position 2 is isoelectronic, the others are isoionic—makes the variations on this theme a polyphonic fugue.



(46) (47)

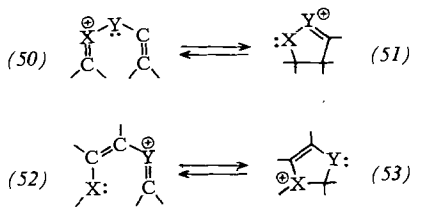
Like isoelectronic substitution in position 1, that in position 3—for a change, an oxygen has been introduced in *(46)*—leads to one resonance structure free of formal charges and two zwitterionic structures. Electrocyclization with its charge migration affords the carbonyl ylide *(47),* a cyclic 1,3-



(48a) (48b) (48c) X, Y = NR, O (49a) (49b)

dipole. Reactions of this type usually take place in the sense of a ring opening, unless subsequent processes follow the thermal or photochemical ring closure.

The multiplicity of possible 1,5-electrocyclizations is increased by *double isoelectronic exchange*; one can imagine that the cyclization of the pentadienyl anion type now takes place in the *cation*. *(48a)* shows this cation for the case of 1,2-disubstitution. The significance of the tripolar resonance structures *(48b)* and *(48c)* is all the smaller, since they violate the "adjacent charge rule". For this reason, *(49a)* dominates on the product side. Usually further steps follow, *e.g.*, proton shift.



Restricting attention to the forms with *one* positive charge, the systems with double isoelectronic replacement in the 2,3-position, *(50)*→*(51)*, and also in the 1,4-position, *(52)*→*(53)*, are schematically formulated; only a limited number of examples has been described. Naturally, the 1,3-, 1,5-, and 2,4-relationships of X and Y are also conceivable. Systems with triple isoelectronic replacement—here the process would take place in a dication—have to our knowledge not been reported so far.

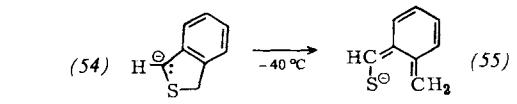
In addition to the already mentioned reviews of 1,5-dipolar cyclizations[29,30], reference may be made to a short review by *Elguero*[31], who recognized the wide scope of the electrocyclic 6π principle for the construction of five-membered rings and placed the emphasis on reactions in the cation.

A complete coverage of the literature will not be attempted in this review. In our limited selection of examples we will give more weight to the didactic point of view than to that of a systematic account. So far the principles of charge distribution and charge migration have been illustrated with complete sets of resonance structures. In the following, we will prefer the short notation by delocalized structures; in other cases the most significant resonance formula serves as an illustration.

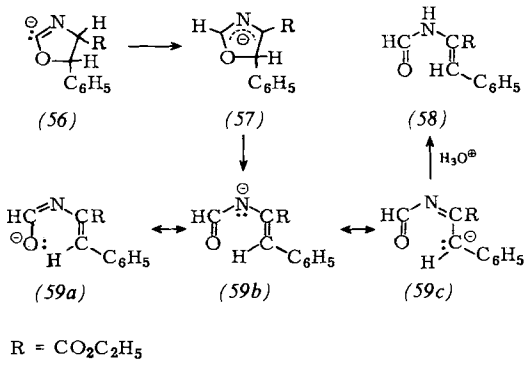
6. Heterosubstituted Pentadienyl Anions (Isoionic Replacement)

We have seen that the placing of the negative charge on a heteroatom which is more strongly electronegative than carbon decisively determines the direction of the electrocyclic reaction: heteroatoms in positions 2 and 4 of the pentadienyl anion favor ring closure, while in positions 1, 3, and 5 they promote ring opening.

Reaction of potassium amide with 1,3-dihydrobenzo[*c*]thiophene generates the anion *(54)* which is of the benzyl type; *i.e.*, two of the carbon atoms of the allyl anion are part of a benzene ring. The NMR spectrum of the ring-opening product was substantially that expected for the *o*-quinodimethane structure *(55)*[32].

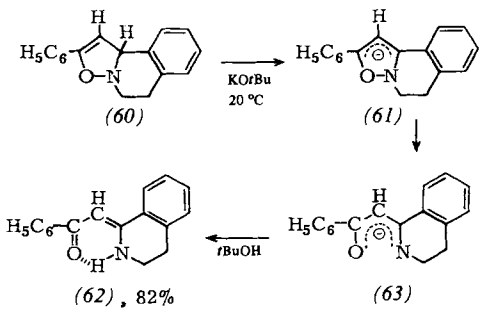


Naturally, *(54)* is not a 4π-system, but an 8π-system, and *(55)* is a 10π-system. In the classification of pericyclic reactions it is permissible to treat benzo-annelated systems as olefinic systems. This phenomenon, nowadays well understood, was one of the happy surprises in the early days of the *Woodward-Hoffmann* rules. Thus, *(55)* can be regarded not only as a pentadienyl anion but, with the inclusion of the double bonds of the 6-membered ring, as a nonatetraenyl anion; disrotation is also predicted for the ring closure of the latter. In the polyene series, the conrotatory ring-opening of *cis*- and *trans*-1,2-diphenylbenzocyclobutenes to the stereoisomeric *o*-quinodimethanes[33] offers an analogy to *(54)*→*(55)*.



R = $CO_2C_2H_5$

On treating α-isocyanoacetic ester with benzaldehyde and potassium *tert*-butoxide in THF, *Schöllkopf et al.*[34] isolated 85% of the formamide derivative *(58)*. The reaction presumably proceeds by the intermolecular proton shift *(56)*→*(57)* and electrocyclic ring opening to *(59)*. The ring cleavage gains high driving force by the distribution of the negative charge on the O- *and* N-atoms in *(59)*.

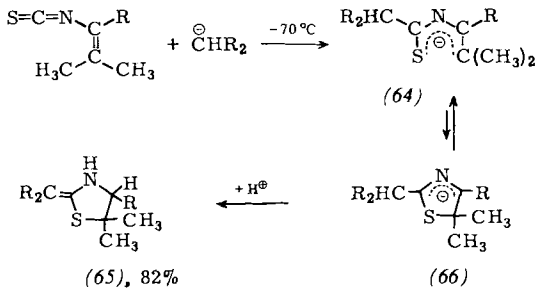


In the presence of potassium *tert*-butoxide in *tert*-butanol, the tricyclic 4-isoxazoline *(60)* undergoes an opening of the hetero-ring to give the enaminoketone *(62)*[35]. Not only the

acquisition of the negative charge by O and N in the pentadienyl anion *(63)*, but also the weakness of the NO σ-bond (53 kcal mol^{-1}) in *(61)* favors the ring opening.

In *(63)* the heteroatoms occupy positions 1 and 5 of the pentadienyl anion. In *(61)* lone electron pairs on both heteroatoms are available for conjugation with the allyl anion system; only the pyramidalization at the nitrogen acts against the antiaromatic 8π-character. A rotation about the terminal bond axes is no longer necessary for the electrocyclic process to occur.

Even in the case of an unfavorable equilibrium a complete cyclization can be induced by favorable secondary reactions.

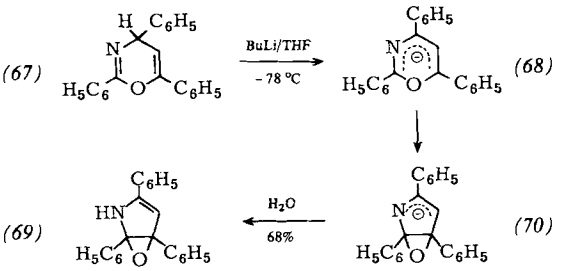


(64)

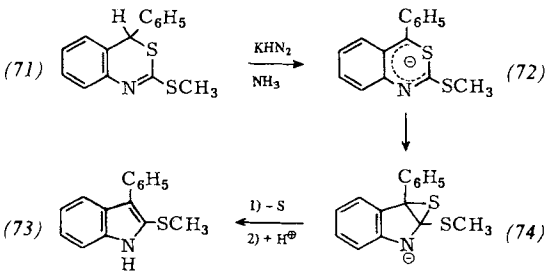
(65), 82% *(66)*

R = $CO_2C_2H_5$

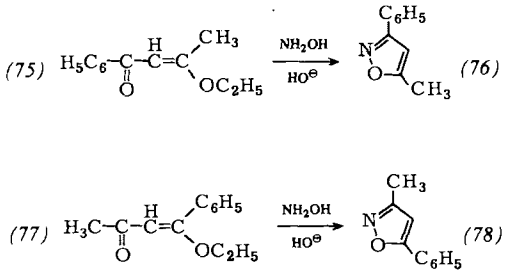
Treatment of potassium malonate with 2-isothiocyanatomethylcrotonic ester furnished the 2-methylenethiazolidine derivative *(65)*[36]. When the intermediate anion *(64)* closes the ring, the S and N atoms lose their portions of the charge. The formation of the cyclic allyl anion *(66)* must be endothermic; however, the subsequent shift of a proton from the malonic ester side chain to position 4 produces a favorable anion, in the stabilization of which the nitrogen atom again participates besides the two ester groups. The product *(65)* is an enamino-β,β-dicarboxylic acid ester.



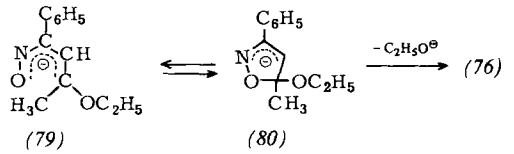
The special characteristic of the deprotonation of triphenyl-4*H*-1,3-oxazine *(67)* studied by *Schmidt et al.*[37] resides in the formation of the 8π-anion *(68)* with its cyclic conjugation. The deep blue color of *(68)* disappears rapidly at −78 °C and hydrolysis yields the bicyclic 2-pyrroline *(69)*. In *(68)* the nitrogen atom does not participate in the stabilization of the negative charge. The energetic preference for an aza-allyl anion and the disappearance of antiaromaticity promote the intraannular electrocyclization. These factors overcome the ring strain which is built up in the formation of the ethylene oxide ring in *(70)*. As in the case of the benzoannelated anions, the 8π-system of *(68)* is theoretically simplified by disregarding the oxygen atom which connects the termini of a pentadienyl anion system.



In the base-catalyzed ring contraction *(71)*—*(73)* according to *Lednicer et al.*[38], we encounter the benzo-annelated 8π-anion *(72)*, in which, in analogy with the preceding example, the S-containing ring is cleaved. Presumably the aromatic nature of the indole *(73)* prompts the cheletropic elimination of sulfur from the anion *(74)*.

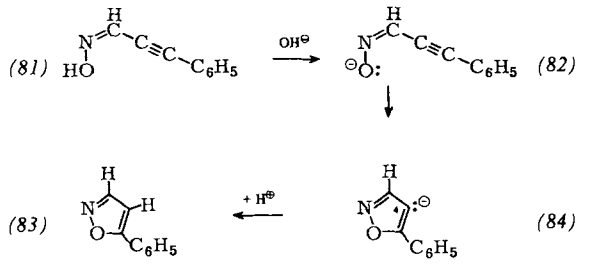


By the action of hydroxylamine on the keto-enol ethers *(75)* and *(77)* in an alkaline medium, *Claisen*[39] obtained the isoxazoles *(76)* and *(78)*. Although the structures were later confirmed[40], many unexplained results[41] still make it doubtful whether the oximate anions, *e.g.*, *(79)*, are intermediates in the formation of *(76)*.



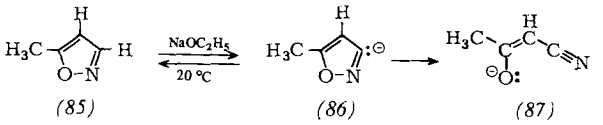
(79) *(80)*

With heteroatoms in positions 1 and 2 of the pentadienyl anion *(79)*, the negative charge migrates during the cyclization to *(80)* from the oxygen to the nitrogen atom. Ethoxide elimination from *(80)* effects aromatization.



The conversion of phenylpropiolaldoxime *(81)* to 5-phenylisoxazole *(83)* with a drop of caustic soda, which was observed by *Claisen*[42], offers an interesting borderline case. As in *(61)*→*(63)*, the rotational symmetry in the distribution of the π-electrons in the CC triple bond and the electronic configuration at the O-atom in *(82)* dispense with the necessity

of 90° rotations about the terminal bond axes. Ring closure leads to the isoxazole anion *(84)*, in which the n-orbital of the carbanionic electron pair is located within the ring plane and no longer maintains allylic resonance. The process *(81)*→*(83)* can be regarded as a nucleophilic *trans*-addition to the CC triple bond.

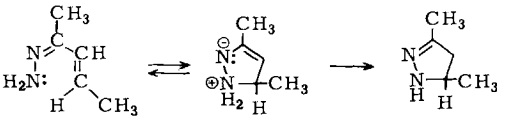


(85) *(86)* *(87)*

The base-induced ring cleavage of isoxazoles, likewise discovered by *Claisen*[43], constitutes a similar process in the opposite direction. Treatment of 5-methylisoxazole *(85)* with ethanolic sodium ethoxide yields the sodium salt of cyanoacetone *(87)*. Whether in this process the anion *(86)* occurs or the opening of the weak N—O bond is synchronized with deprotonation in position 3, is an open question. The whole process may be considered as a *trans*-elimination at the CN double bond of *(85)*.

7. Isoelectronic Exchange in Position 1 of the Pentadienyl Anion

Hydrazones of α,β-unsaturated carbonyl compounds are often not isolable, but isomerize to 2-pyrazolines even at room temperature as, *e.g.*, the hydrazone *(88)* of ethylideneacetone[44].

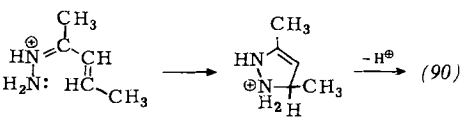


(88) *(89)* *(90)*

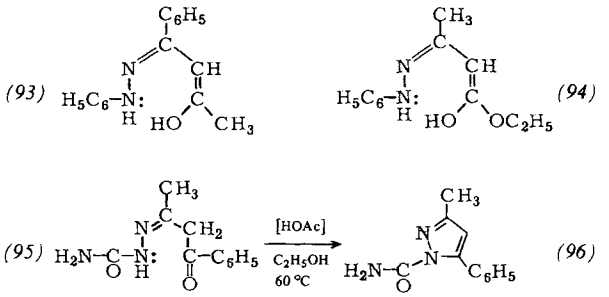
In *(88)* the anionic C-1 of the pentadienyl system *(1a)* is replaced by the isoelectronic amino group; the additional isoionic exchange of the CH in the 2-position by N does not affect the charge distribution. The cyclic zwitterion *(89)* which may exist in an electrocyclic equilibrium with *(88)* contains an aza-allyl anion. It is the subsequent prototropy or sigmatropic 1,4-shift which provides stabilization; the bond energy of the 2-pyrazoline *(90)* surpasses that of *(88)* by about 16 kcal mol^{-1}.

Cannot the formation of pyrazolines also be classified as a nucleophilic addition of the NH_2 group of *(88)* to the electrophilic α,β-unsaturated imine? This is an alternative description of one and the same process, differing only in the choice of words and not in its meaning from that given above. Like the electrocyclization of *(1)*, that of *(88)* requires the two 90° rotations about the axes of the terminal bonds.

The formation of pyrazolines from unsaturated hydrazones is subject to acid catalysis[45]. The role of the acid could consist in an acceleration of the subsequent prototropy, *(89)*→*(90)*. The hypothesis that the weakly basic imine nitrogen of *(88)* is protonated and the cation *(91)* undergoes ring closure to *(92)* is also conceivable, and is even preferred by some authors[45,46]. The cation *(91)* corresponds to *(48)* and differs from the pentadienyl anion by a *double isoelectronic* replacement.



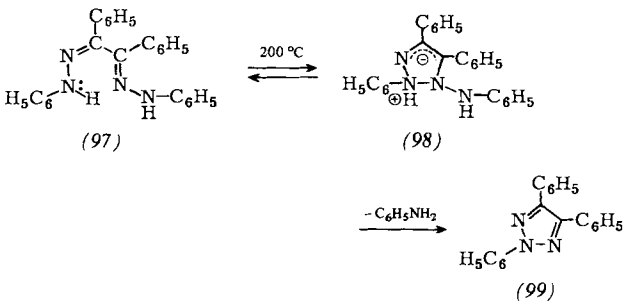
(91) *(92)* *(90)*



(93) *(94)*

(95) *(96)*

According to *E. Fischer et al.*[47], the formation of 5-methyl-1,3-diphenylpyrazole from benzoylacetone and phenylhydrazine proceeds at 50 °C without the addition of acid *via* a labile crystalline intermediate. Dare we assume here an electrocyclization of the enol *(93)* with subsequent aromatization by elimination of water? Does Knorr's pyrazolone synthesis from phenylhydrazine and acetoacetic ester[48] involve a cyclization of the ketene hemiacetal *(94)*? The isolable benzoylacetone semicarbazone *(95)* is converted into *(96)* in the presence of a small amount of acetic acid[49]. Does the acetic acid merely establish the keto-enol equilibrium of *(95)*, or is the electrophilic activity of the carbonyl group increased by *O*-protonation? Mechanistic investigations of these classical syntheses of heterocycles are still lacking.

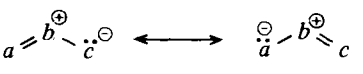


(97) *(98)* *(99)*

V. Meyer et al.[50] prepared 2,4,5-triphenyl-1,2,3-triazole *(99)* by heating benzil phenylosazone *(97)* to 200 °C. The formula *(97)* suggests a pentadienyl anion with an isoelectronic exchange in position 1 and a twofold isoionic replacement in positions 2 and 5. The cyclization *(97)*→*(98)* is probably endergonic, and it is the subsequent formation of the aromatic triazole *(99)* through elimination of aniline which makes up for the thermodynamic driving force.

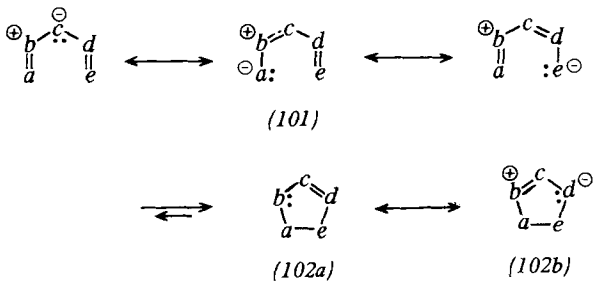
8. Isoelectronic Substitution in Position 2: Cyclizations of Conjugated 1,3-Dipoles of the Allyl Type

1,3-Dipoles are the $_{\pi}4$ reactants in concerted 1,3-dipolar cycloadditions. The all-octet resonance structures *(100)* char-



(100)

acterize 1,3-dipoles of the allyl type[28], which contain NR or O as the middle center *b*; CRR′, NR, and O are interchanged permutatively in the terminal centers *a* and *c*.



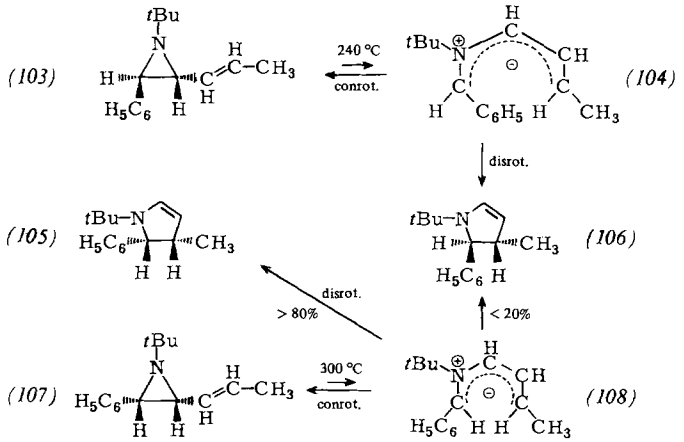
(101)

(102a) *(102b)*

The octet formulas *(101)* of the 1,3-dipole which are conjugated with a double bond *d*=*e* reveal the resonance of pentadienyl anion type with a fixed onium center *b*. In the following the ring-closed product will be represented by the resonance structure *(102a)* which is free of formal charges, although the zwitterionic structure *(102b)* also contributes to a minor extent. With reference to the recent review[30], the plethora of cyclizations will be limited to a few examples.

8.1. Conjugated Azomethine Ylides

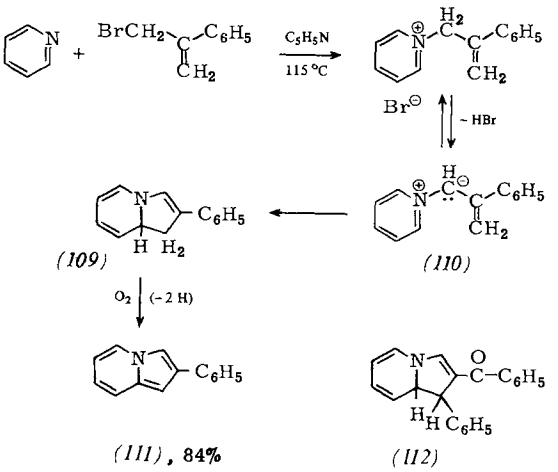
The electrocyclic ring opening of aziridines already discussed for *(18)*⇌*(19)* opens up a path to *vinyl*-substituted azomethine ylides. *Pommelet* and *Chuche*[51] have observed the exclusive formation of the *trans*-2-pyrroline *(106)* from



(103) *(104)* *(105)* *(106)* *(107)* *(108)*

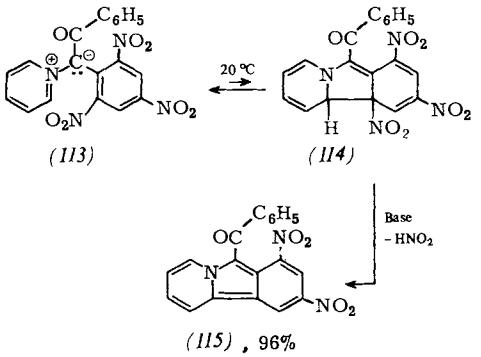
the *trans*-disubstituted aziridine *(103)* at 240 °C. This indicates a sequence of symmetry-allowed steps, namely a conrotatory ring opening of *(103)* and a disrotatory cyclization of *(104)*. Correspondingly, the aziridine *(107)* with *trans*-propenyl and phenyl in the *cis* positions afforded more than 80% of the *cis*-2-pyrroline *(105)*. The concomitant formation of the by-product *(106)* from *(107)* must be the result of a symmetry-forbidden electrocyclic step or a rotation. Only U configurations of the vinylazomethine ylide are presented in the formula scheme. Although W and S configurations may also be more stable in this case, the U configurations are inevitable precursors of the pyrrolines.

In the case of the well-documented pyridinium allylides, *e.g., (110)*, the CN quasi-double bond of the vinylazomethine ylide is part of the aromatic ring. *Pohjala*[52] obtained 2-phenylindolizine *(111)* in 84% yield after refluxing α-bromomethylstyrene in pyridine. The ring closure of *(110)* furnishes the dihydroindolizine *(109)* which is subject to autoxidation. The dihydroindolizine has been isolated in some cases, *e.g., (112)*. Consequently, cyclization does not lose its driving force when the pyridinium aromaticity has to be sacrificed.



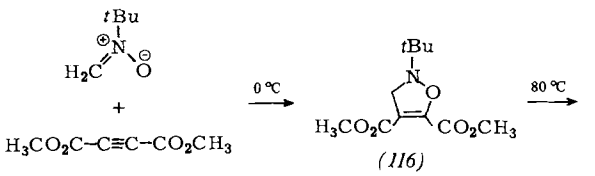
(109) *(110)* *(111)*, 84% *(112)*

In the deep violet isolable pyridinium betaine *(113)* the vinylazomethine ylide structure is embedded in two aromatic nuclei. The base-induced cyclization of this compound to the

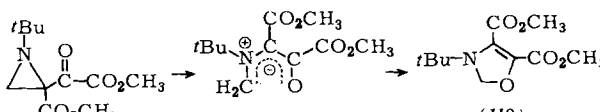


(113) *(114)* *(115)*, 96%

red benzo[*a*]indolizine *(115)* was discovered by *Augstein* and *Kröhnke*[53]. Conceivably, *(114)* is removed from an electrocyclic equilibrium by the elimination of HNO_2 with piperidine. The reaction may be described equally well by an intramolecular nucleophilic substitution of an aromatic nitro group *via (114)* as an intermediate σ-complex.

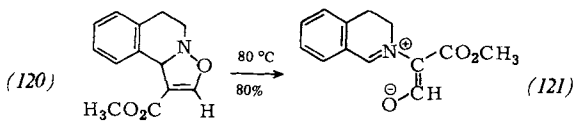


(116)



(117) *(119)* *(118)*

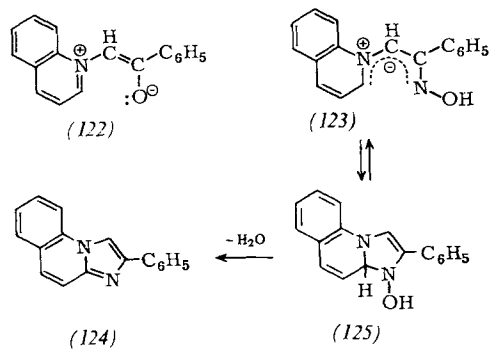
A multi-step sequence suggested by *Baldwin et al.*[54] for the isomerization of the 4-isoxazoline derivative *(116)* to the 4-oxazoline *(118)* calls for the inclusion of the *acyl*azomethine ylide *(119)* as an intermediate. Due to the weakness of the NO σ-bond, the isomerization *(116)*→*(118)* is exothermic



(120) (121)

by about 23 kcal mol^{-1}. The initiating ring contraction *(116)→(117)* probably corresponds in its mechanism to the rearrangement of vinylcyclopropane into cyclopentene.

Depending on the pattern of substitution, the reaction can be stopped at various stages[54,55]. The tricyclic 4-isoxazoline *(120)* that can be obtained from 3,4-dihydroisoquinoline *N*-oxide and propiolic ester isomerizes to the orange crystalline *(121)*[56]. Thus, a benzene ring, an aldehyde and an ester group stabilize the acylazomethine ylide *(121)* to such an extent that ring closure to a 4-oxazoline can no longer be ascertained. However, *(121)* still exhibits the activity of a 1,3-dipole, as disclosed by its cycloadditions to acetylenedicarboxylic ester and other dipolarophiles[55]. Many 4-oxazolines, moreover, maintain thermal equilibria with *C*-acylazomethine ylides[55,57].



(122) (123) (124) (125)

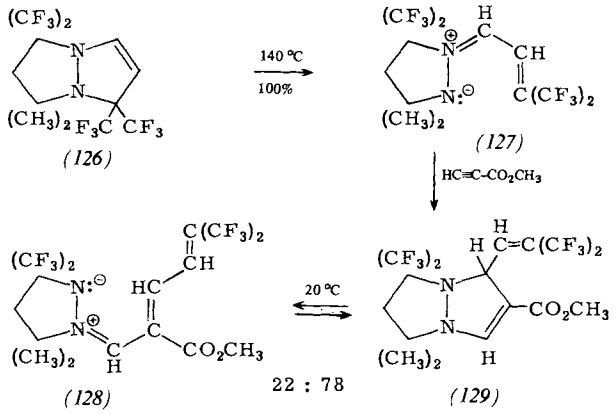
The phenacylquinolinium betaine *(122)* shows no inclination to close the ring. However, the replacement of the oxygen by an imino or oximino group again makes the cyclization energetically attractive. *Kröhnke* and *Zecher*[58] heated *N*-phenacylquinolinium bromide with hydroxylammonium chloride to 130 °C and isolated 87% of the imidazo[1,2-*a*]-quinoline *(124)*. Compound *(123)* may be considered an intermediate. *(125)* is perhaps removed from an equilibrium by elimination of water and rearomatization.

8.2. Conjugated Azomethine Imines

The conjugated double bond may be anchored to the carbon or nitrogen atom of the azomethine imine system. According to *Burger et al.*[59], the 1,5-diazabicyclooctene *(126)*, is accessible by "criss-cross" addition from hexafluoroacetone azine; on heating *(126)*, it is converted into the *C-vinyl*-azomethine imine *(127)*. The inductive stabilization of the anionic charge of *(127)* by the CF_3 groups affects the energy balance.

The 1,3-dipole *(127)* combines with methyl propiolate to give *(129)*, which in turn is subject to an electrocyclic opening of the new ring at room temperature and yields the heptatrienyl anion *(128)*; the CF_3 residues once again contribute to the charge stabilization[59].

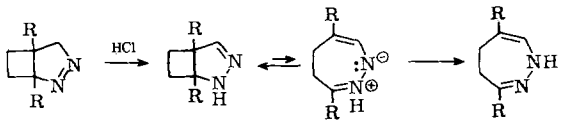
1-Pyrazolines tautomerize under acid catalysis into 2-pyrazolines. The bicyclic diazomethane adduct *(130)*, upon tautomerization to *(131)*, undergoes a ring-opening to the monocyclic *N-vinyl*azomethine imine *(132)*, which is stabilized by prototropy. The direction of this process *(131)→(133)*, dis-



(126) (127) (128) (129)

22 : 78

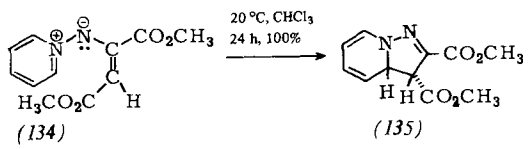
covered by *Prinzbach* and *Martin*[60], is determined by the release of ring strain (about −27 kcal mol^{-1}) which more than compensates the energy required for the conversion of a σ-bond into a π-bond (about +20 kcal mol^{-1}).



(130) (131) (132) (133)

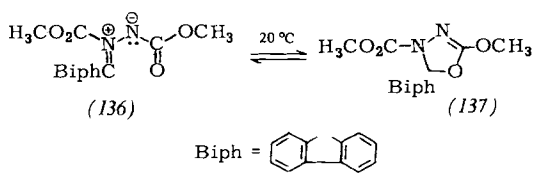
R = CO_2CH_3

N-Aminopyridinium iodide and α-chlorofumaric ester are converted by potassium carbonate into the pyridinium betaine *(134)*, which according to *Sasaki et al.*[61], cyclizes to the dihydropyrazolo[1,5-*a*]pyridine derivative *(135)*.



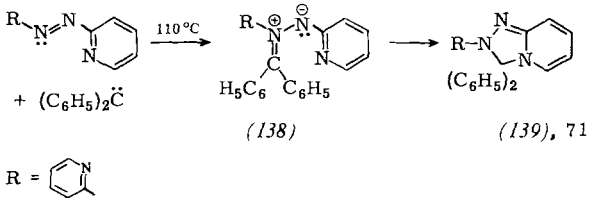
(134) (135)

Nitrogen is set free in the reaction of diazoalkanes with electrophilic azo compounds, and azomethine imines are created, which occasionally can be isolated in crystalline form[62]. The product *(136)* from diazofluorene and dimethyl azodicarboxylate, as an *N-acyl*azomethine imine, closes the ring to form the 1,3,4-oxadiazoline *(137)*. Whereas *(137)* is present in the crystalline state, *Fahr et al.*[63] have revealed a mobile ring-chain tautomerism *(137)→(136)* in solution. Above 50 °C, *(136)* isomerizes irreversibly with acyl migration into fluorenone hydrazone-N^{β}, N^{β}-dicarboxylic ester.



(136) (137)

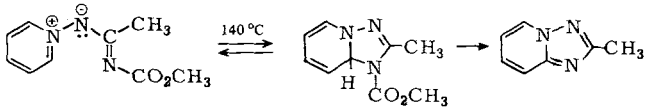
Biph =



(138) (139), 71%

R =

According to *Fahr et al.*[64], diphenyldiazomethane and 2,2′-azopyridine combine to form the dihydro-*s*-triazolo[4,3-*a*]pyridine *(139)*. Since the rate of the evolution of N_2 is that of the self-decomposition of diphenyldiazomethane, diphenylcarbene can be considered responsible for the formation of the *N-imino*-azomethine imine *(138)*.

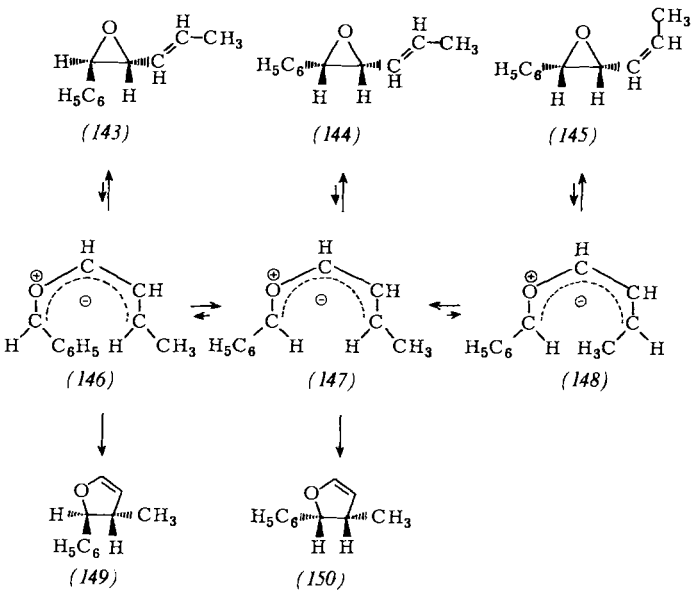


(140) (141) (142), 60%

While in *(138)* the quasi-imino group belongs to a pyridine ring, in *(140)* the latter is integrated into the azomethine imine system. *Kakehi et al.*[65] observed that the electrocyclization *(140)*→*(141)* is followed by aromatization to give *(142)* with formal elimination of methyl formate.

8.3. Conjugated Carbonyl Ylides and Carbonyl Oxides

*Vinyl*carbonyl ylides are obtained by the thermal CC ring-opening of vinyloxiranes; as expected, they enter into electrocyclic ring closure to yield 2,3-dihydrofurans.



(143) (144) (145)

(146) (147) (148)

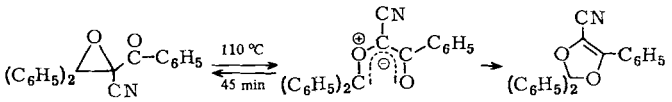
(149) (150)

Stereochemical studies of *Paladini* and *Chuche*[66] with 2-phenyl-3-propenyloxiranes have revealed a pronounced stereoisomerization of the oxiranes after short reaction times. For example, almost identical mixtures of products were reached after 3 h at 240 °C:

(143) → 30% *(143)*, 6% *(144)*, 62% *(150)*, 2% *(149)*
(144) → 30% *(143)*, 9% *(144)*, 61% *(150)*

Recyclization to oxiranes and 1,5-ring closure to dihydrofurans are competing reactions of the vinylcarbonyl ylides *(146)—(148)*. The predominance of the *trans*-oxirane *(143)* in the recovered starting material is due to its higher share in the equilibrium *(143)*⇌*(144)*. The stereoisomerization may be achieved by symmetry-allowed conrotation followed by rotation of the vinylcarbonyl ylide, *(146)*⇌*(147)*, or else through the combination of a conrotatory with a symmetry-forbidden disrotatory reaction step. In experiments at 400 °C, in addition, a low yield of *(145)* from *(144)* indicates a *trans-cis* isomerization in the propenyl side chain; this transformation must result from rotation about the 4,5-bond, *(147)*→*(148)*.

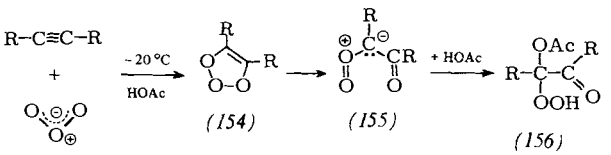
The preferred formation of the *cis*-dihydrofuran *(150)* would correspond to the allowed disrotatory ring closure of the vinylcarbonyl ylide *(147)*, *i.e.*, the sterically preferred U configuration with terminal *exo*-substituents. In view of the exergonic nature of the 1,5-cyclization, one may presume an early transition state; steric hindrance in the vinylcarbonyl ylide therefore affects the energy level of the transition state more strongly than steric factors in the dihydrofuran. The studies of *Eberbach et al.*[67] also support the conclusion that, as compared with the vinylazomethine ylides (Section 8.1), the vinylcarbonyl ylides exhibit greater configurative mobility and a smaller influence of orbital control on the ring closure.



(151) (152) (153), 100%

Since acyl residues and cyano groups stabilize carbonyl ylides better than vinyl and phenyl groups, the conversion of the acyloxirane *(151)* *via* the *acyl*carbonyl ylide *(152)* into the dioxole *(153)* proceeds at a lower temperature than *(143)*→*(146)*, according to *Foucaud et al.*[68].

The key role of the carbonyl oxides within the framework of the *Criegee* mechanism for the ozonolysis of alkenes is no longer questioned nowadays[69,70]. The electrocyclic ring closure of *C-vinyl*carbonyl oxides has not yet been reported. On the other hand, *C*-acylcarbonyl oxides are postulated as intermediates in the ozonolysis of alkynes.



(154) (155) (156)

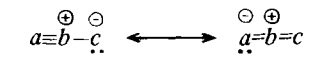
R = CH_2–O–C(=O)–C_6H_5

Criegee and *Lederer*[71] obtained the acetoxyhydroperoxide *(156)* in 83% yield by the action of ozone on 2-butynylene dibenzoate in the presence of acetic acid. The pathway through the 1,2,3-trioxole *(154)* and its electrocyclic ring opening to the acylcarbonyl oxide *(155)* is attractive. The conversion of a C—O bond (+86 kcal mol^{-1}) and an O—O bond (+35 kcal mol^{-1}) into a C=O double bond (−176 kcal mol^{-1}) more than compensates the energy of charge separation. The orbitals of the unshared electron pairs at the O-atoms eliminate the necessity for 90° rotations during the cleavage of the O—O bond.

9. Cyclizations of Conjugated 1,3-Dipoles of the Propargyl-Allenyl Type

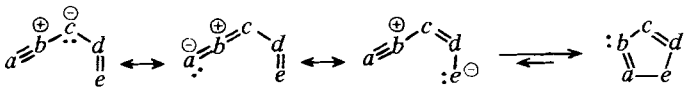
9.1. Mechanistic Considerations

The 1,3-dipoles *(157)* differ from *(100)* by an additional π-bond between *a* and *b*, which requires σ-bonds of the sp-hybrid type for *b*. With the possible exception of the nitrile ylides[72], all nitrilium and diazonium betaines[28] are linear.



(157)

The π-orbitals of the extra bond between *a* and *b* are perpendicular to the molecular orbital of the allyl anion.



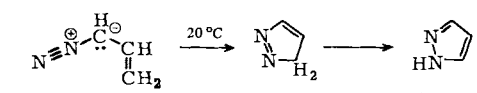
(158) *(159)*

In *(158)* the allyl anion system of the 1,3-dipole of propargyl-allenyl type is extended by an additional double bond *d*=*e*. As in *(101)*, the octet structures *(158)* indicate the fixation of the formal positive charge on *b*, the central atom of the 1,3-dipole, which in this case must be a nitrogen atom; no other element of the first long period harbors an onium charge in the tetracovalent state. A methine group CR or another N-atom can take over the role of *a* in the nitrilium and diazonium betaines, respectively; *c* appears in the subclasses as ylide carbon or imine nitrogen. We are facing in *(158)* a pentadienyl anion with an isoelectronic exchange at *b* and up to four additional isoionic replacements.

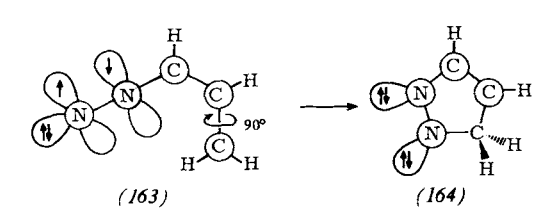
A glance at the scheme *(158)*→*(159)* suggests limitations to the abundance[29]. The conjugated double bond *d*=*e* cannot be located at the terminus *a* of *(157)*, since the resulting 5-membered ring would have to accomodate cumulated double bonds.

Like the concerted 1,3-cycloadditions of *(157)* to dipolarophiles, the cyclization of *(158)* demands the bending of the linear structure *a*—*b*—*c*. A new feature: the ring-closed product *(159)* lacks the allyl anion resonance of the cyclopentenyl anion *(2)*. The n-orbital of the unshared electron pair at *b* is in fact located *in the plane of the ring* and maintains no conjugation with the π-bond in *c*=*d*. Actually, *(159)* constitutes a cyclopentadiene derivative or a five-membered heteroaromatic ring if *e* is capable of conjugation.

Are the numerous known ring closures *(158)*→*(159)* still electrocyclic reactions of the pentadienyl anion type? The cyclization of vinyldiazomethane *(160)*[173] may serve as a model for the discussion of stereoelectronic pathways whose differentiation is, to some extent, more semantic than mechanistic. The 3*H*-pyrazole *(161)* first produced is transformed by prototropy into the aromatic pyrazole *(162)*.

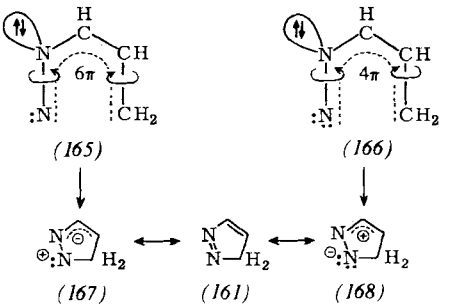


(160) *(161)* *(162)*



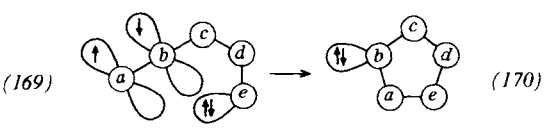
(163) *(164)*

A. In *(163)* the circles demonstrate the 6π-electron system of the pentadienyl anion, the atomic orbitals of which are perpendicular to the plane of the σ-bonds. The extra π-bond of the diazonium group in *(163)*—orbitals in the plane of the paper—is electrophilic. Its two π-electrons are localized as an unshared pair at the inner nitrogen if a nucleophile attacks the outer N-atom. The terminal carbanionic CH_2 group can act as a nucleophile, *one* 90° rotation being required for the conversion *(163)*→*(164)*. Thus, it is not the NN fragment of the pentadienyl system that is involved in the formation of the new σ-bond, but rather the extra π-bond. Hence, of the five π-atomic orbitals that form the pentadienyl system of vinyldiazomethane in *(163) four* are retained during ring closure and constitute the 1,2-diaza-1,3-diene system of the 3H-pyrazole *(164)*.



(165) *(166)* *(167)* *(161)* *(168)*

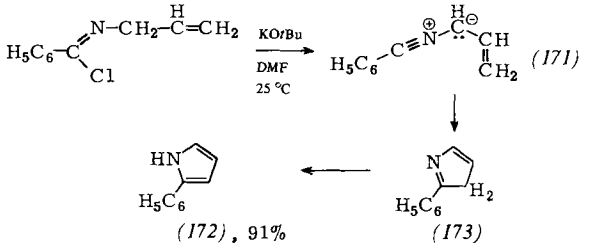
B. In a second model, two 90° rotations about terminal bonds are assumed and the continuous molecular motion is formally broken down into steps. The reaction begins with the bending of the linear diazomethane system of *(163)*; in *(165)*, the electrons of the extra π-bond appear on the inner nitrogen, and a nitrene function, *i.e.*, an electron sextet, arises on the terminal nitrogen. Now either a double-occupied or a vacant atomic orbital of this nitrene nitrogen enters into the pentadienyl system, which either closes the ring as a 6π-system in accordance with *(165)*→*(167)* or undergoes a 4π-cyclization of the pentadienyl cation type, *(166)*→*(168)*. The structures, among which *(167)* contains the allyl anion group and *(168)* that of the allyl cation, are minor resonance contributors of the 1,3-diene system of *(161)*. The distinction between the 6π- and 4π-route is probably only fictitious, particularly as the N-terminus rules out any differentiating between disrotation and conrotation.



(169) *(170)*

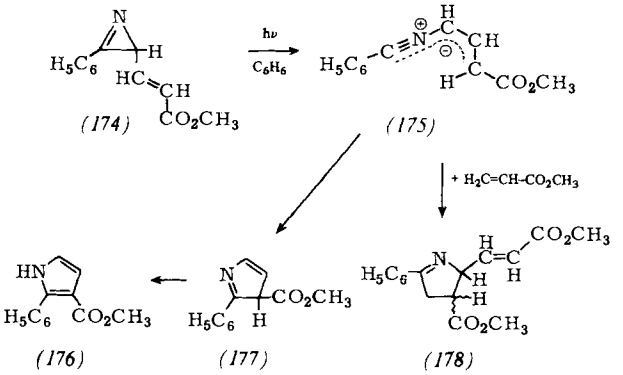
C. A ring closure without rotation is conceivable for *(158)*, *e*=NR or O. The unshared electron pair of the n-orbital at *e* functions as a nucleophile and creates a new σ-bond by overlapping the orbital of the extra π-bond at *a*. The 6π-system of the open-chain species *(169)* is preserved intact in the π-cloud of the aromatic ring *(170)*. A description of the process as a nucleophilic addition of *e* to the electrophilic onium bond $a{=}b^{\oplus}$ would be equivalent.

9.2. Conjugated Nitrile Ylides



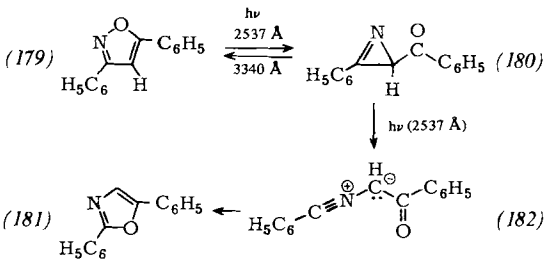
(172), 91% (173)

Nitrile ylides cannot be isolated so far. These 1,3-dipoles were first made available for *in situ* cycloadditions by elimination of HCl from imidoyl chlorides[74]. Recently *Steglich et al.*[75] have set free the benzonitrile *N*-allylide *(171)*, which, as a *vinyl* nitrile ylide, immediately closed the ring; *via* the 3*H*-pyrrole *(173)*, 91% of *(172)* was formed.



(174) (175) (176) (177) (178)

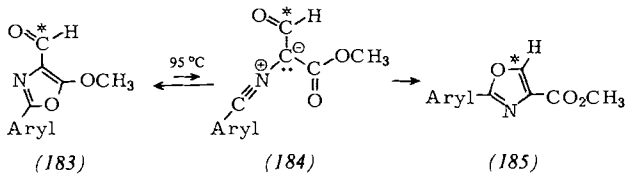
The light-induced electrocyclic ring opening of 2*H*-azirines offers an elegant method for the synthesis of the nitrile ylides. *Padwa et al.*[76] converted the 2*H*-azirine *(174)* into *(175)*, which formed the 3*H*-pyrrole ring *(177) in situ*; the aromatic tautomer *(176)* was isolated in 95% yield. On irradiation of *(174)* in the presence of methyl acrylate, intramolecular cyclization was suppressed in favor of the intermolecular 1,3-dipolar cycloaddition to give *(178)*.



(179) (180) (181) (182)

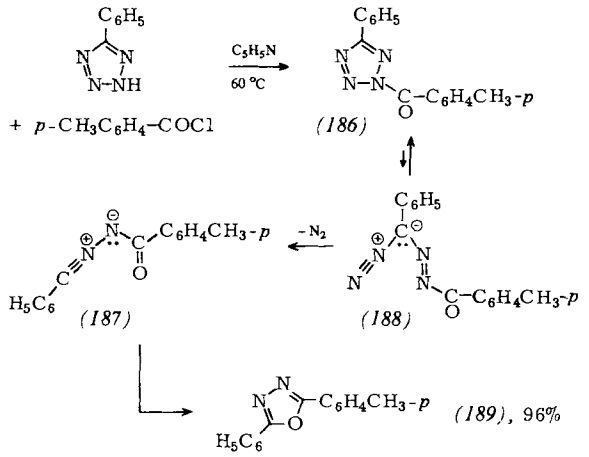
In the surprising photorearrangement of 3,5-diphenylisoxazole *(179)* into 2,5-diphenyloxazole *(181)*, *Singh* and *Ullman*[77] isolated 2-benzoyl-3-phenyl-2*H*-azirine *(180)* as an intermediate. The photochemical behavior of *(180)* is controlled by the wavelength of the light used. Whereas 3340 Å causes the reversal of the ring contraction, *(180)*→*(179)*, shorter wavelength light induces an electrocyclic ring opening to yield the *acyl* nitrile ylide *(182)*, which cyclizes in a dark reaction to the oxazole *(181)*.

Two acyl residues on the nitrile ylide carbon have such a successful stabilizing effect that a *thermal* equilibrium of 4-acyloxazoles with a small concentration of the diacyl nitrile ylide is established. *Cornforth*[78] was the first to observe thermal transformation of 5-methoxyoxazole-4-carbaldehydes *(183)* or -4-carboxamides into methyl oxazole-4-carboxylates *(185)* or their 5-amino derivatives. The interchange of the 5-C atom of the oxazole with the C-atom of the aldehyde or carboxamide side chain, as was to be expected for an intermediate nitrile ylide of type *(184)*, was demonstrated by ^{14}C-labeling[79].



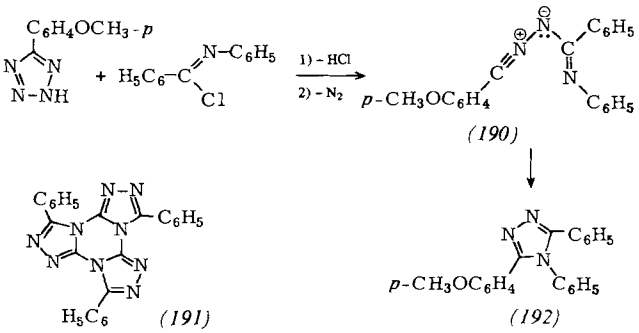
(183) (184) (185)

9.3. Conjugated Nitrile Imines



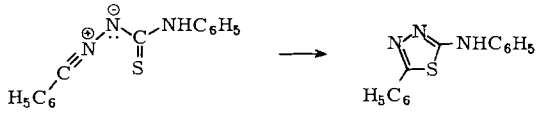
(186) (187) (188) (189), 96%

An excellent synthesis of 1,3,4-oxadiazoles which may bear aryl or alkyl substituents is based on the electrocyclic ring closure of *N-acyl* nitrile imines[80]. 5-Phenyltetrazole reacts with *p*-toluoyl chloride in pyridine to produce 96% of the oxadiazole *(189)*. The evolution of nitrogen obeys first-order kinetics[81], *i.e.*, the steps after the acylation to give *(186)* are rate-determining. The electrocyclic ring opening to the *acylazo* diazoalkane *(188)* probably takes place in an equilibrium that is continuously disturbed by the loss of N_2. For its part, the new *N-acyl* nitrile imine *(187)* closes the oxadiazole ring of *(189)*. The reaction scheme includes two electrocyclic steps of the pentadienyl type. This reaction scheme has been developed into a duplication process which affords polyaryls with alternating benzene and 1,3,4-oxadiazole units[82].



(190) (191) (192)

Imidoyl chlorides react analogously with tetrazoles, *e.g.*, 5-(4-methoxyphenyl)tetrazole with *N*-phenylbenzimidoyl chloride to give the 1,2,4-triazole derivative *(192)* in 99% yield[83]. The electrocyclization of *N-imino* nitrile imines of the type *(190)* provides the key step for this general synthesis of 1,2,4-triazoles. Cyanuric chloride, as a triple aromatic imidoyl chloride, combines with three equivalents of 5-phenyltetrazole to give 70% of *(191)*[84].

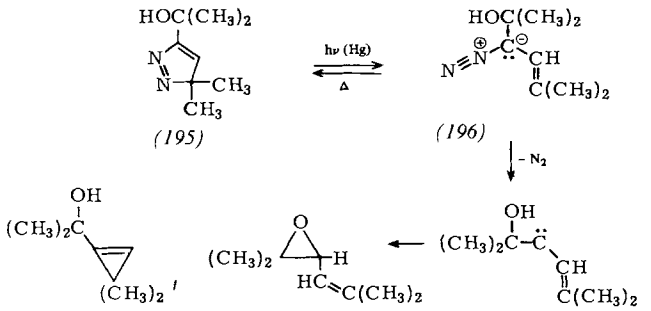


(193) *(194)*

5-Phenyltetrazole and phenyl isothiocyanate at 160 °C furnish the 1,3,4-thiadiazole derivative *(194)* in 64% yield *via* the *N-thiocarbonyl* nitrile imine *(193)*[84].

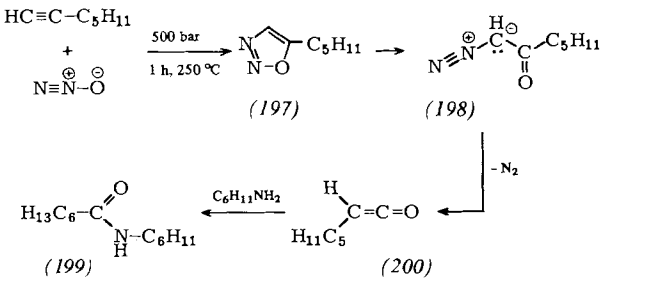
9.4. Conjugated Diazoalkanes

The spontaneous cyclization of *vinyl*diazomethane *(160)* to pyrazole *(162)*[73] has been discussed in Section 9.1; it takes place with a half-conversion time of 3.2 h at 25 °C[85]. *Ledwith* and *Parry*[86] found the photoconversion to be only three times faster than the thermal reaction, and considered it possible that the photochemical step is merely the tautomerization of the 3*H*-pyrazole *(161)* to *(162)*. The cyclization of *trans*-styryldiazomethane is accelerated only slightly by electron-donating substituents ($\rho = -0.40$); *Brewbaker* and *Hart*[85] concluded that there was only a slight loss of charge at the γ-carbon atom in the transition state.



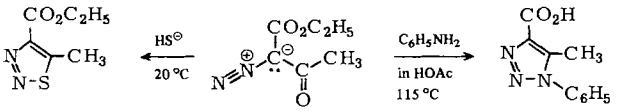
(195) *(196)*

γ,γ-Disubstituted vinyldiazomethanes form the non-aromatic 3*H*-pyrazoles quite slowly. In their photolysis, *Closs* and *Böll*[87] found access to cyclopropenes; the transient red color suggested diazoalkanes to be intermediates. In the photolysis of *(195)*, *Day* and *Whiting*[88] detected spectroscopically up to 65% of the vinyl diazoalkane *(196)* as an intermediate; acetic acid converted *(196)* into the ester with evolution of N_2. Further irradiation of *(196)* is accompanied by the elimination of N_2. The recyclization *(196)*→*(195)* in the dark is slow.



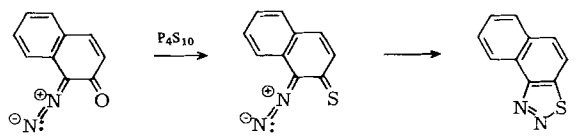
(197) *(198)* *(199)* *(200)*

*Acyl*diazomethanes (diazoketones) are stable and do not undergo ring closure to form 1,2,3-oxadiazoles; this is due to the weakness of the NO σ-bond in the latter and the stabilization of the negative charge by the diazoketone oxygen. 1,2,3-Oxadiazoles are hypothetical, although plausible, intermediates in the 1,3-dipolar cycloadditions of dinitrogen oxide to alkynes. *Buckley* and *Levy*[89] studied the pressure reactions of N_2O with 1-heptyne in the presence of cyclohexylamine and isolated the *N*-cyclohexylamide of heptanoic acid *(199)* in 94% yield. The presumable pathway includes an electrocyclic opening of the 1,2,3-oxadiazole *(197)* to the diazoketone *(198)*. The latter decomposes at 250 °C with Wolff rearrangement, and the intermediate ketene *(200)* is intercepted by cyclohexylamine.



(201) *(202)* *(203)*

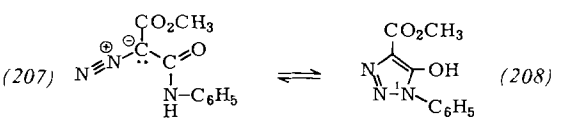
In contrast to the α-diazocarbonyl compounds, the *thiocarbonyl*diazoalkanes undergo ring closure immediately. In 1904, on treating α-diazoacetoacetic ester *(202)* with ammonium hydrogen sulfide, *Wolff* obtained 5-methyl-1,2,3-thiadiazole-4-carboxylic ester *(201)*[90]; the thioacyldiazoalkane probably occurred as an intermediate. The lower bond energy of C=S (128 kcal mol^{-1}) compared with C=O (179 kcal mol^{-1}) causes a shift of the energy balance in favor of the cyclic product.



(204) *(205)* *(206)*

A similar situation is met in the aromatic series. "*o*-Quinone diazides" of type *(204)* exist in the diazoketone form[91]. *Bamberger et al.*[92] converted 1,2-naphthoquinone 1-diazide with P_4S_{10} into the naphthothiadiazole *(206)*, but were unable to isolate the thione *(205)*.

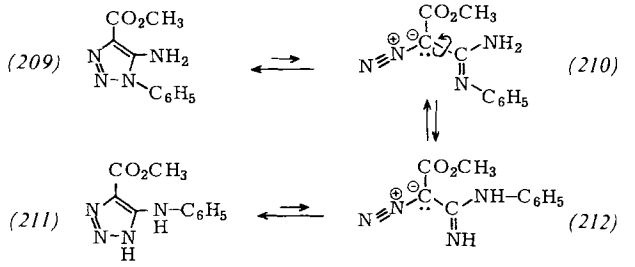
According to *Wolff et al.*, α-diazoacetoacetic ester *(202)* reacts with aniline in boiling acetic acid to give 5-methyl-1-phenyl-1,2,3-triazole-4-carboxylic acid *(203)*[93]. In their tendency to undergo ring closure, *imino*diazoalkanes occupy an intermediate position.



(207) *(208)*

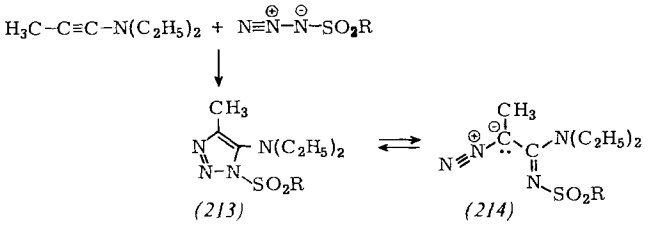
A masterly investigation carried out by *O. Dimroth*[94] in 1910 revealed the tautomerism of the yellow diazomalonic ester anilide *(207)* with the colorless 5-hydroxytriazole-4-carboxylic ester *(208)*. The yellow compound was originally considered to be a triazolonecarboxylic ester, and a keto-enol tautomerism with *(208)* was proposed[95]. The open-chain diazo compound *(207)* was finally recognized without resorting to spectroscopic methods, which were still unknown in 1910.

Kinetic measurements have disclosed a relationship between the rate and the equilibrium constants for the ring opening of *(207)*, when the 1-phenyl in *(207)* is replaced by H, alkyl, or some other aryl residues. The more strongly the 1-substituent of the triazole *(208)* demands a share of the electron pair at N-1, the smaller is the concentration of the cyclic tautomer in the equilibrium mixture, and the rate constants of ring opening increase by a factor of 10^5 [94]. The well-investigated tautomerism *(207)*⇌*(208)* nevertheless still harbors a mystery. In *(207)*, is there an azo coupling with the anilino nitrogen, followed by prototropy to *(208)*, or does a proton shift of *(207)* to the iminol tautomer precede the electrocyclic ring closure?



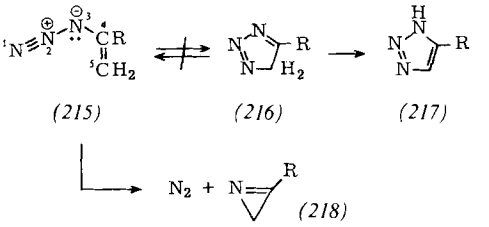
Another discovery of *Dimroth*'s concerns the equilibrium between the 5-amino-1-phenyl-1,2,4-triazole *(209)* and the 5-anilinotriazole *(211)*, which is established at 150 °C or at even lower temperatures with base catalysis, and which in methanol attains a ratio of 30:70 [94]. A migration of the phenyl residue was rigorously excluded, and a reaction pathway *via* the tautomeric amidines *(210)* and *(212)* was proposed.

Lieber et al.[96] introduced substituents into the 1-phenyl residue of 5-amino-1,4-diphenyl-1,2,3-triazole, which is analogous to *(209)*, and observed for the "Dimroth rearrangement" a linear relationship between the logarithms of the rate and equilibrium constants. In a kinetic investigation of the acid catalysis of the isomerization *(209)*⇌*(211)*, *Brown, Hammick,* and *Heritage*[97] noticed a second-order reaction only at low acidities, whereas for pH > 4 a plateau value was reached. This indicates an acid catalysis of the amidine tautomerization, *(210)*⇌*(212)*.



The 1-sulfonyltriazoles arising from the cycloaddition of sulfonyl azides to 1-diethylaminopropyne are surprising in the mobility of the electrocyclic equilibrium with the *amidino*diazoethanes, *e.g. (213)*⇌*(214)*[98]. According to *Himbert* and *Regitz*[99], the equilibrium is established in cold chloroform and contains the following amounts of the triazole derivative *(213)*: 100% for R = $C_6H_4N(CH_3)_2$-*p*, 62% for C_6H_5, 30% for C_6H_4Cl-*p*, and 0% for $C_6H_4NO_2$-*p*. In the case of the 1-aryl-5-aminotriazoles of type *(209)*, the open-chain form *(210)* is not directly detectable. The fact that they are favored in the case of 1-sulfonyltriazoles of type *(213)* originates in a disturbance of the triazole resonance and in a stabilization of the negative charge in the amidinodiazoalkane *(214)* by the sulfonyl group.

9.5. Conjugated Azides

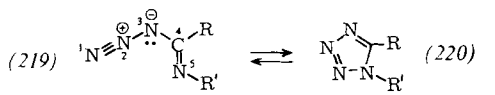


A negative experience may be more exciting than a wagonload of further confirmations of the general reaction scheme: *vinyl* azides *(215)* do not cyclize to 1,2,3-triazoles *(217)*! Instead, 2*H*-azirines *(218)* are formed with evolution of N_2[100], as was first uncovered by *Smolinsky*[101] for *(215)*, R = C_6H_5 (350 °C, gas phase).

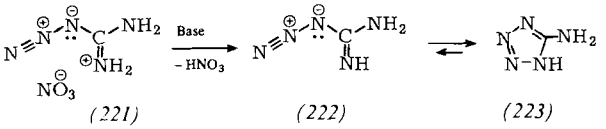
Even if the cyclization *(215)*→*(216)* were deficient in thermodynamic driving force, which is unlikely, the subsequent aromatization of the 4*H*-triazoles, *(216)*→*(217)*, would overcome an unfavorable position of the equilibrium *(215)*⇌*(216)*. Is it conceivable that the prototropy *(216)*→*(217)* is slow enough to be exceeded by the nitrogen-eliminating process *(215)*→*(218)*? This seems all the less probable since *(216)* should be a stronger acid than the 3*H*-pyrazole *(161)* which is passed as an intermediate en route from vinyldiazomethane *(160)* to pyrazole *(162)*. The latter reaction in fact proceeds much faster (E_a = 22.6 kcal mol^{-1}) than the formation of azirines from vinyl azides, for which E_a values of 26.6—30.5 kcal mol^{-1} have been measured[102]. A 3,5-ring closure of *(215)* with simultaneous departure of N_2 (no free nitrene) is favored in the literature as pathway for the formation of 2*H*-azirines from vinyl azides.

Leroy et al.[103] have carried out quantum-chemical calculations on the cyclization of vinyl azide, *(215)*→*(216)*, R = H, in which a 90° rotation about the terminal CC bond, but no rotation about the bond between N-1 and N-2 was assumed; this conforms to reaction path A of Section 9.1. Scanning of the hypersurface with an *ab initio* SCF method indicated an early transition state with a weak 1,5-bond and 25° rotation about the C4—C5 bond. The originally stretched azide system is bent to 129° in the transition state and the electrons of the extra π-bond between N-1 and N-2 are localized as lone pair on N-2. The activation energy was calculated with the STO-3G basis set as 33 kcal mol^{-1}, but with 4-31G as 41 kcal mol^{-1}; still greater is the discrepancy in the heats of the reaction (−56 and −11 kcal mol^{-1}). A comparative calculation of the cyclization of vinyldiazomethane would be desirable.

1,2,3-Triazoles can be obtained from vinyl azides by base catalysis. This conversion, taking place in the anion, will be described in Section 12.2.



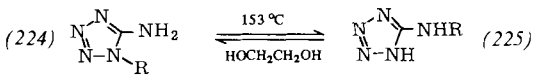
When attempts are made to prepare *imino*azides *(219)* from imidoyl chlorides or nitrilium salts with the azide anion or in other ways, the tetrazoles *(220)* are isolated instead. The aromatic nature of the cyclic product *(220)* is probably responsible for the position of the equilibrium in this highly mobile system. Only electron-attracting substituents are capable of stabilizing the azide form; *inter alia (219)*, $R = CF_3$ and $R' = \beta$-naphthyl[104], and also $R = C_6H_5$, $R' = OH$ or OCH_3[105], have been reported.



(221) *(222)* *(223)*

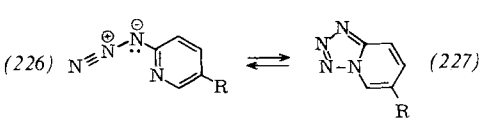
In 1892, in his investigation of aminoguanidines, *Thiele*[106] liberated "Amidotetrazotsäure", *i.e.*, 5-aminotetrazole *(223)*, with sodium acetate from "diazoguanidine nitrate" which *Hantzsch* and *Vagt*[107] correctly formulated as *(221)*. The cyclization of the *guanyl* azide *(222)* occurs in water at pH 9 and 0 °C with a half-conversion time of 2.2 min; the activation energy amounts to 17.8 kcal mol^{-1}[108].

In the same way as for the cyclization *(215)*→*(216)*, R = H, *Leroy et al.*[109] carried out an *ab initio* calculation of the energy surface for the reaction *(219)*→*(220)*, R = R' = H. They based the cyclization on the simple reaction model C (Section 9.1): N-5 moves with its lone pair without rotation toward the extra π-bond located in the plane of the σ-skeleton. The transition state is reached when the azide system has bent to an angle of 136°. Here again the activation energy and the heat of reaction depend to an irritatingly large extent on the basis set: 12.3 and −66 kcal mol^{-1} for STO-3G as well as 24 and −18 kcal mol^{-1} for 4-31G[103].



(224) *(225)*

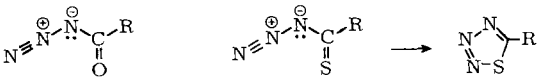
The Dimroth rearrangement of 1- and 5-substituted tetrazoles, *(224)*⇌*(225)*, proceeds *via* the substituted *amidino*azides. Their concentration in the equilibrium with *(224)* and *(225)* is so small that the rearrangement requires high temperatures. *Henry, Finnegan,* and *Lieber*[108] determined the following equilibrium proportions of the 1-substituted tetrazoles *(224)*: 96% for $R = CH_3$, 37% for $R = C_6H_5$, and 21% for $R = C_6H_4Cl$-*p*. Electron-attracting 1-substituents destabilize the tetrazole *(224)* as delineated in Section 9.4 for the 5-amino-1,2,3-triazoles, *(209)*⇌*(211)*. For R = aryl, the logarithms of the rate and equilibrium constants gave linear Hammett plots.



(226) *(227)*

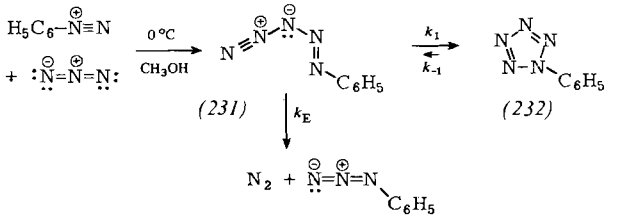
2-Pyridyl azide *(226)*, R = H, is unknown, but exists in the form of tetrazolo[1,5-*a*]pyridine *(227)*, R = H; on cyclization, the aromatic resonance is retained. A small equilibrium concentration of *(226)*, R = H, is exhibited in 1,3-dipolar cycloadditions to enamines[110] or to acetylenecarboxylic esters[111] at elevated temperatures.

Whereas *(227)*, $R = NO_2$, exists in the crystalline state, *Boyer* and *Miller*[112] in 1959 demonstrated the presence of a mobile equilibrium with *(226)*, $R = NO_2$, in solution. Since that time, imidazide-tetrazole equilibria have been observed and measured in so many heteroaromatics that it constitutes the most widely documented 1,5-dipolar cyclization. Electron-attracting substituents and electron-deficient N-heterocycles favor the azide tautomer for two reasons: a) The negative formal charge of the azide experiences additional delocalization; and b) the competing resonance destabilizes the annelated tetrazole ring. *Tišler*[113] and *Butler*[114] reviewed the topic.



(228) *(229)* *(230)*

Acyl azides *(228)* occur in the open-chain form, while *thioacyl* azides *(229)* cyclize completely to 1,2,3,4-thiatriazoles[115]; the analogous situation for acyl- and thioacyldiazomethanes (Section 9.4) indicates comparable resonance energies for azide and diazoalkane systems. Treatment of thioacyl hydrazides with HNO_2 yields 1,2,3,4-thiatriazoles *(230)*, and it is almost inconceivable that the azides *(229)* are not passed as intermediates. In the reaction of thiobenzoyl chloride with the azide anion at −100 °C, *(229)*, $R = C_6H_5$, was not detectable[115]; the electrocyclization to *(230)* is faster than the initial nucleophilic substitution.



(231) *(232)*

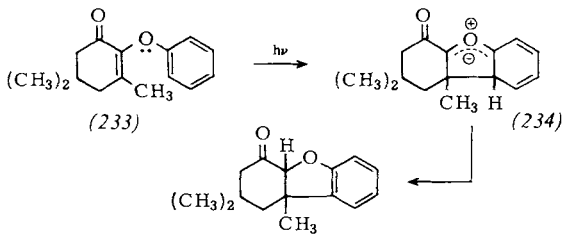
In the *imino* azides *(219)* one notices a pentadienyl anion with one isoelectronic exchange in 2-position and three additional isoionic replacements. With no carbon atom remaining, the *benzene diazo* azide *(231)* represents the logical extreme. Pentazoles are organic compounds *honoris causa*, because they figure as the end of the road in the aromatic azole family.

Prepared by azo coupling of benzenediazonium chloride with lithium azide in methanol, the benzene diazo azide *(231)* is rapidly channeled into two competing processes: The elimination of nitrogen (k_E) to give phenyl azide and the electrocyclic ring closure to *(232)* occur in a ratio of 76:24[116]. The phenylpentazole *(232)* decomposes *via* the open-chain diazo azide *(231)* into phenyl azide and nitrogen with a half-life of 14 min at 0 °C. Not only the fate of a ^{15}N label[116], but also the UV spectrum of the pure and crystallizable phenylpentazole[117] confirms the structure *(232)*. The rate of decomposition of the arylpentazoles depends on the nature of the aryl group in the same way as the rate of the Dimroth rearrangements, *(209)*→*(211)* and *(224)*→*(225)*. For *(232)*, $C_6H_4NO_2$-*p* instead of C_6H_5, the half-life decreases to 2 min, whereas for $C_6H_4N(CH_3)_2$-*p* and $C_6H_4O^{\ominus}$-*p* it increases to 69 and 127 min, respectively, at 0 °C[118].

In an alternative description, the azide ion combines in a 1,3-dipolar cycloaddition with the benzenediazonium ion directly to *(232)*, and in a competing decomposition yields N_2 + phenyl azide *via (231)*. Within this second reaction model, the decomposition of the pentazole *(232)* involves a one-step 1,3-dipolar cycloreversion[119]. The analogy with the imino-azide-tetrazole system is so close that we prefer the scheme with the electrocyclic reaction *(231)*⇌*(232)*.

10. Isoelectronic Exchange in Position 3

10.1. Photocyclizations of Charge-Free Systems

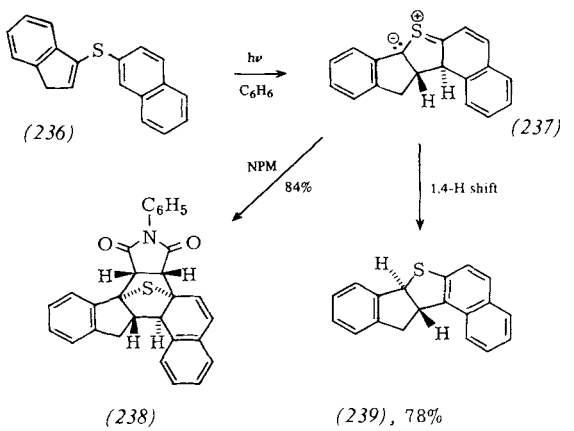


(233) *(234)* *(235)*, 95%

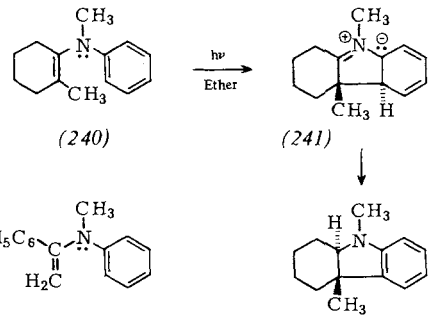
In *(233)* we recognize a derivative of divinyl ether which, for its part, is derived from the pentadienyl anion by isoelectronic replacement of the 3-CH by an oxygen atom. According to *Schultz* and *Lucci*[120], *(233)* undergoes a light-induced cyclization to the hydrobenzofuran derivative *(235)*; the cyclic carbonyl ylide *(234)* is stabilized by the neighboring carbonyl function and is a plausible intermediate. With a concluding prototropy the net process *(233)*→*(235)* may well be exergonic.

In contrast to divinyl sulfide, phenyl vinyl sulfide is subject to photocyclization, and in the presence of iodine it gives a small quantity of benzo[*b*]thiophene[121]. Acyl substitution contributes to stabilization of the thiocarbonyl ylide; compound *(233)* with S in place of the ethereal O on irradition gives *(234)*, S instead of O, in 91% yield[122]. The following example substantiates the conrotation of the electrocyclization that is prescribed by orbital control for the first excited singlet state.

According to *Schultz* and *De Tar*[123], 3-indenyl-2-naphthyl sulfide *(236)* in benzene undergoes a photorearrangement to yield 78% of the pentacyclic dihydrothiophene derivative *(239)*. The *trans* linkage of the five-membered ring in *(239)* is the expected result of a conrotatory photocyclization *(236)*→*(237)* with a subsequent suprafacial 1,4-H shift; the latter is a symmetry-allowed, thermal sigmatropic process. If the irradiation of *(236)* is carried out in the presence of *N*-phenylmaleimide (NPM) as a dipolarophile, the intermediate thiocarbonyl ylide *(237)* is trapped and is converted into the cycloadduct *(238)*. X-Ray structure analysis has elucidated the configuration *(238)* with *trans*-vicinal H atoms at the new σ-bond that is established during the electrocyclization *(236)*→*(237)*. Since triplet sensitizers have no effect, it was assumed that ring closure starts from the S_1 state of *(236)*. However, recent flash photolysis studies with related unsaturated sulfides suggested an excited triplet state as reactive intermediate[123a].

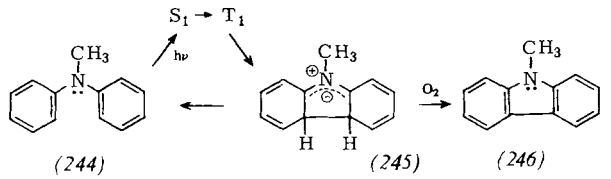


(236) *(237)* *(238)* *(239)*, 78%



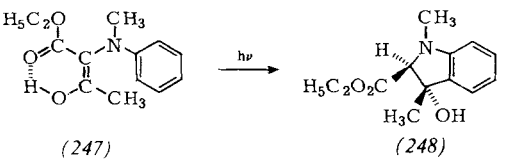
(240) *(241)* *(242)* *(243)*, 75%

Chapman et al.[124] studied the photocyclization of the *N*-cyclohexenylaniline derivative *(240)*, which yielded the tetrahydrocarbazole derivative *(243)*; *trans* linkage of the saturated ring was secured by X-ray structure analysis of a dibromo derivative of *(243)*. Here again the conclusion of conrotatory ring closure to the azomethine ylide *(241)* and a suprafacial 1,4-H shift is probable. An increase in the quantum yield by triplet sensitization was pointed out for another model, *N*-methyl-*N*-(α-phenylvinyl)aniline *(242)*. For direct irradiation a cyclization from the S_1 state seems possible, since triplet quenchers had no effect.



(244) *(245)* *(246)*

In the flash excitation of *N*-methyldiphenylamine *(244)*, *Grellmann et al.*[125] observed the appearance of an intermediate absorbing at 610 nm, which was ascribed to the azomethine ylide *(245)*. In a degassed cyclohexane solution, *(245)* reverted to *(244)* with a half-conversion time of 11 msec at 25 °C, while in the presence of O_2 *N*-methylcarbazole *(246)* was formed. Quantitative experiments revealed an inhibition of the formation of *(245)* by oxygen; a preceding excited triplet state was assumed.

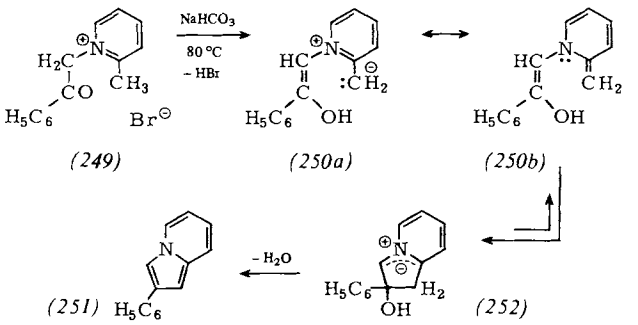


(247) *(248)*

The light-induced cyclization of 2-(*N*-methylanilino)acetoacetic ester *(247)* to the dihydroindole derivative *(248)* is quantitative. The addition of some acetic acid to the medium caused the dehydration of *(248)* to 1,3-dimethylindole-2-carboxylic ester[126].

10.2. Thermal Cyclizations of Charge-Free Systems with Subsequent Reactions

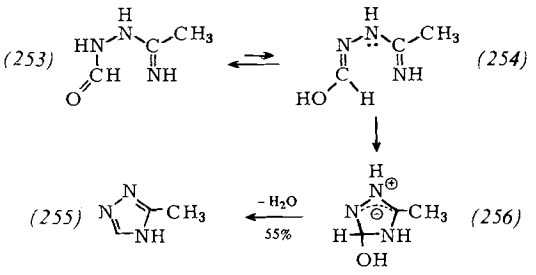
The Chichibabin synthesis of indolizines[127] by the reaction of α-picoline and derivatives with α-haloketones has been studied on hundreds of examples[128]. In the isolable picolinium salts, *e.g.*, *(249)*[127], the acidity of the methyl group is increased to such an extent that even sodium hydrogen carbonate brings about deprotonation.



(249) *(250a)* *(250b)* *(251)* *(252)*

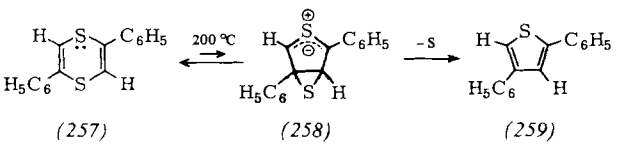
In addition to the zwitterionic structure *(250a)*, the enol can be described by the charge-free formula *(250b)*. Electrocyclization leads to the azomethine ylide *(252)*, which achieves aromaticity by elimination of water to give 2-phenylindolizine *(251)*.

As long ago as 1933, noteworthy studies by *Kröhnke*[129] emphasized the similarity of *N*-acylalkylpyridinium salts to β-diketones and make the occurrence of the enolic form *(250)* plausible. Without mechanistic studies one cannot exclude an alternative in which the ketone form reacts in an aldol type condensation[130].



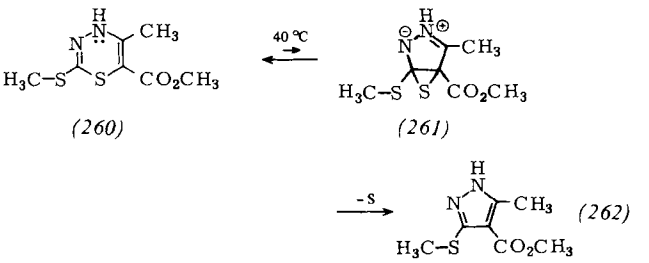
(253) *(254)* *(255)* *(256)*

Does the cyclization of the N^1-formylacetamidrazone *(253)* at 100 °C with the formation of 3-methyl-1,2,4-triazole *(255)*[131] take place *via* the iminol form *(254)*? The azomethine imine *(256)* would be aromatized by dehydration. However, a carbonyl addition starting from *(253)* offers a conceivable course without electrocyclization.



(257) *(258)* *(259)*

In 1954, *Parham* and *Traynelis*[132] observed the thermal loss of sulfur from 2,6-diphenyl-1,4-dithiin *(257)* giving rise to 2,4-diphenylthiophene *(259)* in 69% yield. An intraannular electrocyclization of the divinyl sulfide system present in *(257)* is an attractive pathway for the ring contraction; the thiocarbonyl ylide *(258)*, initially formed in small equilibrium concentration, gains aromaticity by elimination of sulfur; *cf. (74)→(73)* in Section 6. The corresponding ring contraction of 1,4-dithiin-2,3,5,6-tetracarbonitrile proceeds smoothly giving 98% of thiophenetetracarbonitrile[133]. The intermediate thiocarbonyl ylide, analogous to *(258)*, is here stabilized by two cyano residues.

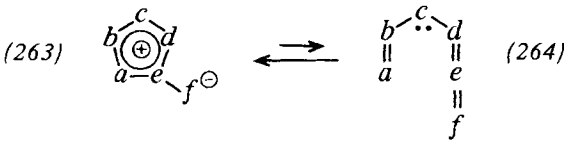


(260) *(261)* *(262)*

An N-function as an onium center should stabilize the cyclic 1,3-dipole more effectively than sulfur, since an iminium ion is better than a sulfonium ion. Several ring contractions of 1,2,4-thiadiazines are known, all based on the capacity of thiirane sulfur to undergo cheletropic elimination. According to *Beyer et al.*[134], even during recrystallization from organic media, the red *(260)* loses sulfur with the formation of the yellow pyrazole *(262)*. The bicyclic azomethine imine *(261)* is a reasonable intermediate.

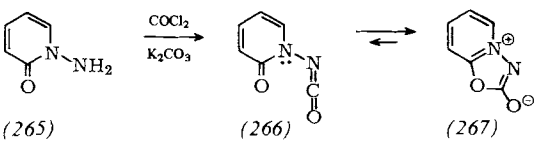
10.3. Formation and Ring Openings of Mesoionic Aromatics

For mesoionic compounds *(263)* of the so-called type A, *Ollis* and *Ramsden*[135] postulated a valence tautomerism with open-chain cumulated systems *(264)*, which contain a pentadienyl anion with isoelectronic replacement in position 3. The energy preference of the mesoionic heterocycle is so great that the spectroscopic detection of *(264)* in the thermal equilibrium with *(263)* has not yet been achieved.

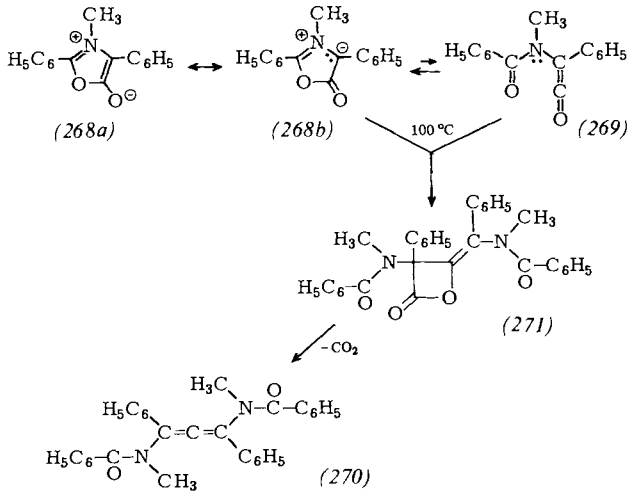


(263) *(264)*

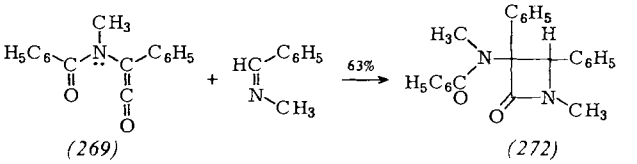
In the first synthesis of an isosydnone, the bicyclic *(267)*, *Hoegerle*[136] treated *(265)* with phosgene and potassium carbonate in chloroform. The isocyanate *(266)* is a likely, though hypothetical intermediate. Analogous acylamino iso*thio*cyanates have been suggested by *Grashey et al.*[137] as intermediates for the formation of 1,3,4-oxadiazolium-2-thiolates from carboxylic acid hydrazides and thiophosgene.



(265) *(266)* *(267)*



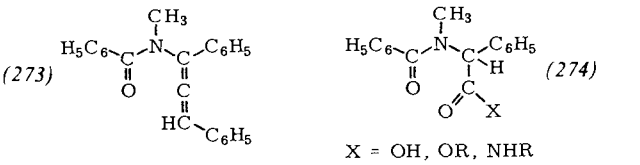
The mesoionic oxazolium-5-olate *(268)* reveals a cyclic azomethine ylide in the resonance structure *(268b)*. Thermolysis at 100 °C afforded the allene derivative *(270)* in 83% yield[138]. It is known that ketene dimers of the β-lactone type produce allenes on heating. More likely than the dimerization of the conjectured open-chain valence tautomer, the benzamidoketene *(269)*, is a combination of *(269)* with *(268)* to form the β-lactone *(271)*, which then loses CO_2. The ketene *(269)* must occur in such low concentrations that the IR absorption of the cumulated system did not become visible.



Further evidence for the intermediacy of the ketene tautomer *(269)* comes from the reaction of the "münchnone" *(268)*—the nomenclature recalls that of "sydnone"—with *N*-benzylidenemethylamine at 80 °C, which furnishes the β-lactam *(272)* in 63% yield[139]. The synthesis of β-lactams from ketenes and azomethines was discovered 70 years ago by *Staudinger*. Carbodiimides, enamines[139], and 3-dimethylamino-2*H*-azirines[140] intercept the ketene tautomer *(269)* in the same way as azomethines.

In contrast to the examples discussed in Section 10.2, the cyclic 1,3-dipole *(268)* is thermodynamically preferred to the open-chain species *(269)*. This can be ascribed to the aromaticity of the mesoionic ring *(268)* with its effective charge delocalization.

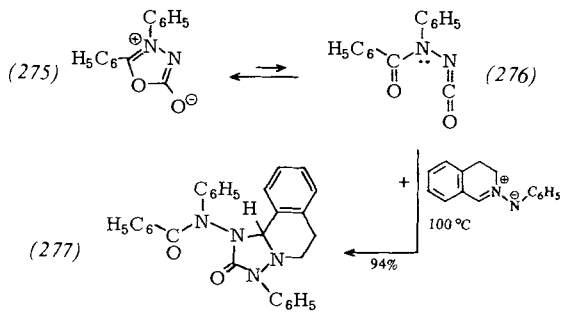
The formation of the allene *(273)* from the münchnone *(268)* with benzylidenetriphenylphosphorane likewise requires the valence-tautomeric ketene *(269)* as a reaction partner[141]. The conversion recalls one of the first carbonyl olefinations, the preparation of tetraphenylallene from diphenylketene and diphenylmethylene(triphenyl)phosphorane by *Staudinger* and *Lüscher*[142].



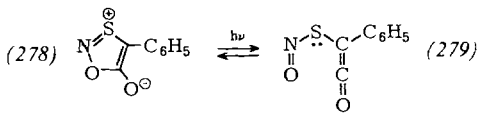
X = OH, OR, NHR

The yellow mesoionic compound *(268)* loses its color in methanol through the formation of *(274)*, X = OCH_3. Alcoholysis, hydrolysis, and ammonolysis find a simple explanation in the occurrence of the ketene form *(269)*[138].

Grashey and *Jänchen*[143] conjectured the isocyanate tautomer *(276)* to be in thermal equilibrium with diphenyl-1,3,4-oxadiazolium-2-olate *(275)* (isosydnone); the reaction with 3,4-dihydroisoquinoline gave rise to the adduct *(277)*,



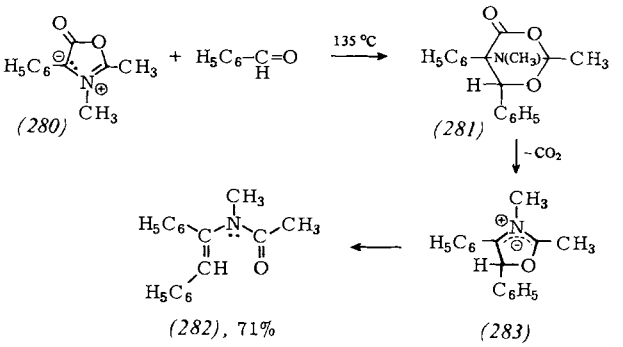
suggesting a 1,3-dipolar cycloaddition to *(276)*. The direction of the addition to *(276)* simulates that for the addition of the same 1,3-dipole to phenyl isocyanate.



The photolysis of the 1,3,2-oxathiazolium-5-olate *(278)* in a solid nitrogen matrix at 10 K[144] provides the only direct evidence for the open-chain cumulated system. The IR absorption at 2120 cm^{-1} was assigned to the ketene *(279)*.

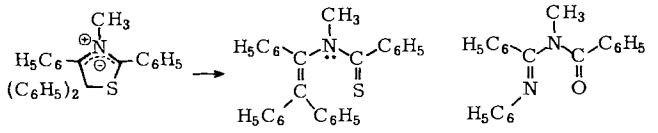
10.4. Cyclic 1,3-Dipoles as Intermediates in Cycloreversions

The above-mentioned mesoionic oxazolone *(268)* appears in the resonance formula *(268b)* as a cyclic azomethine ylide. It is indeed amenable to a variety of 1,3-dipolar cycloadditions[145]. The bicyclic primary adducts lose CO_2; *(268)* and acetylenic dipolarophiles yield pyrroles, whereas ethylene derivatives lead to 2-pyrrolines *via* new azomethine ylide intermediates.



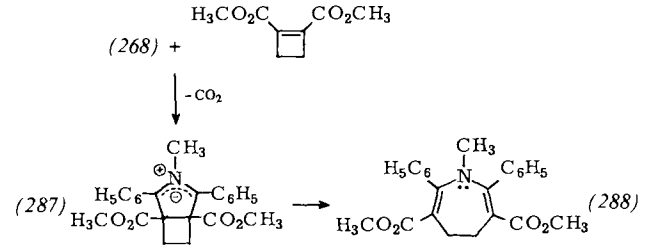
A cyclic azomethine ylide *(283)* is also encountered in the reaction of oxazolium-5-olate *(280)* with benzaldehyde. The cycloaddition to the carbonyl group is followed by loss of CO_2 from *(21)* in a 1,3-dipolar cycloreversion. This leaves a new azomethine ylide *(283)* which, in contrast to *(280)*, is no

longer aromatically stabilized; the α-(*N*-acetyl-*N*-methylamino)stilbene *(282)* emerges from an electrocyclic ring opening[146]. Different substituents in positions 2 and 4 in *(280)* disclose the direction of the addition.



(284) *(285)* *(286)*

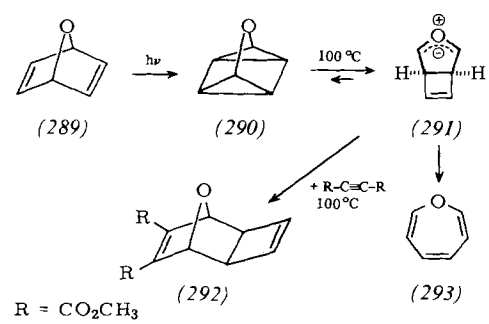
Thiocarbonyl compounds exceed carbonyl compounds in their dipolarophilic activity. Thiobenzophenone reacts with the münchnone *(268)* even at room temperature and, *via* the new azomethine ylide *(284)*, yields the thioenamide *(285)* quantitatively[147]. Nitrosobenzene also induces CO_2 evolution from *(268)* at 20 °C. A 97% yield of the *N*-benzoylamidine *(286)* was obtained[148]. In the initiating cycloaddition and the concluding electrocyclic ring opening the π- and σ-components of the dipolarophilic double bond become separated. Formulas *(282)*, *(285)*, and *(286)* illustrate this "cutting" of the dipolarophile.



(287) *(288)*

Does this cleavage also take place with olefinic dipolarophiles? Here other stabilizations of the new cyclic azomethine ylide prevail: prototropy to a 2-pyrroline or the cycloaddition to a second molecule of the dipolarophile[149]. However, in the adduct of *(268)* to cyclobutene-1,2-dicarboxylic ester, the cleavage was observed by *Martin et al.*[150]. The strain release of the four-membered ring promotes the intracyclic ring opening of the azomethine ylide *(287)* leading to *(288)*.

A particularly elegant intramolecular variant is provided by the ring opening of the 3-oxaquadricyclane *(290)* studied by *Prinzbach et al.*[151]. The photochemical intramolecular [2+2]-cycloaddition of 7-oxanorbornadiene *(289)* is followed by a 1,3-dipolar cycloreversion resulting in the carbonyl ylide *(291)*. If we accept 101 kcal mol^{-1} as the ring strain of the quadricyclane[152] and estimate the strain remaining in *(291)* to be 38 kcal mol^{-1}, the liberation of a strain energy of



(289) *(290)* *(291)* *(292)* *(293)*

R = CO_2CH_3

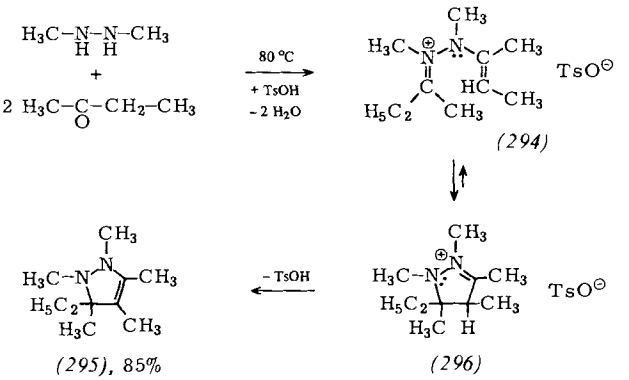
63 kcal mol^{-1} in the process *(290)*→*(291)* makes a reversal unlikely.

The isomerization of *(290)* to the oxepin *(293)* proceeds with a half-conversion time of 25 min at 100 °C[151] and constitutes an intraannular electrocyclic ring opening; *(293)*, in turn, maintains an equilibrium with benzene oxide[153]. The intermediacy of the carbonyl ylide *(291)* can be demonstrated by intercepting the 1,3-dipole with acetylenedicarboxylic ester and formation of *(292)*. The conversion of *(291)* into *(293)* does not involve a conrotatory opening of the cyclobutene ring, but a disrotatory opening of the cyclopentenyl anion type; the cyclobutene double bond does not change its position.

11. Systems with Twofold Isoelectronic Exchange

If the carbanionic function in *(1)* or *(2)* is replaced by a charge-free N-function or by an O atom, the resulting pentadienyl or cyclopentenyl systems are described by zwitterionic or charge-free resonance structures. A *second* isoelectronic exchange gives rise to systems which bear a net positive charge. Depending on the position of the exchange, the formulas harbor either a single cationic charge or two positive and one negative formal charge (Section 5.2).

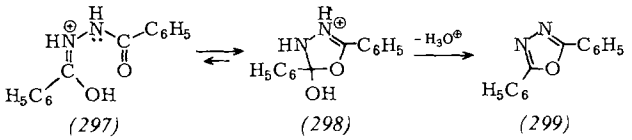
A cyclization in the cation has been discussed above for the acid-catalyzed formation of pyrazolines from α,β-unsaturated hydrazones, *(91)*→*(92)*. An analogous pathway is very likely for the acid-catalyzed condensation of ketones with 1,2-dialkylhydrazines, which has been studied by *Elguero, Jacquier et al.*[154].



(294) *(295)*, 85% *(296)*

The hydrazinium ion *(294)* is the presumed intermediate from 2-butanone and 1,2-dimethylhydrazine in boiling benzene. The cationic character of *(294)* is retained during cyclization, the onium charge in *(296)* being shifted to the neighboring nitrogen. Deprotonation gives the persubstituted 3-pyrazoline *(295)*. The cation *(294)* is derived from the pentadienyl anion structure *(1b)* by isoelectronic exchange in positions 2 and 3, whereas the cation *(91)* shows the replacements in positions 1 and 2.

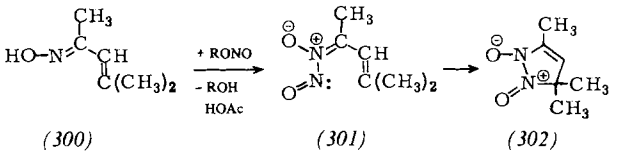
In 1899, *Stollé*[155] synthesized 1,3,4-oxadiazoles from *N,N'*-diacylhydrazines by elimination of water with zinc chloride. Later, polyphosphoric acid at 180 °C was recommended for the preparation of compound *(299)* from *N,N'*-dibenzoylhydrazine in a yield of 92%[156]. The initial protonation probably takes place at the oxygen as in the case of carboxamides with the formation of *(297)*; the proton can be replaced appropriately by other electrophilic agents. Cycliza-



(297) (298) (299)

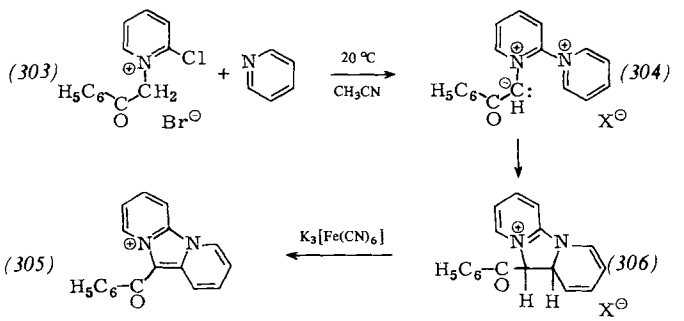
tion to *(299)* is again accompanied by the migration of the positive charge.

A compound obtained by *Harries et al.*[157] from mesityl oxide oxime *(300)* by nitrosation was recognized by *Free-*



(300) (301) (302)

man[158] as trimethyl-5*H*-pyrazole 1,2-dioxide *(302)*. The open-chain precursor, the nitrosonitrone *(301)*, is a pentadienyl anion with double isoelectronic exchange; the onium charge is compensated by the anionic charge of the oxide oxygen on N-2. The reaction can also be regarded as an electrocyclic ring closure of a heterohexatriene (Section 12.5).



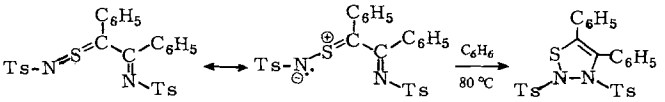
(303) (304) (305) (306)

In the case of isoelectronic replacement of CH by NR in positions 2 *and* 4, the negative charge remains in positions 1, 3, and 5. The open-chain species therefore harbors two positive formal charges and a negative one; two of these charges cancel each other on ring closure. *Kröhnke et al.*[159] treated 2-chloro-1-phenacylpyridinium bromide *(303)* with two equivalents of pyridine. Quaternization is succeeded by deprotonation with a second mole of base leading to *(304)*. As a pyridinio-substituted aromatic azomethine ylide, *(304)* corresponds to the charge type mentioned. The cyclic dipyridodihydroimidazolium ion *(306)* was crystallized as perchlorate and dehydrogenated to the aromatic compound *(305)*.

12. Borderline Cases and Borderline Crossing

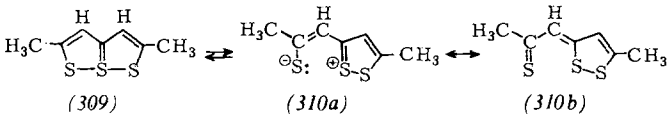
12.1. Isoelectronic Replacement by Elements of Variable Valence

The thione *S*-tosylimide *(307)* resulting from a Wittig reaction can be depicted with tetravalent sulfur without a formal charge—see *(307a)*—or as a sulfonium zwitterion in formula *(307b)*. Viewed from *(307b)*, the ring closure to the Δ^4-1,2,3-thiadiazoline *(308)*[160] appears as the cyclization of an imino-conjugated 1,3-dipole, while in the formulation *(307a)*→*(308)* the transition from tetravalent to divalent sulfur compensates the charge migration in the course of electrocyclization.



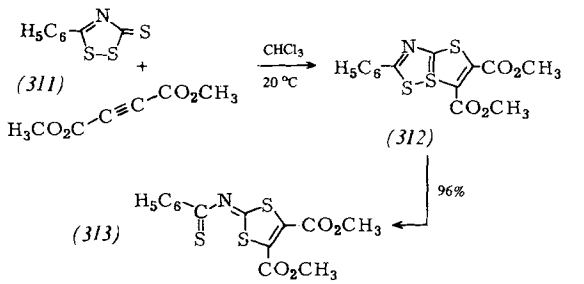
(307a) (307b) (308)

A compound obtained by *Arndt et al.*[161] from 2,4,6-heptanetrione and P_4S_{10} was recognized by X-ray structure analysis[162] to be 2,5-dimethyl-6a-thiathiophthene *(309)*. The three sulfur atoms are arranged colinearly with equal distances of 2.40 Å. The terms "no-bond resonance" and "meribicyclo mesomerism" have been used to described a bonding



(309) (310a) (310b)

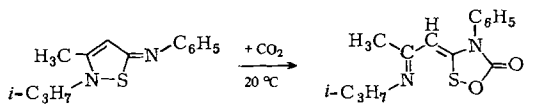
state that is best represented by tetravalent sulfur according to *(309)*. Most reactions of *(309)* find a simple explanation in the assumption of valence tautomerism with the monocyclic 1,2-dithiole structure *(310)*[163]. The ring opening of *(309)* is associated with a change of the valency state of the central sulfur, and the product can be described by a zwitterionic and a charge-free resonance contributor, *(310a)* and *(310b)*.



(311) (312) (313)

Many 1,3-cycloadditions of 1,2-dithiole-3-thiones and related ring systems to dipolarophilic multiple bonds give rise to products whose formation requires a bicyclic intermediate with tetravalent sulfur. *Behringer et al.*[164] treated 5-phenyl-1,2,4-dithiazole-3-thione *(311)* with acetylenedicarboxylic ester and obtained the 2-thiobenzoylimino-1,3-dithiole *(313)*. The ring opening *(312)*→*(313)* is again concurrent with a change in the valence of the sulfur, thus counteracting the effect of charge migration.

An amusing example is offered by 5-imino-3-isothiazoline *(314)* which, according to *Goerdeler et al.*[165], took up carbon



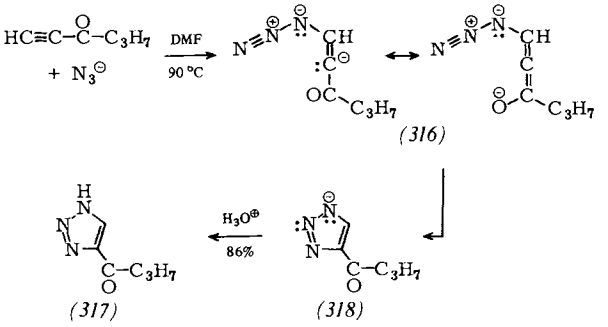
(314) (315), 67%

dioxide under pressure, thus closing a second five-membered ring; electrocyclic opening of the first ring furnished the 1,2,4-oxathiazolidin-5-one *(315)*.

12.2. Additional Anionic Charge in a Conjugated 1,3-Dipole of the Propargyl-Allenyl Type

It has been mentioned in Section 9.5 that thermal electrocyclization of vinyl azides could not be achieved, but the reaction does take place in the deprotonated species.

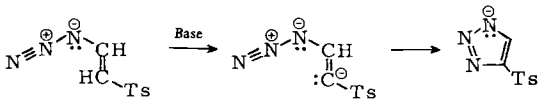
Nesmeyanov et al.[166] treated 1-hexyn-3-one with sodium azide in dimethylformamide (DMF), *i.e.*, in an aprotic medium, and after acidification isolated 4-butyroyl-1,2,3-triazole *(317)*. The direction of the azide addition is dictated by the stabilization of the anion *(316)* as an allenolate. Phenylacetylene is also capable of forming triazoles with sodium



(316) *(317)* *(318)*

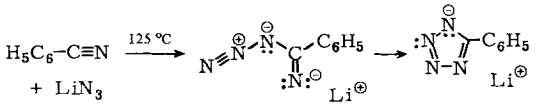
azide if the reaction is run in dimethyl sulfoxide for 160 h at 120 °C[167].

The anion *(316)* constitutes a vinyl azide from which a proton has been removed in position 5; the orbital of the unshared electron pair is located in the σ-plane of the pentadienyl system. This increases the nucleophilicity at C-5 and, furthermore, permits the direct formation of the aromatic triazole anion *(318)* on ring closure. The cyclization *(316)*→*(318)* probably obeys Scheme C of nucleophilic addition described in Section 9.1.



(319) *(320)* *(321)*

1-Azido-2-tosylethylene *(319)* can also be deprotonated with potassium *tert*-butoxide or with sodium toluenesulfinate to *(320)*, again followed by ring closure to the triazole anion *(321)*[168]. The alkaline H,D exchange of *(319)* confirms the acidity of the 5-CH.

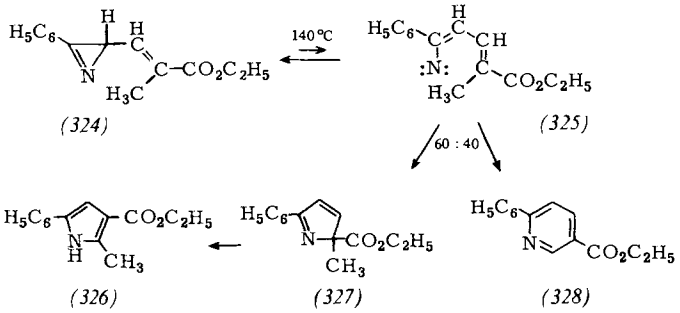


(322) *(323)*

The synthesis of 5-substituted tetrazoles by the 1,3-dipolar cycloaddition of hydrazoic acid to nitriles must often be carried out at elevated temperatures in an autoclave. Faster and less dangerous is the addition of the azide anion to the nitrile group; either ammonium azide in DMF[169] or lithium azide in glycol monoethyl ether at 125 °C[170] are suitable. Finally, the tetrazole is liberated from the salt by mineral acid. The conversion of benzonitrile *via* the anion *(322)* to the 5-phenyltetrazole anion *(323)* serves as an example. The pathway *via (322)* which is analogous to *(316)* and *(320)* deserves preference over a one-step 1,3-cycloaddition in which the reactants combine directly to *(323)*.

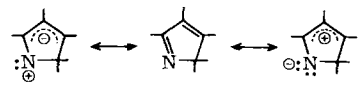
12.3. Cyclization of Butadienylnitrenes and Carbenes

The thermal formation of 2*H*-azirines from vinyl azides has been discussed in Section 9.5. These 2*H*-azirines apparently exist at elevated temperatures in equilibrium with vinylnitrenes.



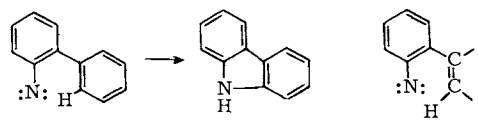
(324) *(325)* *(326)* *(327)* *(328)*

According to *Padwa et al.*[171], the 2*H*-azirine *(324)* rearranges in boiling xylene to the pyrrole derivative *(326)* and to 6-phenylpyridine-3-carboxylic ester *(328)*. The dienic nitrene *(325)* is presumed to be a common intermediate. Insertion into the terminal methyl group with subsequent loss of hydrogen is responsible for the formation of the pyridine derivative *(328)*. A competing process is the electrocyclization to the 2*H*-pyrrole *(327)*, which aromatizes to *(326)* by 1,5-sigmatropic migration of the ester group.



(329a) *(329b)* *(329c)*

The dienylnitrene *(325)* can participate in the electrocyclization as a 6π or a 4π system, depending on whether the nitrogen brings an occupied or an unoccupied orbital into the pentadienyl system. Since the formal cyclization products, *(329a)* or *(329c)*, are both insignificant resonance structures of the α,β-unsaturated imine *(329b)*, the distinction is not meaningful. The close connection with pathway B for the cyclization of vinyldiazomethane (Section 9.1) may be pointed out.

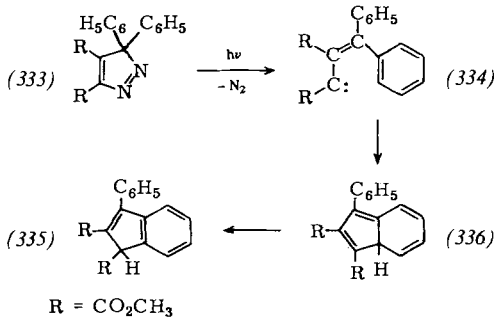


(330) *(331)* *(332)*

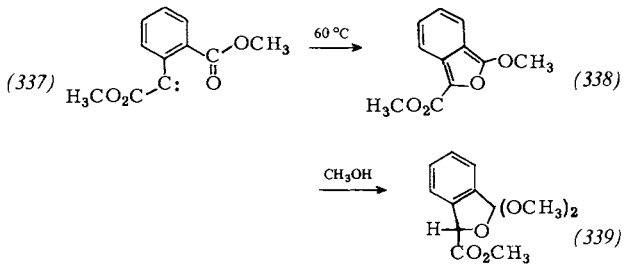
The ring closure of the dienylnitrene *(325)* is the prototype for a large number of cyclizations in which one or both of the ene systems are incorporated into aromatic rings. The synthesis of carbazoles by thermolysis of 2-azidobiphenyl (180 °C) and its derivatives, discovered by *Smith et al.*[172], finds a limit where *o*-substituents of the benzene ring interact with the intermediate nitrenes[173]. The singlet nitrene ap-

pears to be responsible for the ring closure *(330)*→*(331)* in the thermolysis and photolysis of the azide; the photosensitized reaction in fact mainly gives the dimer of *(330)*, 2,2'-azobiphenyl[174]. The deoxidation of 2-nitroso- or 2-nitrobiphenyl with triethyl phosphite also passes through *(330)*, as *Sauer et al.*[175] have established by the agreement of the competition constants in the formation of position-isomeric carbazoles. The synthesis of indoles *via* nitrenes of type *(332)*[176] is also important.

Besides the electrocyclic reaction through a nonaromatic 8a*H*-carbazole, a one-step CH-insertion can be envisaged for *(330)*→*(331)*. The latter is less likely, however. In fact, on thermolysis β,β-dimethyl-*o*-nitrostyrene gives 2,3-dimethylindole[176], which is evidence in favor of an electrocyclic reaction and a 2*H*-indole as an intermediate.



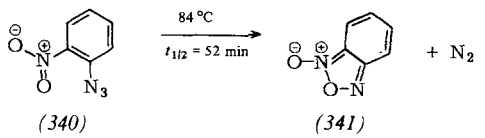
Among the various reaction possibilities, unsaturated carbenes relatively rarely choose pentadienyl cyclization. *Ege*[177] irradiated the 3*H*-pyrazole *(333)* and isolated the indene derivative *(335)* in 65% yield. Should *(334)* avoid the one-step CH insertion in favor of the two-step pathway *via* *(336)*, the analogy with the behavior of dienylnitrenes would be obvious.



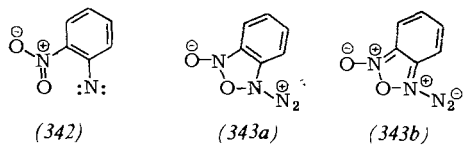
According to *Ibata et al.*[178], the copper-catalyzed decomposition of the corresponding diazo compound goes through the carbene stage *(337)* with pentadienyl cyclization to the benzo[*c*]furan derivative *(338)*. This *o*-quinonoid compound is trapped by the solvent methanol with formation of the cyclic orthobenzoate *(339)* or it may combine with *N*-phenylmaleimide to give the 1,3-cycloadduct.

12.4. Coupling of Ring Closure with the Departure of a Group

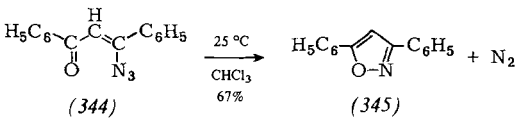
Not all azide thermolyses pass through the free nitrene. In 1899, *Zincke* and *Schwarz*[179] stated that 2-nitrophenyl azide *(340)* loses nitrogen rapidly at 90 °C with the formation of benzofuroxan *(341)*. The elimination of nitrogen from *(340)* at 84 °C is 7000 times faster than that from phenyl



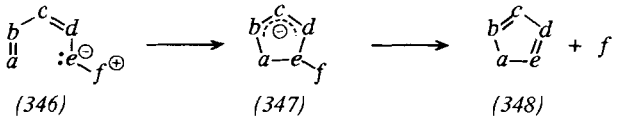
azide[180, 181], although *m*- and *p*-substituents exhibit only a slight influence. This indicates an interaction between the nitro and the azido groups in the rate-determining step and excludes *(342)* as an intermediate.



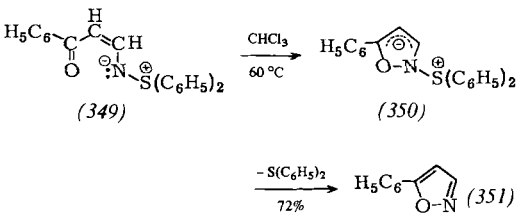
In addition to a one-step process, in which the leaving of N_2 is concerted with the closure of the O—N bond, a two-step sequence may also be assumed: the nitrophenyl azide *(340)* itself isomerizes by an electrocyclization to *(343)* and subsequently N_2 is eliminated to give *(341)*. Structures *(343a)* and *(343b)* differ only in their electron distribution; consequently, a distinction between electrophilic or nucleophilic attack of the nitro oxygen on the azide system is pointless. For illustration, we prefer *(343b)* since electrophilic agents usually attack the azide group at the inner nitrogen atom.



Olefinic azides behave analogously; the β-azido-enone *(344)* loses nitrogen already at 25 °C and gives 3,5-diphenylisoxazole *(345)*[182].



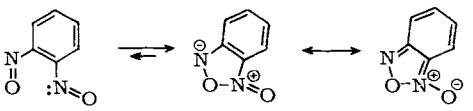
So far it has been impossible to distinguish experimentally the concerted process *(346)*→*(348)* from that with the intermediate *(347)*. On the other hand, it can be shown that leaving groups other than N_2 can take over the role of *f*.



According to *Tamura et al.*[183], the adduct *(349)* from benzoylacetylene and diphenylsulfilimine cyclizes to 5-phenylisoxazole *(351)* in boiling chloroform with elimination of diphenyl sulfide. The electrocyclization product *(350)* is a conceivable intermediate.

12.5. Cyclizations of Heterohexatrienes

Zincke and *Schwarz*[179] described the product of loss of N_2 from 2-nitrophenyl azide *(340)* as *o*-dinitrosobenzene *(352)*, but neither the lack of color nor the chemical properties of this compound are compatible with that structure. In 1903, *Wieland*[184] proposed the furoxan formula for the monocyclic compound, and this insight was later applied to benzofuroxan *(341)*. The cyclization of *(352)* is reversible, as is taught by the rapid isomerization, detectable with NMR, of substituted benzofuroxans[185, 186].



(352) *(341a)* *(341b)*

o-Dinitrosobenzene *(352)* can be regarded as a pentadienyl anion with an isoelectronic 5-exchange; cyclization affords the zwitterion *(341a)*. On the other hand, the resonance structure *(341b)* allows the formal description as a ring closure of the hetero 1,3,5-triene system in *(352)*. This ambiguity is already inherent in the cyclizations *(301)*→*(302)* and *(349)*→*(350)*.

Similar ring-closure reactions of numerous hetero-substituted 1,3,5-hexatrienes bearing carbon functions in positions 1 and 6 or 2 and 5 are associated with a 90° rotation about one of the terminal bond axes. The well-known electrocyclization of 1,3,5-hexatrienes to cyclohexadienes plays an important part also in the heterocyclic series[187]. The closure of *five*-membered rings constitutes a second electrocyclic reaction type of heterohexatrienes, the significance and scope of which has been recognized by *George et al.* and will be the subject of the following paper[188].

13. Epilogue

There is still a deplorable lack of studies on the kinetics and mechanism of 1,5-electrocyclizations. It is conceivable, if not probable, that not all the reactions compiled in this review are tailored after the same mechanistic model. In our discussion we often had to contend ourselves with speculation instead of undisputed knowledge. It is a matter of definition, to what extent the range of mechanisms can be generalized with the term *electrocyclic*.

In the pentadienyl anion cyclization we are undoubtedly facing an archetype which permits the collective description of a colorful variety of reactions. The classification system introduced is suitable to pigeon-hole hundreds of scattered examples from the literature. Hopefully, the knowledge of such a general reaction principle will stimulate further experimental activity.

The first papers on the rules of conservation of orbital symmetry prompted an almost unparalleled development of theory and practice. Should the concept of electrocyclizations of the pentadienyl anion type prove fruitful in heterocyclic chemistry, it would add to the great scientific harvest associated with the names of *R. B. Woodward* and *R. Hoffmann*.

Received: February 28, 1980 [A 321 IE]
German version: Angew. Chem. *92*, 979 (1980)
Translated by AD-EX (Translations) Ltd., London

[1] *R. B. Woodward, R. Hoffmann*, J. Am. Chem. Soc. *87*, 395 (1965).
[2] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[3] *J. B. Hendrickson*, Angew. Chem. *86*, 71 (1974); Angew. Chem. Int. Ed. Engl. *13*, 47 (1974).
[4] *H. C. Longuet-Higgins, E. W. Abrahamson*, J. Am. Chem. Soc. *87*, 2045 (1965).
[5] *H. E. Zimmerman*, Acc. Chem. Res. *4*, 272 (1971).
[6] *M. J. S. Dewar*, Angew. Chem. *83*, 859 (1971); Angew. Chem. Int. Ed. Engl. *10*, 761 (1971).
[7] *R. B. Bates, D. A. McCombs*, Tetrahedron Lett. *1969*, 977.
[8] *L. H. Slough*, J. Org. Chem. *32*, 108 (1967).
[9] *M. A. Laurent*, C. R. Acad. Sci. *19*, 353 (1844).
[10] *D. H. Hunter, S. K. Sim*, J. Am. Chem. Soc. *91*, 6202 (1969); Can. J. Chem. *50*, 669, 678 (1972).
[11] *D. H. Hunter, S. K. Sim, R. P. Steiner*, Can. J. Chem. *55*, 1229 (1977).
[12] *D. R. Hunter, R. P. Steiner*, Can. J. Chem. *53*, 355 (1975).
[13] *G. Boche, K. Buckl, D. Martens, D. R. Schneider, H.-U. Wagner*, Chem. Ber. *112*, 2961 (1979).
[14] *R. Huisgen, W. Scheer, H. Huber*, J. Am. Chem. Soc. *89*, 1753 (1967).
[15] 1,2,3-Triphenylaziridine: *C. H. Ross*, Dissertation, Universität München 1975, p. 14ff.
[16] *S. W. Staley, N. J. Pearl*, J. Am. Chem. Soc. *95*, 2731 (1973).
[17] *W. J. Hehre*, University of California at Irvine, private communication 1973.
[18] *R. B. Bates, W. H. Deines, D. A. McCombs, D. E. Potter*, J. Am. Chem. Soc. *91*, 4608 (1969).
[19] Cyclopentane 7.2 kcal mol^{-1}, cyclopentene 6.8 kcal mol^{-1}; *P. von R. Schleyer, J. E. Williams, K. R. Blanchard*, J. Am. Chem. Soc. *92*, 2377 (1970).
[20] *C. W. Shoppee, G. N. Henderson*, J. Chem. Soc. Perkin Trans. I *1975*, 765.
[21] *D. J. Atkinson, M. J. Perkin, P. Ward*, J. Chem. Soc. *C 1971*, 3247.
[22] *H. Kloosterziel, J. A. A. van Drunen, P. Galama*, J. Chem. Soc. Chem. Commun. *1969*, 885.
[23] *G. J. Heiszwolf, H. Kloosterziel*, Recl. Trav. Chim. Pays-Bas *86*, 807 (1967); *G. J. Heiszwolf, J. A. A. van Drunen, H. Kloosterziel, ibid. 88*, 1377 (1969); *H. Kloosterziel, J. A. A. van Drunen, ibid. 89*, 368 (1970).
[24] *R. B. Bates, S. Brenner, C. M. Cole, E. W. Davidson, G. D. Forsythe, D. A. McCombs, A. S. Roth*, J. Am. Chem. Soc. *95*, 926 (1973).
[25] *W. T. Ford, M. Newcomb*, J. Am. Chem. Soc. *96*, 309 (1974).
[26] *D. H. Hunter, R. E. Klinck, R. P. Steiner, J. B. Stothers*, Can. J. Chem. *54*, 1464 (1976).
[27] *R. Hoffmann, R. A. Olofson*, J. Am. Chem. Soc. *88*, 943 (1966).
[28] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565 (1963); J. Org. Chem. *41*, 403 (1976).
[29] *H. Reimlinger*, Chem. Ber. *103*, 1900 (1970).
[30] *E. C. Taylor, I. J. Turchi*, Chem. Rev. *1979*, 181.
[31] *J. Elguero*, Bull. Soc. Chim. Fr. *1971*, 1925.
[32] *H. Kloosterziel, J. A. A. v. Drunen*, Tetrahedron Lett. *1973*, 1023.
[33] *R. Huisgen, H. Seidl*, Tetrahedron Lett. *1964*, 3381.
[34] *U. Schöllkopf, F. Gerhart, R. Schröder, D. Hoppe*, Justus Liebigs Ann. Chem. *766*, 116 (1972).
[35] *R. Huisgen, K. Niklas*, unpublished work; *K. Niklas*, Dissertation, Universität München 1975, p. 86ff.
[36] *D. Hoppe*, Justus Liebigs Ann. Chem. *1976*, 2185.
[37] *R. R. Schmidt, W. J. W. Mayer, H.-U. Wagner*, Justus Liebigs Ann. Chem. *1973*, 2010.
[38] *D. Lednicer, D. E. Emmert*, J. Heterocycl. Chem. *8*, 903 (1971).
[39] *L. Claisen*, Ber. Dtsch. Chem. Ges. *59*, 144 (1926).
[40] *B. Eistert, E. Merkel*, Chem. Ber. *86*, 895 (1953).
[41] *A. Quilico* in *H. Weißberger:* The Chemistry of Heterocyclic Compounds, Vol. 17. Wiley Interscience, New York 1962, p. 14ff. 96ff.
[42] *L. Claisen*, Ber. Dtsch. Chem. Ges. *36*, 3664 (1903).
[43] *L. Claisen*, Ber. Dtsch. Chem. Ges. *25*, 1776 (1892).
[44] *K. von Auwers, P. Heimke*, Justus Liebigs Ann. Chem. *458*, 186 (1927).
[45] *H. Ferres, W. R. Jackson*, Chem. Commun. *1969*, 261.
[46] *G. Coispeau, J. Elguero*, Bull. Soc. Chim. Fr. *1970*, 2717.
[47] *E. Fischer, C. Bülow*, Ber. Dtsch. Chem. Ges. *18*, 2135 (1895).
[48] *L. Knorr*, Ber. Dtsch. Chem. Ges. *16*, 2597 (1883).
[49] *A. Michael, J. Ross*, J. Am. Chem. Soc. *53*, 2394 (1931).
[50] *K. Auwers, V. Meyer*, Ber. Dtsch. Chem. Ges. *21*, 2806 (1888).
[51] *J. C. Pommelet, J. Chuche*, Can. J. Chem. *54*, 1571 (1976).
[52] *E. Pohjala*, Tetrahedron Lett. *1972*, 2585.

[53] *W. Augstein, F. Kröhnke*, Justus Liebigs Ann. Chem. *697*, 158 (1966).
[54] *J. E. Baldwin, R. G. Pudussery, A. K. Qureshi, B. Sklarz*, J. Am. Chem. Soc. *90*, 5325 (1968).
[55] *R. Huisgen, K. Niklas*, unpublished work; *K. Niklas*, Dissertation, Universität München 1975, pp. 17, 20, 24.
[56] *H. Seidl, R. Huisgen, R. Knorr*, Chem. Ber. *102*, 904 (1969).
[57] *F. Texier, R. Carrié*, Bull. Soc. Chim. Fr. *1971*, 4119.
[58] *F. Kröhnke, W. Zecher*, Chem. Ber. *95*, 1128 (1962).
[59] *K. Burger, H. Schickaneder, C. Zettl*, Synthesis *1976*, 803; Angew. Chem. *89*, 1 (1977); Angew. Chem. Int. Ed. Engl. *16*, 55 (1977).
[60] *H. Prinzbach, H.-D. Martin*, Chimia *23*, 37 (1969).
[61] *T. Sasaki, K. Kanematsu, A. Kakehi*, J. Org. Chem. *37*, 3106 (1972).
[62] *R. Huisgen, R. Fleischmann, A. Eckell*, Tetrahedron Lett. *1960*, No. 12, p. 1; Chem. Ber. *110*, 500 (1977).
[63] *E. Fahr, K. Döppert, F. Schneckenbach*, Justus Liebigs Ann. Chem. *696*, 136 (1966).
[64] *E. Fahr, J. Markert, N. Pelz*, Justus Liebigs Ann. Chem. *1973*, 2088.
[65] *A. Kakehi, S. Ito, K. Uchiyama, Y. Konno, K. Kondo*, J. Org. Chem. *42*, 443 (1977).
[66] *J.-C. Paladini, J. Chuche*, Bull. Soc. Chim. Fr. *1974*, 197.
[67] *W. Eberbach, B. Burchardt*, Chem. Ber. *111*, 3665 (1978); *W. Eberbach, W. Seiler*, Tetrahedron Lett. *1978*, 4875.
[68] *B. Moisan, A. Robert, A. Foucaud*, Tetrahedron *30*, 2867 (1974).
[69] *R. Criegee*, Angew. Chem. *87*, 765 (1975); Angew. Chem. Int. Ed. Engl. *14*, 745 (1975).
[70] *P. S. Bailey:* Ozonation in Organic Chemistry. Kap. VI. Academic Press, New York 1978.
[71] *R. Criegee, M. Lederer*, Justus Liebigs Ann. Chem. *583*, 29 (1953).
[72] *P. Caramella, K. N. Houk*, J. Am. Chem. Soc. *98*, 6397 (1976).
[73] *D. W. Adamson, J. Kenner*, J. Chem. Soc. *1935*, 286; *C. D. Hurd, S. C. Liu*, J. Am. Chem. Soc. *57*, 2656 (1935).
[74] *R. Huisgen, H. Stangl, H. J. Sturm, H. Wagenhofer*, Angew. Chem. *74*, 31 (1962); Angew. Chem. Int. Ed. Engl. *1*, 50 (1962); *R. Huisgen, H. Stangl, H. J. Sturm, R. Raab, K. Bunge*, Chem. Ber. *105*, 1258 (1972).
[75] *N. Engel, W. Steglich*, Angew. Chem. *90*, 719 (1978); Angew. Chem. Int. Ed. Engl. *17*, 676 (1978).
[76] *A. Padwa, J. Smolanoff, A. Tremper*, J. Am. Chem. Soc. *97*, 4682 (1975).
[77] *B. Singh, E. F. Ullman*, J. Am. Chem. Soc. *89*, 6911 (1967); *B. Singh, A. Zweig, J. B. Gallivan, ibid. 94*, 1199 (1972).
[78] *J. W. Cornforth* in: The Chemistry of Penicillin. Princeton University Press, Princeton 1949, p. 700.
[79] *C. G. Stuckwisch, D. D. Powers*, J. Org. Chem. *25*, 1819 (1960).
[80] *R. Huisgen, J. Sauer, H. J. Sturm, J. H. Markgraf*, Chem. Ber. *93*, 2106 (1960).
[81] *R. Huisgen, H. J. Sturm*, unpublished work; *H. J. Sturm*, Dissertation, Universität München 1960.
[82] *J. Sauer, R. Huisgen, H. J. Sturm*, Tetrahedron *11*, 241 (1960); *R. Huisgen, C. Axen, H. Seidl*, Chem. Ber. *98*, 2966 (1965).
[83] *R. Huisgen, J. Sauer, M. Seidel*, Chem. Ber. *93*, 2885 (1960).
[84] *R. Huisgen, H. J. Sturm, M. Seidel*, Chem. Ber. *94*, 1555 (1961).
[85] *J. L. Brewbaker, H. Hart*, J. Am. Chem. Soc. *91*, 711 (1969).
[86] *A. Ledwith, D. Parry*, J. Chem. Soc. *B 1967*, 41.
[87] *G. L. Closs, W. A. Böll*, Angew. Chem. *75*, 640 (1963); Angew. Chem. Int. Ed. Engl. *2*, 399 (1963); J. Am. Chem. Soc. *85*, 3904 (1963).
[88] *A. C. Day, M. C. Whiting*, J. Chem. Soc. *C 1966*, 1719.
[89] *G. D. Buckley, W. J. Levy*, J. Chem. Soc. *1951*, 3016.
[90] *L. Wolff*, Justus Liebigs Ann. Chem. *333*, 1 (1904).
[91] Tautomerism with 80—90% of 1,2,3-benzoxadiazole has recently been deduced from the PE spectrum of *o*-quinone diazide in the gas phase; *R. Schulz, A. Schweig*, Angew. Chem. *91*, 737 (1979); Angew. Chem. Int. Ed. Engl. *18*, 692 (1979). Confirmation by another method would be desirable.
[92] *E. Bamberger, M. Baum, L. Schlein*, J. Prakt. Chem. [2] *105*, 266 (1923).
[93] *L. Wolff, R. Krüche*, Justus Liebigs Ann. Chem. *394*, 48 (1912).
[94] *O. Dimroth*, Justus Liebigs Ann. Chem. *364*, 183 (1909); *373*, 336 (1910).
[95] *O. Dimroth*, Justus Liebigs Ann. Chem. *335*, 1 (1904); *338*, 143 (1905).
[96] *E. Lieber, C. N. R. Rao, T. S. Chao*, J. Am. Chem. Soc. *79*, 5962 (1957).
[97] *B. R. Brown, D. U. Hammick, S. G. Heritage*, J. Chem. Soc. *1953*, 3820.
[98] *R. E. Harmon, F. Stanley, S. K. Gupta, J. Johnson*, J. Org. Chem. *35*, 3444 (1970).
[99] *G. Himbert, M. Regitz*, Justus Liebigs Ann. Chem. *1973*, 1505.
[100] Review: *G. L'abbé*, Angew. Chem. *87*, 831 (1975); Angew. Chem. Int. Ed. Engl. *14*, 775 (1975).
[101] *G. Smolinsky*, J. Org. Chem. *27*, 3557 (1962).
[102] *G. L'abbé, G. Mathys*, J. Org. Chem. *39*, 1778 (1974).
[103] *L. A. Burke, G. Leroy, M. T. Nguyen, M. Sana*, J. Am. Chem. Soc. *100*, 3668 (1978).
[104] *E. Zbiral, J. Stroh*, Justus Liebigs Ann. Chem. *725*, 29 (1969).
[105] *F. Eloy*, J. Org. Chem. *26*, 953 (1961).
[106] *J. Thiele*, Justus Liebigs Ann. Chem. *270*, 1, 54 (1892).
[107] *A. Hantzsch, A. Vagt*, Justus Liebigs Ann. Chem. *314*, 339 (1901).
[108] *R. A. Henry, W. G. Finnegan, E. Lieber*, J. Am. Chem. Soc. *76*, 88 (1954); *77*, 2264 (1955).
[109] *L. A. Burke, J. Elguero, G. Leroy, M. Sana*, J. Am. Chem. Soc. *98*, 1685 (1976).
[110] *R. Fusco, S. Rossi, S. Maiorana*, Tetrahedron Lett. *1965*, 1965.
[111] *R. Huisgen, K. von Fraunberg, H. J. Sturm*, Tetrahedron Lett. *1969*, 2589.
[112] *J. H. Boyer, E. J. Miller*, J. Am. Chem. Soc. *81*, 4671 (1959).
[113] *M. Tišler*, Synthesis *1973*, 123.
[114] *R. N. Butler*, Adv. Heterocycl. Chem. *21*, 402 (1977).
[115] Review: *A. Holm*, Adv. Heterocycl. Chem. *20*, 145 (1976).
[116] *R. Huisgen, I. Ugi*, Chem. Ber. *90*, 2914 (1957).
[117] *I. Ugi, H. Perlinger, L. Behringer*, Chem. Ber. *91*, 2324 (1958).
[118] *I. Ugi, R. Huisgen*, Chem. Ber. *91*, 531 (1958).
[119] *I. Ugi*, Tetrahedron *19*, 1801 (1963).
[120] *A. G. Schultz, R. D. Lucci*, J. Org. Chem. *40*, 1371 (1975).
[121] *S. H. Groen, R. M. Kellogg, J. Buter, H. Wynberg*, J. Org. Chem. *33*, 2218 (1968).
[122] *A. G. Schultz, W. Y. Fu, R. D. Lucci, B. G. Kurr, K. M. Lo, M. Boxer*, J. Am. Chem. Soc. *100*, 2140 (1978).
[123] *A. G. Schultz, M. B. De Tar*, J. Am. Chem. Soc. *98*, 3564 (1976).
[123a] *T. Wolff*, J. Am. Chem. Soc. *100*, 6157 (1978).
[124] *O. L. Chapman, G. L. Eian, A. Bloom, J. Clardy*, J. Am. Chem. Soc. *93*, 2918 (1971); *T. Wolff, R. Waffenschmidt ibid. 102*, 6098 (1980).
[125] *K.-H. Grellmann, G. M. Sherman, H. Linschitz*, J. Am. Chem. Soc. *85*, 1881 (1963); *H. Linschitz, K. H. Grellmann, ibid. 86*, 303 (1964); *E. W. Förster, K.-H. Grellmann, ibid. 94*, 634 (1972).
[126] *A. G. Schultz, W. K. Hagmann*, J. Chem. Soc. Chem. Commun. *1976*, 726.
[127] *A. E. Tschitschibabin*, Ber. Dtsch. Chem. Ges. *60*, 1607 (1927).
[128] Reviews: *W. L. Mosby* in *A. Weissberger:* The Chemistry of Heterocyclic Compounds. Vol. 15/1. Wiley Interscience, New York 1961, p. 239; *T. Uchida, K. Matsumoto*, Synthesis *1976*, 209.
[129] *F. Kröhnke*, Ber. Dtsch. Chem. Ges. *66*, 604 (1933); *F. Kröhnke, W. Heffe, ibid. 70*, 864 (1937).
[130] *D. R. Bragg, D. G. Wibberley*, J. Chem. Soc. *1963*, 3277.
[131] *H. Paul, G. Hilgetag, G. Jähnchen*, Chem. Ber. *101*, 2033 (1968).
[132] *W. E. Parham, V. J. Traynelis*, J. Am. Chem. Soc. *76*, 4960 (1954).
[133] *H. E. Simmons, R. D. Vest, D. C. Blomstrom, J. R. Roland, T. L. Cairns*, J. Am. Chem. Soc. *84*, 4746 (1962).
[134] *H. Beyer, E. Bulka, F. W. Beckhaus*, Chem. Ber. *92*, 2593 (1959).
[135] *W. D. Ollis, C. A. Ramsden*, Adv. Heterocycl. Chem. *19*, 1, 13 (1976).
[136] *K. Hoegerle*, Helv. Chim. Acta *41*, 548 (1958).
[137] *R. Grashey, N. Keramaris, M. Baumann*, Tetrahedron Lett. *1970*, 5078.
[138] *H. O. Bayer, R. Huisgen, R. Knorr, F. C. Schaefer*, Chem. Ber. *103*, 2581 (1970).
[139] *E. Funke, R. Huisgen*, Chem. Ber. *104*, 3222 (1971).
[140] *J. Lukáč, H. Heimgartner*, Helv. Chim. Acta *62*, 1236 (1979).
[141] *J. Wulff, R. Huisgen*, Chem. Ber. *102*, 1841 (1969).
[142] *G. Lüscher*, Dissertation, ETH Zürich 1922.
[143] *R. Grashey, E. Jänchen*, unpublished work; *E. Jänchen*, Dissertation, Universität München 1977, p. 48.
[144] *I. R. Dunkin, M. Poliakoff, J. J. Turner, N. Harrit, A. Holm*, Tetrahedron Lett. *1976*, 873.
[145] Review: *R. Huisgen*, J. Chem. Soc. Spec. Publ. *21*, 51 (1967).
[146] *R. Huisgen, E. Funke*, Angew. Chem. *79*, 320 (1967); Angew. Chem. Int. Ed. Engl. *6*, 365 (1967); *R. Huisgen, E. Funke, H. Gotthardt, H.-L. Panke*, Chem. Ber. *104*, 1532 (1971).
[147] *R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, E. Brunn*, Tetrahedron Lett. *1967*, 1809; *E. Funke, R. Huisgen, F. C. Schaefer*, Chem. Ber. *104*, 1550 (1971).
[148] *E. Brunn, E. Funke, H. Gotthardt, R. Huisgen*, Chem. Ber. *104*, 1562 (1971).
[149] *H. Gotthardt, R. Huisgen*, Chem. Ber. *103*, 2625 (1970).
[150] *H. D. Martin, M. Hekman*, Angew. Chem. *84*, 995 (1972); Angew. Chem. Int. Ed. Engl. *11*, 926 (1972).
[151] *H. Prinzbach, H. Babsch*, Angew. Chem. *87*, 772 (1975); Angew. Chem. Int. Ed. Engl. *14*, 753 (1975). See also *W. Eberbach, M. Perroud-Argüelles, H. Achenbach, E. Druckrey, H. Prinzbach*, Helv. Chim. Acta *54*, 2579 (1971).
[152] *P. von R. Schleyer, E. J. Williams, K. R. Blanchard*, J. Am. Chem. Soc. *92*, 2377 (1970).
[153] *E. Vogel, W. A. Böll, H. Günther*, Tetrahedron Lett. *1965*, 609.
[154] *L. J. Chapelle, J. Elguero, R. Jacquier, G. Tarrago*, Bull. Soc. Chim. Fr. *1970*, 3147.
[155] *R. Stollé*, Ber. Dtsch. Chem. Ges. *32*, 797 (1899).
[156] *F. D. Popp*, J. Chem. Soc. *1964*, 3503.
[157] *C. Harries, R. Gley*, Ber. Dtsch. Chem. Ges. *32*, 1330 (1899).
[158] *J. P. Freeman*, J. Org. Chem. *27*, 1309 (1962).
[159] *K. H. Duchardt, F. Kröhnke*, Justus Liebigs Ann. Chem. *1977*, 1692.
[160] *T. Saito, S. Motoki*, J. Org. Chem. *42*, 3922 (1977).
[161] *F. Arndt, P. Nachtwey, J. Push*, Ber. Dtsch. Chem. Ges. *58*, 1633 (1925).
[162] *S. Bezzi, C. Garbuglio, M. Mammi, G. Traverso*, Gazz. Chim. Ital. *88*, 1226 (1958).
[163] Reviews: *N. Lozac'h* in *M. J. Janssen:* Organosulfur Chemistry. Wiley Interscience, New York 1967, p. 179; *E. Klingsberg*, Q. Rev. Chem. Soc. *23*, 536 (1969); *R. D. Hamilton, E. Campaigne* in *A. Weissberger,*

E. C. Taylor: Special Topics in Heterocyclic Chemistry. Wiley Interscience, New York 1977, p. 300.
[164] *H. Behringer, D. Bender, J. Falkenberg, R. Wiedenmann,* Chem. Ber. *101,* 1428 (1968).
[165] *J. Goerdeler, R. Büchler, S. Solyom,* Chem. Ber. *110,* 285 (1977).
[166] *A. N. Nesmeyanov, M. I. Rubinskaya,* Dokl. Akad. Nauk SSSR, Ser. Khim. *158 (2),* 408 (1964).
[167] *F. P. Woerner, H. Reimlinger,* Chem. Ber. *103,* 1908 (1970).
[168] *J. S. Meek, J. S. Fowler,* J. Am. Chem. Soc. *89,* 1967 (1967); J. Org. Chem. *33,* 985 (1968).
[169] *W. G. Finnegan, R. A. Henry, R. Lofquist,* J. Am. Chem. Soc. *80,* 3908 (1958).
[170] *R. Huisgen, J. Sauer, H. J. Sturm, J. H. Markgraf,* Chem. Ber. *93,* 2106 (1960).
[171] *A. Padwa, J. Smolanoff, A. Tremper,* J. Org. Chem. *41,* 543 (1976).
[172] *P. A. S. Smith, B. B. Brown,* J. Am. Chem. Soc. *73,* 2435 (1951).
[173] Review: *P. A. S. Smith* in *W. Lwonski:* Nitrenes. Wiley Interscience, New York 1970, p. 129ff., 150ff.
[174] *J. S. Swenton,* Tetrahedron Lett. *1968,* 3421.
[175] *J. Sauer, J. Engels,* Tetrahedron Lett. *1969,* 5175.
[176] *R. J. Sundberg, T. Yamazaki,* J. Org. Chem. *32,* 290 (1967).
[177] *G. Ege,* Tetrahedron Lett. *1963,* 1667.
[178] *M. Hamaguchi, T. Ibata,* Chem. Lett. *1976,* 287.
[179] *Th. Zincke, P. Schwarz,* Justus Liebigs Ann. Chem. *307,* 28 (1899).
[180] *K. K. Russel,* J. Am. Chem. Soc. *77,* 3487 (1955).
[181] *T. F. Fagley, J. R. Sutter, R. L. Oglukian,* J. Am. Chem. Soc. *78,* 5567 (1958).
[182] *U. Türck, H. Behringer,* Chem. Ber. *98,* 3020 (1965).
[183] *Y. Tamura, K. Sumoto, H. Matsuchima, H. Taniguchi, M. Ikeda,* J. Org. Chem. *38,* 4324 (1973).
[184] *H. Wieland,* Justus Liebigs Ann. Chem. *329,* 225, 241 (1903); *H. Wieland, L. Semper, ibid. 358,* 36 (1908).
[185] *G. Englert,* Z. Elektrochem. Angew. Phys. Chem. *65,* 854 (1961).
[186] *A. J. Boulton, A. R. Katritzky, M. J. Sewell, B. Wallis,* J. Chem. Soc. *B 1967,* 914.
[187] *J. C. Jutz,* Fortschr. Chem. Forsch. *73,* 125 (1978).
[188] *M. V. George, A. Mitra, K. B. Sukumaran,* Angew. Chem. *92,* 1005 (1980); Angew. Chem. Int. Ed. Engl. *19,* 973 (1980).

Thermal and Photochemical Transformations of Hetero-1,3,5-hexatrienes into Five-Membered Rings—Possible Pericyclic Reactions[**]

By Manapurathu V. George, Abijit Mitra, and Kutikat B. Sukumaran[*]

Heterosubstituted 1,3,5-hexatrienes undergo thermal and photochemical cyclizations, most of which can be viewed as pericyclic reactions. Numerous cyclizations of this type have been reported in the literature. This article presents a systematic account of such reactions, classified according to the number and nature of the heteroatoms.

1. Introduction

The thermal and photochemical transformations of 1,3,5-hexatrienes to 1,3-cyclohexadienes and the analogous ring-opening reactions are well-known examples of electrocyclic reactions[1,2]. The principle of the conservation of orbital symmetry requires a disrotatory mode for the thermal ring closure of 1,3,5-hexatrienes, which is classified as a $[_\pi 2_s + _\pi 2_s + _\pi 2_s]$-process; the photocyclization follows the conrotatory mode. Numerous examples of such thermal and photochemical reactions are reported in the literature. A second conceivable mode of transformation of 1,3,5-hexatrienes is the intramolecular thermal cycloaddition to give bicyclo[3.1.0]hexenes, which as a $[_\pi 4_a + _\pi 2_a]$ reaction is also symmetry allowed. For photocyclizations, the Woodward-Hoffmann rules predict two routes for the formation of the same bicyclo[3.1.0]hexene system, namely $[_\pi 4_s + _\pi 2_a]$ or $[_\pi 4_a + _\pi 2_s]$.

Also, 1,3,5-hexatrienes containing heteroatoms such as oxygen, nitrogen, and sulfur, in principle, can undergo thermal electrocyclic reactions to give hetero-1,3,5-cyclohexadienes[3] or the $[_\pi 4 + _\pi 2]$-type to give heterobicyclo[3.1.0]hexenes or products derived there from. It is evident from the literature that, in addition to the above cyclizations, monocyclic five-membered rings can be formed from hetero-1,3,5-hexatrienes; these reactions can also be considered as pericyclic or electrocyclic reactions, respectively. In this review, selected examples of these types of reactions will be discussed particularly in order to stimulate further research and clarify mechanistic details.

2. Cyclizations of 1,3,5-Hexatriene and Hetero-1,3,5-hexatrienes

2.1. All-Carbon Systems

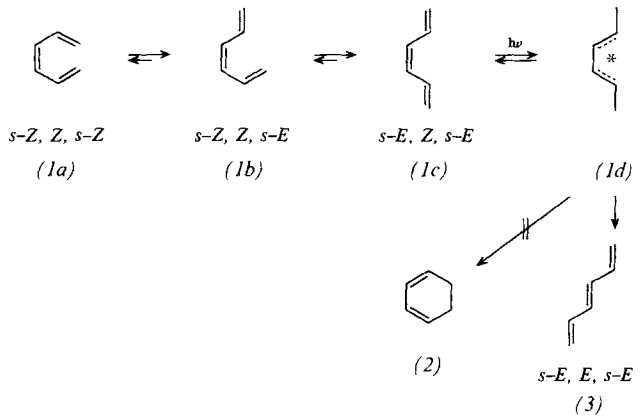
Generally 1,3,5-hexatrienes containing no heteroatoms undergo thermal electrocyclizations leading to 1,3-cyclohexadienes, and these reactions do not depend significantly on the preferred conformations of the 1,3,5-trienes. Thermal $[_\pi 4_a + _\pi 2_a]$-reactions leading to bicyclo[3.1.0]hexenes are rare.

In contrast, the photoreactions of 1,3,5-hexatrienes show a strong dependence on the conformational preferences of the

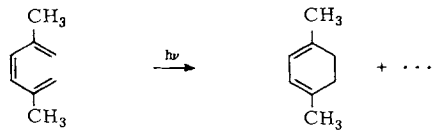
[*] Prof. Dr. M. V. George
Department of Chemistry, Indian Institute of Technology
Kanpur 208016 (India) and
The Radiation Laboratory, University of Notre Dame
Notre Dame, Ind. 46556 (USA)
Dr. A. Mitra, Dr. K. B. Sukumaran
Department of Chemistry, Indian Institute of Technology
Kanpur 208016 (India)

[**] Document No. NDRL-1955 from the Notre Dame Radiation Laboratory.

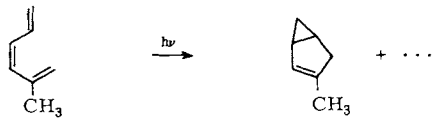
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1212-0973 $ 02.50/0*



starting trienes. *Havinga* and co-workers[4,5] have shown that the product composition resulting from the irradiation of 1,3,5-hexatriene systems reflect both qualitatively and quantitatively the composition of the ground state conformational equilibrium. Thus it has been shown that the unsubstituted (*Z*)-1,3,5-hexatriene, which predominantly exists in the stretched *s-E,Z,s-E* form *(1c)*, does not give rise to any 1,3-cyclohexadiene *(2)*. The excited state relaxes back either to the (*Z*)-triene *(1)* or to the (*E*)-isomer *(3)*.

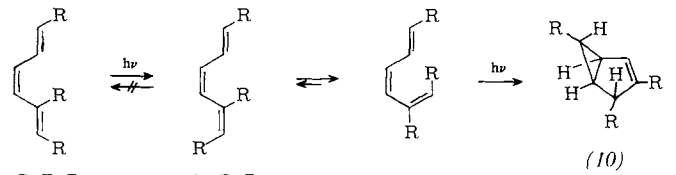


(4) s-Z, Z, s-Z *(5)*

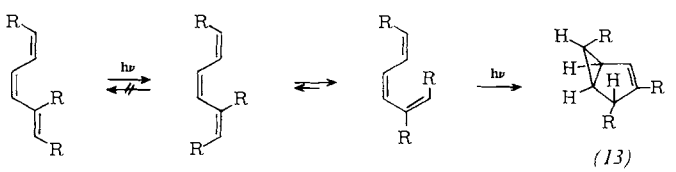


(6) s-Z, Z, s-E *(7)*

In contrast, (*Z*)-2,5-dimethyl-1,3,5-hexatriene *(4)*, which exists predominantly in the *s-Z,Z,s-Z* form, cyclizes to *(5)* with a fair quantum yield. (*Z*)-2-Methyl-1,3,5-hexatriene, which exists predominantly in the *s-Z,Z,s-E* form, is transformed upon irradiation into 3-methylbicyclo[3.1.0]hex-2-ene *(7)*, along with other products.



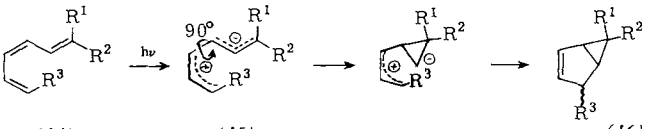
Z, Z, E *E, Z, E* *E, Z, E* *(10)*
(8) *(9)*



Z, Z, Z *E, Z, Z* *E, Z, Z* *(13)*
(11) *(12)*

R = C_6H_5

These photorearrangements are known to occur through the $\pi \rightarrow \pi^*$-singlet excited states, and a high stereospecificity is associated with these reactions. *Padwa et al.*[6] have shown that the formation of the bicyclo[3.1.0]hexene proceeds through the $[{}_\pi 4_s + {}_\pi 2_a]$-scheme. For example, the irradiation of (1*Z*,3*Z*,5*E*)-1,2,6-triphenyl-1,3,5-hexatriene *(8)* gives 4-*exo*,6-*exo*,3,4,6-triphenylbicyclo[3.1.0]hex-2-ene *(10)* as the major product, whereas the *Z,Z,Z*-isomer *(11)* under similar conditions gives preferentially the 4-*exo*,6-*endo*-bicyclo derivative *(13)*. It has been suggested that the trienes *(8)* and *(11)* undergo initial *cis,trans*-isomerization to give *(9)* and *(12)*. The thermodynamically favored conformers then photocyclize to *(10)* and *(13)*.



(14) *(15)* *(16)*

Dauben et al.[7,8] have also shown that the photorearrangement of conjugated trienes occurs from the *s-Z,Z,s-E* forms. These authors postulate a relaxation of the electronically excited state of *(14)* to the vibrationally excited zwitterion *(15)*, further reaction of which should occur from a conformation in which the central bond of the bisallyl system is twisted through 90°. An electrocyclization of the allyl anion moiety with subsequent ion recombination is considered responsible for the formation of the bicyclo[3.1.0]hexene *(16)*. Quantum chemical calculations by *Salem et al.*[9–12] support the view that zwitterionic intermediates are involved in these photoreactions.

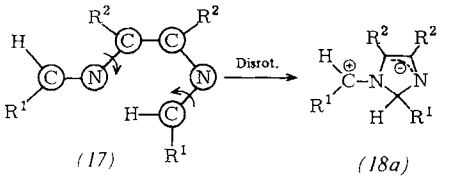
Recent studies by *Courtot et al.*[13], however, have demonstrated the occurrence of cycloadditions of the $[{}_\pi 4_a + {}_\pi 2_a]$-type; these reactions might involve vibrationally excited ground states.

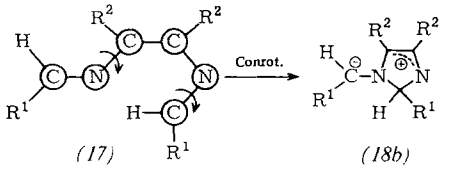
2.2. Heterosystems

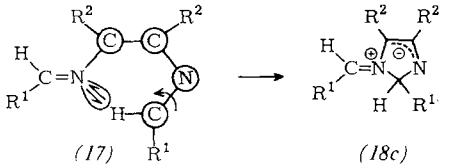
Cyclizations of hetero-1,3,5-hexatrienes to five-membered rings would also appear to proceed from the *s-Z,Z,s-E* form. The electron count for the one-step cyclization of hetero-1,3,5-hexatrienes allows several possible descriptions, which using the arbitrarily selected example *(17)*, are illustrated below.

1) The formation of *(18a)* can be considered as a pentadienyl anion cyclization[14], which involves two 90° twists with disrotation.
2) In the case of a conrotatory cyclization of the pentadienyl cation type, 4π-electrons are involved in the electrocyclization, while the π-electrons of the CN double bond remain on the terminal C-atom of *(18b)*.
3) An intramolecular nucleophilic addition of the nitrogen lone pair to the heterodiene system involves only *one* 90°-twist, with the formation of *(18c)*.

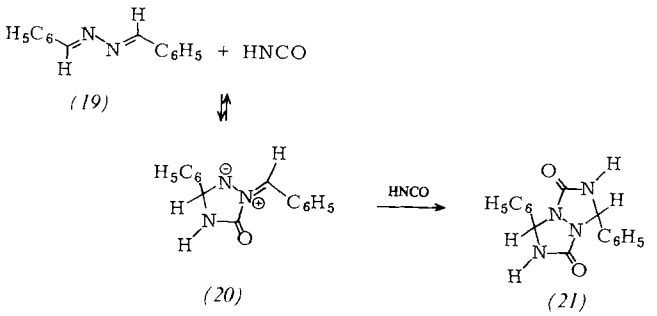
The electron count leads to three different resonance structures of the same species *(18)*. It is very difficult, if not impossible, to distinguish between these three reaction paths.



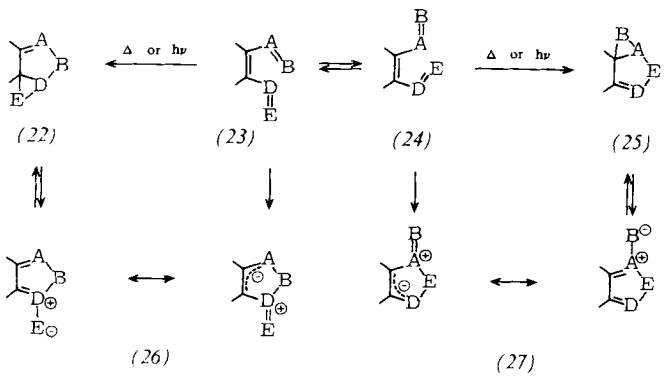




The same type of mechanistic problems and ambiguity were observed by *Huisgen*[14] for the electrocyclization of conjugated 1,3-dipoles of the propargyl-allenyl type.



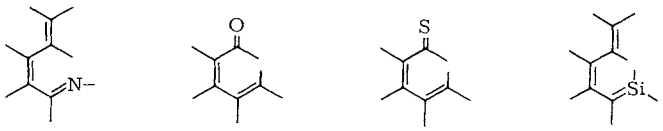
The close analogy to the first step of the "criss-cross addition" of unsaturated systems to azines[15] is also emphasized. For example, the formation of the bisadduct *(21)*[15a], is preceded by formation of a zwitterionic monoadduct from benzylideneazine *(19)* and cyanic acid; *(20)*, as an azomethine imine accepts a second molecule of HNCO in a 1,3-dipolar cycloaddition[16]. The diazadiene system in *(19)* reacts formally as an allyl anion.



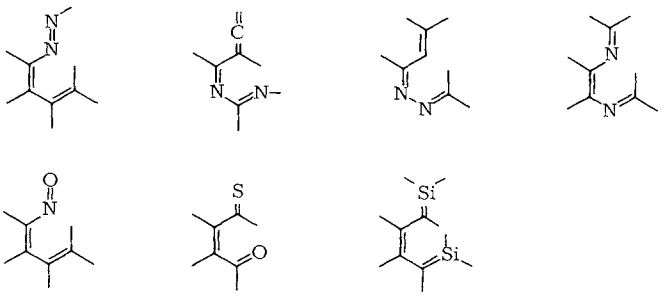
A further conceivable mode of cyclization for the hetero-1,3,5-hexatrienes *(23)* and *(24)* is the thermal $[_\pi 4_a + _\pi 2_a]$-cycloaddition, for which, however, no examples are known. At best, the heterobicyclo[3.1.0]hexenes *(22)* and *(25)* can be postulated as intermediates on the pathway to *(26)* and *(27)*; undoubtedly, there is a greater likelihood of the direct cyclization *(23)*→*(26)* and *(24)*→*(27)*. In contrast, the allowed photoadditions *(23)*→*(22)* and *(24)*→*(25)* of the type $[_\pi 4_s + _\pi 2_a]$ or $[_\pi 4_a + _\pi 2_s]$ are well documented.

Depending on the nature of the substrate and the type of heteroatoms, a variety of products can be formed from these reactions. Although the mechanistic similarities of the examples cited below are by no means certain, we prefer to base our description on the pericyclic reaction scheme. The skeletons of the hetero-1,3,5-hexatrienes discussed here are listed in Scheme 1.

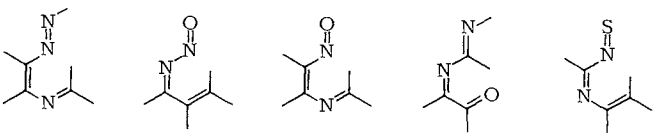
Systems with one heteroatom



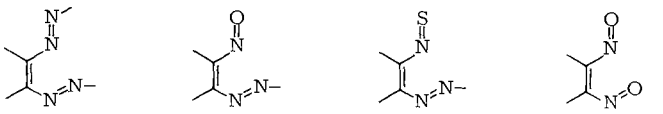
Systems with two heteroatoms



Systems with three heteroatoms



Systems with four heteroatoms

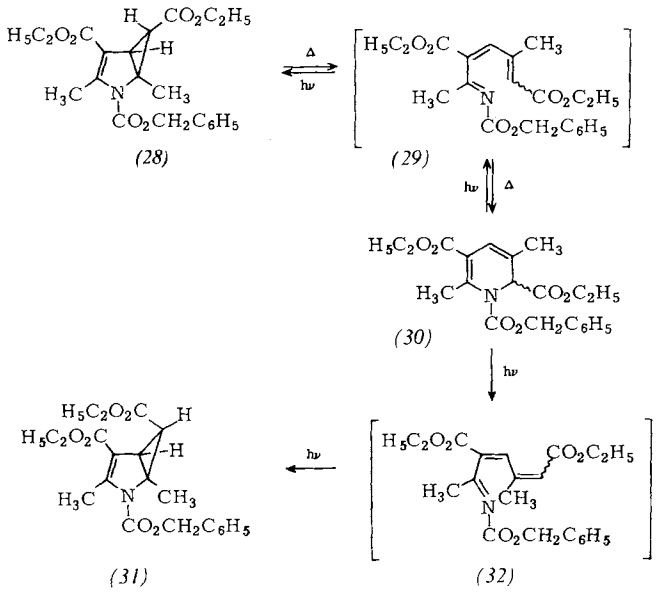


Scheme 1

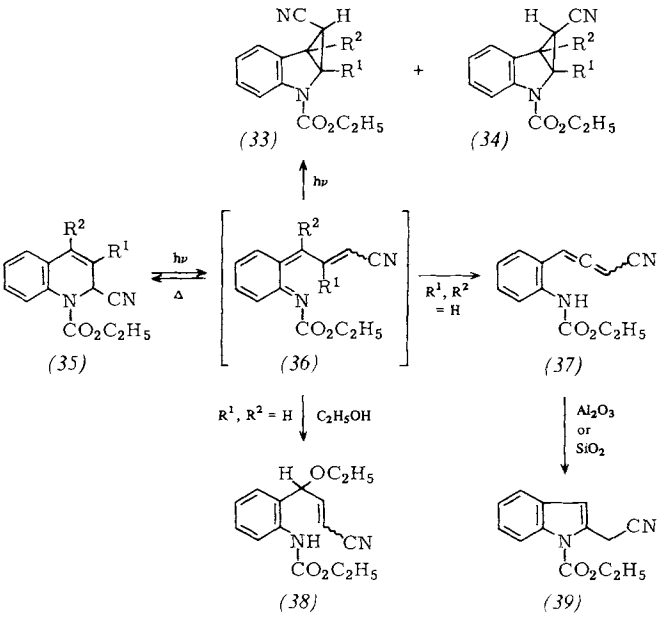
3. Triene Systems with One Heteroatom

3.1. One Nitrogen Atom

Biellmann and *Goeldner*[17] have shown that thermolysis of the homopyrrole *(28)* gives a nearly quantitative yield of the 1,2-dihydropyridine derivative *(30)*. Subsequent photolysis gives a mixture of the homopyrroles *(28)* and *(31)*. It has been suggested that the thermolysis of *(28)* initially involves a cycloreversion to the 1-azahexatriene derivative *(29)*,



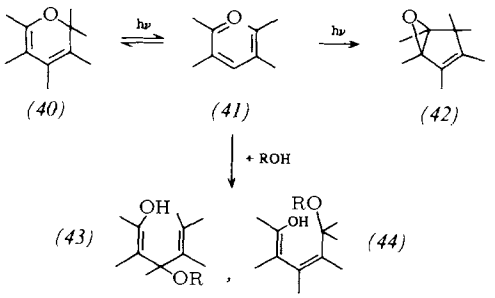
which then undergoes a disrotatory electrocyclization. The formation of the homopyrrole on irradiation of *(30)* can be rationalized in terms of a sequence of two photoreactions. The conrotatory ring opening of *(30)*—clearly the steric course cannot be ascertained—is followed by a photocycloaddition of the types $[{}_{\pi}4_{s}+{}_{\pi}2_{a}]$ and $[{}_{\pi}4_{a}+{}_{\pi}2_{s}]$.



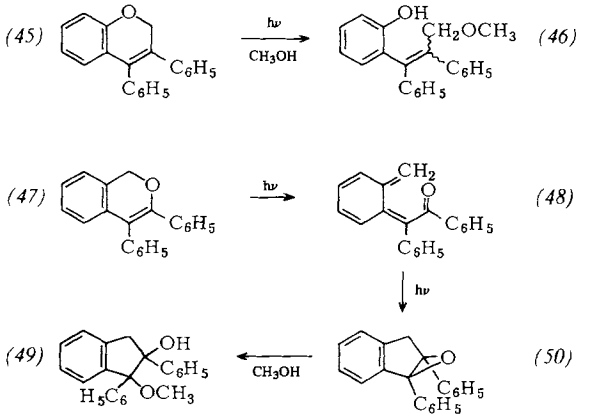
Ikeda et al.[18] have shown that the photolysis of the 2-cyano-1,2-dihydroquinoline-1-carboxylate *(35)*, $R^1=R^2=H$, in ethanol leads to a mixture of the allene *(37)* and the ethanol adduct *(38)*. The allene *(37)* as such could not be isolated, but rearranged to the 2-cyanomethylindole-1-carboxylate *(39)* on chromatography. The rearrangement of the energetically disfavored *o*-quinonoid system of *(36)* to the benzene derivative is responsible for both allene formation and alcohol addition. For certain 4-substituted or 3,4-disubstituted derivatives of *(35)*, *Ikeda* and co-workers[19] observed the photochemical transformation to the cyclopropa[*b*]indoles *(33)* and *(34)*; here also, the *o*-quinonoid 1,3,5-hexatrienes of type *(36)* would be involved as intermediates[20].

3.2. One Oxygen Atom

In a detailed investigation, *Padwa* and co-workers[21-25] have studied the phototransformations of chromenes, isochromenes, and chromanones. The 2*H*-pyran moiety *(40)* first undergoes an electrocyclic ring opening to the dienone



(41), which in certain cases cyclizes to the 6-oxabicyclo[3.1.0]hexene *(42)*. Additionally, solvent adducts of types *(43)* and *(44)* are formed.

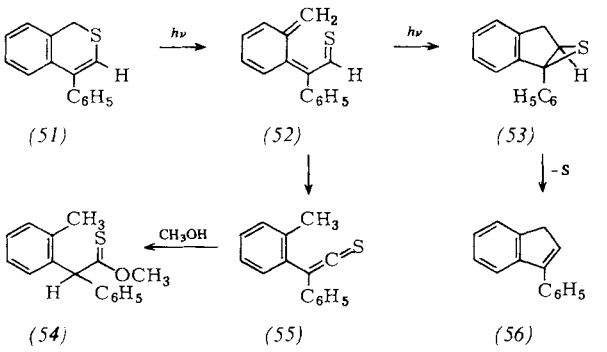


As a specific example, the photolysis of the 2*H*-chromene *(45)* in methanol is chosen which affords, *via* the pathway mentioned earlier, *i.e.* through the dienone, the methanol adduct *(46)*[24]. In contrast, the irradiation of the isochromene *(47)* yields the indene oxide *(50)* and its methanol adduct *(49)*. The *o*-quinonoid dienone *(48)* is the logical intermediate. The independently demonstrated photolysis of the epoxide *(50)*→*(49)* in methanol makes the proposed reaction pathway plausible.

The ring-opening reactions of monocyclic 2*H*-pyrans *(40)* have been examined by different workers[26-28]. According to *Gosnik*, substituents exert an appreciable effect on the equilibrium *(40)*⇌*(41)*[27,28].

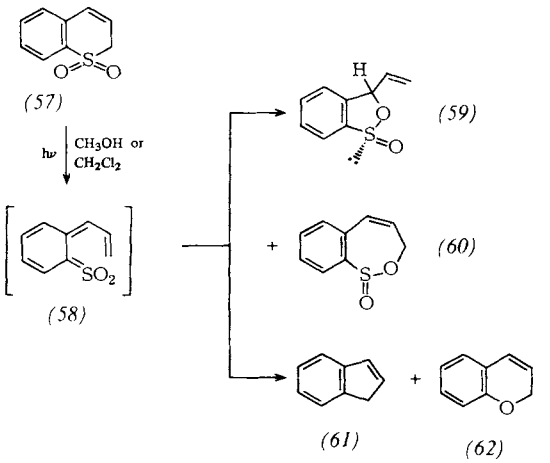
3.3. One Sulfur Atom

The photolysis of 4-phenylisothiochromene *(51)* in methanol, for example, which has also been studied by *Padwa et al.*[24], yields 3-phenylindene *(56)* and methyl α-phenyl-α-*o*-



(51) (52) (53) (54) (55) (56)

tolylthionoacetate *(54)*. The photo-ring opening to *(52)* and the subsequent photocyclization to *(53)* occur as described in the oxygen series; however, the thiirane *(53)* undergoes loss of sulfur. The heterohexatriene *(52)* can also undergo 1,5-H-shift to the thioketene *(55)*, which in turn immediately reacts with methanol to form the ester *(54)*.

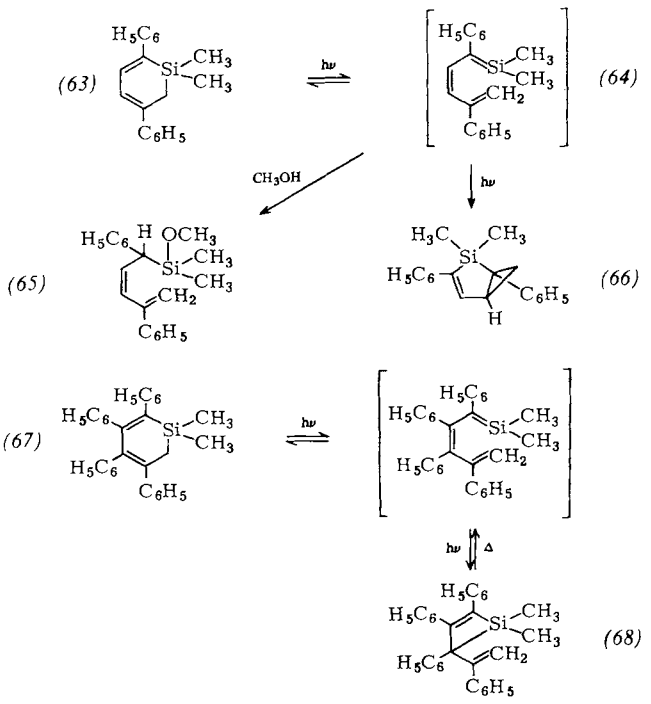


(57) (58) (59) (60) (61) (62)

According to *Hall* and *Smith*[29], the cyclic sulfone *(57)* can surprisingly also undergo electrocyclic photolysis to give the sulfene *(58)*. In any case, the formation of *(58)* enables one to explain the formation of the *cis*- and *trans*-sultines *(59)*, through an electrocyclization of the pentadienyl anion type, whereas the formation of the seven-membered sultine *(60)* is based on the heptatrienyl anion mode of cyclization. These processes profit from the restoration of benzenoid character, starting from the *o*-quinonoid *(58)*. The photochemical cleavage of SO_2 from *(58)* could lead to a carbenoid intermediate, whose 4π-electron system cyclizes to the indene *(61)*. The formation of the 2*H*-chromene *(62)* is based on formal loss of SO and is more difficult to explain.

3.4. One Silicon Atom

It speaks for the generality of the electrocyclic reactions that both the photo-ring opening of the 1-sila-2,4-cyclohexadiene *(63)* and also the subsequent photocycloaddition with the formation of *(66)*, occur in a similar fashion, as shown by *Sakurai et al.*[30]. The intermediacy of the heterohexatriene *(64)* is demonstrated through the isolation of the methanol adduct *(65)*, which is obtained on photolysis in methanol/benzene, along with the 2-silabicyclo[3.1.0]hexene *(66)*. The photolysis of the tetraphenyl derivative *(67)* is an interesting silabutadiene cyclization to give *(68)*. The thermal reversion *(68)*→*(67)* profits from the loss of the silacyclobutene ring strain.

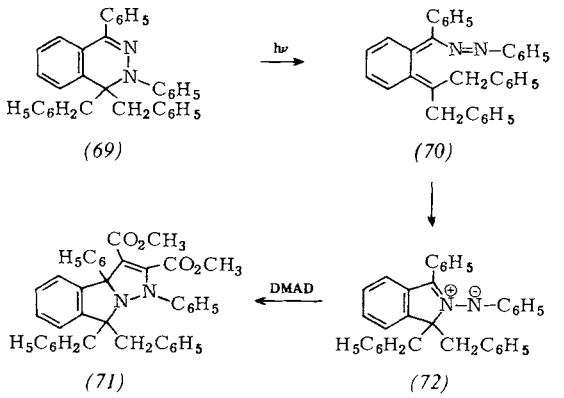


(63) (64) (65) (66) (67) (68)

4. Trienes with Two Heteroatoms

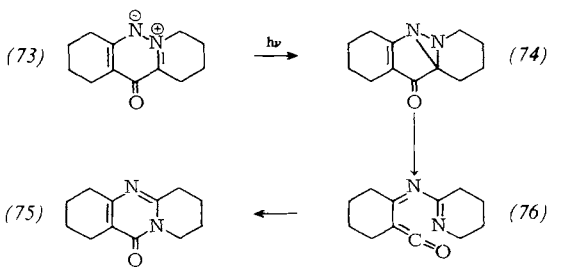
4.1. Two Nitrogen Atoms

4.1.1. 1,2-, 1,3-, and 2,3-Diaza-1,3,5-hexatrienes



(69) (70) (71) (72)

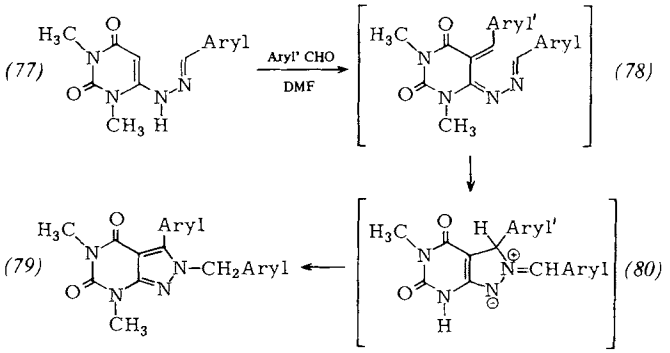
It has been observed by *Singh*[31] that 1,1-dibenzyl-2,4-diphenyl-1,2-dihydrophthalazine *(69)* photolyzes to the stable azomethine imine *(72)*, wherein the ring closure of the 1,2-



(73) (74) (75) (76)

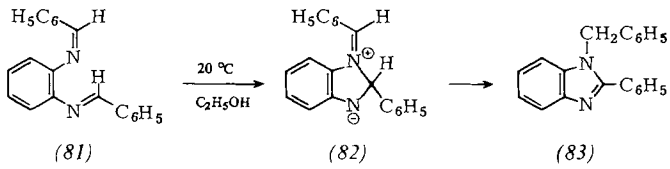
diazahexatriene *(70)* could well be a subsequent thermal reaction. The 1,3-dipole *(72)* reacts with suitable dipolarophiles; for example, with dimethyl acetylenedicarboxylate (DMA) the adduct *(71)* is formed.

Ning et al.[32] have reported that the cyclic azomethine imine *(73)* undergoes photoisomerization to the pyridoquinazolinone *(75)*. The electrocyclic ring closure *(73)*→*(74)*, the cycloreversion *(74)*→*(76)*, and the renewed electrocyclization form a plausible explanation, the last reaction probably being a thermal step.



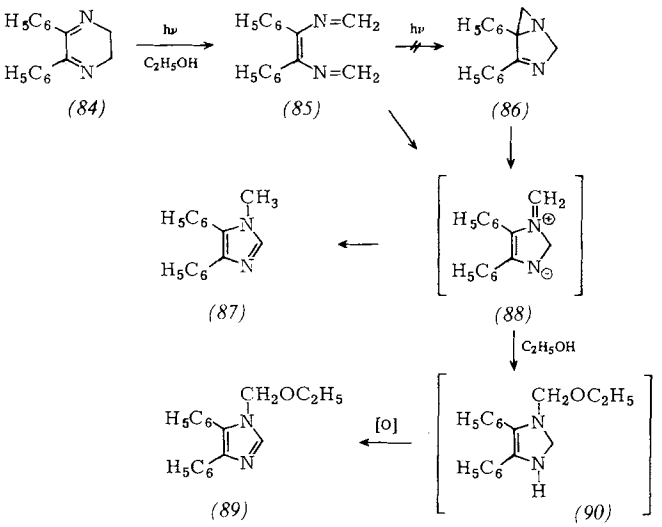
Yoneda et al.[33] have treated 6-(2-arylmethylenehydrazino)-1,3-dimethyluracil *(77)* with aromatic aldehydes in boiling dimethylformamide (DMF), whereby the 3-aryl-2-arylmethyl-5,7-dimethylpyrazolo[3,4-*d*]pyrimidines *(79)* are formed. One might suspect that the aldehyde reacts with the nucleophilic 5-position of the uracil derivatives and that the 2,3-diazahexatriene derivative *(78)* undergoes an electrocyclization to the azomethine imine *(80)*; *(80)* then tautomerizes to the aromatic pyrazole derivative *(79)*.

4.1.2. 2,5-Diaza-1,3,5-hexatrienes

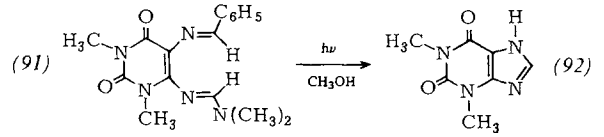


A possible route to this system is provided by the reaction of *o*-phenylenediamines with aldehydes, which were investigated as early as 1877 by *Ladenburg* and co-workers[34]. In later studies by *Hinsberg*[35] and *O. Fischer*[36], the products were recognized as benzimidazoles which are formed through bis(azomethine) intermediates. For example, the reaction of *o*-phenylenediamine with benzaldehyde at −20 °C yields the bis(benzylidene) derivative *(81)*, which at room temperature undergoes cyclization to 1-benzyl-2-phenylbenzimidazole *via (82)*.

Open-chain 2,5-diazahexatrienes have been postulated as intermediates in the phototransformations of 2,3-dihydropyrazines[37,38]. *Beak* and *Miesel*[37] obtained a mixture of the 1-methyl- and 1-ethoxymethyl-5,6-diphenylimidazole *(87)* and *(89)* by the irradiation of the 5,6-diphenyl derivative *(84)* in ethanol. The ring opening to the bis(azomethine) *(85)* and its cyclization to the zwitterion *(88)* constitute a plausible explanation. Subsequent reactions are the tautomerization to *(87)*



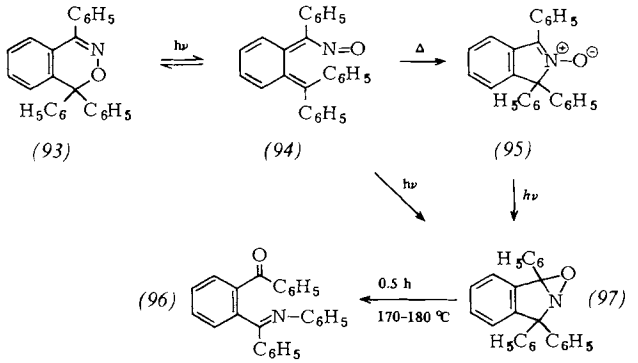
and the addition of alcohol, which is followed by autoxidation to *(89)*. The authors did not observe any evidence for the occurrence of the diazabicyclohexene derivative *(86)*.



In the 2,5-diazahexatriene *(91)*, the CC-double bond is part of the uracil system. *Yoneda et al.*[39] obtained the theophylline *(92)*, upon irradiation in methanol. The reaction could occur *via* intermediates which correspond to *(88)* and *(90)*, wherein the N-methoxybenzyl and the dimethylamino group are probably removed by hydrolysis during work-up.

4.2. One Nitrogen and One Oxygen Atom

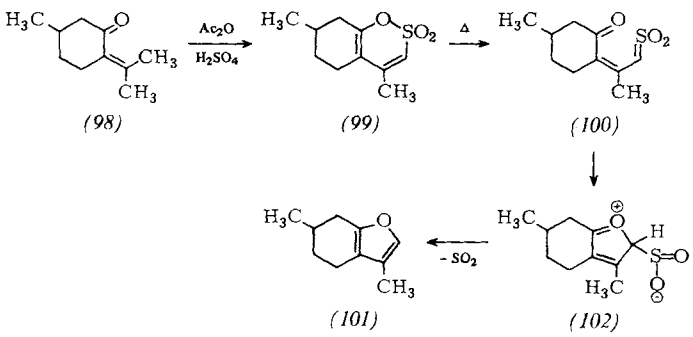
The action of light on 1,1,4-triphenyl-1*H*-2,3-benzoxazine *(93)* leads to the tricyclic oxaziridine *(97)*[40]; the nitroso intermediate *(94)* could undergo direct photocycloaddition or



might first be involved in the ring closure of the nitrone *(95)*, which then forms the oxaziridine *(97)* through a known photochemical reaction. This alternative pathway thus constitutes two electrocyclic steps. Upon heating of *(97)*, the anil of 1,2-dibenzoylbenzene *(96)* is formed, either directly or indirectly *via* the nitrone *(95)*.

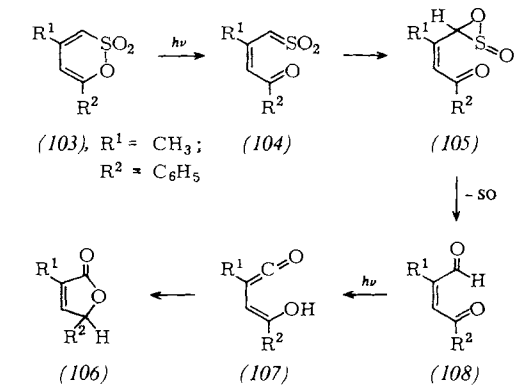
4.3. One Oxygen and One Sulfur Atom

Doubly unsaturated six-membered sultones behave like potential heterohexatrienes with O- and S-functions[41].



(98) *(99)* *(100)* *(101)* *(102)*

Triebs[42] observed a thermal SO_2 cleavage from sultones of type *(99)*—this can be prepared from the enone *(98)* with acetic anhydride and concentrated sulfuric acid—with the formation of the furan *(101)* in our example. The seemingly mysterious transformation finds a ready explanation in the three-step reaction pathway, which consists of electrocyclic ring opening to give *(100)*, closure of the five-membered ring in *(102)*, and an aromatization with loss of SO_2. Subsequent studies have shown that the pyrolysis of sultones constitute a synthetic route to furan derivatives[43].

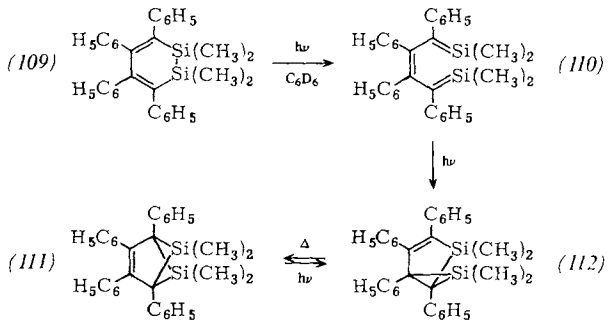


(103), R^1 = CH_3; R^2 = C_6H_5 *(104)* *(105)* *(106)* *(107)* *(108)*

The photolysis of sultones can take a different course with the formation of butenolides. *Gorewit* and *Rosenblum*[44] have shown that the carbon framework remains intact in the transformation of *(103)* into *(106)*. Several subsequent light-induced steps have been proposed: the α,β-unsaturated sulfene *(104)* should produce the diacylalkene *(108)* with SO loss, which in the next step induces a 1,5-H-shift to the enolketene *(107)*. Thermal intramolecular addition completes the process. We feel that a possible pathway for the transformation of *(104)*→*(108)* is through the intermediacy of the three-membered sultine *(105)*, which can readily undergo cheletropic SO elimination.

4.4. Two Silicon Atoms

The photolysis of 1,2-disila-3,5-cyclohexadiene *(109)* has been reported by *Sakurai et al.*[45] to give a quantitative yield of the bicyclohexene derivative *(112)*, presumably formed through the disilahexatriene intermediate *(110)*. Heating



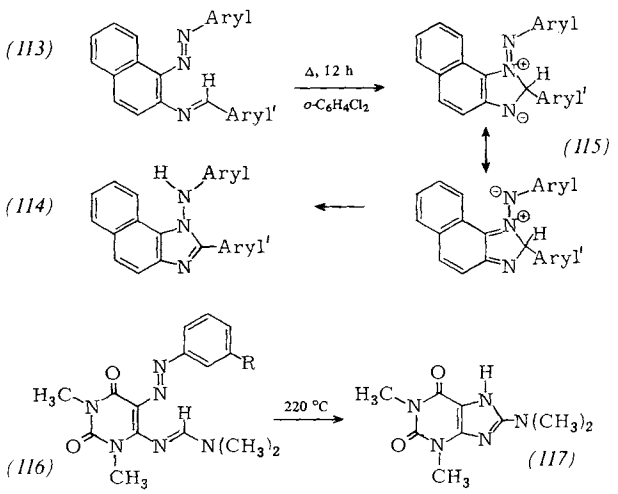
(109) *(110)* *(111)* *(112)*

(112) results in an allyl shift, which leads to the 5,6-disilabicyclo[2.1.1]hexene derivative *(111)*. Interestingly, irradiation of *(111)* causes the reverse isomerization to *(112)*.

5. Triene Systems with Three Heteroatoms

5.1. Three Nitrogen Atoms

On heating 1-arylazo-2-naphthylamines with aromatic aldehydes isomeric products were isolated instead of the azomethines *(113)*; they were identified as N-arylaminonaph-



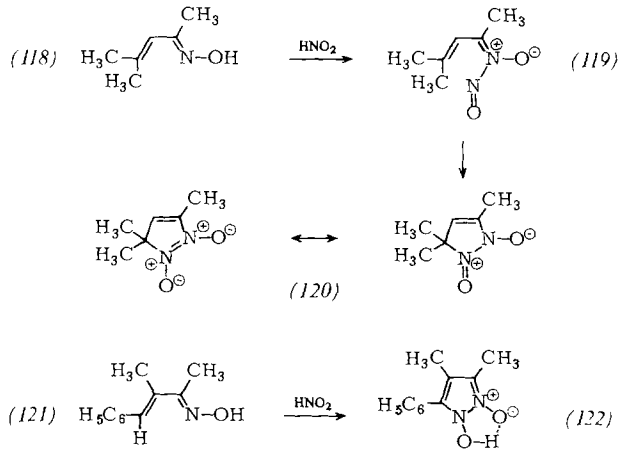
(113) *(114)* *(115)* *(116)* *(117)*

thoimidazoles *(114)* by *O. Fischer et al.*[46]. Under carefully controlled conditions, the heterotrienes *(113)* were isolable[47]; in solvents such as boiling toluene they rearrange smoothly to the imidazoles *(114)*, presumably through the intermediate *(115)*.

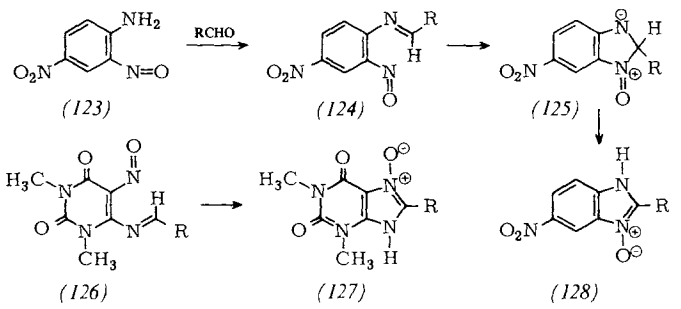
An analogous reaction pathway is presumably applicable to the transformation of 5-arylazo-6-aminouracil with dimethylformamide dimethylacetal, which yields the imidazole *(117)*; the amidine *(116)* reacting in the same way as the azomethine *(113)*; after cyclization, arylamine elimination allows the aromatization to *(117)*[33].

5.2. One Oxygen and Two Nitrogen Atoms

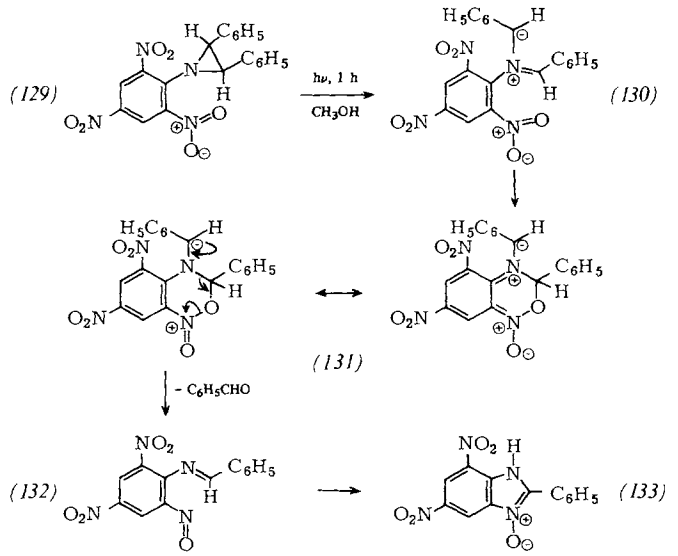
The product obtained from the reaction of mesityl oxide oxime *(118)* and nitrous acid was formulated as "nitrimine"[48] or as *N*-nitrosonitrone[49] *(119)*, until *Freeman*[50] characterized it as 3,3,5-trimethyl-3*H*-pyrazole 1,2-dioxide, which is



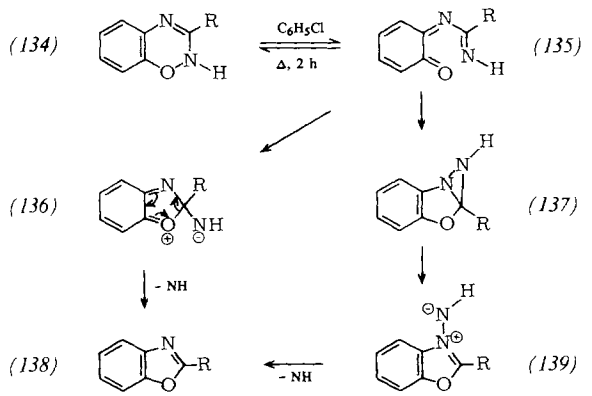
represented by two resonance structures in *(120)*. Ring closure of the nitroso compound *(119)* provides a plausible explanation. Treatment of the α,β-unsaturated ketoxime *(121)* with nitrous acid gives the 3*H*-pyrazole analogous to *(120)* which can tautomerize to the 1-hydroxypyrazole 2-oxide *(122)*[51].



On reaction of 4-nitro-2-nitrosoaniline *(123)* with benzaldehyde, the azomethine *(124)* cannot be isolated but cyclizes immediately *via (125)* to the benzimidazole *N*-oxide *(128)*[52]. A similar reaction pathway has also been described in the 6-amino-1,3-dimethyl-5-nitrosouracil series *(126)*, giving xanthine *N*-oxides *(127)*[53].



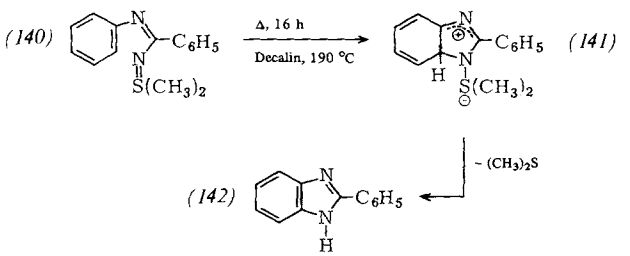
The phototransformations of *N*-*o*-nitrophenylaziridines into benzimidazole *N*-oxides, which have been studied by *Heine et al.*[54], deserve mention in connection with heterohexatrienes. The initial step in the irradiation of *(129)* might involve the well-documented electrocyclic ring opening to the azomethine ylide *(130)*. The electrocyclization to *(131)* is not adversely affected by the two onium centers in the heterohexatrine *(130)*. The subsequent elimination of benzaldehyde can be considered as a retro-Diels-Alder reaction. In the case of the nitrosoazomethine *(132)*, one obtains an intermediate which cyclizes in a manner analogous to *(124)*→*(128)*. It is not clear which steps in the reaction pathway besides the initial step are photochemical processes. The formation of the benzimidazole *N*-oxides from *o*-nitroanilines and aromatic aldehydes[55,56] could possibly occur through analogous pathways.



The transformation of 3-*p*-tolyl-2*H*-1,2,4-benzoxadiazine *(134)* into 2-*p*-tolylbenzoxazole *(138)* occurs in boiling chlorobenzene in 80% yield, as observed by *Rees et al.*[57]. The net loss of NH and the liberation of ammonia suggests the involvement of redox processes. As there are examples for the elimination of NH from azomethine imines, the authors proposed a stepwise reaction pathway, involving first the electrocyclic ring opening to the quinone imine *(135)*, followed by an intramolecular $[{}_{\pi}4_a + {}_{\pi}2_a]$ reaction in forming an NN bond. The diaziridine *(137)* then gives the azomethine imine *(139)*, which loses NH. In the more simple pathway through *(136)* also, the fate of NH is not clear.

5.3. One Sulfur and Two Nitrogen Atoms

The sulfimide *(140)* constitutes a heterohexatriene of this type. In refluxing decalin, *(140)* gives 2-phenylbenzimidazole *(142)* in 9% yield, presumably *via (141)* as intermediate; the major products are 2-phenylquinazoline (19%) and triphe-

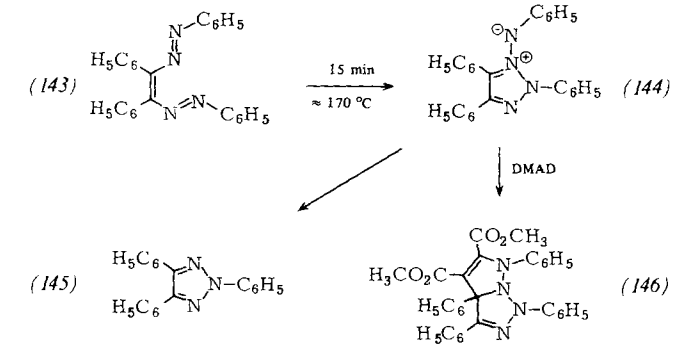


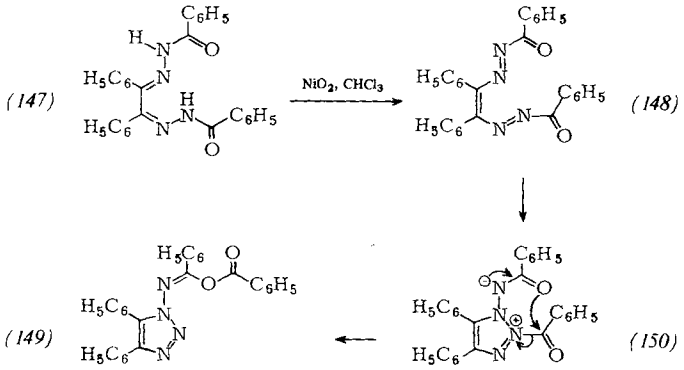
nyl-1,3,5-triazine (65%)[58]. The irradiation of *(140)* gives *(142)* in better yields (30%). *Gilchrist et al.*[58] formulated the reaction *via* a nitrene, which results from N=S cleavage; the pathway *via (141)* offers an alternative.

6. Triene Systems with Four Heteroatoms

6.1. Four Nitrogen Atoms

1,2-Bis(phenylazo)alkenes are converted into 1,2,3-triazoles on heating or irradiation[59-61]. Thus, the stilbene derivative *(143)* at 170 °C yields 85% of 2,4,5-triphenyl-1,2,3-triazole *(145)*[59]. The intermediacy of the aromatic azomethine imine *(144)* has been demonstrated by trapping with suitable dispolarophiles—*(146)* is a typical cycloadduct[59].

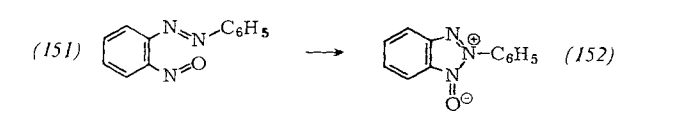


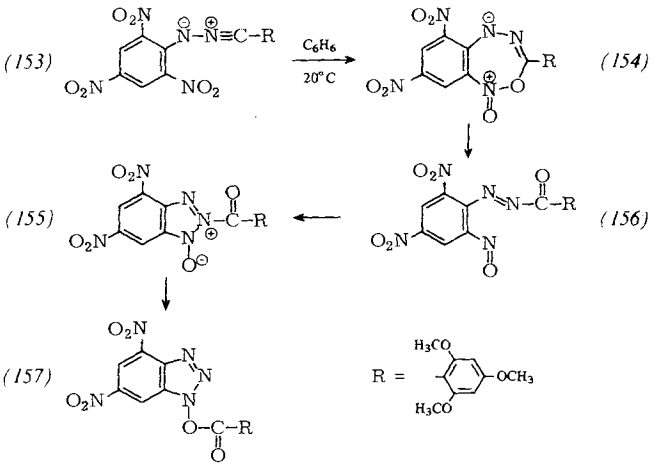


One would expect the bisazo compound *(148)* to be formed on oxidation of benzil bis(benzoylhydrazone) *(147)*. Instead, 26% of the triazole derivative *(149)* was isolated[62]. Here too, one can expect a heterohexatriene cyclization to give *(150)*, followed by an acyl shift with formation of *(149)*. The reactions of other 1,2-diketone bis(benzoylhydrazones) have also been studied[62,63].

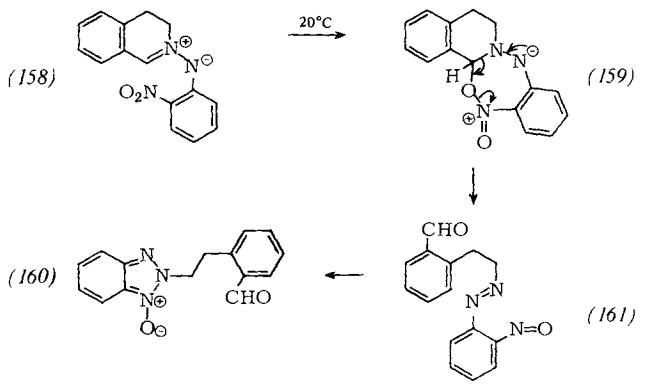
6.2. One Oxygen and Three Nitrogen Atoms

In an attempt to reduce *o*-nitrobenzene with sodium hydrogen sulfide to the *o*-nitroso compound *(151)*, *Bamberger* and *Hübner* obtained 2-phenylbenzotriazole 1-oxide *(152)*[64]. The formation of an aromatic heterocycle could significantly contribute to the driving force for cyclization.





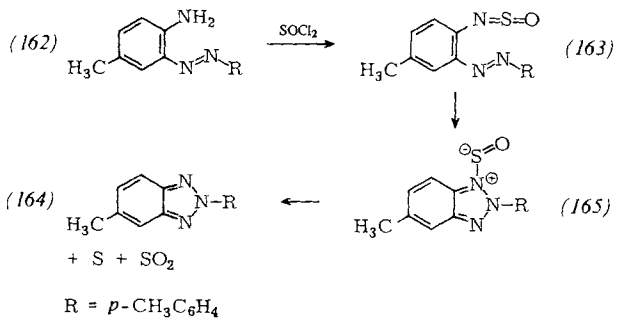
Nitrilimines are unstable 1,3-dipoles which add *in situ* to dipolarophiles. In an attempt to liberate *(153)* from its precursor (hydrazidoyl halide), *Huisgen* and *Weberndörfer*[65] obtained a 71% yield of the 1-hydroxybenzotriazole derivative *(157)*. In the electrocyclic sequence *(153)*→*(154)*→*(156)*, an oxygen atom of the nitro group is transferred to the second side chain. The heterotriene *(156)* closes the five-membered ring according to the scheme observed from *(151)*, followed by the acyl shift *(155)*→*(157)*. The same multistep transformation was observed for *N*-(4-bromo-2-nitrophenyl)-*C*-phenylnitrilimine by *Barnish* and *Gibson*[66].



Azomethine imines of type *(158)* of the 3,4-dihydroisoquinoline series can be intercepted by dipolarophiles, with the formation of cycloadducts. In the absence of dipolarophiles, *(158)* isomerizes to the benzotriazole 1-oxide *(160)* in 80% yield, as reported by *Grashey*[67]. The apparently surprising reaction sequence consists of three electrocyclic steps; in the last step again there is an interaction between nitroso and azo groups.

6.3. One Sulfur and Three Nitrogen Atoms

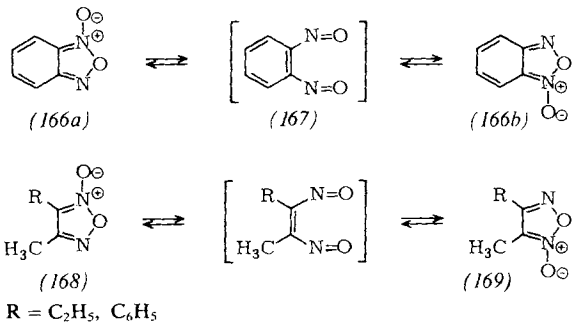
In the treatment of the amine *(162)* with thionyl chloride *Michaelis* and *Erdmann*[68] isolated the benzotriazole deriva-



tive *(164)*, instead of the usual *N*-sulfinylamine *(163)*—which in this case is formed initially as well. The interaction of the heterocumulene with the azo group could proceed *via (165)*; S and SO_2 were observed as disproportionation products of the liberated SO.

6.4. Two Oxygen and Two Nitrogen Atoms

Substituted benzofuroxans have not been isolated as the expected isomers. The explanation is found in a fast equilibrium—illustrated in *(166a)* and *(166b)* for the unsubstituted species—*via* the heterohexatriene *o*-dinitrosobenzene *(167)*.



The temperature dependence of the NMR spectrum offers the key to the rate constant and activation enthalpy of this process[69,70]. Similar isomerisation equilibria are observed for the unsymmetrically substituted, mononuclear furoxans *(168)* and *(169)*[71].

7. Conclusion

In this brief review an attempt has been made to rationalize several reported reactions in terms of heterohexatriene cyclizations. It is needless to state that this analysis implying mechanistic uniformity is an oversimplication. Many of the described reactions may not proceed in a concerted manner, but may involve biradicals. Further work will be necessary to clarify these details.

The authors thank Professor Rolf Huisgen, Universität München, for carefully reading the manuscript and for numerous suggestions and helpful discussions, as well as for translating the text into German. The help rendered by Dr. S. Lahiri, Dr. V. Bhat, and Mr. Ch. Vijaya Kumar of the Indian Institute of Technology, Kanpur in preparing this manuscript is gratefully acknowledged. The preparation of this article was supported by the Department of Science and Technology, Government of India, Indian Institute of Technology, Kanpur and the Office of Basic Energy Sciences of the U. S. Department of Energy.

Received: February 1, 1979;
supplemented: October 27, 1980 [A 343 IE]
German version: Angew. Chem. *92*, 1005 (1980)

[1] For a general review, see *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[2] For a general review on thermal pericyclic reactions, see *J. B. Hendrickson*, Angew. Chem. *86*, 71 (1974); Angew. Chem. Int. Ed. Engl. *13*, 47 (1974).
[3] For the formation of six-membered aromatic and heteroaromatic rings, see *J. C. Jutz*, Top. Curr. Chem. *73*, 125 (1978).
[4] *P. J. Vroegop, J. Lugtenburg, E. Havinga*, Tetrahedron *29*, 1393 (1973).
[5] For a review on the photochemistry of trienes, see *H. J. C. Jacobs, E. Havinga*, Adv. Photochem. *11*, 305 (1979).
[6] *A. Padwa, L. Brodsky, S. Clough*, J. Am. Chem. Soc. *94*, 6767 (1972).
[7] *W. G. Dauben, M. S. Kellogg*, J. Am. Chem. Soc. *94*, 8951 (1972).
[8] *W. G. Dauben, M. S. Kellogg, J. I. Seeman, N. D. Vietmeyer, P. H. Wenschuh*, Pure Appl. Chem. *33*, 197 (1973); *W. G. Dauben, E. L. McInnis, D. M. Michno* in *P. de Mayo*: Rearrangements in Ground and Excited States, Vol. 3. Academic Press, New York 1980, p. 91.
[9] *V. Bonačič-Koutecký, P. Hiberty, J. Koutecký, C. Leforestier, L. Salem*, Angew. Chem. *87*, 599 (1975); Angew. Chem. Int. Ed. Engl. *14*, 575 (1975).
[10] *L. Salem*, Science *191*, 822 (1976).
[11] *W. G. Dauben, L. Salem, N. J. Turro*, Acc. Chem. Res. *8*, 41 (1975).
[12] *L. Salem*, Acc. Chem. Res. *12*, 87 (1979).
[13] *P. Courtot, J.-Y. Salun, R. Rumin*, Tetrahedron Lett. *1976*, 2061.
[14] For a review on the pentadienyl anion type cyclizations, see the preceding article by *R. Huisgen*, Angew. Chem. *92*, 979 (1980); Angew. Chem. Int. Ed. Engl. *19*, 947 (1980).
[15] a) *J. R. Bailey, N. H. Moore*, J. Am. Chem. Soc. *39*, 279 (1917); b) *J. R. Bailey, N. H. Moore, A. T. McPherson, ibid. 39*, 1322 (1917); c) *T. Wagner-Jauregg*, Ber. Dtsch. Chem. Ges. *63*, 3213 (1930); d) *K. Burger, F. Hein, C. Zettl, H. Schickaneder*, Chem. Ber. *112*, 2609 (1979); e) *T. Wagner-Jauregg*, Synthesis, 349 (1976).
[16] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. Int. Ed. Engl. *2*, 569 (1963).
[17] *J. F. Biellmann, M. P. Goeldner*, Tetrahedron *27*, 2957 (1971).
[18] *M. Ikeda, S. Matsugashita, H. Ishibashi, Y. Tamura*, J. Chem. Soc. Chem. Commun. *1973*, 922.
[19] a) *M. Ikeda, S. Matsugashita, F. Tabusa, H. Ishibashi, Y. Tamura*, J. Chem. Soc. Chem. Commun. *1974*, 433; b) *M. Ikeda, S. Matsugashita, Y. Tamura*, J. Chem. Soc. Perkin I *1976*, 2587; *1977*, 1770; c) *M. Ikeda, S. Matugashita, F. Tabusa, Y. Tamura, ibid. 1977*, 1166.
[20] It has been stated in ref. [19c] that the authors have evidence to show that azaheterotrienes are not involved in the formation of cycloprop[*b*]indoles. This evidence, however, has not been cited in the paper.
[21] *A. Padwa, A. Au, W. Owens*, J. Chem. Soc. Chem. Commun. *1974*, 675.
[22] *A. Padwa, G. A. Lee*, J. Am. Chem. Soc. *96*, 1634 (1974).
[23] *A. Padwa, A. Au*, J. Am. Chem. Soc. *96*, 1633 (1974); *97*, 242 (1975).
[24] *A. Padwa, A. Au, G. A. Lee, W. Owens*, J. Org. Chem. *40*, 1142 (1975).
[25] *A. Padwa, W. Owens*, J. Org. Chem. *42*, 3076 (1977).
[26] *P. Schiess, R. Seeger, C. Suter*, Helv. Chim. Acta *53*, 1713 (1970).
[27] *E. N. Marvell, G. Caple, T. Chadwick, T. Gosnik, G. Zimmer*, J. Org. Chem. *37*, 2992 (1972); *E. N. Marvell, T. Gosnik, ibid. 37*, 3036 (1972).
[28] *T. Gosnik*, J. Org. Chem. *39*, 1942 (1974).
[29] *C. R. Hall, D. J. H. Smith*, Tetrahedron Lett. *1974*, 3633.
[30] *Y. Nakadaira, S. Kanouchi, H. Sakurai*, J. Am. Chem. Soc. *96*, 5621 (1974).
[31] *B. Singh*, J. Am. Chem. Soc. *91*, 3670 (1969).
[32] *R. Y. Ning, J. F. Blount, W. Y. Chen, P. B. Madan*, J. Org. Chem. *40*, 2201 (1975).
[33] *F. Yoneda, M. Higushi, T. Nagamatsu*, J. Am. Chem. Soc. *96*, 5607 (1974).
[34] *A. Ladenburg*, Ber. Dtsch. Chem. Ges. *10*, 1123 (1877); *11*, 590, 1648 (1878); *A. Ladenburg, I. Engelbrecht, ibid. 11*, 1653 (1878); *A. Ladenburg, L. Rügheimer, ibid. 11*, 1656 (1878).
[35] *O. Hinsberg*, Ber. Dtsch. Chem. Ges. *19*, 2025 (1886); *20*, 1585 (1887); *O. Hinsberg, F. Funcke, ibid. 27*, 2197 (1894); *O. Hinsberg, P. Koller, ibid. 29*, 1497 (1896).
[36] *O. Fischer*, Ber. Dtsch. Chem. Ges. *25*, 2826 (1892).
[37] *P. Beak, J. L. Miesel*, J. Am. Chem. Soc. *89*, 2375 (1967).
[38] *D. R. Arnold, V. Y. Abraitus, D. McLeod, Jr.*, Can. J. Chem. *49*, 923 (1971).
[39] *F. Yoneda, M. Higuchi, M. Kawamura*, Heterocycles *4*, 1659 (1976).
[40] *B. Singh*, J. Am. Chem. Soc. *90*, 3893 (1968).
[41] For a review on sultones, see *A. Mustafa*, Chem. Rev. *54*, 195 (1954).
[42] *W. Triebs*, Ber. Dtsch. Chem. Ges. *70*, 85 (1937).
[43] *T. Morel, P. E. Verkade*, Recl. Trav. Chim. Pays-Bas *67*, 539 (1948); *70*, 35 (1951); *F. Bohlmann, C. Fischer*, Chem. Ber. *107*, 1767 (1974).

[44] B. Gorewit, M. Rosenblum, J. Org. Chem. 38, 2257 (1973).
[45] Y. Nakadira, S. Kanouchi, H. Sakurai, J. Am. Chem. Soc. 96, 5623 (1974).
[46] O. Fischer, W. Meier, H. Schwappacher, H. Kracker, J. Prakt. Chem. [2] 104, 102 (1922); O. Fischer, E. Thiel, F. Stauber, W. Hild, G. Seufert, H. Hojer, F. Manntiechler, F. Elflein, K. Müller, ibid. 107, 16 (1924).
[47] A. Mitra, S. M. S. Chauhan, M. V. George, J. Org. Chem. 45, 3182 (1980).
[48] C. Harries, R. Gley, Ber. Dtsch. Chem. Ges. 32, 1330 (1899).
[49] R. Fusco, G. Trisoglio, Atti Accad. Naz. Lincei, Classi Sci. Fis. Mat. Nat. Rend. [7] 2, 681, 751 (1941).
[50] J. P. Freeman, J. Org. Chem. 27, 1309 (1962).
[51] J. P. Freeman, J. J. Gannon, J. Heterocycl. Chem. 3, 544 (1966); J. Org. Chem. 34, 194 (1969).
[52] M. Z. Nazer, J. Petridou, M. J. Haddadin, C. H. Issidorides, Heterocycles 6, 541 (1977); D. W. Russel, Chem. Commun. 1965, 498.
[53] E. C. Taylor, E. E. Garcia, J. Am. Chem. Soc. 86, 4721 (1964); see also H. Goldner, G. Dietz, E. Carstens, Justus Liebigs Ann. Chem. 692, 134 (1966); H. Goldner, G. Dietz, E. Carstens, ibid. 693, 233 (1966).
[54] H. W. Heine, G. J. Blosick, G. B. Lowrie III, Tetrahedron Lett. 1968, 4801.
[55] G. W. Stacy, B. V. Ettling, A. J. Papa, J. Org. Chem. 29, 1537 (1964).
[56] R. Marshall, D. J. Sears, D. M. Smith, J. Chem. Soc. C 1970, 2144.
[57] T. L. Gilchrist, C. J. Harris, M. E. Peek, C. W. Rees, J. Chem. Soc. Chem. Commun. 1975, 962.
[58] T. L. Gilchrist, C. J. Moody, C. W. Rees, J. Chem. Soc. Perkin I 1975, 1964.
[59] C. S. Angadiyavar, K. B. Sukumaran, M. V. George, Tetrahedron Lett. 1971, 633; K. B. Sukumaran, C. S. Angadiyavar, M. V. George, Tetrahedron 28, 3987 (1972).
[60] K. B. Sukumaran, S. Satish, M. V. George, Tetrahedron 30, 445 (1974).
[61] M. Bauer, G. R. Bedford, A. R. Katritzky, J. Chem. Soc. 1964, 751.
[62] K. S. Balachandran, M. V. George, Tetrahedron 29, 2119 (1973).
[63] M. Shaban, M. Nassr, E. ElAshray, M. Mustafa, Org. Prep. Proced. Int. 9, 117 (1977).
[64] E. Bamberger, R. Hübner, Ber. Dtsch. Chem. Ges. 36, 3822 (1903).
[65] R. Huisgen, V. Weberndörfer, Chem. Ber. 100, 71 (1967).
[66] L. T. Barnish, M. S. Gibson, Chem. Ind. (London) 1965, 1699; J. Chem. Soc. C 1968, 8.
[67] R. Grashey, Angew. Chem. 74, 155 (1962); Angew. Chem. Int. Ed. Engl. 1, 158 (1962).
[68] A. Michaelis, G. Erdmann, Ber. Dtsch. Chem. Ges. 28, 2192 (1895).
[69] A. R. Katritzky, S. Oksne, R. K. Harris, Chem. Ind. (London) 1961, 990.
[70] P. Diehl, H. A. Christ, F. B. Mallory, Helv. Chim. Acta 45, 504 (1962); F. B. Mallory, S. L. Manatt, C. S. Wood, J. Am. Chem. Soc. 87, 5433 (1965).
[71] F. B. Mallory, A. Cammarata, J. Am. Chem. Soc. 88, 61 (1966).

Reversible Topotactic Redox Reactions of Solids by Electron/Ion Transfer[**]

By Robert Schöllhorn[*]

Solids having suitable structural and electronic properties are able to form intercalation compounds by reversible redox reactions at room temperature *via* topotactic electron/ion transfer processes. The host lattices range from inorganic solids with different structural dimensionality to organic molecular solids. Similarly, depending on the host lattice type, the guest species may vary from protons and metal ions to large inorganic and organic molecular ions. The possibilities of a systematic "tailoring" of new stable or metastable compounds, the controlled modification of physical properties of solids, and the technical application of electronic/ionic conductors, provide a wide and attractive field for academic and applied research in an interdisciplinary area that involves solid state chemistry and physics, molecular chemistry, electrochemistry, and interface science.

1. Introduction

The formation of intercalation compounds by the uptake or exchange, respectively, of guest molecules, atoms and ions by host lattices having suitable structures is a well-known example for solid state reactions at low temperatures[1]. As concerns the mechanism of reaction, two different cases have to be distinguished: (a) host lattices which are insulators and whose effective lattice matrix charge remains constant in the course of intercalation or exchange reactions *e.g.* zeolites[2], sheet silicates[3], polyphosphates[4]; (b) host lattices with electronic conductivity, whose effective lattice charge may be altered by the intercalation, thus introducing a new dimension into the reaction mechanism. The intercalation is proceeding in this case under synchronous uptake of ions and electrons into the solid [cf. Section 2, eq. (1), Fig. 1]. The rapid development of the chemistry of intercalation compounds within the last ten years is essentially related to the latter mentioned type of reaction. Besides long known solids such as graphite[5], molybdenum sulfide[6] and tungsten trioxide[7], a large number of electronically conducting host lattices are accessible today; with respect to structure and composition their range extends from inorganic solids with framework lattices to organic solids with molecular lattices. A similar variety is found with regard to the (ionic) guest species which, depending upon the nature of the host lattice, include small ions like H^+, main group and transition metal ions, as well as large molecular ions (*e.g.* metal complex ions, heterocyclic ions, dye cations).

From the chemical standpoint the process associated with direct intercalation is to be considered as a reversible topotactic redox reaction by electron/ion transfer[8–11]. This concept enables the consideration of intercalation reactions which are correlated with a change in the electronic state of the host lattice under a common viewpoint, also in cases

[*] Prof. Dr. R. Schöllhorn
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9—11, D-4400 Münster (Germany)

[**] The term "topotactic" refers to solid state reactions which are characterized by the fact that defined lattice matrix elements specific to the original solid phase remain unaltered in the course of the reaction with respect to their structural organization (for semantic aspects cf. [13]).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-0983 $ 02.50/0

where neutral guest molecules are the only reacting species[12].

Topical interest in the type of reaction under consideration stems from different motivations. From a preparative point of view topotactic redox processes allow the systematic synthesis of an unusual variety of electron/ion conducting compounds *via* solid state reactions at ambient temperature; many of these materials are metastable and cannot be obtained by other preparative techniques. Investigation of the reaction mechanisms leads to new information on the relationship between structure, degree of order, and reactivity of solids. The possibility of a variation of redox state and composition provides a flexible model for the systematic modification of the physical properties of solids (optical and magnetic properties, transport phenomena, phase transitions, superconductivity) with conservation of the original host lattice matrix.

In connection with the problem of economic energy conversion and storage, topotactic redox systems with metal guest ions are of importance as electron/ion conducting reversible electrodes for high energy density secondary batteries. As regards application they are also of interest, *e.g.* in heterogeneous catalysis and electrocatalysis; metal oxide hydrogen bronzes are used as nonemissive optical display systems.

In the following review we shall first outline some of the general reaction principles and thereafter discuss the characteristics of particular systems using structural aspects as a guideline. Some special topics (ionic conductivity, physical properties, application) will also be briefly considered.

2. General Aspects

The principle of the process under discussion can be defined schematically as the bulk reaction of an electronically conducting host lattice (Z) that contains an intracrystalline system of accessible vacant lattice sites (□) with mobile guest ions (A) of an electrolyte phase which is in contact with the solid. Synchronously with the uptake of the guest ions—which diffuse from the interface host lattice/electrolyte into the bulk of the solid—an equivalent amount of electrons enters or leaves, respectively, the conduction band of the solid [eqs. (1) and (2)]. The electrons are provided and consumed by concurrent chemical or electrochemical reactions. It is understood that the process is reversible and that the host matrix retains its basic structural integrity during the course of foreward and backward reaction (topotactic process[13]).

$$x\,A^{\oplus} + x\,e + \square_x[Z] \rightleftarrows A_x^{\oplus}[Z]^{x\ominus} \quad (1)$$

$$x\,A^{\ominus} + \square_x[Z] \rightleftarrows [Z]^{x\oplus}A_x^{\ominus} + x\,e \quad (2)$$

While a large number of host lattices are known to undergo electron/cation transfer reactions [eq. (1), Fig. 1], there are few examples of reversible electron/anion transfer processes [eq. (2)], the most well-known being graphite, which is redox-amphoteric and is open to both types of reactions. It is clear for steric and energetic reasons that anion intercalation will be unfavorable in most cases. We shall therefore restrict our discussion to *electron/cation transfer*. In this case the solid can be described in the reduced state by a macroanion matrix $[Z]^{x-}$ with intercalated mobile guest cations A^+.

Equation (1) represents a homoionic process; the redox reaction may also proceed, however, by synchronous or consecutive cointercalation of different guest cations:

$$x\,A^{\oplus} + y\,B^{\oplus} + (x+y)\,e + [Z] \rightarrow A_x^{\oplus}B_y^{\oplus}[Z]^{(x+y)\ominus} \quad (3a)$$

$$x\,A^{\ominus} + x\,e + B_y^{\oplus}[Z]^{y\ominus} \rightarrow A_x^{\oplus}B_y^{\oplus}[Z]^{(x+y)\ominus} \quad (3b)$$

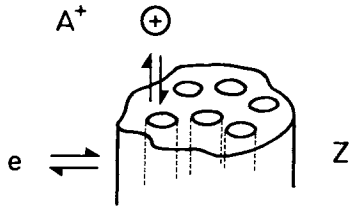


Fig. 1. Schematic illustration of reversible topotactic redox reactions by electron/cation transfer; Z = host lattice with accessible unoccupied lattice sites; A^+ = guest cation.

The intercalated compounds may in addition undergo cation exchange reactions according to

$$x\,A^{\oplus} + B_x^{\oplus}[Z]^{x\ominus} \rightarrow x\,B^{\oplus} + A_x^{\oplus}[Z]^{x\ominus} \quad (4)$$

With regard to the structural and physical properties of potential host lattices, there are a number of obvious requirements:

- In order to secure the stability of the host lattice matrix, the bonding between the atoms which constitute the matrix must be strong and has to include covalent (spacially directed) components. There are exceptions from this principle, *e.g.* in the case of rather small guest species such as protons, which may react reversibly even with molecular solids.
- A compound system of interconnected vacant lattice sites sharing polyhedral faces has to provide adequate space for the location and transport of guest cations.
- An energetically suitable conductivity band of the host matrix is required for the reversible uptake of electrons.
- The ionic mobility of the guest species must be high inside the solid, *i.e.* lattice positions have to be energetically approximately equivalent and the potential changes along the diffusion path should be small.

It is thus apparent that topotactic redox reactions of electronic/ionic conductors may essentially proceed only at intermediate temperatures: at high temperatures the matrix itself will become unstable, while at low temperatures the mobility of guest ions will be inhibited by large activation energy barriers for translation.

Independent of their chemical composition the host lattices may be divided into the following categories according to their essential structural characteristics (Fig. 2):

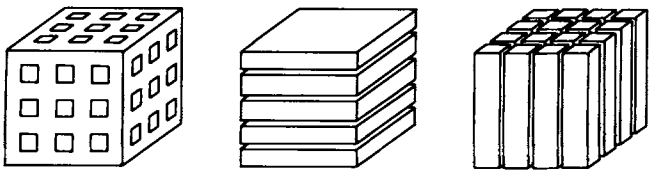


Fig. 2. Scheme of basic host lattice types with different structural dimensionality (see text).

Three-dimensional systems consisting of a framework host matrix that contains interconnected or isolated empty "channels" of unoccupied lattice sites which share polyhedral faces. There are naturally rather rigorous restrictions with respect to the dimensions of the guest cations which have to be below a critical radius that depends upon the host lattice.

Two-dimensional systems with neutral layered units as the matrix elements. The van der Waals gap between the layers represents a two-dimensionally infinite array of neighboring vacant lattice positions. As a consequence of the structural pecularities and the relatively weak coherence forces between the layer units, even large molecular guest ions may be accommodated *via* changes in the interlayer spacing. The flexibility of two-dimensional systems is characterized by the fact that complex solvated phases may form *via* the additional uptake of neutral polar molecules from the electrolyte medium [eq. (5)]. The solvated phases exhibit polyelectrolyte character, *i.e.* cation and solvate exchange properties.

$$x\,A^{\oplus} + x\,e + y\,\mathrm{solv} + [Z] \rightleftarrows (A^{\oplus})_x(\mathrm{solv})_y[Z]^{x\ominus} \qquad (5)$$

One-dimensional systems consisting of chain-type units separated by van der Waals gaps which provide neighboring empty lattice sites. Their structural flexibility is even higher as compared to layered lattices; they are, however, rather susceptible to lattice defects like all quasi one-dimensional systems[14].

Molecular solids have low lattice energies and low electronic conductivities; they may undergo topotactic redox reactions under certain conditions (cf. Section 7).

The majority of the host lattices investigated so far belong to the first two categories. With respect to chemical composition, the most variable group of host lattices are binary and multinary compounds of transition metals which easily undergo changes in the oxidation state with electronegative elements (chalcogenides, oxides). The formal oxidation state of the host matrix metal component is usually nonintegral in the reduced state. Thermodynamically unstable "empty" host lattices can be obtained by topotactic oxidation of ternary phases (prepared at high temperatures) which contain mobile metal ions (alkali ions, Cu^+, Tl^+) *e.g.* $CrSe_2$ from $NaCrSe_2$[15] or β-V_2O_5 from β-$Cu_xV_2O_5$[16]. For some ternary phases oxidation to zero negative charge on the host lattice is not possible [eq. (6)]; this may be due to electronic or structural reasons[17,18].

$$A_n^{\oplus}[Z]^{n\ominus} \rightleftarrows A_{n-x}^{\oplus}[Z]^{(n-x)\ominus} + x\,e + x\,A^{\oplus} \quad (x<n) \qquad (6)$$

Host lattices with framework structure intercalate only metal ions and protons. Host lattices with layer and chain structures may take up metal ions as well as molecular ions; both cation types can be solvated by neutral molecules *via* cation dipole interaction. The electronic conductivity of the host lattice may be either of semiconducting or metallic type and varies normally with the extent of reduction; considerable work has been devoted recently to the question of localized and delocalized electronic states[19,20].

Topotactic redox reactions can be performed either by chemical or electrochemical methods. The intercalation *e.g.* of lithium ions may be achieved by reaction of the host lattice with solutions of Li in liquid ammonia[19] or with butyllithium in aprotic solvents[21]; the electron donors are butyl carbanions or solvated electrons $e(NH_3)_x$, respectively. In aqueous electrolytes $S_2O_4^{2-}$, SO_3^{2-} *etc.* may be used as electron donors[8,9]; chemical reoxidation is performed *e.g.* with O_2, I_2, $[Fe(CN)_6]^{3-}$ as the electron acceptors. Direct thermal intercalation of neutral guest molecules into layered host lattices is well-known[22,23] and has recently been shown to proceed *via* molecular redox disproportionation[24,25].

A most important and versatile method for preparative as well as for analytical purposes is the electrochemical technique, which provides information on reversibility, intermediate stages, thermodynamic data and ionic mobility. Single crystal or polycrystalline host lattice electrodes can be intercalated and deintercalated by cathodic reduction or anodic oxidation in aqueous or nonaqueous electrolytes containing the appropriate guest ions [eq. (1), Fig. 3]. Cyclic voltammetry studies provide qualitative data on the reversibility of the

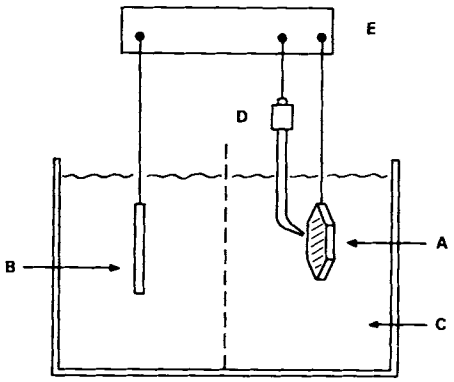


Fig. 3. Scheme of electrochemical reduction and oxidation of host lattice electrodes. (A) single crystal or polycrystalline working electrode; (B) counterelectrode; (C) aqueous or nonaqueous electrolyte containing guest cations; (D) Luggin capillary with reference electrode; (E) electronic equipment for control of potential and current.

reaction[8b,10,26,27]. Galvanostatic reduction and oxidation at constant current (coulometric titration) yields quantitative information on phase ranges and intermediate stages, provided equilibrium potential is maintained and side reactions are excluded. Thermodynamic data and chemical diffusion coefficients can be derived from EMF measurements at equilibrium potentials and from DC polarization studies, respectively[28]. *In situ* studies by X-ray and neutron diffraction methods provide evidence of structural changes and ordering states in the course of electrode reactions[29-32]. Lattice distortions, point defects and extended defects, which may be either inherent to the host lattice or develop during intercalation, strongly affect the kinetics, mechanism and extent of topotactic redox reactions; hysteresis phenomena and partial or total irreversibility are frequent consequences in such cases[33-35].

The general outline presented here does not account for the specific characteristics of particular systems; these will be discussed in the following sections with the dimensionality of the host lattice as the ordering scheme.

3. Host Lattices with Framework Structures

As discussed above solids with three-dimensional matrix will for steric reasons accept only metal guest ions, whose radii cannot exceed an upper critical value. The compounds investigated so far belong essentially to the transition metal oxides and chalcogenides. In terms of structure and reactivity they may be divided into systems with interconnected and with isolated channels.

3.1. Interconnected Lattice Channels

With respect to chemical reactivity the most versatile framework structures examined as yet are the rhombohedral molybdenum cluster chalcogenides Mo_6X_8 and $A_xMo_6X_8$ (X = S, Se; A = metal cation) which have gained considerable interest because of their remarkable physical properties (superconductivity, magnetic behavior, lattice instabilities)[36]. They are prepared from the elements at high temperatures (1300—1600 K), with the exception of Mo_6S_8 which was found to be formed on leaching of *e.g.* $Fe_2Mo_6S_8$ or $Ni_2Mo_6S_8$ with dilute mineral acids[37,38]. The structure of the binary phases can be described as a three-dimensional arrangement of Mo_6X_8 units which contain distorted octahedral Mo_6 metal clusters (Fig. 4). These units are joined *via*

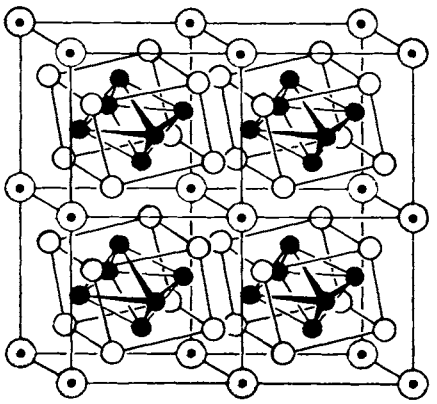


Fig. 4. Structure of Mo_6S_8. Dotted circles indicate unoccupied (channel) positions at the unit cell origin; ● = Mo, ○ = S.

Mo—S bonds to form a framework lattice that is characterized by intersecting infinite channels of neighboring vacant lattice sites running along the three rhombohedral axes. In the ternary phases the vancant lattice positions are (partially) occupied by the A metal atoms, whose location depends upon the stoichiometry x, the size and the oxidation state of A. X-Ray data established an unusually strong thermal motion for small A atoms[36].

Electrochemical studies on the molybdenum cluster chalcogenides revealed that they are able to undergo reversible topotactic redox reactions by electron/ion transfer at room temperature [eq. (7)][11,39,40]. Guest cations can be alkali, al-

$$x\,A^{\oplus} + x\,e + Mo_6X_8 \rightleftarrows A_x^{\oplus}[Mo_6X_8]^{x\ominus} \qquad (7)$$

kaline earth, transition and post transition metal ions; they all show rather high ionic mobility at 300 K. The upper critical guest ion radius corresponds to ≈ 120 pm for Mo_6S_8. Depending upon the guest cation line phases and nonstoichiometric phase ranges are observed (Table 1); some of these compounds are metastable phases.

Table 1. Ternary molybdenum cluster chalcogenides $A_xMo_6X_8$ obtained by cathodic reduction of the host lattice Mo_6X_8 in aqueous or organic electrolytes containing the guest cations A^{n+}; x_m = maximum stoichiometry observed.

Ternary Phase	Stoichiometry	Ternary Phase	Stoichiometry
$Li_x[Mo_6S_8]$	$x=0.8$; $2.4\leq x\leq 3.6$	$Zn_x[Mo_6Se_8]$	$x=1$; $x=2$
$Li_x[Mo_6Se_8]$	$x_m=3.6$	$Cd_x[Mo_6S_8]$	$x_m=2$
$Na_x[Mo_6S_8]$	$x_m=3.6$	$Cd_x[Mo_6Se_8]$	$x=1$; $x=2$
$Mn_x[Mo_6S_8]$	$x_m=1.3$	$Cu_x[Mo_6S_8]$	$0.7\leq x\leq 4$
$Fe_x[Mo_6S_8]$	$x_m=2$	$Cu_x[Mo_6Se_8]$	$0\leq x\leq 4$
$Co_x[Mo_6S_8]$	$x_m=2$	$Cu_x[Ag_{0.7}Mo_6S_8]$	$0\leq x\leq 3.3$
$Ni_x[Mo_6Se_8]$	$x_m=1.8$	$Zn_x[Ag_{0.7}Mo_6S_8]$	$x_m=1.65$
$Zn_x[Mo_6S_8]$	$x=1$; $x=2$	$Li_x[Ag_{0.7}Mo_6S_8]$	$x_m=3.2$

Because of their low redox potential, alkali and alkaline earth compounds decompose in H_2O; they can be obtained by cathodic reduction of Mo_6X_8 electrodes in aprotic organic electrolytes containing the guest ions. Chemical preparation is possible by reaction of Mo_6X_8 with the guest metals dissolved in liquid NH_3. In Figure 5 the potential/charge trans-

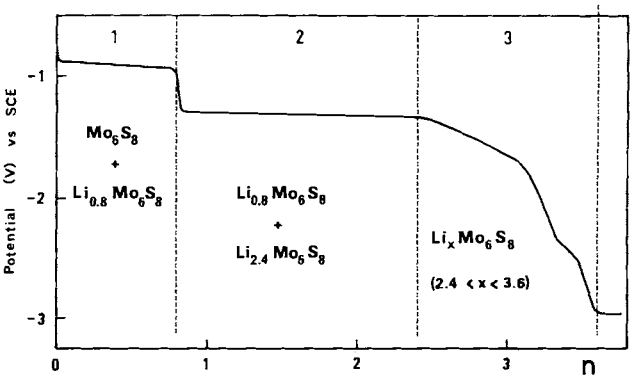


Fig. 5. Galvanostatic cathodic reduction of Mo_6S_8 in Li^+/propylene carbonate. Potential/charge transfer curve and phase diagram; n = integral charge transfer (mole/mol Mo_6S_8). 1, 2, 3 see text.

fer curve is given for the cathodic reduction of Mo_6S_8 in Li^+/dimethoxyethane. The charge transfer n (mole/mol Mo_6S_8) is numerically equivalent to the integral lithium content x in the overall reduction [eq. (8)]. Two potential

$$x\,Li^{\oplus} + x\,e + Mo_6S_8 \rightleftarrows Li_x^{\oplus}[Mo_6S_8]^{x\ominus} \qquad (8)$$

plateaus are observed (region 1, 2) as well as a region with continuous steep increase in potential (3). X-Ray studies showed that in agreement with thermodynamical considerations the plateau regions correspond to two phase ranges $Mo_6S_8/Li_{0.8}Mo_6S_8$ and $Li_{0.8}Mo_6S_8/Li_{2.4}Mo_6S_8$, while in region 3 a nonstoichiometric phase $Li_xMo_6S_8$ appears with $2.4\leq x\leq 3.6$[11,39,40] (Li metal deposition starts at $n=3.6$). The reversibility and the high ionic mobility of Li^+ is substantiated by cyclic voltammetry studies (Fig. 6) and by ^{7}Li-NMR data which show a rather low activation energy $E_A = 8.9$ kJ mol^{-1}.

It is remarkable that the molybdenum cluster chalcogenides are ionic conductors at ambient temperature even for

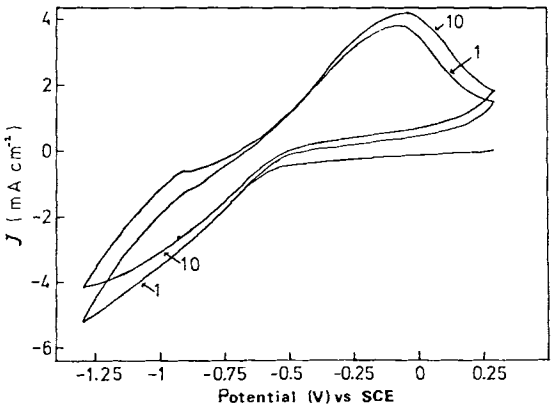


Fig. 6. Cyclic voltammogram of Mo_6S_8 electrode in Li^+/dimethoxyethane, $v = 300$ mV min^{-1} [11]. I = current density. The numbers on the curves indicate the cycle.

transition metal ions, *e.g.* Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}. The latter can be intercalated reversibly by cathodic reduction in aqueous electrolytes; they show solid solution ranges with triclinic lattice distortions at higher metal content. In contrast, line phases only with orthorhombic symmetry are observed for the bivalent post-transition metal ions Zn^{2+} and Cd^{2+}; values for the molar free energy ΔG^0 have been obtained from EMF measurements for zinc molybdenum selenides[41]:

$$Zn + Mo_6Se_8 \rightarrow ZnMo_6Se_8 \quad \Delta G^0 = -75.3 \text{ kJ/mol} \quad (9)$$
$$Zn + ZnMo_6Se_8 \leftarrow Zn_2Mo_6Se_8 \quad \Delta G^0 = -68.5 \text{ kJ/mol} \quad (10)$$

Large nonstoichiometric phase ranges are found for the copper compounds. They can be prepared either from aqueous Cu^{2+} or from organic electrolytes (Cu^+/CH_3CN). The oxidation state of Cu in the ternary chalcogenides is assumed to be $+1$[36]. For selenides $Cu_xMo_6Se_8$ the phase range is $0 < x < 4$, and a continuous change in lattice parameters is observed[41] (Fig. 7). Hysteresis phenomena are found for the

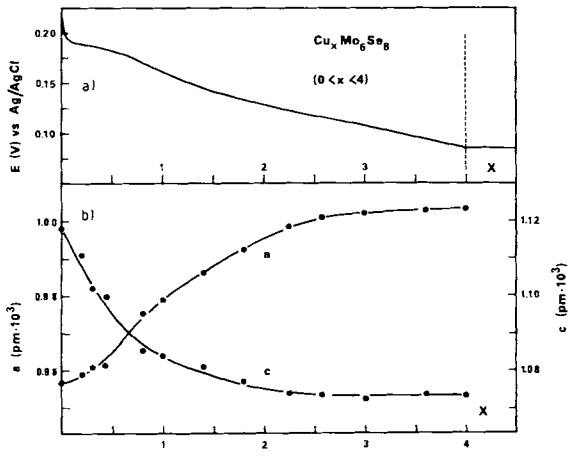


Fig. 7. Formation of $Cu_xMo_6Se_8$ by cathodic reduction of Mo_6Se_8 in Cu^{2+}/H_2O. (a) potential *vs.* composition, x = Cu content; (b) dependence of the hexagonal lattice parameters a, c on x.

sulfide $Cu_xMo_6S_8$: the lower phase limit corresponds to $x = 1.2$ on oxidation of $Cu_xMo_6S_8$ and to $x = 0.7$ on reduction of Mo_6S_8[39]. The hysteresis is reversible and is assumed to be related to the density anomaly of Mo_6S_8[42], to the fact that different positions can be occupied by Cu, and to small dimensional changes of the lattice positions with changes in the rhombohedral angle. A lower phase limit of $x = 1$ was reported in an X-ray study on the anodic oxidation of $Cu_2Mo_6S_8$ in aqueous electrolyte[43]; for thermally prepared phases the lower limit is $x = 1.2$[42].

An investigation on the system Cu/Mo_6S_8 in the temperature range $396\text{ K} < T < 443\text{ K}$ was performed recently in a solid state cell with doped CuBr as the electrolyte[44]. Partial copper ion conductivities and diffusion coefficients were determined as a function of copper content ($1.5 < x < 3.5$) and of temperature. The ionic transport properties were found to be excellent; the chemical diffusion coefficient amounts to 4.8×10^{-5} cm^2 s^{-1} at 441 K for $Cu_{3.3}Mo_6S_8$. From the dependence of the equilibrium EMF of the cell

Pt/Cu/Cu solid electrolyte/$Cu_xMo_6S_8$/Pt

on x and T the copper chemical potential, partial enthalpies and partial entropies were derived. The interpretation of the data is based on a model that takes into account the electronic configuration as well as the distribution of Cu between two types of lattice positions (Fig. 8).

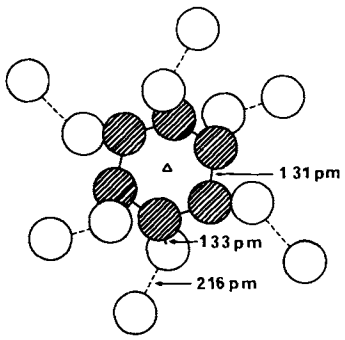


Fig. 8. Cluster of twelve partially occupied Cu^+ positions in $Cu_xMo_6S_8$ viewed along the threefold axis; Cu-1 sites shaded, Cu-2 sites unshaded. The six peripheral sites belong to nearest-atom positions of adjacent clusters [36, 44].

Ternary phases $Tr_xMo_6S_8$ ($x \approx 1$) with partial occupation of the channel sites by large cations, *e.g.* Ag^+, Sn^{2+}, Pb^{2+}, can be prepared only at high temperatures. The Tr^{n+} ions are located close to the origin of the unit cell and show no ionic mobility. There is, however, an excess of unoccupied channel lattice sites, and quaternary phases may be obtained by cathodic reduction of these compounds in electrolytes containing small guest ions A^{n+} [eq. (11)]. Data on the phase limits of $A_xAg_{0.7}Mo_6S_8$ are given in Table 1[41].

$$xA^{\oplus} + xe + TrMo_6X_8 \rightleftarrows A_x[TrMo_6X_8] \quad (11)$$

The "ionic-covalent" bonding model which has been proposed recently to explain the stabilizing effect of A^+ guest ions on the Mo_6X_8 lattice and to understand the influence of A^+ on changes in physical properties implies a maximum electron transfer to the host lattice matrix of ≈ 4 for sulfides and of ≈ 3 for selenides (*i.e.* $[Mo_6S_8]^{4-}$ and $[Mo_6Se_8]^{3-}$)[36]. This model is in agreement with the maximum stoichiometries observed for ternary phases prepared at high temperatures. From the data on selenides obtained at 300 K by cathodic reduction (Table 1) however, an electron transfer

corresponding to $[Mo_6Se_8]^{4-}$ is, calculated (*e.g.* $(Cu^+)_4[Mo_6Se_8]^{4-}$) which is inconsistent with the bonding scheme suggested.

The galvanostatic oxidation of the binary copper sulfide $Cu_{1+x}S$ has been studied in aqueous Cu^{2+} electrolyte; the phase diagram as well as thermodynamic data of intermediate phases were determined[45]. Bornite Cu_5FeS_4, which has a pseudocubic lattice, was shown to have a reversible redox region ($Cu_{5-x}FeS_4$) with $0<x<2$, *i.e.* a part of the Cu atoms are mobile and can be removed from the host lattice[46]. Alkali tungsten oxide bronzes A_xWO_3 with defect perovskite structure show high electronic conductivities[47]; the activation energy for alkali ion transport is, however, rather high. Li_xWO_3 can be used as a nonpolarizing electrode with β-alumina[48].

3.2. Isolated Parallel Lattice Channels

Among the binary and ternary compounds of sulfur and selenium with transition metals in lower oxidation states a series of phases is known which are semiconductors or metals and whose structures can be described in terms of a matrix M_yX_z that contains isolated parallel channels. These channels may be either empty or (partially) filled with large metal ions, *e.g.* Tl^+, K^+ (Table 2). Evidence that chalcogenide systems of this structure type may participate in topotactic redox reactions came originally from studies on Nb_3S_4 and Nb_3Se_4 which demonstrated that both compounds may act as host lattices with mono- or bivalent cations [eq. (12)][10, 16, 35]. The hexagonal niobium chalcogenides consist of a framework of NbX_6 octahedra joining common faces and edges with empty lattice channels of ≈ 130 pm diameter running in the direction of the c axis (Fig. 9)[49]. The metal atoms form Nb—Nb chains parallel to the c axis which are supposed to be responsible for the high electronic conductivity and the superconducting behavior[50]. Cyclic voltammetry studies indicate high ionic mobility in the lattice channels; lattice parameter changes on intercalation are very small as a consequence of the rigid lattice structure. The stoichiometries of the reduction products are, however, rather low ($Na_{0.2}Nb_3S_4$, $K_{0.2}Nb_3S_4$) which has been attributed to a restricted accessibility of the solid volume due to inherent lattice defects (Fig. 10). This assumption is supported by the observation that ternary phases $Na_xNb_3S_4$ and $K_xNb_3S_4$ prepared at high temperatures have considerably higher redox capacity, since the Nb_3S_4 structure is stabilized under thermal equilibrium conditions by the alkali cations[35]. Because of its small ionic radius the influence of defects should be less important for Li^+: cathodic reduction of Nb_3S_4 in Li^+/propylene carbonate leads in fact to $Li_xNb_3S_4$ with $x \approx 1$ (Fig. 11).

Table 2. Binary and ternary transition metal chalcogenides with isolated parallel lattice channels.

Cpd.	Ref.	Cpd.	Ref.
$A_xTi_3S_4$	[16]	V_5S_8	[16, 55]
$Tl_xTi_6Se_8$	[51]	TlV_5S_8	[16, 54]
Nb_3X_4 (X = S, Se, Te)	[49]	TlV_5Se_8	[51]
$A_xNb_3S_4$	[35]	$TlTi_5Se_8$	[51]
$Tl_xV_6S_8$	[52]	Nb_2Se	[53]

$$\frac{x}{n}A^{n\oplus} + xe + Nb_3X_4 \rightleftarrows A^{n\oplus}_{x/n}[Nb_3X_4]^{x\ominus} \qquad (12)$$

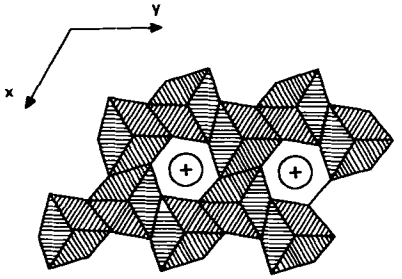


Fig. 9. Structure of Nb_3S_4 and Ti_3S_4 with isolated channels (cross-section perpendicular to channels); positions of guest cations in reduced phases are indicated by circles [16].

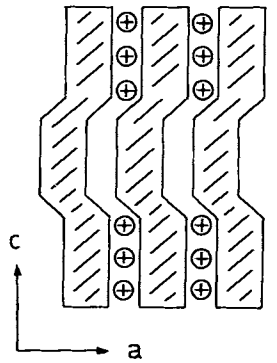


Fig. 10. Scheme of $A^+_x[Nb_3S_4]^{x-}$ structure with partially inaccessible channel volume originating from lattice defects (cross section parallel to channel axes, negative charges of the Nb_3S_4 matrix ommitted) [35].

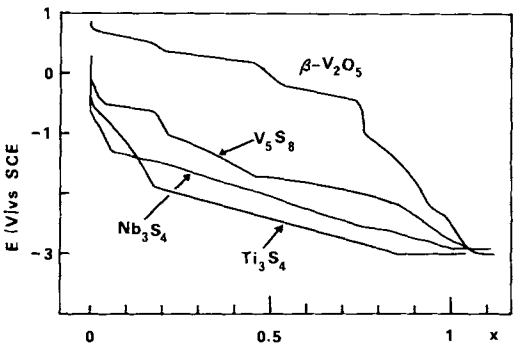


Fig. 11. Potential/charge transfer curve for cathodic reduction of Ti_3S_4, Nb_3S_4, V_5S_8 and β-V_2O_5 to the corresponding Li^+ phases. Electrolyte: 1 M Li^+/propylene carbonate, 298 K; x = e/unit formula [16].

The formation of $K_{0.3}Ti_3S_4$ has been reported recently[16]: its structure can be considered as a partially filled up version of the Nb_3S_4 type. The K^+ ions in the lattice channels are mobile at room temperature. On anodic oxidation in aqueous electrolytes the empty host lattice Ti_3S_4 is obtained which undergoes topotactic redox reactions with cations up to a radius of ≈ 130 pm. The upper limit for $Li_xTi_3S_4$ is equivalent to $x = 0.8$ (Fig. 11); variations of lattice parameters with x are rather small again due to the rigid host structure.

Large parallel channels filled up with Tl atoms are found in the titanium and vanadium chalcogenides $TlTi_5Se_8$, TlV_5S_8 and V_5S_8 (Table 2). Their monoclinic structure is, however, quite different from the Nb_3S_4 type; the structure consists of a distorted framework of MX_6 octahedra sharing faces and edges. The Tl atoms reside in large rectangular channels parallel to the b axis. TlV_5S_8 exhibits metallic conductivity; the Tl atoms are mobile and on anodic oxidation in aqueous electrolytes V_5S_8 is obtained[16]. The binary phase can be reduced and oxidized in electrolytes like Nb_3S_4—with clear changes, however, in lattice parameters due to the higher lattice flexibility. The upper stoichiometric limits for the copper and lithium phase are $Cu_{0.3}V_5S_8$ and $Li_{1.0}V_5S_8$, respectively.

A considerable number of transition metal oxide bronzes $A_xM_yO_z$ are known to have crystal structures with cations A (alkali cations, NH_4^+, Tl^+, Cu^+) positioned in channels inside the M_yO_z matrix[56,57]. Tetragonal tungsten bronzes Na_xWO_3 have been used as reversible electrodes in solid state cells with β-alumina as the electrolyte[58]. An NMR analysis of Li diffusion in the lithium vanadate β-$Li_xV_2O_5$ demonstrated a rather low activation energy of 6.4 kJ mol^{-1}[59]; it has been employed as reversible electrode material[60]. β-$Cu_xV_2O_5$ ($0.26<x<0.64$), which has a V_2O_5 network structure with Cu^+ in channel positions[61], may be oxidized anodically to the metastable binary oxide β-V_2O_5[16] with empty channels. On cathodic reduction in aqueous or organic electrolytes, alkali and transition metal ions can be reversibly inserted into the host lattice (Fig. 11). The high ionic mobility of guest ions can be attributed to the fact that the cations may occupy different positions[62].

Binary transition metal oxides MO_2 with rutile structure have empty lattice channels parallel to the tetragonal c axis and should be able to accept small ions such as Li^+. Metastable ternary phases Li_xMO_2 have actually been reported for the following oxides: TiO_2, VO_2, CrO_2, MnO_2, WO_2, RuO_2, OsO_2 and IrO_2[63–65]. Formation of ternary phases with Li^+ on electrochemical or chemical reduction has also been observed for a series of nonstoichiometric binary oxides of V, Cr, Mo, W with complex framework structures[66–68].

4. Host Lattices with Layered Structures

As compared to three-dimensional systems, host lattices with layer structures are characterized by their ability to intercalate besides metal ions a large variety of molecular species of different size and geometry with expansion of the lattice perpendicular to the layer planes. In addition they exhibit specific structural features on intercalation and deintercalation related to changes in the stacking sequence of the layer units; in extreme cases total one-dimensional disorder may be observed. We shall exclude here graphite from discussion, since its intercalation chemistry has been treated extensively in recent reports[69,70].

4.1. Layered Chalcogenides

A large number of transition metals M are able to form dichalcogenides MX_2 with the highly polarizable anions X = S, Se, Te which have hexagonal structures related to the CdI_2 type (Fig. 12, Table 3). The lattice can be described in terms of a stacking of elastic $(MX_2)_\infty$ sheets of ≈600 pm in thickness which are held together essentially by weak van der Waals interactions. The MX_2 layer units themselves consist of two anion sheets with the metal atoms in the central plane;

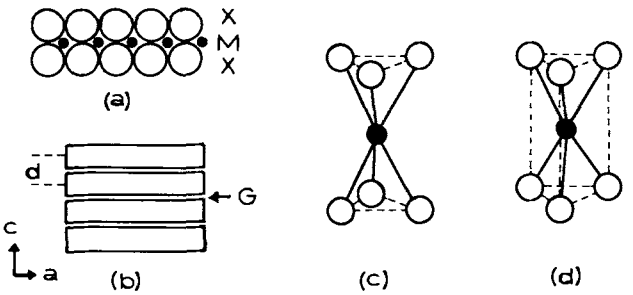


Fig. 12. Structure scheme of layered transition metal dichalcogenides MX_2. (a) X—M—X single layer, (b) layer stacking in the crystal lattice, d = interlayer spacing, G = van der Waals gap, (c), (d) octahedral and trigonal-prismatic coordination of M.

Table 3. Layered binary and ternary phases which undergo reversible topotactic redox reactions.

MX_2 [a]	Ta_2S_2C	MoO_3	$Li_xV_3O_8$
A_xMX_2 [a]	$K_2Ni_3S_4$	$Mo_{18}O_{52}$	FeOCl
MPX_3 [b]	$K_2Pt_4S_6$	V_2O_5	UO_2F_2
$CrPS_4$		ε-$Cu_xV_2O_5$	

[a] M = group 4—6 elements, Re, Sn; A = alkali metal, Ag, Tl, Cu; X = S, Se. [b] M = Mn, Fe, Ni, Zn; X = S, Se.

there is strong ionic/covalent bonding between M and X (Fig. 12). Modifications differ in the coordination of the intralayer metal atoms (octahedral or trigonal prismatic) and in the mode of stacking of the MX_2 layers[71,72].

The strong anisotropy of the layered transition metal dichalcogenides with respect to structure and physical properties extends also to their chemical reactivity. *Rüdorff* first observed alkali metal intercalation into dichalcogenides and proposed an ionic structure model[73]. Compounds with Lewis base molecules were prepared originally by *Weiss* and *Ruthardt*[74]. Intercalation by electrochemical methods was subsequently reported[8b,75,76] and interpreted as reversible topotactic redox reactions[8]. Recent investigations on the mechanism of thermal Lewis base intercalation established that these reactions also are correlated with redox processes and the formation of products with ionic structure[12,24,25].

In order to give an impression of the wide variety of topotactic reactions of layered dichalcogenides, a schematic overview on the characteristic reaction pathways (which also applies to other layered host lattices with redox properties) is shown in Figure 13. We shall divide here the reactions of dichalcogenides into three groups according to the guest species involved: intercalation of metal ions, intercalation of solvated ions, and intercalation of neutral molecules with Lewis base function.

The reversible formation of *intercalation compounds with metal ions* according to eq. (13) (Fig. 13) has been observed for the electropositive alkali and alkaline earth elements, Eu,

$$x\,A^{\oplus} + x\,e + MX_2 \rightleftarrows A_x^{\oplus}[MX_2]^{x\ominus} \qquad (13)$$

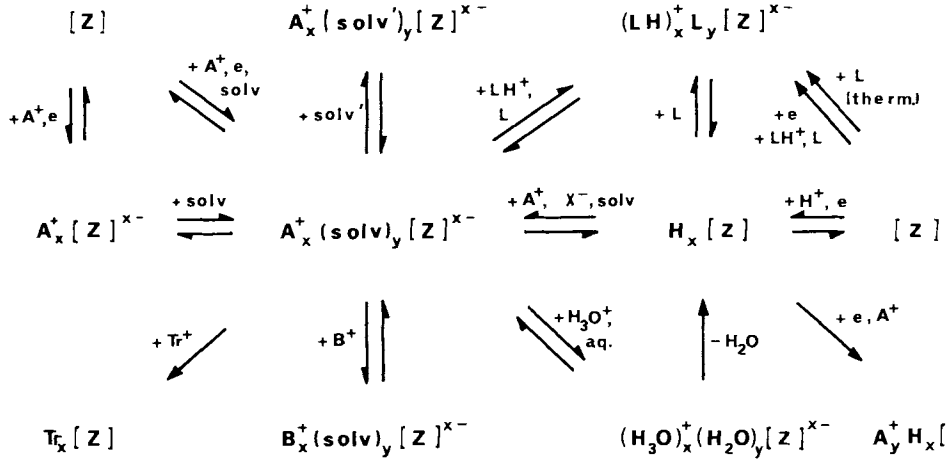


Fig. 13. Scheme of topotactic redox, exchange and solvation reactions of layered host lattices with electronic conductivity. Z = host lattice; A^+, B^+ = guest cations; solv = neutral polar solvent molecules (*e.g.* H_2O, NH_3, formamide); L = Lewis base (*e.g.* pyridine); R^- = anion base (*e.g.* OH^-, NH_2^-, CH_3O^-); Tr = cation with low solvation energy (Cu^+, Ag^+, Tl^+) [86].

Yb, and the post-transition metals Cu, Ag, Tl. Convenient ways of chemical preparation of the alkali compounds are the reaction of the dichalcogenides with alkali metal solutions in liquid NH_3[19,73] or with *n*-butyllithium solutions[21]. Electrochemical formation is achieved by cathodic reduction of MX_2 electrodes in nonprotolytic electrolytes, *e.g.* solutions of alkali ions in dimethyl sulfoxide or cyclopropylene carbonate[34,77]. The intercalation of the metal ions leads to an increase of the interlayer spacing *d* (distance between neighboring layers in the direction of the hexagonal c axis), which is related to the size of the guest ion. The upper limit for *x* in A_xMX_2 depends on the chalcogenide and on the guest metal ion. Several intermediate phase ranges were found for the larger alkali metals (Fig. 14). For low *x* values, higher stage phases are observed with the guest metal ions intercalated in

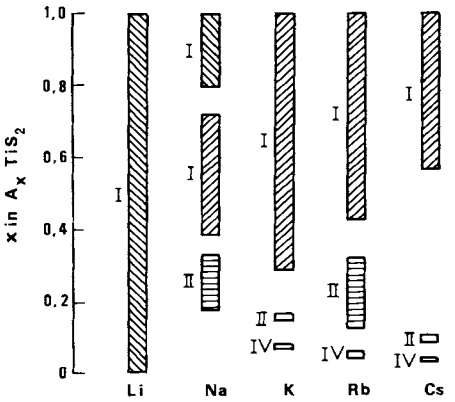


Fig. 14. Limits of A_xTiS_2 phases. I, II, IV = first, second and fourth stage compounds [19, 34].

only every second or fourth interlayer space. The intercalation is associated with changes in the stacking mode of the layers; Na^+, K^+, Rb^+ and Cs^+ may occupy either octahedral or trigonal prismatic sites depending upon the cation size, the cation concentration and the nature of the dichalcogenide[19]. The electronic band structure of the host lattice seems to play an important role in the stability of the ternary phases. While alkali compounds of dichalcogenides with a broad t_{2g} conduction band are rather stable (*e.g.* A_xTiS_2), it is found that compounds of chalcogenide host lattices with filled-up d_{z^2} band have low stability (*e.g.* A_xMoS_2[77,78], Fig. 15). Lithium compounds have been extensively studied because of their application as reversible battery electrodes[34].

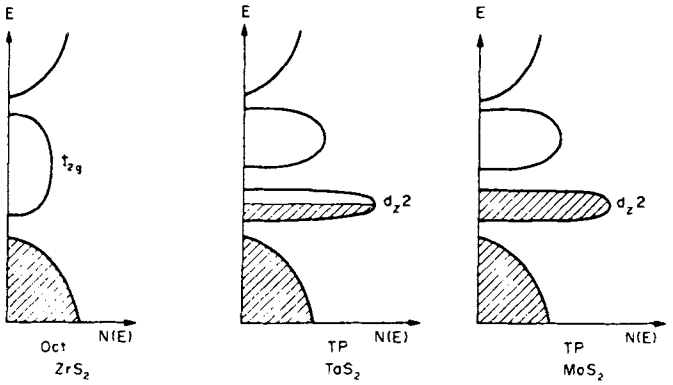


Fig. 15. Band structure scheme of layered dichalcogenides of transition elements of subgroups 4, 5 and 6 [19]. Examples ZrS_2, TaS_2 and MoS_2. Oct = octahedral, TP = trigonal prismatic.

In the case of Li_xTiS_2 a homogeneous phase range of $0 \leq x \leq 1$ has been observed[79]. Free energies and enthalpies of formation for Li and Na phases have been evaluated from electrochemical data[34,80].

Cu_xMX_2 and Ag_xMX_2 can be obtained from aqueous electrolytes; both cations reside in tetrahedral interlayer sites. The occupation is a function of temperature, and order-disorder transitions have been found for Cu_xNbS_2 and Cu_xTaS_2[81]. The existence of ordered intermediate structures (Fig. 16) in Na_xTiS_2 has been proven recently by X-ray investigations on the cathodic reduction of TiS_2 single crystals in NaI/propylene carbonate at 300 K[32]. Support for Li ordering states in Li_xTiS_2 follows from *in situ* X-ray investigations on TiS_2 electrodes[29], electrochemical potential stepping techniques[82], and perturbed angular correlation studies[83].

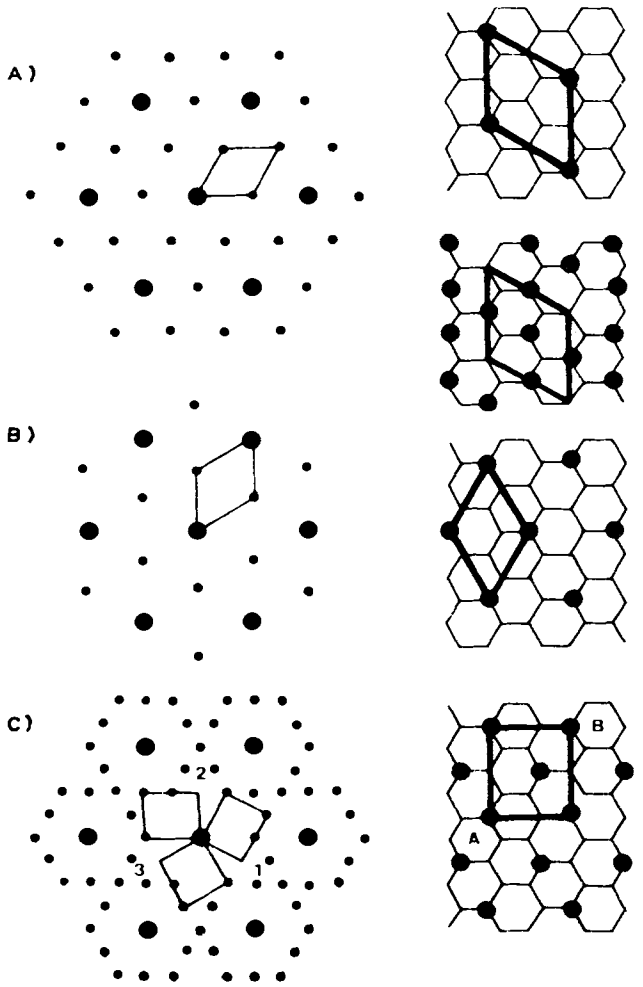


Fig. 16. Ordered states of Na_xTiS_2 phases at room temperature. Superstructure patterns and corresponding unit cells; n refers to stage number [32]. A) above: $a_A = 2a$, $n = 2$, $x = 1/8$; below: $a_A = 2a$, $n = 1$, $x = 3/4$; B) $a_B = a$, $n = 3$, $x = 1/9$; $n = 2$, $x = 1/6$; C) A = 2, B = $a\,|\,\bar{3}$; $n = 2$, $x = 1/4$, $n = 1$, $x = 1/2$.

Metastable layered binary sulfides and selenides may be prepared by oxidation of thermally stable ternary phases, *e.g.* $CrSe_2$, $Cr_{0.5}Ti_{0.5}S_2$ and VS_2 are obtained on oxidation of $LiVS_2$, $Na_{0.5}Ti_{0.5}Cr_{0.5}S_2$ and K_xCrSe_2[8a, 15, 84].

Cathodic reduction (or chemical reduction *e.g.* with $S_2O_4^{2-}$) of layered dichalcogenides in electrolytes with strongly polar solvents leads to uptake of neutral solvent molecules along with cations into the solid [eq. (14), Fig. 17].

$$x\,A^{\oplus} + x\,e + y\,\mathrm{solv} + MX_2 \rightleftarrows A_x^{\oplus}(\mathrm{solv})_y[MX_2]^{x\ominus} \qquad (14)$$

The resulting *solvated phases* exhibit polyelectrolyte character and consist of two-dimensional macroanions $[MX_2]_\infty^{x-}$ with mobile solvated cations in the interlayer space[8, 9, 85, 86]; they undergo ion and solvent exchange reactions (Fig. 13). An extraordinary variety of phases can be obtained by the choice of cation (*e.g.* main group and transition metal ions, metal complex ions, protonated amines and quaternary ions, cationic dyes) and solvent (inorganic and organic polar molecules). The solvate structures are principally governed by the ion/dipole interaction between cations and solvent molecules.

Hydrated chalcogenides $A_x^+(H_2O)_y[MX_2]^{x-}$ with alkali and alkaline earth ions show rather simple correlations between solvate structure and cation hydration energies. For cations with a charge/radius ratio $e/r < 1$ only monolayers of H_2O are observed, while cations with $e/r > 1$ are able to form hydrates with bilayers and monolayers of H_2O in dependence of the H_2O activity (Fig. 17, 18). The average lattice expan-

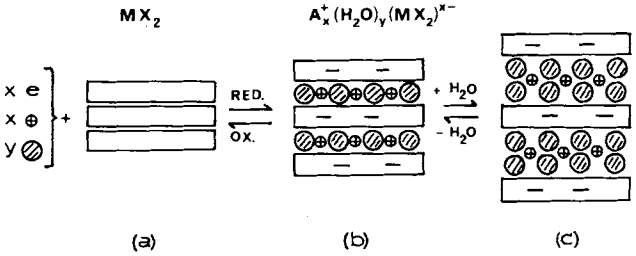


Fig. 17. Scheme of formation of hydrated layered chalcogenides by cathodic reduction of MX_2 in aqueous electrolytes. (a) host lattice; (b) monolayer hydrate; (c) bilayer hydrate; ⊕ = guest cation A^+; ◍ = H_2O.

sions of $\Delta d \approx 300$ pm and $\Delta d \approx 600$ pm are equivalent to one and two times, respectively, the van der Waals diameter of H_2O. Octahedral coordination of the cations by water was found for the bilayer hydrate $Na_{0.6}(H_2O)_2VS_2$[87], whereas trigonal prismatic sites could be established for H_2O and K^+ in the monolayer hydrates $K_{0.5}(H_2O)_{0.5}NbS_2$ and $K_{0.3}(H_2O)_yTaS_2$[88]. The position and anisotropic mobility of H_2O in monolayer hydrates is discussed in Section 8.

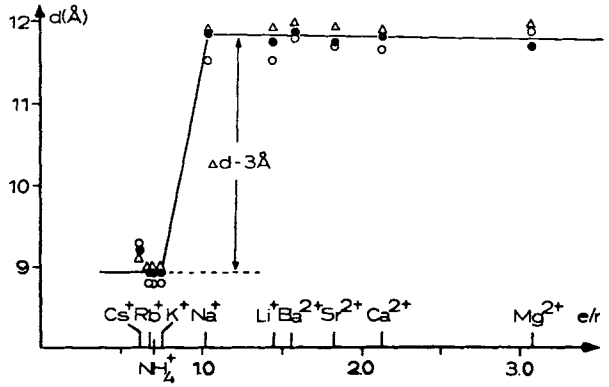


Fig. 18. Dependence of the interlayer spacing d of hydrated layered transition metal sulfides on the charge/radius ratio e/r of the guest cation [85].
○ = $A_{0.5/x}^{x+}(H_2O)_y[TiS_2]^{0.5-}$; ● = $A_{0.5/x}^{x+}(H_2O)_y[NbS_2]^{0.5-}$;
△ = $A_{0.3/x}^{x+}(H_2O)_y[TaS_2]^{0.3-}$.

The maximum reduction stage in aqueous electrolytes essentially depends upon the electronic nature of the host lattice and varies between $x \approx 0.25$ and $x = 0.5$ (*e.g.* $Na_{0.33}^+(H_2O)_y[TiS_2]^{0.33-}$, $K_{0.5}^+(H_2O)_y[NbS_2]^{0.5-}$). Hydrated sulfides $A_x(H_2O)_yMoS_2$ and $A_x(H_2O)_ySnS_2$ are rather unstable towards oxidation to the binary phases[78, 89, 90]; for chromium sulfides $A_x(H_2O)_yCrS_2$ a limited redox range $0.4 < x < 0.7$ is found which is likely to be due to the instability of Cr^{4+} in sulfides[17].

Evidence for the occurrence of intermediates in the cathodic reduction and anodic oxidation of dichalcogenide electrodes in aqueous electrolytes came from investigations on single crystal and polycrystalline MS_2 electrodes by cyclic voltammetry[8b]. This was confirmed by a recent *in situ* neutron diffraction study on the structural changes of 2H-TaS_2

electrodes in the course of galvanostatic reduction in K^+/D_2O[12,31]. The overall reaction proceeds according to equation (15) with formation of $K_{0.5}(D_2O)_{0.5}TaS_2$ as the final product.

$$x\,K^{\oplus} + x\,e + y\,D_2O + TaS_2 \rightleftarrows K_x^{\oplus}(D_2O)_y[TaS_2]^{x\ominus} \quad (15)$$

The potential/charge transfer curve shows three potential plateaus (regions 1—3) and a steep continuous rise in potential (region 4) (Fig. 19a). The neutron diffraction data obtained simultaneously with the reduction indicate the formation and disappearance of intermediate phases. Detailed

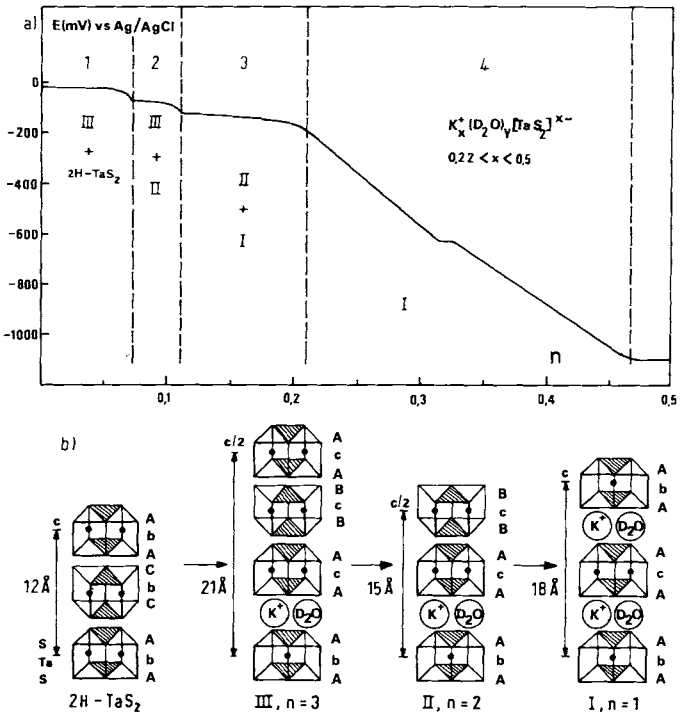


Fig. 19. Galvanostatic cathodic reduction of 2H-TaS_2 in K_2SO_4/D_2O. (a) potential/charge transfer curve and phase diagram, $n = e/TaS_2$; (b) scheme of structural transformations in the course of the reduction [31]. I, II, III = compounds of the first, second and third stage.

analysis revealed the existence of three two-phase ranges 1—3 with the formation of third stage, second stage and first stage hydrates (Fig. 19b):

$K^+_{0.21}(D_2O)_{0.79}[TaS_2]^{0.21-}_3$

$K^+_{0.22}(D_2O)_{0.78}[TaS_2]^{0.22-}_2$

$K^+_{0.21}(D_2O)_{0.79}[TaS_2]^{0.21-}$

In region 4 there exists a nonstoichiometric first stage phase. Anodic oxidation proceeds *via* the same stages in inverse sequence. The formation of higher stage intermediates was also observed for other MX_2 host lattices with different guest ions and seems to be a general phenomenon in topotactic electrode reactions of layered chalcogenides that is likely to be related to stable intermediate electronic states. Kinetic factors become of importance with increasing guest-ion size (*e.g.* large transition metal complexes, dye cations) and may prevent the isolation of pure intermediates[12,31].

The intercalation of protonated Lewis bases (amines, heterocycles) with low solvation energy in aqueous electrolytes results in the formation of homosolvated phases as a consequence of the equilibrium

$$LH^{\oplus} + H_2O \rightleftarrows L + H_3O^{\oplus}$$

On cathodic reduction of *e.g.* TaS_2 in aqueous pyridinium ion (pyH^+) solutions, $(pyH^+)_{0.25}(py)_{0.25}[TaS_2]^{0.25-}$ is obtained with pyridinium ions solvated by neutral pyridine molecules in the interlayer space [eq. (16)][8b,25,91]. Three intermediate phases have been identified with the pyridine ring planes either parallel or perpendicular to the host layer planes.

$$0.5\,pyH^{\oplus} + 0.25\,e + 0.25\,H_2O + TaS_2 \rightarrow (pyH^{\oplus})_{0.25}(py)_{0.25}[TaS_2]^{0.25\ominus} + 0.25\,H_3O^{\oplus} \quad (16)$$

Spontaneous intercalation is observed on reaction of dichalcogenides with aqueous base solutions, *e.g.* alkali hydroxides, NH_3, organic amines. The process involves partial hydrolysis of the host lattice layers with formation of H_2S, which itself acts as the electron donor yielding elemental sulfur[8c,85]:

$$\frac{x}{2}HS^{\ominus} + MX_2 \rightarrow \frac{x}{2}S + \frac{x}{2}H^{\oplus} + [MX_2]^{x\ominus} \quad (17)$$

A large variety of inorganic and organic *neutral molecular compounds with Lewis base character* (NH_3, hydrazines, amines, heterocycles, acid amides, *N*-oxides, phosphanes, *etc.*) are able to form *Lewis base intercalation compounds* L_yMX_2 with layered dichalcogenides by direct thermal reaction[22,23]. The lattice expansions are dependent upon size and arrangement of the guest molecules and interlayer spacings up to 5000 pm are measured for strongly anisometric guest species, *e.g. n*-alkylamines[92-94]. The interaction host lattice/guest molecule has been interpreted in terms of a charge transfer from the guest donor molecules to the acceptor host lattice[22,23,95,99]. Recent investigations led, however, to the hypothesis that the direct intercalation of Lewis base compounds generally proceeds *via* topotactic redox reactions to phases with ionic structures[12,24,25]. This concept is supported by studies on the mechanism of intercalation of NH_3 and pyridine. In contrast with previous models[96,97] (Fig. 20a), ^{1}H-NMR measurements on $TaS_2(NH_3)_{1.0}$ and $TiS_2(NH_3)_{1.0}$ established a position of NH_3 in the interlayer space with the C_3 axis oriented parallel to the layer planes (Fig. 20b)[95],

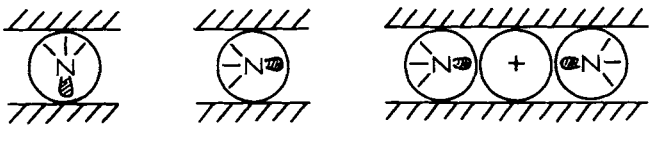


Fig. 20. Structure models for the position of NH_3 between the metal sulfide layers in $TaS_2 \cdot (NH_3)$. a, b: C_3 axis of NH_3 perpendicular and parallel to the layer planes, c: ionic model [12, 24].

which is obviously an unfavorable position for charge transfer between the nitrogen lone pair and the MX_2 layers. An investigation on the mechanism of NH_3 intercalation into TaS_2 demonstrated that a redox process is correlated with

this reaction that involves the oxidation of a fraction of the guest molecules with formation of N_2[24]. The electrons are transferred to the TaS_2 layers, while the protons are accepted by NH_3 molecules [eq. (18)—(20)].

$$2NH_3 \rightarrow N_2 + 6H^{\oplus} + 6e \quad (18)$$

$$xe + TaS_2 \rightarrow [TaS_2]^{x\ominus} \quad (19)$$

$$H^{\oplus} + NH_3 \rightarrow NH_4^{\oplus} \quad (20)$$

The resulting product $(NH_4^+)_x(NH_3)_{1-x}[TaS_2]^{x-}$ with $x \approx 0.1$ has ionic structure with NH_4^+ cations solvated by neutral NH_3 molecules. This bonding scheme explains *e.g.* the unusual orientation of NH_3 by conventional ion/dipole interactions (Fig. 20c). The thermal intercalation of pyridine in TaS_2 was found to proceed similarly *via* a redox process associated with a molecular disproportionation of a part of the guest molecules yielding dipyridine [eq. (21)—(23)]. The product has again ionic structure:

$$x\,py \rightarrow \frac{x}{2}(py\text{-}py) + xH^{\oplus} + xe \quad (21)$$

$$x\,py + xH^{\oplus} \rightarrow x(pyH^{\oplus}) \quad (22)$$

$$xe + TaS_2 \rightarrow [TaS_2]^{x\ominus} \quad (23)$$

$(py)_{0.5-2x}(pyH^+)_x(py\text{-}py)_{x/2}[TaS_2]^{x-}$ with the ring planes perpendicular to the hexagonal c axis ($x \approx 0.2$; Fig. 21d)[25, 98, 99]. The appearance of higher stage intermediates during thermal intercalation of NH_3 and pyridine has been investigated by neutron diffraction[100]. Less complex reaction mechanisms

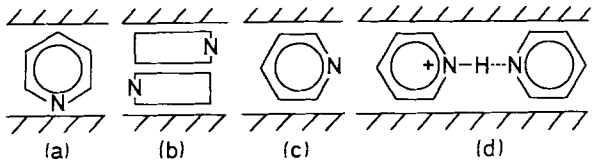


Fig. 21. Structure models for the position of pyridine in $MX_2(py)_{0.5}$ [12, 25, 99].

should be observed for guest species with low ionization potential and able to form stable radical cations, *e.g.* aromatic Lewis bases; indirect evidence for this process has recently been reported for phenylenediamine intercalation[83]. Direct ionization was assumed to occur in the thermal intercalation of metallocenes[101] which can also be obtained by cathodic reduction of MX_2 in electrolytes containing metallocenium ions[31].

A series of binary and ternary chalcogenides with layered structures related to the CdI_2 and $CrCl_3$ type have been reported to undergo topotactic redox reactions: tantalum sulfide carbide Ta_2S_2C[9, 102, 103], phosphorus sulfides MPX_3[91, 104, 105], $CrPS_4$[106] and the thiometallates $K_2Ni_3S_4$ and $K_2Pt_4S_6$[85, 86, 107]. Their reactivity is rather similar to that of the layered dichalcogenides.

4.2. Layered Oxides

As a consequence of the high electronegativity and low polarizability of oxygen, metal/oxygen bonds have more ionic character as compared to metal/sulfur bonds. The structures of oxides and sulfides are therefore generally quite different[72].

The binary oxide of molybdenum(VI) MoO_3 has a typical layer structure: edge- and vertex-sharing distorted MoO_6 octahedra form two-dimensional puckered $(MoO_3)_x$ units which are separated in the orthorhombic crystal lattice by van der Waals gaps (Fig. 22). The semiconducting MoO_3 is

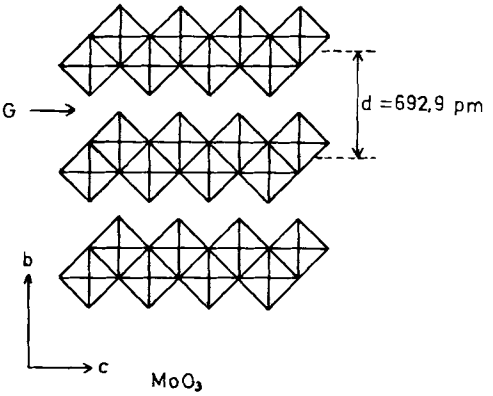


Fig. 22. Structure of MoO_3; cross section perpendicular to the layer planes; G = van der Waals gap.

able to undergo a wide range of topotactic redox and exchange reactions which are surprisingly similar to those observed for layered dichalcogenides (Fig. 13)[10, 67, 86, 108]. In aqueous electrolytes containing main group or transition metal ions dark blue hydrated phases with metallic luster are obtained [eq. (24)]. These reactions are strongly dependent upon pH values and may lead to the formation of mixed

$$xA^{\oplus} + xe + yH_2O + MoO_3 \rightleftarrows A_x^{\oplus}(H_2O)_y[MoO_3]^{x\ominus} \quad (24)$$

metal cation/hydrogen bronzes. To illustrate this, Figure 23 shows the potential/charge transfer curve for the cathodic re-

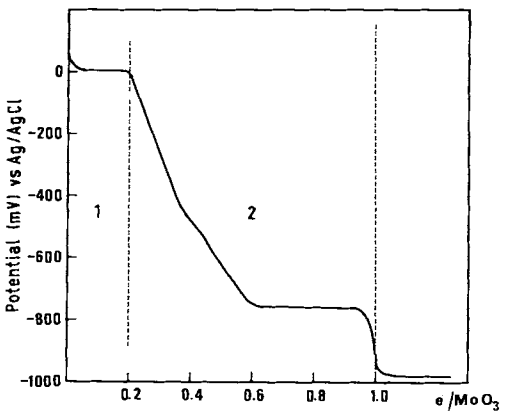


Fig. 23. Galvanostatic cathodic reduction of MoO_3 in Na^+/H_2O: potential/charge transfer curve.

duction of MoO_3 in 1 N Na_2SO_4 (pH = 6). The starting region 1 corresponds to a two-phase range with the formation of $H_{0.2}MoO_3$ at constant potential; in region 2, which exhibits a nonstoichiometric and a two-phase range, hydrated Na^+ and H_3O^+ ions enter the lattice simultaneously. After a charge transfer of $1\,e/MoO_3$ the potential of H^+ discharge is reached, the composition of the final product is $Na_{0.5}^+H_{0.5}^+(H_2O)_y[MoO_3]^-$. Oxidation/reduction cycles show a limited kinetically accessible reversible range of $0.4 \leq x \leq 1$ which is likely due to small structural distortions.

Transition metal complex ions as well as a large number of organic ions can be intercalated by cathodic reduction in aqueous and organic electrolytes. Thermal intercalation of Lewis base compounds can be achieved and is assumed to proceed as a molecular redox disproportionation[108].

MoO_3 is of interest as cathode material for organic electrolyte lithium batteries because of the high energy density of the couple Li/MoO_3[109]. As reaction product, the formation of lower molybdenum oxides has been proposed[110]; from X-ray data a ternary phase with a structure similar to high temperature Li_2MoO_3 was suggested as the product[63]. A study on the discharge reaction mechanism revealed that the process is in fact a reversible topotactic redox reaction [eq. (25)]; the kinetically accessible range corresponds to $0.1 < x < 1.5$[67].

$$x\,Li^{\oplus} + x\,e + MoO_3 \rightleftarrows Li_xMoO_3 \qquad (25)$$

$Mo_{18}O_{52}$ has a lattice structure closely related to the MoO_3 type and shows similar reactivity[67,108]. Several layered oxides of vanadium have been studied with respect to topotactic redox activity. The binary vanadium oxide V_2O_5 forms layered ternary phases $Li_xV_2O_5$ on cathodic reduction in organic Li^+ electrolytes and on reaction with butyllithium or LiI [eq. (26)][63,111,112]. Hydrated vanadium oxides

$$x\,LiI + V_2O_5 \rightarrow Li_xV_2O_5 + \frac{x}{2}\,I_2 \qquad (26)$$

$A_x^+(H_2O)_y[V_3O_8]^{x-}$ can be obtained from the ternary oxide $Li_xV_3O_8$ which show a limited redox range[113]. ε-$Cu_xV_2O_5$[114] yields on anodic oxidation in aqueous H_2SO_4 ε-$(H_3O^+)_{0.2}(H_2O)_y[V_2O_5]^{0.2-}$, which can be reversibly reduced in aqueous metal ion solutions to the hydrated phases ε-$A_x^+(H_2O)_y[V_2O_5]^{x-}$ $(0.2 < x < 0.8)$[115]. On cathodic reduction in A^+/(DMSO) the orthorhombic oxide chloride FeOCl forms solvated layered phases $A_x^+(DMSO)_y[FeOCl]^{x-}$ (A = alkali ion, H^+, $(CH_3)_4N^+$; $x = 0.1$—0.5)[116]. $Li_{0.5}FeOCl$ can be prepared by reaction of the oxide halide with butyllithium[117]. The thermal intercalation of metallocenes and of pyridine into the FeOCl lattice has been reported[117-119]. Analytical and mass spectrometric investigations on the reaction of pyridine with FeOCl to give $(py)_{1/3}FeOCl$ revealed the formation of bipyridyl and of chloropyridine; this would suggest a redox mechanism similar to that established for $MX_2(py)_{0.5}$ *(vide supra)* and a simultaneous topochemical modification of the host matrix[91]. On cathodic reduction of FeOCl in aqueous pyridinium solutions $(pyH^+)_x(py)_{1/3-x}[FeOCl]^{x-}$ is obtained ($x \approx 0.2$).

A large number of other layered materials exhibiting electronic conductivity have been described (metal chalcogenides, oxides, halides, carbides, nitrides, *etc.*[72]) and it is likely that many of them are potential candidates for topotactic redox reactions. Besides graphite, only few other host lattices are known so far which lead to products with inverse polarity $[Z]^{x+}A_x^-$ [eq. (2)]; interesting systems in this connection would be layered rare earth halides, *e.g.* PrI_2[72]—which is a metallic conductor $[PrI_2]^+(e)$ and should, in principle, be able to undergo electron/anion transfer reactions.

5. Linear Chain Systems

Relatively few studies have hitherto been devoted to host lattices with M_xX_y (M = metal, X = nonmetal) chains as the host lattice matrix. This is due, in part, to the low structural stability of one-dimensional elements and the ease of irreversible modification by chemical attack. Most investigations have concentrated on the transition metal trichalcogenides MX_3 (M = Ti, Zr, Hf, Nb, Ta; X = S, Se)[19,34]. The structure of $NbSe_3$ (Fig. 24) can be described geometrically by distorted $NbSe_6$ trigonal prisms sharing opposite trigonal faces to form $(NbSe_3)_\infty$ chains. The structures of the other compounds differ, in the main, with respect to the arrangement of the chains. Two of the chalcogen atoms are closer to each other with a X—X linkage, *i.e.* $M^{4+}X^{2-}(X_2)^{2-}$. The trichalcogenides can intercalate Li [eq. (27)] in organic electrolytes;

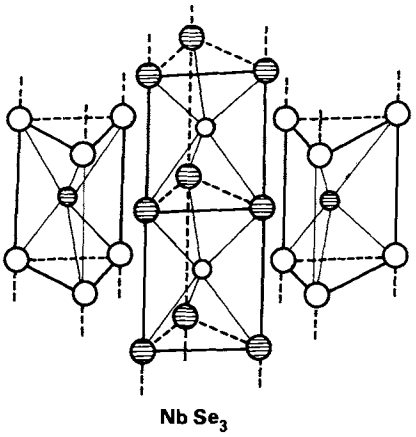


Fig. 24. Structure scheme of niobium triselenide with $(NbSe_3)_\infty$ chains. Large circles Se; small circles Nb.

$$x\,Li^{\oplus} + x\,e + MX_3 \rightarrow Li_x(MX_3) \qquad (27)$$

the reaction with *n*-butyllithium yields a maximum value of $x = 3$. Electrochemical studies on TiS_3 showed reversibility of the intercalation only for low values of x[63,120]. This has been attributed to irreversible attack at the polysulfide bridges which is probably associated with a change of the transition metal coordination from trigonal prismatic to octahedral coordination and with the formation of Li_2S. For $NbSe_3$, a larger reversibility range was observed; the higher stability of $NbSe_3$ may be related to the fact that Nb prefers trigonal prismatic coordination to octahedral coordination. Structural studies show strong line-broadening and extensive lattice disorder which is in part due to co-intercalation of solvent species.

The ternary alkali sulfides of iron $AFeS_2$ (A = K, Rb, Cs) consist of negatively charged chains built up of FeS_4 tetrahedra sharing opposite edges; the alkali ions occupy positions between the chains. Topotactic ion exchange of K^+ for alkaline earth ions in aqueos electrolytes has been reported[121]. The $AFeS_2$ structure contains vacant lattice sites between the chains, and in a recent electrochemical investigation the formation of Li_xKFeS_2 in organic Li^+ electrolytes was established with $x = 1$[122]. The initial reaction corresponds to a two phase region $KFeS_2/LiKFeS_2$ and the lattice symmetry changes from monoclinic to tetragonal. On subsequent oxidation/reduction cycling an extended nonstoichiometric phase region is found [eq. (28)]. X-Ray investiga-

$$LiKFeS_2 \rightleftarrows Li_{1-y}KFeS_2 + yLi^{\oplus} + ye \quad (28)$$

tions suggest a CuTe like structure for $Li_{1-y}KFeS_2$ ($0 \leq y \leq 0.75$). $Sr_{0.5}FeS_2$ and $Ba_{0.5}FeS_2$ also show reversible reactions with Li.

The structure of the niobium chalcogenide Nb_2Se_9 is also characterized by metal/sulfur chain elements[123]. Intercalation of Li with the formation of $Li_8Nb_2Se_9$ has been reported[124]. By thermal methods (iodine vapor transport) $NbSe_4I_{0.33}$ can be obtained; the iodine atoms are located between the $NbSe_4$ chains[125] and the structure may be described as $[NbSe_4]^{x+}[I_{0.33}]^{x-}$. It would be of interest to find out whether iodine is mobile in this compound, thus allowing topotactic electron/anion transfer [eq. (2)].

6. Hydrogen Bronzes and Electron/Proton Transfer

We shall here define hydrogen bronzes as solid compounds $H_x[Z]$ with electronic conductivity which contain mobile hydrogen atoms and are able to undergo reversible topotactic electron/proton transfer according to the formal scheme:

$$xH^{\oplus} + xe + [Z] \rightleftarrows H_x^{\oplus}[Z]^{x\ominus} \quad (29)$$

Hydrogen ions are the smallest guest ions available and strong pecularities are observed with respect to mobility, bonding and structural features as compared to other atomic and molecular guest ions. Because of their exceptionally small radius and consequent high charge density, protons polarize considerably their surrounding, which leads to partially covalent bonding to the host lattice. Besides line phases, large nonstoichiometric regions are frequently found; mixed metal cation/hydrogen bronzes may be obtained from electrolytes containing both H^+ and metal ions A^+ [eq. (30), Fig. 23].

$$xH^{\oplus} + yA^{\oplus} + (x+y)e + [Z] \rightleftarrows H_x^{\oplus}A_y^{\oplus}[Z]^{(x+y)\ominus} \quad (30)$$

A special type of reactivity is observed in the case of hydrogen bronzes with layered structure which may react as solid Brønsted acids with neutral or ionic Lewis bases [eq. (31), (32); Fig. 13].

$$H_x[Z] + L \rightleftarrows (LH^{\oplus})_x[Z]^{x\ominus} \quad (31)$$

$$H_x[Z] + xA^{\oplus} + xX^{\ominus} \rightleftarrows A_x^{\oplus}[Z]^{x\ominus} + xHX \quad (32)$$

(L = neutral Lewis base, *e.g.* H_2O, NH_3, pyridine; $X = OH^{\ominus}$, $NH_2^{\ominus}$, $OCH_3^{\ominus}$, *etc.*)

The first systematic studies were performed on H_xWO_3 and H_xMoO_3 by *Glemser*, who recognized the "genotypic" character and reversibility of the formation process[7, 126]. *Brénet et al.* and *Feitknecht et al.* observed a solid solution range H_xMnO_2 on the reduction of MnO_2[127, 128]. In recent years a considerable number of hydrogen bronzes have been prepared and characterized, most of them derived from transition metal oxides and chalcogenides with framework and layer structures (Table 4). Although the preparation of these phases is frequently possible by chemical reduction of the host lattice (*e.g.* Zn/HCl, N_2H_4, *etc.*) the most suitable way is the electrochemical technique (acid electrolytes), which also yields information on phase ranges and thermodynamic data and allows the convenient isolation of intermediates. Compounds with low stability at ambient temperature can be prepared by low temperature electrolysis in nonaqueous acid electrolytes. An indirect method of preparation for layered hydrogen bronzes is the dehydration of oxonium compounds $(H_3O^+)_x(H_2O)_y[Z]^{x-}$, which are readily accessible by ion-exchange with acids of the corresponding alkali phases (Fig. 13).

Table 4. Hydrogen bronzes of transition metal compounds with framework and layer structures (x = maximum H content observed).

Cpd.	x	Ref.	Cpd.	x	Ref.
H_xWO_3	0.6	[7, 129]	$H_xV_3O_8$	1.5	[113]
H_xReO_3	0.8	[115, 132]	H_xNiO_2	2	[146, 147]
H_xBaRuO_3	0.4	[115, 133]	H_xFeOCl	0.5	[116]
H_xTiO_2	small	[143, 150]	H_xTiS_2	0.3	[12]
H_xIrO_2	small	[148c]	H_xVS_2	0.3	[115]
H_xVO_2	1.0	[152]	H_xNbS_2	0.8	[30, 139]
H_xRuO_2	small	[154]	$H_xTaS_2(1T)$[a]	0.3	[115]
H_xMnO_2	0.5	[127, 128, 146]	$H_xTaS_2(2H)$[a]	0.8	[30, 139]
H_xPbO_2	0.02	[151]	H_xCrS_2	0.3	[17]
β-$H_xV_2O_5$	0.5	[16, 41]	H_xMoS_2	0.3	[89]
H_xMoO_3	2	[10, 126, 135]	$H_xV_5S_8$	0.8	[16, 41]
$H_xMo_{18}O_{52}$	8	[108, 115]	$H_xAg_{0.7}Mo_6S_8$	0.2	[41]
ϵ-$H_xV_2O_5$	0.8	[115]	H_xZrCl	1	[153]
			H_xZrBr	1	[153]

[a] 1T, 2H: stacking modifications of TaS_2.

Among the materials with framework host structures, tungsten(VI) oxide, which has a distorted ReO_3 type lattice, was studied in more detail. On reduction of WO_3 in aqueous HCl/Zn the color changes from faintly yellow to dark blue, with formation of H_xWO_3. The following nonstoichiometric phase ranges have been detected: tetragonal $0.15 < x < 0.23$, tetragonal $0.33 < x < 0.5$, and cubic $0.5 < x < 0.6$[7, 129]. Corresponding potential steps are found in potential/charge transfer curves on reduction of WO_3 in aqueous H_2SO_4; the upper composition limit on cathodic reduction is $x = 0.6$. Enthalpies of formation from $H_{2(g)}$ and $WO_{3(s)}$ at 298 K have been determined for $H_{0.18}WO_3$ (-4.8 kJ mol^{-1}) and $H_{0.35}WO_3$ (-9.6 kJ mol^{-1})[130]. Recent structural studies on the cubic phase show that the hydrogen atoms are attached to the WO_3 lattice by $-OH$ bonds[131].

The structurally related cubic oxide ReO_3 exhibits metallic conductivity and has been reported to yield a gold-colored orthorhombic hydrogen bronze $H_{0.15}ReO_3$ on reduction with ethanol or partial disproportionation in water[132]. Cathodic reduction of ReO_3 in aqueous H_2SO_4 was found to be reversible with an upper composition limit of $x = 0.8$; several potential steps occurring in the course of galvanostatic reduction indicate the presence of intermediate phases[115]. $BaRuO_3$, whose structure is also related to the perovskite type lattice, absorbs gaseous H_2 at room temperature to yield $H_{0.3}BaRuO_3$[133]; on (reversible) cathodic reduction of the ternary phase in 1 N H_2SO_4 the upper composition limit turns out to be $H_{0.4}BaRuO_3$[115]. Oxide hydrogen bronzes derived from host lattices with the more compact rutile type structure usually exhibit low x values except for H_xVO_2 and H_xMnO_2 (Table 4). Hydrogen bronzes of metal chalcogenides with framework structures seem to be rather unstable at ambient temperature; $H_{0.2}Ag_{0.7}Mo_6S_8$ can be prepared by cathodic reduction of $Ag_{0.7}Mo_6S_8$ at 230 K in CH_3OH/HCl electrolyte. The cluster halide Nb_6I_{11} is able to react with gaseous hy-

drogen to give HNb_6I_{11}; hydrogen is located inside the Nb_6 octahedra. The reaction seems, however, to be irreversible[134].

Of the hydrogen bronzes with layered structures H_xMoO_3 has been studied in most detail. Reduction of MoO_3 with *e.g.* Zn/HCl yields dark-blue bronzes. Four different phases have been reported: (I) blue orthorhombic $0.23<x<0.4$, (II) blue monoclinic $0.85<x<1.04$, (III) red monoclinic $1.55<x<1.72$ and (IV) olive green, $x=2$[126,135]. Electrochemical and X-ray studies revealed a strong influence of kinetics on oxidation and reduction[10,115]. On galvanostatic reduction of MoO_3 electrodes in 0.1 N H_2SO_4 a phase range of $0.25<x<0.5$ was observed for I; in the region $0.5<x<1.67$ potentials differ significantly from equilibrium values even at low current densities and a mixture of phases I, II and III is found. On reoxidation, however, pure phases III ($1.59<x<1.67$) and II ($0.94<x<1.01$) can be observed (Fig. 25). The reoxidation of phase I is kinetically hindered. The

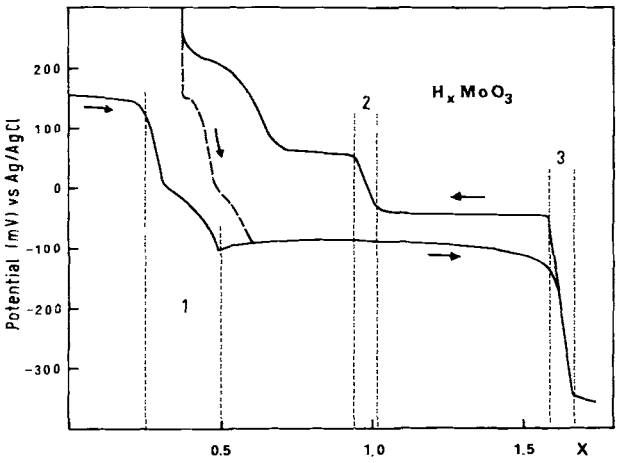


Fig. 25. Formation of H_xMoO_3 by cathodic reduction of MoO_3 in 0.1 M H_2SO_4: potential/charge transfer curve and phase diagram on reduction and reoxidation.

hysteresis found is fully reversible in the range $\approx 0.4<x<1.67$; it is obvious that structural reasons are responsible for this phenomenon. The line phase $H_{2.0}MoO_3$ can be obtained by cathodic reduction only in concentrated acid electrolytes. In the presence of metal ions mixed metal cation/hydrogen bronzes are formed[10] (Fig. 23). The enthalpies of formation of the four hydrogen bronzes H_xMoO_3 have been determined by solution calorimetry; the values (for formation from $H_{2(g)}$ and $MoO_{3(s)}$ at 300 K) are between -18.2 and -83.9 kJ mol^{-1}[136].

Elastic and inelastic neutron diffraction studies on $H_{0.3}MoO_3$ show hydrogen to be attached as —OH to bridging oxygen atoms within the MoO_3 layers, while peaks associated with —OH_2 groups appear in inelastic neutron scattering spectra of $H_{0.93}MoO_3$, $H_{1.86}MoO_3$, and $H_{2.0}MoO_3$[137,138].

H_xMoO_3 reacts as a solid Brønsted acid with Lewis bases (NH_3, N_2H_4, organic amines *etc.*) yielding the corresponding intercalation compounds [eq. (31)] with partially protonated bases, *e.g.* the pyridine compound of $H_{0.5}MoO_3$[10,108]:

$$(pyH^{\oplus})_x(py)_{0.3-x}[H_{0.5-x}MoO_3]^{x\ominus}$$

Neutralization with aqueous metal hydroxides leads in a reversible reaction to hydrated phases [eq. (32), Fig. 13][10,86]. The layered hydrogen bronzes $H_xMo_{18}O_{52}$, $H_xV_3O_8$ and ε-$H_xV_2O_5$ show analogous reactivity[108,113,115].

Hydrogen bronzes of layered transition metal dichalcogenides H_xMX_2 may be prepared either by cathodic reduction of binary chalcogenides in aqueous or nonaqueous solutions of strong acids [eq. (29)][12,30,139], or by dehydration of the oxonium compounds $(H_3O^+)_x(H_2O)_y[MX_2]^{x-}$[86]. Like the layered oxide bronzes they react as solid Brønsted acids with Lewis bases[85] and may form mixed metal cation/hydrogen bronzes.

Neutron diffraction and neutron scattering studies revealed characteristic differences for H position and bonding depending upon the coordination of the intralayer transition metal atoms in the host lattice. For 2H-TaS_2 and 2H-NbS_2 with trigonal prismatic environment of Nb and Ta hydrogen was found to be located *inside* the MX_2 layers in trigonal prismatic sites with hydrogen/metal four-center bonding[30] (Fig. 26). By way of contrast, in hydrogen bronzes derived from 1T-TaS_2 and TiS_2 with octahedral sites for Ti and Ta hydrogen is positioned close to the van der Waals gap approximately at the height of the sulfur atom planes[12].

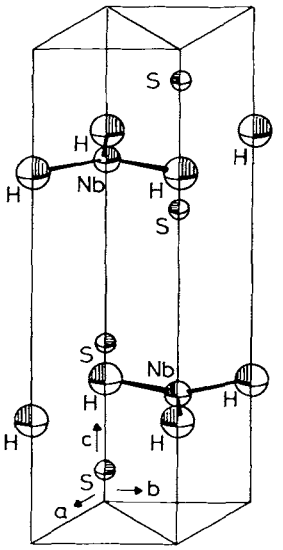


Fig. 26. Hexagonal unit cell of $H_{0.8}NbS_2$. Each hydrogen atom is bound to three Nb atoms in adjacent unit cells [30].

$H_{0.3}CrS_2$ and $H_{0.3}MoS_2$ (distorted MoS_2 lattice) are examples of metastable phases that can only be obtained from the corresponding ternary alkali sulfides A_xMS_2 *via* hydration and ion-exchange with acids[17,89]. Reversible electron/proton transfer in limited ranges correlated with partial protonation and deprotonation of guest cations is found for Lewis base intercalation compounds on oxidation and reduction[25,91], *e.g.*:

$$(pyH^{\oplus})_n(py)_m[TaS_2]^{n\ominus} + xe + xH^{\oplus} \rightleftarrows (pyH^{\oplus})_{n+x}(py)_{m-x}[TaS_2]^{(n+x)\ominus} \quad (33)$$

These systems, like the oxonium compounds, can be considered as solvated hydrogen bronzes.

Regarding the mobility of H in hydrogen bronzes, there is some disagreement on quantitative data in the literature. For polycrystalline samples of H_xWO_3 with $x<0.5$ a diffusion constant for hydrogen of $D=7\times10^{-6}$ cm^2 s^{-1} at 300 K with an activation energy $E_a=5.5$ kJ mol^{-1} was established by ^{1}H-NMR studies; rapid diffusion was reported even at 80 K[140]. Later ^{1}H-NMR studies on single crystals, however, showed lower values of $D\approx10^{-11}$ cm^2 s^{-1} and activation energies of 14—19 kJ mol^{-1} which seem to be more consistent with the proposed structures[131,141-143]. The lower diffusion coefficients were confirmed by inelastic neutron scattering data[131]. Similar values were established by electrochemical methods for H_xNiO_2 ($D\approx10^{-11}$ cm^2 s^{-1})[144]. For $H_{1.6}MoO_3$ an activation energy for H transport of 30 kJ mol^{-1} was found by NMR measurements[145]. Further data and a comparison of these with hydrogen mobilities in metal/hydrogen systems are urgently needed.

As regards their application, hydrogen bronzes are of present or potential future interest in several sectors: reversible electrode materials, electrochromic devices for nonemissive displays, heterogeneous catalysis, electrocatalysis (fuel cells, solar H_2O photolysis) *etc.* Some systems have been in use for a long time, *e.g.* manganese dioxide and nickel hydroxide as electrode materials in primary and secondary galvanic cells. In a simplified model, charge and discharge reactions can be described (for the topotactic range) by equations (34) and (35)[127,128,146,147]. Reversible deprotonation of intercalated H_2O molecules in hydrated layered nickel hydroxides may play an additional role.

$$MnO_2 + xH^{\oplus} + xe \rightleftarrows H_x[MnO_2] \quad (x_{max}\approx0.5) \quad (34)$$

$$H_{2-x}[NiO_2] + xH^{\oplus} + xe \rightleftarrows H_2[NiO_2] \quad (x_{max}\approx1.5) \quad (35)$$

Electron/proton transfer processes correlated with strong changes in color depending upon the oxidation state of the host matrix have been the subject of extensive studies in connection with their use as passive display devices[148]. The most promising system at the moment seems to be WO_3/H^+, which changes in color/bleaching cycles from faint yellow to dark blue due to the reversible formation of hydrogen bronzes:

$$WO_3 + xH^{\oplus} + xe \rightleftarrows H_x[WO_3] \quad (\text{yellow}\rightleftarrows\text{blue}) \quad (36)$$

The catalytic activity of H_xMoO_3 was first demonstrated in the reduction of NO by H_2[126]. H_xMoS_2 may play a role in hydrodesulfurization by activated MoS_2 catalysts. Studies on hydrogen spillover in metal/metal oxide systems have been reported[149], and the effect of hydrogen in TiO_2 photoanodes has recently been investigated[150]. It seems rather likely that in addition to interface reactions contributions of bulk topotactic electron/proton transfer processes play an important role in heterogeneous catalysis and electrocatalysis by semiconducting or metallic transition metal compounds. This is also the case for many related processes, *e.g.* corrosion, reduction of metal oxides by H_2 *etc.*; similarly, physical properties of solids may be altered significantly by small amounts of hydrogen in the lattice. Obviously, these aspects have not received adequate attention so far; one of the reasons for this is the fact that H concentrations and phase ranges in hydrogen bronzes can be very small and may thus escape detection by conventional analytical techniques.

A typical example for the important influence of minor amounts of hydrogen has been given lately in a study on the reaction mechanism of PbO_2 electrodes in lead acid batteries. The authors were able to show that the initial high current density observed on discharge is correlated with the formation of the hydrogen bronze H_xPbO_2, *i.e.* rapid electron/proton transfer in the solid phase[151] [eq. (37)]; x amounts to ≈0.02.

$$PbO_2 + xe + xH^{\oplus} \rightleftarrows H_x[PbO_2] \quad (37)$$

In conclusion it should be stated that investigation of the formation, reactivity, and properties of hydrogen bronzes is an attractive but largely undeveloped field which merits further systematic research both from the academic as well as the technological point of view.

7. Molecular Solids

We consider here molecular solids as lattices which consist of discrete neutral or ionic molecular units of low or medium molecular weight. They are characterized in general by low electronic conductivities and by modest lattice energies which consequently should prevent topotactic redox processes. Exceptions should be expected under the following conditions[155]: (a) extensive intermolecular electron delocalization, *e.g.* by charge transfer and metal d-orbital interaction[156,157], (b) small size of the guest ion resulting in minor steric perturbation of the host lattice and (c) appropriate intracrystalline diffusion pathways for guest ions with small activation energies. Obviously electron/proton transfer is thus expected to be the most likely type of reaction in molecular solids, though larger guest species have been found to intercalate.

Probably the earliest systems studied were solid oxygen-carrying metal chelates. [2,2'-Ethylenebis(nitrilomethylidine)diphenolato]cobalt(II) and substituted derivatives form red-brown crystals which turn black on exposure to air with reversible uptake of molecular oxygen[158-160]; depending upon the ligands, the cobalt/O_2 ratio is 2:1 or 1:1. The mode of stacking of the planar chelate molecules is such that large open channels are provided in one lattice direction for diffusion and location of oxygen. Cobalt(II) is oxidized on uptake of O_2, but the correct oxidation state has not yet been established. The cobalt chelates have been used for the generation of pure oxygen from air for welding purposes.

A large number of other planar metal chelates are known to have similar structures with columnar stacking of the complex units; their electronic conductivity parallel to the complex chains strongly increases on partial oxidation of the metal ions due to interaction between partially filled d-orbitals (one-dimensional metals and semiconductors). Bis(benzildioximato) complexes of nickel(II) and palladium(II) can be oxidized by halogens (Y=Br, I) to tetragonal columnar phases $[MR_2]Y$ with intermolecular metal-metal bonding; the halogen is located in channels parallel to the complex chains and is likely to be present principally as Y_3^- anions. Partial removal of the halogen under retention of the tetragonal lattice structure was observed over a large nonstoichiometric range for the bromine compounds [eq. (38); $z_{max}=0.8$]. Dynamic redox equilibria have been suggested

$$[MR_2]^{n\oplus}(Y)^{n\ominus} \rightleftarrows [MR_2]^{(n-x)\oplus}(Y_{1-z})^{(n-x)\ominus} + \frac{z}{2}Y_2 \quad (38)$$

for the lattice anions, *e.g.* $Y_2 + Y^- \rightleftarrows Y_3^-$[161]. One may assume that similar reactions will be observed for partially oxidized phthalocyanines[162]. It should be noted that phthalocyanines and related metal chelates have considerable electrocatalytic activity for oxygen reduction (fuel cells)[163] which may well be correlated to topotactic redox processes.

The migration of new phases from anode to cathode in applied electric fields has been observed on single crystals of the partially oxidized platinum complex salt $K_2[Pt(CN)_4]Br_{0.3}(H_2O)_{2.3}$, which has a columnar structure and behaves as a one-dimensional metallic conductor. Electron microprobe and X-ray analysis suggest the migration and discharge of Br^- to Br_2 at the anode with concurrent reduction of the metal[164]. Proton injection and reduction of the metal was found in a study on single crystals of $K_{1.46}[Pt(C_2O_4)_2](H_2O)_x$ under similar conditions. Solid state galvanic cells with electrodes of these materials using gelatine/HCl electrolyte produced open cell potentials of 0.33—0.52 V[165]. No details on structural changes have been reported.

Topotactic electron/proton transfer processes of tantalum halide cluster complexes and amminechloroplatinum complexes have recently been investigated[155]. The anodic oxidation of Magnus Green salt $[Pt(NH_3)_4][PtCl_4]$ electrodes in aqueous H_2SO_4 electrolyte proceeds in a two phase region. The structure of the tetragonal product can be described as consisting of chains of partially oxidized PtX_4 moieties with Pt—Pt bonding and hydrated HSO_4^- anions in the interchain space (Fig. 27). The compound shows a nonstoichiometric

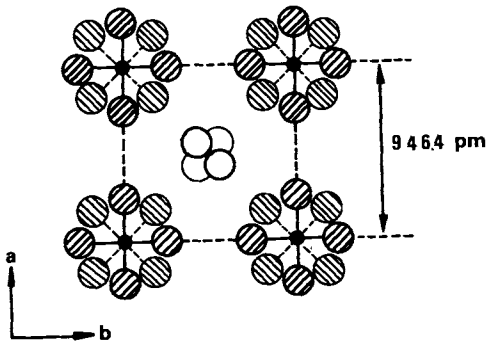


Fig. 27. Structure model of tetragonal $[Pt(NH_3)_4PtCl_4]^{0.5+}(H_{1.5}SO_4)^{0.5-}(H_2O)_y$ with partially oxidized PtX_4 chains and hydrated interchain anions (H_2O molecules not indicated). ● = Pt, ○ = O, ◍ = Cl, ◎ = NH_3.

phase region due to reversible electron/proton transfer [eq. (39), $0 \leq x \leq 0.1$]. Structurally related phases can be obtained

$$[Pt(NH_3)_4PtCl_4]^{0.5\oplus}(H_{1.5}SO_4)^{0.5\ominus}(H_2O)_y \rightleftarrows [Pt(NH_3)_4PtCl_4]^{(0.5+x)\oplus}(H_{1.5-x}SO_4)^{(0.5+x)\ominus}(H_2O)_y + xH^\oplus + xe \quad (39)$$

with other anions, *e.g.* BF_4^-, ClO_4^-, $H_2PO_4^-$ in the corresponding electrolytes; the isomeric Peyrones chloride *cis*-$Pt(NH_3)_2Cl_2$ reacts analogously.

The metal cluster halide $Ta_6Cl_{14}(H_2O)_8$ is able to undergo similar topotactic redox reactions in the solid state by anodic oxidation and cathodic reduction [eq. (40), $0 \leq x \leq 1.5$]. The accessible range for change of the oxidation state of Ta cor-

$$[Ta_6Cl_{14}](H_2O)_8 \rightleftarrows [Ta_6Cl_{14}]^{x\oplus}(OH^\ominus)_x(H_2O)_{8-x} + xH^\oplus + xe \quad (40)$$

responds to +2.33 to +2.58; proton transport is assumed to proceed *via* the hydrogen bond system that connects the cluster units. $Nb_6Cl_{14} \cdot 8H_2O$ may similarly be oxidized, but cathodic reduction is hindered for kinetic reasons[155].

Research on *organic molecular systems* with electronic conductivity has, in the last years, strongly centered on charge transfer complexes with columnar structures which behave as one-dimensional metals, *e.g.* tetracyanoquinone (TCNQ)/tetrathiofulvalene[157, 166]. Charge transfer complexes of this type have been studied as reversible galvanic cell cathodes; no structural data were reported[166, 167]. It is interesting to note, however, that water strongly influences the electrode processes. Recently, it could be demonstrated for the quinolinium salt of tetracyanoquinone that reversible electron/proton transfer may occur in these solids [eq. (41)][155].

$$(C_9H_7NH)^\oplus[(TCNQ)_2]^\ominus + xe + xH^\oplus \rightleftarrows (C_9H_7NH)^\oplus(H^\oplus)_x[(TCNQ)_2]^{(1+x)\ominus} \quad (41)$$

Semiconducting organic molecular solids with extended π bonding systems, *e.g.* dyes and salts of aromatic radical ions have been investigated with respect to their properties as electrochromic display materials[168]. There is little information on the reaction mechanism; since most of these systems are known to undergo electron/proton transfer in homogeneous solution[169], one may assume that this also holds for the solid state. The electronic conductivity of crystalline polyacetylenes has been shown to increase strongly by topotactic doping with oxidants[166, 170].

It has long been known that biological systems exhibit a degree of topological ordering on the molecular scale which is much higher than was originally assumed. Certain phenomena in living cells, *e.g.* energy conversion and storage, require fast electron/proton transfer over extended distances which is only possible in highly ordered domains; these processes may well be considered as topotactic redox reactions.

8. Fast Ion Transport and Molecular Dynamics

Interest in fast ion transport phenomena of cations and anions in solids at lower temperatures has focussed in the past decade essentially on insulator type electrolytes[171]. Systematic experimental research and theoretical studies[172] on electronic/ionic conductors have intensified only in recent years with the discovery of fast ion transport at room temperature in intercalation compounds of host lattices with alkali metals (Li, Na, K)[19, 34] as well as transition metals (Cu, Ag, Fe, Co, Ni, Zn)[10, 173]. NMR and electrochemical techniques have been used to obtain data for chemical diffusion coefficients and activation energies[28, 175]. For alkali ions in layered dichalcogenides A_xMX_2 the activation energies were found to depend upon the stoichiometric factor x, the site geometry of A^+ and the ionicity of the host structure[19]. Deviations from the ideal stoichiometry of the host lattice may strongly affect the guest ion mobility[33-35]. The existence of ordered domain structures has recently been proven by single crystal studies on Na_xTiS_2[32] and is also likely to occur in Li_xTiS_2[82, 83]. Chemical diffusion coefficients of 10^{-6} to

10^{-10} cm^2 s^{-1} in Li_xTiS_2 and Na_xTiS_2 were determined by electrochemical pulse techniques[33]. Electron microscopy and diffraction studies on Cu_xTaS_2 and Cu_xNbS_2 showed that the guest ions undergo order/disorder transformations which depend upon the Cu content; above $\approx$330 K the Cu ions behave as a two-dimensional liquid[81]. Chemical diffusion coefficients for Cu^+ in the solid solution range of $Cu_xMo_6S_8$ have been measured by the electrochemical pulse technique[44].

Regarding *molecular guest species,* investigations of the temperature dependent dynamics by NMR and inelastic neutron scattering may provide useful structural information. For the layered NH_3 intercalation compounds $TiS_2(NH_3)$ and $TaS_2(NH_3)$ strong anisotropic mobility of the guest molecules was found (Section 4, Fig. 20). Molecular diffusion and reorientation rates exceed 10^5 s^{-1} above 160 K; rotation about the C_3 axis of NH_3 continues down to $\approx$5 K with a rate of $\approx 10^8$ s^{-1}[95]. From inelastic neutron scattering data, an activation energy for translational motion of 9.6 kcal mol^{-1} could be derived[176]. A domain model for NH_3 diffusion in dichalcogenides has been proposed[174].

Extreme anisotropic mobility of water molecules at 300 K in monolayer hydrates $A_x^+(H_2O)_y[MX_2]^{x-}$ (A = alkali cation, M = Nb, Ta) was observed by ^{1}H-NMR studies[177]. The spectra show the calculated signal for an isolated two spin system which results from two-dimensional diffusion of H_2O in the interlayer space without activation of the rotation around the C_2 axis of H_2O (Fig. 28). The anisotropic motion

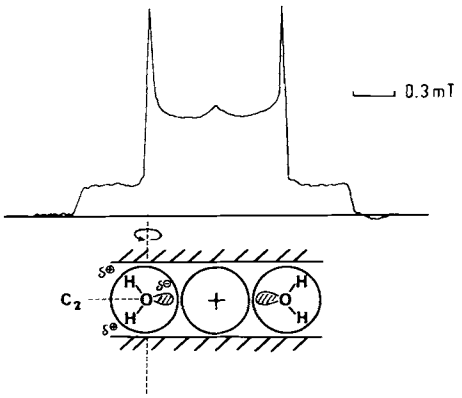


Fig. 28. ^{1}H-NMR spectrum of $K_{0.5}^+(H_2O)_{0.5}[NbS_2]^{0.5-}$ (integrated signal) at 290 K and below scheme of the orientation of H_2O molecules in the interlayer space.

is a consequence of the electrostatic interaction of the negatively charged $[MX_2]^{x-}$ layers with the positively polarized hydrogen atoms of water; the negative H_2O dipole ends are engaged in cation/dipole interaction with neighboring A^+ cations in the electrolyte layers. At temperatures of 370—420 K a single line spectrum is found indicating activation of the C_2 axis rotation; the transition to the rigid lattice at lower temperatures is dependent upon the hydration energy of the cations. pH-dependent structural changes in the two-dimensional electrolyte layers of hydrated chalcogenides have been investigated by H-NMR[12].

Proton spin-lattice relaxation time studies on $TaS_2(py)_{0.5}$ showed that the pyridine molecules form a rigid lattice with slow molecular motions up to 300 K[178]. Methyl group rotation down to low temperatures was observed by H-NMR techniques for monomethylpyridine intercalation compounds of TaS_2[179].

9. Physical Properties

The relationship between structural dimensionality and composition of solid compounds and the corresponding physical properties has been a major recent topic in solid state science. Extensive studies have been devoted particularly to anisotropy phenomena of quasi one-dimensional and two-dimensional systems[22,166]. An intriguing aspect in this context which has stimulated a great deal of research is the possibility of achieving systematic changes in physical properties of solids *via* topotactic redox reactions with conservation of the original host lattice structure.

Of the intercalation compounds of host lattices with two-dimensional structure, those of graphite have been widely studied[69,70] with respect to transport properties, electronic structure, optical properties, and lattice dynamics. Strong enhancement was found for basal plane conductivities σ_a in graphite on intercalation of acceptor host molecules. For $C_{16}AsF_5$ the conductivity $\sigma_a = 6 \times 10^{-5}\ \Omega^{-1}$ cm^{-1} exceeds that of copper metal, while the strong anisotropy is reflected in the ratio $\sigma_a/\sigma_c = 10^6$[180].

Marked anisotropy is similarly observed for layered dichalcogenides. Depending upon the nature of the guest species dramatic changes in the physical properties can occur. The intercalation of organic and inorganic cations in superconducting tantalum chalcogenides was found to strongly increase the critical temperatures T_c of the phase transition normal state/superconducting state[22,23]. The solvated alkali tantalum sulfides $A_x^+(solv)_y[TaS_2]^{x-}$ were shown to be superconducting polyelectrolytes[181]. The T_c enhancement was assumed to be related to the elimination of Fermi surface instabilities (charge density waves[182]) by the intercalation of guest species. Intercalated dichalcogenides are Type II superconductors and exhibit anisotropic critical field and current values; they represent the most anisotropic superconducting materials known. Measurements of magnetic proper-

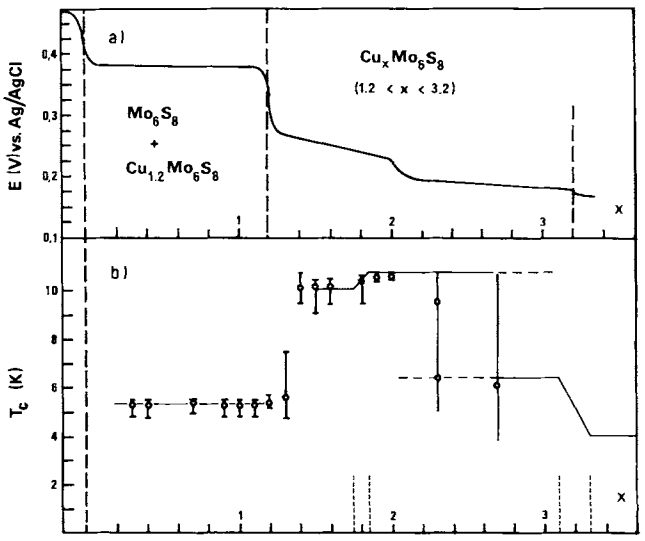


Fig. 29. Superconducting $Cu_xMo_6S_8$ phases prepared by reduction and oxidation of $Cu_2Mo_6S_8$. (a) potential/composition curve; (b) dependence of the critical transition temperature T_c on integral Cu content x [39].

ties and normal state conductivity also reveal strong anisotropy. The localization of the d-electrons in alkali metal compounds A_xMS_2 was found to increase in the series M = Ti, V, Cr[183]. Charge transfer to the host layers in dependence of type and concentration of the guest species has been studied by spectroscopic methods[22,83].

The correlation between composition, lattice parameter changes, electrochemical potential and superconducting transition temperatures of $Cu_xMo_6S_8$ prepared by electrochemical intercalation has recently been reported (Fig. 29)[39,43]. The structural transitions and T_c values were found to be close to those of samples obtained by thermal methods[36,42]. An increase in T_c of up to 7 K has been observed on the intercalation of K^+ ions into the empty lattice channels of Nb_3S_4[35].

10. Technological Application

Solids which undergo reversible topotactic redox reactions are of interest in several fields regarding application. One major area is the use of such systems as reversible cathodes for high energy density battery cells[34,46,63,67,184,185] *via* the formation of ternary phases with metal guest ions. It is obvious that topotactic battery electrode processes should be superior to electrode reactions correlated with the formation of new phases under complete structural reorganization. Basic requirements for cathode materials with topotactic reactivity are (a) high free energy of reaction, (b) little change in free energy over the composition range, (c) minor structural changes, (d) high mobility of the guest ions in the solid phase, (e) quantitative reversibility of the reaction, and (f) high electronic conductivity. Research has concentrated mainly on cells with Li anodes in organic electrolytes[26] because of the low specific weight of this element, the high mobility of Li^+ ions in host lattices, small structural changes on intercalation (small ionic radius of Li^+), and high free energies of formation of ternary phases with chalcogenides and oxides of transition metals in higher oxidation states (Table 5). Since higher maximum Li contents are usually observed

Table 5. Calculated energy densities of lithium organic cells with reversible topotactic cathode reactions.

Cathode	Energy Density (Wh/kg)
TiS_2	481
$V_{0.75}Fe_{0.25}S_2$	510
VSe_2	246
MoO_3	542
Cr_3O_8	940
MnO_2	530

for host lattices with two- and one-dimensional structures as compared to solids with framework structure, these have received favored attention. Examples of compounds which have been studied in more detail are the layered dichalcogenides MX_2[34], phosphorus sulfides MPX_3[104,105], transition metal trichalcogenides MX_3[120], and the oxides MoO_3[67], V_2O_5[63], Cr_3O_8[64], MnO_2[109], FeOCl[116,117].

Much work has been devoted to the development of Li/TiS_2 cells, since TiS_2 is the lightest in weight and the most economical among the layered dichalcogenides. The reaction $Li + TiS_2 \rightleftarrows Li_xTiS_2$ ($0 \leq x \leq 1$) takes place with a high free energy of formation of 206 kJ mol^{-1} and with little changes in lattice parameters and in free energy over the composition range (Fig. 30). The use of topotactic photointercalation electrodes for energy storage has been proposed recently[186].

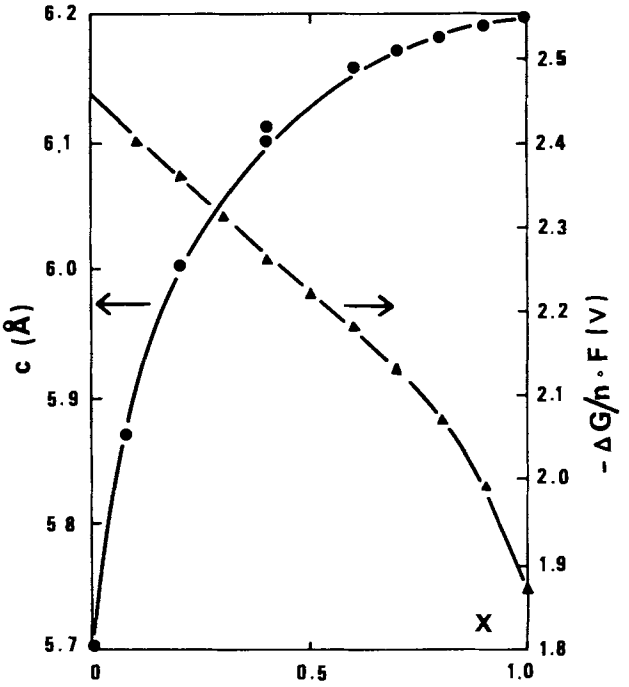


Fig. 30. Li_xTiS_2: variation of the hexagonal c axis lattice parameter and the partial molar free energy of formation with x [34].

The application of hydrogen bronzes and molecular organic solids liable to electron/proton transfer as nonemissive electrochromic display systems has been discussed in Sections 6 and 7.

Graphite donor and acceptor intercalation compounds have been studied because of their catalytic activity for a wide range of molecular reactions: NH_3-synthesis, reduction, oxidation, halogenation, polymerization and esterification of organic compounds, and Fischer-Tropsch synthesis[187]. Layered transition metal sulfides (MoS_2, WS_2) doped with Ni and Co are the major hydrodesulfurization catalysts in the petroleum industry; Ni and Co intercalation has been suggested to be involved in the catalytic activity. The formation of bipyridyl on the intercalation of TaS_2 and FeOCl with pyridine was shown to proceed at temperatures as low as 400 K[25,91]. Furthermore, it now seems likely that topotactic electron/proton transfer reactions may play an essential role in many heterogeneous catalytic and electrocatalytic processes (Section 6).

Graphite acceptor intercalation compounds with electronic conductivities higher than metallic copper have been already mentioned, as has also the strong increase in superconducting transition temperatures of layered and framework chalcogenides after intercalation; these two examples may suffice to illustrate further potential lines of future application of topotactic redox reactions *via* modification of materials properties.

11. Conclusions

In the present paper an attempt has been made to give an overview on a rapidly developing interdisciplinary field of research. The exciting variety of solid state redox reactions at room temperature and the corresponding changes in physical properties provide a wide and promising area for future research. Although the basic concept is clear now and presents a fairly consistent picture, extended systematic studies will be needed to elucidate particular points regarding *e.g.* the detailed description of changes in geometric and electronic structure in the course of topotactic redox reactions, the influence of lattice defects on kinetics, the temperature-dependence of transport properties, molecular dynamics and ordering states of guest species, thermodynamic correlations, and interfacial phenomena. The possibilities of a systematic "tailoring" of new metastable materials with unusual properties have been demonstrated and will certainly remain one important line of future investigations. It is also reasonable to predict that in addition to the systems already known, new ways for the practical application of solids with electronic/ionic conductivity will be perceived in the coming years.

With respect to his own contributions cited in the reference section the author is indebted to many co-workers for their support; this pertains also to the collaboration with several colleagues: Dr. J. O. Besenhard (Technische Universität München), Dr. A. Lerf (Institut für Tieftemperaturforschung Garching), Dr. C. Riekel (Institut Laue-Langevin Grenoble) and Dr. F. Sernetz (CERN Genf). The valuable experimental assistance of Herr K. Wagner is gratefully acknowledged. Thanks are also due to Prof. A. Weiss (Universität München), who succeeded many years ago to convince the author of the merits of research in solid state chemistry. Financial support has been provided by the Fonds der Chemischen Industrie, by the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and by the Institut Laue-Langevin, Grenoble.

Received: July 4, 1980 [A 342 IE]
German version: Angew. Chem *92*, 1015 (1980)

[1] *R. M. Barrer* in *L. Mandelcorn:* Nonstoichiometric Compounds. Academic Press, New York 1964, p. 309.
[2] *W. M. Meier, J. B. Uytterhoeven*, Adv. Chem. Ser. *121* (1973).
[3] *R. F. Grim:* Clay Mineralogy. McGraw-Hill, New York 1968; *Ar. Weiss* in *A. Eglinton, M. T. J. Murphy:* Organic Geochemistry. Springer, Berlin 1979, p. 737; *B. K. Theng:* The Chemistry of Clay-Organic Reactions. A. Hilger, London 1974.
[4] *Ar. Weiss, E. Michel*, Z. Anorg. Allg. Chem. *296*, 313 (1958); *306*, 277 (1960).
[5] *K. Fredenhagen, G. Cadenbach*, Z. Anorg. Allg. Chem. *158*, 249 (1926); *K. Fredenhagen, M. Suck, ibid. 178*, 353 (1929).
[6] *W. Rüdorff, H. Sick*, Angew. Chem. *71*, 127 (1959).
[7] *O. Glemser, H. Sauer*, Z. Anorg. Allg. Chem. *252*, 144 (1943); *O. Glemser, Ch. Neumann, ibid. 265*, 288 (1951).
[8] a) *R. Schöllhorn, A. Lerf*, Z. Naturforsch. *B 29*, 804 (1974); b) *R. Schöllhorn, H. Meyer*, Mater. Res. Bull. 9, 1237 (1974); c) *R. Schöllhorn, E. Sick, A. Lerf, ibid. 10*, 1005 (1975).
[9] *R. Schöllhorn, W. Schmucker*, Z. Naturforsch. *B 30*, 975 (1975).
[10] *R. Schöllhorn, R. Kuhlmann, J. O. Besenhard*, Mater. Res. Bull. *11*, 83 (1976).
[11] *R. Schöllhorn, M. Kümpers, J. O. Besenhard*, Mater. Res. Bull. *12*, 781 (1977).
[12] *R. Schöllhorn*, Physica *99B*, 89 (1980).
[13] *J. R. Günter, H. R. Osswald*, Bull. Inst. Chem. Res., Kyoto Univ. *53*, 249 (1975).
[14] *H. J. Keller:* Chemistry and Physics of One-Dimensional Materials. Plenum Press, New York 1977.
[15] *C. F. van Bruggen, R. J. Haange, G. A. Wiegers, D. K. G. De Boer*, Physica *99B*, 166 (1980).
[16] *R. Schöllhorn, W. Schramm, D. Fenske*, Angew. Chem. *92*, 477 (1980); Angew. Chem. Int. Ed. Engl. *19*, 492 (1980).
[17] *R. Schöllhorn, R. Arndt, A. Kubny*, J. Solid State Chem. *29*, 259 (1979).
[18] *A. J. Jacobson, M. S. Whittingham, S. M. Rich*, J. Electrochem. Soc. *126*, 887 (1979).
[18a] *F. Lévy:* Intercalated Layered Materials. D. Reidel, Dordrecht 1979.
[19] *J. Rouxel* in [18a], p. 201; Physica *99B*, 3 (1980).
[20] *C. Haas*, Solid State Commun. *26*, 709 (1978); *C. F. van Bruggen, C. Haas, G. A. Wiegers*, J. Solid State Chem. *27*, 9 (1979).
[21] *M. B. Dines*, Mater. Res. Bull. *10*, 287 (1975).
[22] *G. V. Subba Rao, M. W. Schafer*, in [18a], p. 99.
[23] *F. R. Gamble, T. H. Geballe* in *N. B. Hannay:* Treatise on Solid State Chemistry. Vol. 3. Plenum Press, New York 1976.
[24] *R. Schöllhorn, H. D. Zagefka*, Angew. Chem. *89*, 193 (1977); Angew. Chem. Int. Ed. Engl. *16*, 199 (1977).
[25] *R. Schöllhorn, H. D. Zagefka, T. Butz, A. Lerf*, Mater. Res. Bull. *14*, 369 (1979).
[26] *J. O. Besenhard, G. Eichinger*, J. Electroanal. Chem. *68*, 1 (1976); *G. Eichinger, J. O. Besenhard, ibid. 72*, 1 (1976).
[27] *M. Armand*, Thèse, Inst. Nationale Polytechnique de Grenoble 1978.
[28] *G. J. Dudley, B. C. H. Steele*, J. Solid State Chem. *31*, 233 (1980).
[29] *R. R. Chianelli, J. C. Scanlon, B. M. L. Rao*, J. Electrochem. Soc. *125*, 1563 (1978).
[30] *C. Riekel, H. G. Reznik, R. Schöllhorn, C. J. Wright*, J. Chem. Phys. *70*, 5203 (1979).
[31] *C. Riekel, H. G. Reznik, R. Schöllhorn*, J. Solid State Chem. *34*, 253 (1980).
[32] *T. Hibma*, Physica *99B*, 136 (1980).
[33] *D. A. Winn, J. M. Shemilt, B. C. H. Steele*, Mater. Res. Bull. *11*, 559 (1976).
[34] *M. S. Whittingham*, Prog. Solid State Chem. *12*, 41 (1978).
[35] *R. Schöllhorn, W. Schramm*, Z. Naturforsch. *B 34*, 697 (1979).
[36] *K. Yvon*, Curr. Top. Mater. Sci. *3*, 54 (1978); *Ø. Fischer*, Appl. Phys. *16*, 1 (1978).
[37] *R. Chevrel, M. Sergent, J. Prigent*, Mater. Res. Bull. 9, 1487 (1974).
[38] *Ø. Fischer, R. Odermatt, G. Bongi, H. Jones, R. Chevrel, M. Sergent*, Phys. Lett. *45A*, 87 (1973).
[39] *R. Schöllhorn, M. Kümpers, A. Lerf, E. Umlauf, W. Schmidt*, Mater. Res. Bull. *14*, 1039 (1979).
[40] *M. Kümpers*, Dissertation, Universität Münster 1980.
[41] *P. Dolscheid, W. Schramm, R. Schöllhorn*, unpublished.
[42] *R. Flükiger, A. Junod, R. Baillif, P. Spitzli, A. Treyvaud, A. Paoli, H. Devantay, J. Muller*, Solid State Commun. *23*, 699 (1977); *R. Flükiger, R. Baillif, J. Muller*, J. Less-Common Met. 1980, in press.
[43] *M. Tovar, L. E. De Long, D. C. Johnston, M. B. Maple*, Solid State Commun. *30*, 551 (1979).
[44] *G. J. Dudley, K. Y. Cheung, B. C. H. Steele*, J. Solid State Chem. *32*, 259, 269 (1980).
[45] *H. J. Mathieu, H. Rickert*, Z. Phys. Chem. (Frankfurt am Main) *79*, 315 (1972).
[46] *B. C. H. Steele* in [171b], p. 47.
[47] *M. J. Sienko*, Adv. Chem. Ser. *39*, 224 (1963); *J. B. Goodenough*, Bull. Soc. Chim. Fr. *4*, 1200 (1965); *A. Ferretti, D. B. Rogers, J. B. Goodenough*, J. Phys. Chem. Solids *26*, 2007 (1965).
[48] *M. S. Whittingham, R. A. Huggins*, Nat. Bur. Stand. (US) Spec. Publ. *364*, 51 (1972).
[49] *K. Selte, A. Kjekshus*, Acta Crystallogr. *17*, 1568 (1964); *A. F. J. Ruysink, F. Kadijk, A. J. Wagner, A. J. Jellinek, ibid. B 24*, 1614 (1968).
[50] *E. Amberger, K. Polborn, P. Grimm, M. Dietrich, B. Obst*, Solid State Commun. *26*, 943 (1978).
[51] *K. Klepp, H. Boller*, Abstracts VIth Int. Conf. Solid Compounds of the Transition Elements, Stuttgart 1979, p. 66.
[52] *M. Vlasse, L. Fournès*, Mater. Res. Bull. *11*, 1527 (1976).
[53] *B. R. Conard, L. J. Norrby, H. F. Franzen*, Acta Crystallogr. *B 25*, 1729 (1969).
[54] *L. Fournès, M. Vlasse, M. Saux*, Mater. Res. Bull. *12*, 1 (1977).
[55] *I. Kawada, M. Nakano-Onoda, M. Ishii, M. Saeki*, J. Solid State Chem. *15*, 246 (1975).
[56] *P. Hagenmuller* in *A. T. Trottmann-Dickenson:* Comprehensive Inorganic Chemistry. Vol. 4. Pergamon Press, New York 1973, p. 541.
[57] *M. S. Whittingham* in [171c], p. 367.
[58] *M. S. Whittingham, R. A. Huggins*, J. Chem. Phys. *54*, 414 (1971).
[59] *J. Gendell, R. M. Cotts, M. J. Sienko*, J. Chem. Phys. *37*, 220 (1962).
[60] *M. S. Whittingham* in [171a], p. 429; *A. V. Popov, Y. G. Metlin, Y. D. Tretyakov*, J. Solid State Chem. *31*, 23 (1980).
[61] *J. Galy, D. Lavaud, A. Casalot, P. Hagenmuller*, J. Solid State Chem. *2*, 531 (1970).
[62] *J. Galy, J. Darriet, A. Casalot, B. Goodenough*, J. Solid State Chem. *1*, 339 (1970).
[63] *M. S. Whittingham*, J. Electrochem. Soc. *123*, 315 (1976).
[64] *J. O. Besenhard, R. Schöllhorn*, J. Electrochem. Soc. *124*, 968 (1977).

[65] *D. W. Murphy, F. J. Di Salvo, J. N. Carides, J. V. Waszak*, Mater. Res. Bull. *13*, 1395 (1978).
[66] *D. W. Murphy, P. A. Christian, F. J. Di Salvo, J. N. Carides*, J. Electrochem. Soc. *126*, 497 (1979).
[67] *J. O. Besenhard, R. Schöllhorn*, J. Power Sources *1*, 267 (1976).
[68] *P. Cignini, M. Icovi, S. Panero, G. Pistoia, C. Temperoni*, J. Electroanal. Chem. *102*, 333 (1979).
[69] *A. Hérold* in [18a], p. 321; Franco American Conf. on Intercalation Compounds of Graphite, Mater Sci. Eng. *31*, 1—350 (1977).
[70] Proceedings of the Int. Conf. on Layered Materials and Intercalates, Physica *99 B*, 1—503 (1980); *C. F. van Brüggen, C. Haas, H. W. Myron:* Layered Materials and Intercalates. North Holland, Amsterdam 1980.
[71] *J. A. Wilson, A. D. Yoffe*, Adv. Phys. *18*, 193 (1969).
[72] *F. Hulliger* in *F. Lévy:* Physics and Chemistry of Materials with Layered Structures. Vol. 5. D. Reidel, Dordrecht 1976.
[73] *W. Rüdorff*, Chimia *19*, 489 (1965).
[74] *Ar. Weiss, R. Ruthardt*, Z. Naturforsch. *B 24*, 256 (1969); *R. Ruthardt*, Dissertation, Universität München 1969.
[75] *M. S. Whittingham*, J. Chem. Soc. Chem. Commun. *1974*, 328.
[76] *G. V. Subba Rao, J. C. Tsang*, Mater. Res. Bull. *9*, 921 (1974).
[77] *J. O. Besenhard, H. Meyer, R. Schöllhorn*, Z. Naturforsch. *B 31*, 907 (1976).
[78] *R. Schöllhorn, A. Weiss*, J. Less-Common Met. *36*, 229 (1974).
[79] *J. Bichon, M. Danot, J. Rouxel*, C. R. Acad. Sci. *C 276*, 1283 (1973).
[80] *A. S. Nagelberg, W. L. Worrel*, J. Solid State Chem. *29*, 345 (1979).
[81] *R. de Ridder, D. van Dyck, G. van Tendeloo, J. van Landuyt, S. Ammelinckx*, Phys. Status Solidi *A 39*, 383 (1977).
[82] *A. H. Thompson*, J. Electrochem. Soc. *126*, 608 (1979).
[83] *T. Butz, A. Vasquez, H. Saitovitch, R. Mühlberger, A. Lerf*, Physica *99 B*, 69 (1980).
[84] *D. W. Murphy, C. Cros, F. J. Di Salvo, J. V. Waszak*, Inorg. Chem. *16*, 3027 (1977).
[85] *A. Lerf, R. Schöllhorn*, Inorg. Chem. *16*, 2950 (1977).
[86] *R. Schöllhorn* in *M. S. Whittingham, A. J. Jacobson:* Intercalation Chemistry. Academic Presss, New York 1980, in press.
[87] *A. J. A. Boos-Albernik, R. J. Haange, G. A. Wiegers*, Abstr. Vth Int. Conf. Solid Compounds of the Transition Elements, Uppsala 1976, p. 60.
[88] *H. A. Graf, A. Lerf, R. Schöllhorn*, J. Less-Common Met. *55*, 213 (1977).
[89] *R. Schöllhorn, M. Kümpers, D. Plorin*, J. Less-Common Met. *58*, 55 (1978); *M. Kümpers, R. Schöllhorn*, Z. Naturforsch. *B 35*, 929 (1980).
[90] *R. Schöllhorn, W. Roer, K. Wagner*, Monatsh. Chem. *110*, 1147 (1979).
[91] *H. D. Zagefka*, Dissertation, Universität Münster 1980.
[92] *Ar. Weiss, R. Ruthardt*, Z. Naturforsch. *B 28*, 249 (1973).
[93] *R. Schöllhorn, E. Sick, A. Weiss*, Z. Naturforsch. *B 28*, 168 (1973).
[94] *F. R. Gamble, J. H. Osiecki, M. Cais, R. Pisharody, F. J. Di Salvo, T. H. Geballe*, Science *174*, 493 (1971).
[95] *F. R. Gamble, B. G. Silbernagel*, J. Chem. Phys. *63*, 2544 (1975); *B. G. Silbernagel, M. B. Dines, F. R. Gamble, L. A. Gebhard, M. S. Whittingham, ibid. 65*, 1906 (1976).
[96] *J. Cousseau, L. Trichet, J. Rouxel*, Bull. Soc. Chim. Fr. *1973*, 872.
[97] *J. V. Acrivos, S. F. Mayer, T. H. Geballe:* Colloque Weyl III. Springer, New York 1973, p. 341.
[98] *C. Riekel, D. Hohlwein, R. Schöllhorn*, J. Chem. Soc. Chem. Commun. *1976*, 863.
[99] *F. R. Gamble, J. H. Osiecki, F. J. Di Salvo*, J. Chem. Phys. *55*, 3525 (1971).
[100] *C. Riekel, R. Schöllhorn*, Mater. Res. Bull. *11*, 369 (1976); *C. Riekel, C. O. Fischer*, J. Solid State Chem. *29*, 181 (1979).
[101] *M. B. Dines*, Science *188*, 1210 (1975); *R. P. Clement, W. B. Davies, K. A. Ford, M. L. H. Green, A. J. Jacobson*, Inorg. Chem. *17*, 2754 (1978).
[102] *R. Schöllhorn, A. Weiss*, Z. Naturforsch. *B 28*, 716 (1973).
[103] *R. Brec, J. Ritsma, G. Ouvrard, J. Rouxel*, C. R. Acad. Sci. *C 281*, 531 (1975); Inorg. Chem. *16*, 660 (1977).
[104] *A. Le Méhauté, G. Ouvrard, R. Brec, J. Rouxel*, Mater. Res. Bull. *12*, 1191 (1977); *R. Brec, D. M. Schleich, G. Ouvrard, A. Louisy, J. Rouxel*, Inorg. Chem. *18*, 1814 (1979).
[105] *A. H. Thompson, M. S. Whittingham*, Mater. Res. Bull. *12*, 741 (1977).
[106] *A. Louisy, J. Ouvrard, D. M. Schleich, R. Brec*, Solid State Commun. *1980*, im Druck.
[107] *R. Schöllhorn* in *J. Wood, O. Lindqvist, C. Helgesson, N. G. Vannerberg:* Reactivity of Solids. Plenum Press, New York 1977, p. 719.
[108] *R. Schöllhorn, T. Schulte-Nölle, G. Steinhoff*, J. Less-Common Met. *71*, 71 (1980).
[109] *F. W. Dampier*, J. Electrochem. Soc. *121*, 656 (1974).
[110] *J. P. Gabano, Y. Jumel, J. P. Gomis*, Abstr. 144th Meet. Electrochem. Soc., Boston 1973, p. 134; *A. N. Dey*, Br. Pat. 1325055 (1973); US-Pat. 3808052 (1974).
[111] *M. S. Whittingham, M. B. Dines*, J. Electrochem. Soc. *124*, 1387 (1977).
[112] *P. G. Dickens, S. J. French, A. T. Hight, M. F. Pye*, Mater. Res. Bull. *14*, 1295 (1979).
[113] *R. Schöllhorn, F. Klein-Reesink, R. Reimold*, J. Chem. Soc. Chem. Commun. *1979*, 398.
[114] *J. Galy, D. Lavaud, A. Casalot, P. Hagenmuller*, J. Solid State Chem. *2*, 531 (1970).
[115] *B. Schlasche, K. Wagner, R. Schöllhorn*, unpublished.
[116] *H. Meyer, A. Weiss, J. O. Besenhard*, Mater. Res. Bull. *13*, 913 (1978).
[117] *P. Palvadeau, L. Coic, J. Rouxel, J. Portier*, Mater. Res. Bull. *13*, 221 (1978).
[118] *F. Kanamaru, M. Shimada, M. Koizumi, M. Takano, T. Takada*, J. Solid State Chem. *7*, 297 (1973).
[119] *Th. R. Halbert, J. Scanlon*, Mater. Res. Bull. *14*, 415 (1979).
[120] *D. W. Murphy, F. A. Trumbore*, J. Electrochem. Soc. *123*, 960 (1976).
[121] *H. Boller*, Monatsh. Chem. *109*, 975 (1978).
[122] *A. J. Jacobson, M. S. Whittingham, S. M. Rich*, J. Electrochem. Soc. *126*, 887 (1979).
[123] *A. Meerschaut, L. Guémas, R. Berger, J. Rouxel*, Acta Crystallogr. *B 35*, 1747 (1979).
[124] *D. W. Murphy, F. A. Trumbore, J. N. Carides*, J. Electrochem. Soc. *124*, 325 (1977).
[125] *A. Meerschaut, P. Palvadeau, J. Rouxel*, J. Solid State Chem. *20*, 21 (1977).
[126] *O. Glemser, G. Lutz*, Z. Anorg. Allg. Chem. *264*, 17 (1951); *O. Glemser, U. Hauschild, G. Lutz, ibid. 269*, 93 (1952); *O. Glemser*, Nachr. Akad. Wiss. Göttingen, Math. Phys. Kl. 2A, 221 (1955); *O. Glemser, G. Lutz, H. Meyer, ibid. 285*, 173 (1956).
[127] *J. Brénet, P. Malessan, A. Grund*, C. R. Acad. Sci. *242*, 111 (1956).
[128] *W. Feitknecht, H. R. Osswald, U. Feitknecht-Steinmann*, Helv. Chim. Acta *43*, 1947 (1960).
[129] *P. G. Dickens, R. J. Hurditch*, Nature *215*, 1266 (1967); in *L. Eyring, M. O. Keefe:* The Chemistry of Extended Defects in Nonmetallic Solids. North Holland, Amsterdam 1960, p. 555.
[130] *P. G. Dickens, J. H. Moore, D. J. Neild*, J. Solid State Chem. *7*, 241 (1973).
[131] *C. J. Wright*, J. Solid State Chem. *20*, 89 (1977); *P. J. Wiseman, P. G. Dickens, ibid. 6*, 374 (1973).
[132] *N. Kimizuka, T. Akahane, S. Matsumoto, K. Yukino*, Inorg. Chem. *15*, 3178 (1976).
[133] *M. Shelef, R. A. Dalla Betta, K. Otto*, J. Inorg. Nucl. Chem. *38*, 99 (1976).
[134] *A. Simon*, Z. Anorg. Allg. Chem. *355*, 311 (1967).
[135] *J. J. Birtill, P. G. Dickens*, Mater. Res. Bull. *13*, 311 (1978).
[136] *J. J. Birtill, P. G. Dickens*, J. Solid State Chem. *29*, 367 (1979).
[137] *F. A. Schröder, H. Weitzel*, Z. Anorg. Allg. Chem. *435*, 247 (1977).
[138] *P. G. Dickens, J. J. Birtill, C. J. Wright*, J. Solid State Chem. *28*, 185 (1979).
[139] *D. W. Murphy, F. J. Di Salvo, G. W. Hull, J. V. Waszak, S. F. Mayer, G. R. Steward, S. Early, J. V. Acrivos, T. H. Geballe*, J. Chem. Phys. *62*, 967 (1975).
[140] *M. A. Vannice, M. Boudart, J. J. Fripiat*, J. Catal. *17*, 359 (1970).
[141] *P. G. Dickens, D. W. Murphy, T. K. Halstead*, J. Solid Chem. *6*, 370 (1973).
[142] *M. S. Whittingham, R. A. Huggins*, J. Chem. Phys. *54*, 414 (1971); in *J. S. Anderson, M. W. Roberts, F. S. Stone:* Reactivity of Solids. Chapman and Hall, London 1972, p. 125.
[143] *L. Glasser*, Chem. Rev. *75*, 21 (1975).
[144] *D. M. MacArthur*, J. Electrochem. Soc. *117*, 729 (1970).
[145] *A. Cirillo, J. J. Fripiat*, J. Phys. (Paris) *39*, 247 (1978).
[146] Electrochemistry, Vol. 4. Specialist Periodical Reports. The Chemical Society, London 1974.
[147] *J. McBreen*, Electrochim. Acta *20*, 221 (1975).
[148] a) *I. F. Chang, B. L. Gilbert, T. I. Sun*, J. Electrochem. Soc. *122*, 955 (1975); b) *B. Reichman, A. J. Bard, ibid. 126*, 2133 (1979); c) *S. Gottesfeld, J. D. E. McIntyre, ibid. 126*, 742, 2171 (1979).
[149] *P. A. Sermon, G. C. Bond*, J. Chem. Soc. Faraday Trans. *72*, 730 (1976); B. S. Hobbs, A. C. C. Tseung, J. Electrochem. Soc. *119*, 580 (1972).
[150] *D. S. Ginley, M. L. Knotek*, J. Electrochem. Soc. *126*, 2163 (1979).
[151] *J. Pohl, H. Rickert*, Z. Phys. Chem. (Frankfurt am Main) *112*, 117 (1978).
[152] *A. Wadsley* in *L. Mandelcorn:* Nonstoichiometric Compounds. Academic Press, New York 1964, p. 161; *O. Glemser, A. Schwarzmann*, Z. Anorg. Allg. Chem. *278*, 249 (1955).
[153] *A. W. Struss, J. D. Corbett*, Inorg. Chem. *16*, 360 (1977).
[154] *K. Doblhofer, M. Metikos, Z. Ogumi, H. Gerischer*, Ber. Bunsenges. Phys. Chem. *82*, 1046 (1978).
[155] *R. Schöllhorn, K. Wagner, H. Jonke*, Angew. Chem. *93* (1981), in press.
[156] *H. Meier:* Organic Semiconductors. Verlag Chemie, Weinheim 1974.
[157] *J. T. Devreeze, R. P. Evrard, V. E. van Doren:* Highly Conducting One-Dimensional Solids. Plenum Press, New York 1979.
[158] *P. Pfeiffer, E. Breith, E. Lübbe, T. Tsumaki*, Justus Liebigs Ann. Chem. *503*, 84 (1933).
[159] *T. Tsumaki*, Bull. Chem. Soc. Jpn. *13*, 252 (1938).
[160] *A. E. Martell, M. Calvin:* Chemistry of Metal Chelate Compounds. Prentice Hall, New York 1952; *L. H. Vogt, H. M. Faigenbaum, S. E. Wiberley*, Chem. Rev. *63*, 269 (1963).
[161] *J. S. Miller, C. H. Griffiths*, J. Am. Chem. Soc. *99*, 749 (1977).
[162] *J. L. Peterson, C. S. Schramm, D. R. Stojakovic, B. M. Hofmann, T. J. Marks*, J. Am. Chem. Soc. *99*, 286 (1977).

[163] *J. O. M. Bockris, S. Srinavasan:* Fuel Cells. McGraw-Hill, New York 1969; *G. Sandstede:* From Electrocatalysis to Fuel Cells. University of Washington Press, Seattle 1972; *A. D. Franklin*, Nat. Bur. Stand. (US) Spec. Publ. *455*, 241 (1976).
[164] *P. S. Gomm, A. E. Underhill*, J. Chem. Soc. Chem. Commun. *1971*, 511.
[165] *F. N. Lecrone, J. H. Perlstein*, J. Chem. Soc. Chem. Commun. *1972*, 75.
[166] *J. S. Miller, A. J. Epstein:* Synthesis and Properties of Low-Dimensional Materials. Academy of Science, New York 1978.
[167] *F. Gutmann, A. M. Hermann, A. Rembaum*, J. Electrochem. Soc. *114*, 323 (1967); *P. Weidenthaler, E. Pelinka*, Collect. Czech. Chem. Commun. *34*, 1482 (1969).
[168] *I. F. Chang:* Proc. of the Int. Symp. on Nonemissive Electrooptic Displays. Plenum Press, New York 1976; *J. Bruininck, C. G. A. Kregting*, J. Electrochem. Soc. *125*, 1397 (1978); *J. E. Kuder, J. M. Pochan, S. R. Turner, D. T. Hinman, ibid. 125*, 1750 (1978); *R. Jasinski, ibid. 126*, 167 (1979).
[169] *S. Hünig*, Angew. Chem. *90*, 927 (1978); Angew. Chem. Int. Ed. Engl. *17*, 875 (1978).
[170] *G. Wegner*, Pure Appl. Chem. *49*, 443 (1977).
[171] a) *W. van Gool:* Fast Ion Transport in Solids. North Holland, Amsterdam 1973; b) *G. Mahan, W. L. Roth:* Superionic Conductors. Plenum Press, New York 1976; c) *P. Hagenmuller, W. van Gool:* Solid Electrolytes. Academic Press, New York 1978.
[172] *L. Heyne* in *S. Geller:* Solid Electrolytes. Springer, Berlin 1977, p. 169.
[173] *F. M. R. Engelsman, G. A. Wiegers, F. Jellinek, B. van Laar*, J. Solid State Chem. *6*, 574 (1973).
[174] *M. S. Whittingham*, Electrochim. Acta *20*, 575 (1975).
[175] *M. S. Whittingham, B. G. Silbernagel* in [171c], p. 93; *C. Berthier, Y. Chabre, P. Segranson*, Physica *99B*, 107 (1980).
[176] *C. Riekel, A. Heidemann, B. E. F. Fender, G. C. Stirling*, J. Chem. Phys. *71*, 530 (1979); *C. Riekel, R. Schöllhorn, F. Tomkinson*, Z. Naturforsch. *A 35*, 590 (1980).
[177] *A. Lerf, P. Burkert, J. O. Besenhard, R. Schöllhorn*, Z. Naturforsch. *B 32*, 1033 (1977); *U. Röder, W. Müller-Warmuth, R. Schöllhorn*, J. Chem. Phys. *70*, 2864 (1979).
[178] *S. Wada, H. Alloul, P. Molinié*, J. Phys. (Paris) *39*, L243 (1978).
[179] *M. Molitor, W. Müller-Warmuth, R. Schöllhorn*, unpublished.
[180] *J. E. Fischer*, Physica *99B*, 383 (1980).
[181] *R. Schöllhorn, A. Lerf, F. Sernetz*, Z. Naturforsch. *B 29*, 810 (1974); *F. Sernetz, A. Lerf, R. Schöllhorn*, Mater. Res. Bull. *9*, 1597 (1974); *A. Lerf, F. Sernetz, W. Biberacher, R. Schöllhorn, ibid. 14*, 797 (1979).
[182] *J. A. Wilson, F. J. Di Salvo, S. Mahajan*, Adv. Phys. *24*, 117 (1975).
[183] *G. A. Wiegers*, Physica *99B*, 151 (1980).
[184] *D. W. Murphy, F. A. Trumbore*, J. Cryst. Growth *39*, 185 (1977).
[185] *H. Ikeda, S. Uens, T. Saito, S. Nakaido, H. Tamaru*, Denki Kagaku *45*, 391 (1977).
[186] *H. Tributsch*, presented in a lecture at the Tagung der Fachgruppe Photochemie der GDCh, Göttingen 1979.
[187] *L. B. Ebert*, Annu. Rev. Mater. Sci. *6*, 181 (1976); *M. S. Whittingham, L. B. Ebert* in [18a], p. 533.

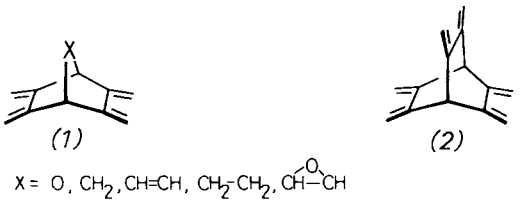
COMMUNICATIONS

Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying publication on submission of their manuscript. The same reasons should be clearly apparent from the manuscript. In cases where the editorial staff decide, after due consultation with independent referees, that these conditions are not met, manuscripts will be returned to the authors with the request to submit them for publication in a specialist journal catering for scientists working in the field concerned.

2,3,5,6,7,8-Hexakis(methylene)bicyclo[2.2.2]octane[**]

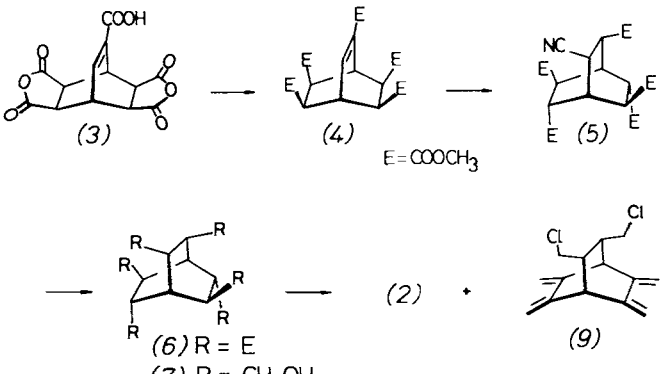
By *Olivier Pilet* and *Pierre Vogel*[*]

The 2,3,5,6-tetrakis(methylene)bicyclo[2.2.*n*]alkanes *(1)* have interesting spectroscopic[1] and chemical properties[2]. We report now the synthesis and a few properties of the hexaene *(2)*[3], a system ($D_3 \rightleftarrows D_3$ or D_{3h} symmetry) that occupies a place between barrelene[4] and triptycene[5].



Methyl bicyclo[2.2.2]oct-2-ene-2,3,5,6,7-pentacarboxylate *(4)* was obtained by heating a 3:1 mixture of maleic anhydride and coumalic acid to 200 °C without solvent, yielding *(3)* (65%)[6], followed by esterification (MeOH, $CHCl_3$, TosOH, 6 d, 87%). The all-*cis* configuration of the ester groups in *(4)* was indicated by $^3J_{H,H} = 2.0$ Hz between 2,6-H and 1 H and between 4-H and 3,5-H[7] and by $^3J_{C,H} \approx 2$ Hz between C-7, C-8 and 2,4,6-H and 1,3,5-H, respectively[8].

When *(4)* (50 g) was heated to 80 °C for 20 h with KCN (13 g), $(CH_3)_2C(OH)CN$ (13 g), and tetrabutylammonium cyanide (2 g) in dry CH_3CN (750 ml), *(5)* was obtained (>95%) which yielded the all-*trans* hexaester *(6)* (80% based on *(4)*) after hydrolysis (53 g in 500 ml 80% aq. AcOH + 15 ml H_2SO_4, 130 °C, 4 d) followed by esterification with MeOH ($CHCl_3$, TosOH). Reduction with $LiAlH_4$ (7 mol. equiv.) in THF (80 °C, 50 h) yielded *(7)* (41%). Chlorination with $SOCl_2$/pyridine (80 °C, 4 h) furnished *(8)* (45%). Treatment with potassium *tert*-butoxide (20 mol. equiv.) in THF (50 °C, 3 d) led to a 85:15 mixture (60%) of *(2)* and *(9)*. Compound *(2)* was isolated by fractional crystallization (hexane) as colorless crystals that polymerized upon heating under Ar.



[*] Dipl.-Chem. O. Pilet, Prof. Dr. P. Vogel
Institut de chimie organique de l'Université
2, rue de la Barre, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the "Swiss National Science Foundation" (FN 2'891-0.77) and "Stipendienfonds der Basler Chemischen Industrie".

Table 1. Melting points and selected spectroscopic data of compounds *(2)*, *(4)*, *(6)*, *(7)*, and *(8)*.

(2): IR (CCl_4): 3087, 2990, 2960, 1780, 1660, 1640, 1615, 1440, 1425, 1410, 1390, 1370, 1255, 1210, 1995, 890 cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 3.78$ (s, 2H), 5.01 (s, 6H), 5.35 (s, 6H); MS (70 eV): $m/e = 183$ (5%), 182 (M^+, 17), 181 (6), 167 (13), 166 (10), 165 (22), 51 (100)

(4): m.p. 137—138 °C; IR (KBr): 3010, 2970, 1740 cm^{-1}; ^{1}H-NMR (C_6D_6): $\delta = 2.54$ (dd, 3,5-H, $J = 10.4$, 2.0 Hz), 2.89 (dd, 2,6-H, $J = 10.4$, 2.0 Hz), 3.35, 3.37, 3.40 (s, 15H, CH_3OOC), 3.45 (m, 4-H, $J = 7.0$, 2.0 Hz), 3.99 (m, 1-H, $J = 2.1$ Hz), 7.79 (dm, 8-H, $J = 7.0$ Hz)

(6): m.p. 184—185 °C; IR ($CHCl_3$): 3010, 2960, 2860, 1740 (s), 1440, 1380, 1300 cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 3.81$ (s, 18H), 3.71 (s, 2H), 3.13 (s, 6H)

(7): m.p. 290—294 °C; IR (KBr): 3330, 2960, 2940, 2900, 1480, 1450, 1380 cm^{-1}; ^{1}H-NMR (D_2O): $\delta = 1.33$ (m, 6H), 1.65 (m, 2H), 3.45 (m, 12H)

(8): m.p. 178—182 °C; IR (KBr): 3000, 2970, 2920, 1460, 1445, 1315, 1300 cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 1.4$—2.0 (m, 6H); 3.3—4.0 (m, 12H); 5.13 (br. s, 2H)

Its structure was given by its spectra (Table 1) and its reactivity toward tetracyanoethylene (TCNE).

The UV absorption spectrum of *(2)* (Fig. 1) shows a relatively intense band at $\lambda_{max} = 247$ nm ($\varepsilon = 18\,500$) without the Franck-Condon fine structure usually observed for the rigid 2,3-bis(methylene)bicyclo[2.2.n]alkanes[9] and the tetraenes *(1)*[1a]. This suggests superposition of two allowed transitions of very similar energies (vibronic coupling?). The shoulder at $\lambda = 268$ nm might be due to the Franck-Condon contour of the lowest energy band or to a low intensity (perhaps symmetry forbidden) transition[10].

TCNE in excess added at 20 °C to *(2)*, gives the mono-, bis-, and trisadducts. Preliminary kinetic measurements gave $k_1 \approx 0.1$, $k_2 \approx 0.07$, and $k_3 \approx 0.0017$ l mol^{-1} s^{-1} at 27 °C in toluene. (Concerning the differences observed in the Diels-Alder reactivities, see[11].)

Received: June 16, 1980 [Z 621 IE]
German version: Angew. Chem. *92*, 1036 (1980)

[1] a) *P. Vogel*, Chimia *31*, 53 (1977); *R. Gabioud, P. Vogel*, Tetrahedron *36*, 149 (1980), and references cited therein; b) *M. Mohraz, C. Batich, E. Heilbronner, P. Vogel, P.-A. Carrupt*, Recl. Trav. Chim. Pays-Bas *98*, 361 (1979).

[2] *P.-A. Carrupt, P. Vogel*, Tetrahedron Lett. *1979*, 4533; *Y. Bessière, P. Vogel*, Helv. Chim. Acta *63*, 232 (1980).

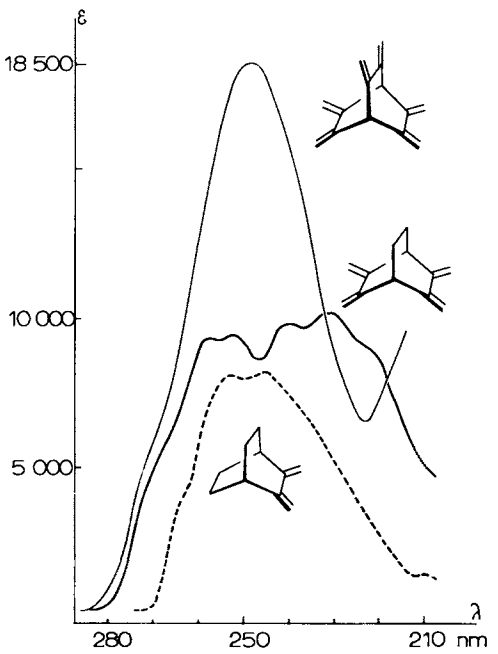


Fig. 1. UV absorption spectra (isooctane) of 2,3-bis(methylene)-, 2,3,5,6-tetrakis(methylene)-, and 2,3,5,6,7,8-hexakis(methylene)bicyclo[2.2.2]octane *(2)*.

[3] The generic name hericene is proposed for bicycloalkanes in which all methylene groups are methylene-substituted, after the Latin *hericeus* for hedgehog.

[4] *H. E. Zimmerman, R. M. Paufler*, J. Am. Chem. Soc. *82*, 1514 (1960); *C. W. Jefford, T. W. Wallace, M. Acar*, J. Org. Chem. *42*, 1654 (1977).

[5] *P. D. Bartlett, E. S. Lewis*, J. Am. Chem. Soc. *72*, 1005 (1950); *C. F. Wilcox, Jr., A. C. Craig*, J. Org. Chem. *26*, 2491 (1961).

[6] *O. Diels, K. Alder*, Justus Liebigs Ann. Chem. *490*, 257 (1931).

[7] *F. Iordache, F. Chiraleu, M. Avram*, Rev. Roum. Chim. *20*, 233 (1975); Chem. Abstr. *83*, 57812j (1975).

[8] *T. Spoormaker, M. J. A. de Bie*, Recl. Trav. Chim. Pays-Bas *98*, 380, 59 (1979).

[9] *P. Asmus, M. Klessinger*, Tetrahedron *30*, 2477 (1974).

[10] PE spectrum of *(2)* see *M. Mohraz, W. Jian-qi, E. Heilbronner, P. Vogel, O. Pilet*, Helv. Chim. Acta *63*, 568 (1980).

[11] *M. Hardy, P.-A. Carrupt, P. Vogel*, Helv. Chim. Acta *59*, 1685 (1976); *H.-U. Pfeffer, M. Klessinger*, Chem. Ber. *112*, 890 (1979); *H.-D. Scharf, H. Plum, J. Fleischlauer, W. Schleker, ibid. 112*, 862 (1979); *R. Sustmann, M. Böhm, J. Sauer, ibid. 112*, 833 (1979); *C. Rücker, D. Lang, J. Sauer, H. Friege, R. Sustman, ibid. 113*, 1663 (1980).

Oxygen Atoms Produced by Microwave Discharge: Reaction with Arenes[**]

By *Elazar Zadok, Bonita Sialom*, and *Yehuda Mazur*[*]

We recently found that ground state oxygen atoms produced by microwave discharge can be effectively used for preparative scale oxidations of unsaturated compounds in condensed phases[1].

These oxidations involve passing O_2 or a mixture of N_2O and N_2 diluted with He in a flow system at 4 torr, through a microwave discharge and then onto the surface of a stirred substrate as neat liquid or in solution[1].

Using this method we have oxidized three mono- and three poly-substituted benzene derivatives (Table 1). The reactions were performed on 1—2 g of neat liquid substrate for 1—2 h, using O_2 discharge, and the conversions were *ca.* 30%. Products were identified after separation by preparative GC and their relative yields determined by analytical GC. The relative rates were established by reacting mixtures of substrates and comparison of the product yields. It was found that the product ratios were independent of reaction time.

The products of these oxidations are mainly phenols derived from direct ring hydroxylation as well as from replacement of the substituent by the OH group. In the polymethylated arenes, minute amounts (less than 1%) of rearranged phenol products of 1,2-methyl migration were also formed. In addition, methyl substituents were partly oxidized to give benzyl alcohol and benzaldehyde or their respective derivatives. Similar products and in the same ratios were obtained when the source of ground state oxygen atoms was a mixture of N_2O and N_2.

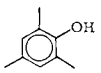
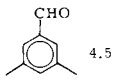
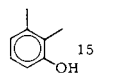
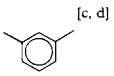
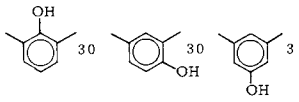
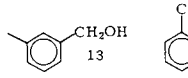
Table 1 shows that substituted arenes are hydroxylated mainly at the *ortho* positions, regardless of the size of the substituent. The substitution pattern and the relative rates for the ring substitution in the different substrates indicate that the ground state oxygen atom behaves as a radical reagent having a moderate electrophilic character[2].

The results of the oxidations in the condensed phase are similar to those obtained by *Grovenstein et al.*[3] in gas phase reaction, in which the ground state oxygen atoms were formed by photolysis of N_2O in the presence of Hg vapor[4]. A significant difference is, however, the absence in the gas

[*] Prof. Dr. Y. Mazur, E. Zadok, M. Sc., B. Sialom, M. Sc.
Department of Organic Chemistry, The Weizmann Institute of Science
Rehovot (Israel)

[**] This work was supported by the USA—Israel Binational Science Foundation, Jerusalem.

Table 1. Product distribution from reactions of arenes with ground state oxygen atoms produced by microwave discharge of O_2/He.

Substrate	Relative rate [e]	Relative yields of products [%] derived from oxidation of an aromatic CH bond	Substituent cleavage	methyl shift	methyl oxidation
 [a]	1.0	 *ortho* 71, *meta* 7, *para* 16	 1		 3  2
 [b]	1.3	 *ortho* 59, *meta* 15, *para* 21	 5		
 [b]	3.7	 *ortho* 65, *meta* 1, *para* 19	 15		
 [b,c]	28.5	 92	 3	 0.5	 4.5
 [c,d]	3.5	 15, 8	 40	 1	 36
 [c, d]	5.0	 30, 30, 3	 4.5	 0.5	 13, 19

[a] At −78 °C. [b] At −30 °C. [c] Also done by microwave discharge of N_2O/N_2. [d] At −25 °C. [e] For ring substitution.

phase reaction of the rearranged phenols and of benzylic oxidation products[5]. Oxidation of naphthalene in solution with ground state oxygen atoms gave α- and β-naphthols in 7:1 ratio. The corresponding acetates were obtained in the same ratio when the reaction was performed in acetic anhydride in the presence of traces of sulfuric acid.

Experimental

Oxidation of naphthalene: A steady flow of O_2 and He (0.7 l/min, 7:1 ratio) at 4 torr was passed through a quartz U-tube containing a magnetically stirred methyl caproate solution of naphthalene (1 g in 5 ml). The side arm of the U-tube was connected by a gas discharge cavity to the microwave generator (Kiva MPG-2, 2450 MHz, 100 watt), which was placed 5 cm above the substrate surface. After reaction for 1 h at 5 °C the material was chromatographed on silica gel to give 600 mg starting compound, 280 mg of α-naphthol, 40 mg of β-naphthol, and small amounts of other oxidation products.

Received: July 30, 1980 [Z 622 IE]
German version: Angew. Chem. *92*, 1037 (1980)

CAS Registry numbers:
Naphthalene, 91-20-3; α-naphthol, 90-15-3; β-naphthol, 135-19-3; methylbenzene, 108-88-3; *tert*-butylbenzene, 98-06-6; methoxybenzene, 100-66-3; 1,3,5-trimethylbenzene, 108-67-8; 1,2-dimethylbenzene, 95-47-6; 1,3-dimethylbenzene, 108-38-3; *o*-methylphenol, 95-48-7; *m*-methylphenol, 108-39-4; *p*-methylphenol, 106-44-5; *o*-*tert*-butylphenol, 88-18-6; *m*-*tert*-butylphenol, 585-34-2; *p*-*tert*-butylphenol, 98-54-4; *o*-methoxyphenol, 90-05-1; *m*-methoxyphenol, 150-19-6; *p*-methoxyphenol, 150-76-5; 2,4,6-trimethylphenol, 527-60-6; 2,3-dimethylphenol, 526-75-0; 3,4-dimethylphenol, 95-65-8; 2,6-dimethylphenol, 576-26-1; 2,4-dimethylphenol, 105-67-9; 3,5-dimethylphenol, 108-68-9; phenol, 108-95-2; 2,3,5-trimethylphenol, 697-82-5; 2,5-dimethylphenol, 95-87-4; benzaldehyde, 100-52-7; benzyl alcohol, 100-51-6; 3,5-dimethylbenzaldehyde, 5779-95-3; 2-methylbenzaldehyde, 529-20-4; 3-methylbenzyl alcohol, 587-03-1; 3-methylbenzaldehyde, 620-23-5; oxygen atom, 17778-80-2

[1] *E. Zadok, D. Amar, Y. Mazur,* J. Am. Chem. Soc. *102*, 6369 (1980).
[2] *R. Ito, T. Migita, N. Morikawa, O. Simamura,* Tetrahedron *21*, 955 (1965).
[3] *E. Grovenstein, A. Mosher,* J. Am. Chem. Soc. *92*, 3810 (1970).
[4] For other gas-phase oxidations of aromatic compounds, see: *R. A. Bonanno, P. Kim, J. Lee, S. R. Timmons,* J. Chem. Phys. *57*, 1377 (1972); *T. M. Sloane, ibid. 67*, 2267 (1977); *J. S. Gaffney, R. Attkinson, J. N. Pitts,* J. Am. Chem. Soc. *98*, 1828 (1976); *G. Boocock, R. J. Cvetanović,* Can. J. Chem. *39*, 2436 (1961); *G. R. H. Jones, R. J. Cvetanović, ibid. 39*, 2444 (1961).
[5] Comparison of our results with those recently published by *Takamuku, Sakurai et al. (A. Hori, H. Matsumoto, S. Takamuku, H. Sakurai,* J. Chem. Soc. Chem. Commun. *1978*, 16 and Chem. Lett. 467 (1978); *S. Takamuku, H. Matsumoto, A. Hori, H. Sakurai,* J. Am. Chem. Soc. *102*, 1441 (1980)), on the reaction of ground state oxygen atoms producted by γ-radiolysis of liquid CO_2, shows considerable differences in the relative distribution of the oxidation products. γ-Radiolysis leads to comparatively small yields of *o*-phenols and complete lack of substituent cleavage products.

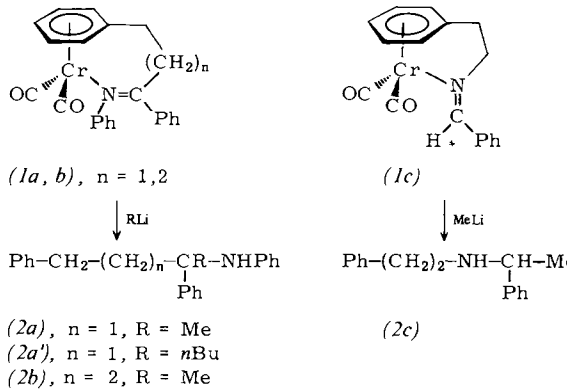
New Arene(dicarbonyl)chromium Chelates: Application to Asymmetric Synthesis of Amines

By *Arlette Solladié-Cavallo, Jean Suffert,* and *Jean-Luc Haesslein*[*]

We have found that arene(dicarbonyl)chromium chelates *(1a—d)* (synthetized by irradiation of arene(tricarbonyl)chromium complexes *(3a—d)* (Scheme 1) undergo, with alkyllithium compounds, nucleophilic addition on the azomethine carbon; hydrolysis of the intermediates then leads in good yields to the chiral amines *(2)* (Table 1).

[*] Dr. A. Solladié-Cavallo, J. Suffert, J. L. Haesslein
Laboratoire de Chimie Organique de l'Ecole Nationale Supérieure de Chimie, ERA du C.N.R.S., n° 687
Université Louis Pasteur
P.O. Box 296/R8, F-67008 Strasbourg (France)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1212-1005 $ 02.50/0*



(1a, b), n = 1,2 — *(1c)*

RLi / MeLi

$Ph-CH_2-(CH_2)_n-\underset{Ph}{\underset{|}{C}}R-NHPh$ — $Ph-(CH_2)_2-NH-\underset{Ph}{\underset{|}{C}}H-Me$

(2a), n = 1, R = Me
(2a'), n = 1, R = *n*Bu
(2b), n = 2, R = Me
(2c)

Table 1. Reaction conditions and yields of reactions of *(1)* with alkyllithium compounds.

Reactant (Chelate)	R in RLi	Reaction conditions T [°C]	t [h]	Yield [%]	Product (Amine)
(1a)	Me	0	16	98	*(2a)*
(1a)	*n*Bu	−30	15	40	*(2a')*
(1a)	1,3-Dithian-	0	15	0	—
	2-yl	50	10	0	—
(1b)	Me	0	16	60	*(2b)*
(1c)	Me	0	16	88	*(2c)*
(1*S*)-*(1d)* [1]	Me	0	16	98	*(2d)* [a]
(1*S*)-*(1d)* [1]	Me	−20	24	72	*(2d)* [b]

[a] $[\alpha]_D^{20} = -8.6$ ($c = 0.4$; $CHCl_3$); optical purity 77%, calculated with $[\alpha]_D^{20}$(max) $= \pm 11.2$. [b] $[\alpha]_D^{20} = -10.5$ ($c = 0.4$; $CHCl_3$); optical purity 94%, calculated as in [a].

A benzene solution of the chelate *(1)* is added dropwise, under argon, to a diethyl ether solution of the alkyllithium compound (see Table 1). Decomplexation occurs during work-up (H_2O/NH_4Cl), leading to the racemic amines *(2a–c)* which are purified by chromatography and identified by elemental analysis, mass spectra, IR, and ^{1}H-NMR (Table 2).

Chemical yields depend on reaction temperature but the absence of reaction with 2-lithio-1,3-dithiane may be ascribed mainly to steric hindrance.

When the optically pure chelate (1*S*)-*(1d)*[1] is used (Scheme 1), the amine *(2d)* obtained is up to 94% optically pure. Nucleophilic addition of alkyllithium compounds to the optically pure arene(tricarbonyl)chromium complexe (1*S*)-*(3d)* proceeds without asymmetric induction.

The new chelates *(1)* are good precursors of the chiral amines *(2)*; replacement of the phenyl groups on the azine methine function by alkyl groups or hydrogen should provide an efficient route to a large number of chiral amines.

Received: November 14, 1979 [Z 623 IE]
German version: Angew. Chem. *92*, 1038 (1980)

Table 2. Selected physical and spectroscopic data of the chiral amines *(2a–d)*. IR in $CHCl_3$, ^{1}H-NMR in $CDCl_3$/TMS.

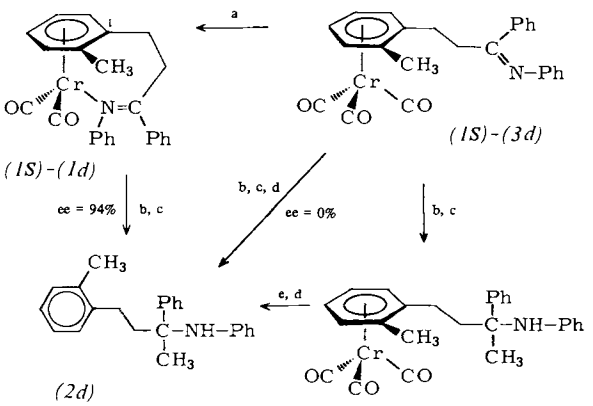
(2a): m.p. 89 °C; IR: 3420 (NH), 3050–3000 (CH arom.), 2930–2850 cm^{-1} (CH_2); ^{1}H-NMR: $\delta = 1.65$ (s, CH_3), 1.80–2.80 (m, $(CH_2)_2$), 3.95 (s, NH), 6.10–7.60 (m, 15 H, arom.)

(2a'): IR: 3420 (NH), 3060–3010 (CH arom.), 2930–2860 cm^{-1} (CH_2); ^{1}H-NMR: $\delta = 0.5$–2.70 (m, $(CH_2)_2$ und C_4H_9), 3.93 (s, NH), 6.10–7.70 (m, 15 H, arom.)

(2b): IR: 3420 (NH), 3060–3020 (CH arom.), 2930, 2860 cm^{-1} (CH_2); ^{1}H-NMR: $\delta = 1.57$ (s, CH_3), 1.4–3.0 (m, $(CH_2)_3$), 3.97 (s, NH), 6.10–7.60 (m, 15 H, arom.)

(2c): IR: 3400 (NH), 3060–3040 (CH arom.), 2960–2900 cm^{-1} (CH_2); ^{1}H-NMR: $\delta = 1.35$ (d, CH_3), 2.12 (s, NH), 2.70 (br. $(CH_2)_2$), 3.70 (q, CH—N), 6.90–7.30 (m, 10 H, arom.)

(2d): IR: 3415 (NH), 3050–3000 (CH arom.), 2935–2870 cm^{-1} (CH_2); ^{1}H-NMR: $\delta = 1.66$ (s, CH_3), 1.98 (s, CH_3), 1.90–2.80 (m, $(CH_2)_2$), 3.95 (s, NH), 6.10–7.60 (m, 15 H, arom.)



Scheme 1. a) *hν*/benzene; b) RLi, −20 °C; c) H_2O/NH_4Cl; d) *hν*/O_2; e) chromatography. ee = enantiomeric excess.

[1] (1*S*)-*(1d)* was synthesized from (1*S*)-(+)-tricarbonyl(*o*-methylbenzaldehydato)chromium; *A. Solladié-Cavallo, G. Solladié, E. Tsamo*, J. Org. Chem. *44*, 4189 (1979).

Phosphorus Triiodide and Diphosphorus Tetraiodide, New Reagents for Deprotecting Acetals and Ketals[**]

By *Jean-Noël Denis* and *Alain Krief*[*]

On continuing our investigations on the reactivity of PI_3 and P_2I_4 towards organic molecules[1], we found that these reagents allow the transformation of ketals into aldehydes or ketones[2]. Only few nonaqueous deprotections have so far been reported for these protecting groups[3].

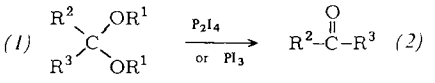


Table 1. Yields and conditions for reaction of aldehydes and ketones with P_2I_4 (method A) or PI_3 (method B).

R^1	R^2	R^3	Yield [%] [a]	Method	T [°C]	t [h]
CH_3	C_9H_{19}	CH_3	91	A	20	0.2
			85	B	20	0.2
CH_3	C_8H_{17}	H	63	A	20	0.2
			60	B	20	0.2
CH_3	C_8H_{17}	H	64	A	20	0.2 [b]
			57	B	20	0.2 [b]
CH_3	$-(CH_2)_2CH(tBu)(CH_2)_2-$		78	A	20	0.25
			81	B	20	0.25
CH_3	C_6H_5	CH_3	67	A	20	0.25 [c]
			75	B	20	0.25 [c]
C_2H_5	C_9H_{19}	CH_3	65	A	20	0.3 [d]
C_2H_5	C_9H_{19}	CH_3	85	A	60	4
			79	B	60	4
C_2H_5	$-(CH_2)_2CH(tBu)(CH_2)_2-$		65	A	60	6
			58	B	60	4

[a] Yields of purified products. [b] Reactions were conducted in the presence of propene, giving a 10% increase in the yield of carbonyl compound. [c] This ketone contains ≈5% of an unidentifed product; it is absent if the reaction is conducted with an excess of P_2I_4 (0.55 mol) or PI_3 (1.1 mol) per mol of ketal. The ketone is thus formed in 79 and 77% yield respectively after stirring at (20 °C, 15 min). [d] 0.92 mol of ethyl iodide is formed per mol of ketal.

[*] Dipl.-Chem. J. N. Denis, Prof. Dr. A. Krief
Departement de Chimie, Facultés Universitaires N. D. de la Paix
61, rue de Bruxelles, B-5000 Namur (Belgium)

[**] The authors acknowledge award of a fellowship by Roussel Uclaf Company (France) to *J. N. D.* and financial support of this work by FNRS.

The reactions are particularly easy with dimethoxyalkanes *(1)*, $R^1 = CH_3$, which produce the corresponding carbonyl compounds *(2)* on stirring at room temperature for about 15 minutes in dichloromethane with 0.275 or 0.370 molar equivalent, respectively, of P_2I_4 (method A) or PI_3 (method B).

Work-up is usually performed by addition of water to the reaction medium, to solubilize the phosphorus by-products, and the organic phase is further extracted with water.

The diethoxyalkanes *(1)*, $R = C_2H_5$, are less reactive and require heating (60 °C, 2—4 h) to produce similar yields of *(2)* since appreciable amounts of intermediates, which decompose on heating, are formed at room temperature even in the case of ketones.

The behavior of ketals towards PI_3 or P_2I_4 differs from that of acetals: while the ketone is already present prior to the hydrolysis, the formation of the aldehyde requires the hydrolysis of an intermediate containing the phosphorus atom.

We also observed the concomitant formation of methyl- or ethyl iodide, depending on the nature of the starting ketal (≈ 0.8 mol per mol of protected carbonyl compound).

Received: July 4, 1980 [Z 624 IE]
German version: Angew. Chem. *92*, 1039 (1980)

CAS Registry numbers:
(1), (R',$R^3 = CH_3$, $R^2 = C_9H_{19}$), 68298-50-0; *(1)*, ($R' = CH_3$, $R^2 = C_8H_{17}$, $R^3 = H$), 18824-63-0; *(1)*, ($R' = CH_3$, R^2,$R^3 = (CH_2)_2CH(t\text{-}Bu)(CH_2)_2$), 944-19-4; *(1)*, ($R'$,$R^3 = CH_3$, $R^2 = C_6H_5$), 4316-35-2; *(1)*, ($R' = C_2H_5$, $R^2 = C_9H_{19}$, $R^3 = CH$), 75717-48-5; *(1)*, ($R' = C_2H_5$, R^2,$R^3 = (CH_2)_2CH(t\text{-}Bu)(CH_2)_2$), 1900-58-9; *(2)*, ($R^2 = C_9H_{19}$, $R^3 = CH_3$), 112-12-9; *(2)*, ($R^2 = C_8H_{17}$, $R^3 = H$), 124-19-6; *(2)*, (R^2,$R^3 = (CH_2)_2CH(t\text{-}Bu)(CH_2)_2$), 98-53-3; *(2)*, ($R^2 = C_6H_5$, $R^3 = CH_3$), 98-86-2; *(2)*, ($R^2 = C_9H_{19}$, $R^3 = CH_3$), 112-12-9; PI_3, 134555-01-1; P_2I_4, 13455-00-0

[1] *J.-N. Denis, A. Krief*, J. Chem. Soc. Chem. Commun. *1980*, 544; Tetrahedron Lett. *1979*, 3995; *A. Krief*, Aldrichimica Acta, in press.
[2] *H. Meerwein* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie. Vol. VI/3. Thieme, Stuttgart 1965, p. 199.
[3] *M. E. Jung, W. A. Andrus, P. L. Orstein*, Tetrahedron Lett. *1977*, 4175; *A. Bowers, L. C. Ibanez, H. J. Ringold*, Tetrahedron *7*, 138 (1959).

Water Gas Shift Reaction with the Aid of Selenium/Platinum Catalyst[1]

By *Nobuaki Kambe, Fumihiko Morimoto, Kiyoshi Kondo,* and *Noboru Sonoda*[*]

We recently reported[1] that carbon monoxide reacts with water and selenium in the presence of base to form selane (hydrogen selenide, H_2Se) and CO_2 [eq. (1)].

$$CO + Se + H_2O \rightarrow H_2Se + CO_2 \quad (1)$$

Meanwhile, we have found that selane (hydrogen selenide, H_2Se) decomposes to hydrogen and selenium on platinum black [eq. (2)].

$$H_2Se \xrightarrow{Pt} H_2 + Se \quad (2)$$

Reaction (2) was found to proceed smoothly at 200 °C, and at such a high temperature the reaction (1) did not require the presence of base. The combination of these two reactions (1) and (2) would thus provide a new system for the water gas shift reaction [eq. (3), Table 1].

$$CO + H_2O \xrightarrow{Se/Pt} CO_2 + H_2 \quad (3)$$

[*] Prof. Dr. N. Sonoda [+], Dr. K. Kondo [+], N. Kambe, F. Morimoto
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)
[+] Authors to whom correspondence should be addressed.

As shown by the control experiments using selenium or platinum black alone (runs 1, 7), both elements are necessary for catalytic formation of H_2 and CO_2. The experiment in run 1 corresponds to the reaction formulated in eq. (1). The conversion[3] of CO into CO_2 in run 4 after 20 h is 43%.

Table 1. Water gas shift reaction [a] catalyzed by selenium/platinum [a].

Run	Catalyst		Products	
	Se [mmol]	Pt [mmol]	H_2 [mmol]	CO_2 [mmol]
1	1	—	0.1	1.0
2	1	0.01	1.6	2.3
3	1	0.1	5.7	5.9
4	1	1	21.1	20.8
5	0.1	0.1	2.1	2.0
6	0.1	1	12.1	12.0
7	—	1	0.9	0.9

[a] See *Experimental* for reaction conditions.

The reaction of CO with H_2O in the co-presence of selane and platinum black under identical conditions likewise affords CO_2 and H_2 [eq. (4)].

$$CO + H_2O \xrightarrow{H_2Se/Pt} CO_2 + H_2 \quad (4)$$

Experimental

A) Water gas shift reaction (3), run 4 in Table 1: Metallic selenium (0.079 g, 1 mmol), platinum black (0.195 g, 1 mmol), and water (10 ml) are placed with a magnetic stirring bar in a glass tube inserted in a 50 ml stainless steel autoclave, and the apparatus is then flushed several times with carbon monoxide, and finally charged with CO at *ca.* 30 bar at room temperature. The reaction is carried out at 200 °C for 20 h with vigorous stirring. On completion of the reaction, the resulting gas is collected in a gas sampler and analyzed by gas chromatography: the resulting gas is found to consist of carbon monoxide (27.7 mmol), carbon dioxide (20.8 mmol), and hydrogen (21.1 mmol).

B) Decomposition of hydrogen selenide on platinum black (2): H_2Se (0.162 g, 2 mmol), platinum black (0.195 g, 1 mmol), and water (10 ml) are placed in the same apparatus as in (A) at room temperature under nitrogen (≈ 30 bar). After reaction at 200 °C for 1 h, 1.9 mmol of H_2 is found.

C) Water gas shift reaction (4): H_2Se (0.162 g, 2 mmol), platinum black (0.195 g, 1 mmol), and water (10 ml) are allowed to react at ≈ 30 bar as described in (A). The reaction is carried out at 200 °C for 20 h with vigorous stirring. The amounts of H_2 and CO_2 formed are 32.4 and 31.6 mmol, respectively.

Received: December 3, 1979 [Z 625a IE]
German version: Angew. Chem. *92*, 1040 (1980)

[1] A new system utilizing the reducing ability of carbon monoxide, Part 2.—Part 1: *N. Sonoda, K. Kondo, K. Nagano, N. Kambe, F. Morimoto*, Angew. Chem. *92*, 317 (1980); Angew. Chem. Int. Ed. Engl. *19*, 308 (1980).
[2] Recent advances in water gas shift reaction are focused on the homogeneous catalytic systems: *C.-H. Cheng, D. E. Hendriksen, R. Eisenberg*, J. Am. Chem. Soc. *99*, 2791 (1977); *R. M. Laine, R. G. Rinker, P. Ford, ibid.* *99*, 252 (1977); *C.-H. Cheng, R. Eisenberg, ibid. 100*, 5968 (1978); *P. C. Ford, R. G. Rinker, C. Ungermann, R. M. Laine, V. Landis, S. A. Moya, ibid. 100*, 4595 (1978); *T. Yoshida, Y. Ueda, S. Otsuka, ibid. 100*, 3941 (1978).
[3] Conversion after 5 h is 10%, and increases almost linearly with respect to time.

Selenium-Catalyzed Reduction of Aromatic Nitro Compounds to Amines by CO/H_2O in the Presence of Triethylamine[1]

By *Toshiyuki Miyata, Kiyoshi Kondo, Shinji Murai, Tsuneaki Hirashima,* and *Noboru Sonoda*[*]

In the preceding paper[2] we described a new water gas shift reaction system using catalytic amounts of selenium and platinum black. In connection with this system, we now wish to report a new catalytic reduction of aromatic nitro compounds to aromatic amines with carbon monoxide and water in the presence of selenium and triethylamine [eq. (1)]. Examples are given in Table 1.

$$ArylNO_2 + 3CO + H_2O \xrightarrow{Se/Et_3N} ArylNH_2 + 3CO_2 \quad (1)$$

Table 1. Yields of isolated amines on Se-catalyzed reduction of nitrobenzenes according to eq. (1), based on nitrobenzene derivative.

No.	Aryl	Yield [%]
1	C_6H_5	86
2	p-$MeOC_6H_4$	40
3	p-ClC_6H_4	35
4	p-BrC_6H_4	25
5	p-MeC_6H_4	70

It is noteworthy that selenium, which is a main group element, catalyzes this reaction; until now however, only complexes of the transition metals rhodium[2,3], osmium[3], iridium[3], and iron[3] have been found to be effective catalysts for this reduction.

The yields of arylamines are moderate to good. The presence of triethylamine is essential for the reduction.

We have already reported two closely related reactions; (i) selenium/triethylamine catalyzed carbonylation of anilines with CO/O_2 to produce urea derivatives[4] and (ii) the selane/triethylamine promoted carbonylation of anilines with carbon monoxide to afford formanilides[5]. Under the present reduction conditions, subsequent carbonylation of aniline produced to diphenylurea was found to proceed only to a small extent; but the production of formanilide was not observed.

It is plausible that the most important reducing species in the present reaction system may be selane (hydrogen selenide, H_2Se)[6]. In a control experiment designed to test this assumption, reaction of nitrobenzene with selane under N_2 afforded aniline quantitatively [eq. (2)].

$$PhNO_2 + 3H_2Se \rightarrow PhNH_2 + 2H_2O + 3Se \quad (2)$$

Experimental

Freshly distilled nitrobenzene (1.23 g, 10 mmol), water (0.63 g, 35 mmol), metallic selenium (0.016 g, 0.2 mmol), and triethylamine (2.02 g, 20 mmol) in tetrahydrofuran (THF) (20 ml) are placed with magnetic stirring bar in a 50-ml stainless steel autoclave. The apparatus is then flushed several times with CO and charged with CO at 30 bar. The reaction is conducted at 80 °C for 5 h with vigorous stirring. After the reaction, CO is released and air is introduced into the reaction mixture to precipitate selenium. Filtration followed by evaporation gives a mixture of products shown by GLC analyses to contain aniline (0.80 g, 8.6 mmol) and diphenylurea (0.068 g, 0.34 mmol).

Received: July 1, 1980 [Z 625 b IE]
German version: Angew. Chem. 92, 1040 (1980)

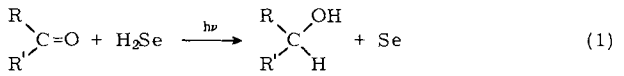
[*] Prof. Dr. N. Sonoda [†], Dr. K. Kondo, Prof. Dr. S. Murai
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)
Dr. T. Hirashima, T. Miyata
Osaka Municipal Technical Research Institute
2-1-1, Oogimachi, Kita-ku, Osaka 530 (Japan)
[†] Author to whom correspondence should be addressed.

[1] A new system utilizing the reducing ability of carbon monoxide, Part 3.—Part 2: *N. Kambe, F. Morimoto, K. Kondo, N. Sonoda*, Angew. Chem. 92, 1040 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1007 (1980).
[2] *A. F. M. Iqbal*, Tetrahedron Lett. *1971*, 3385.
[3] *K. Cann, T. Cole, W. Slegeir, R. Pettit*, J. Am. Chem. Soc. *100*, 3969 (1978).
[4] *K. Kondo, N. Sonoda, S. Tsutsumi*, J. Chem. Soc. Chem. Commun. *1972*, 307.
[5] *K. Kondo, N. Sonoda, H. Sakurai*, J. Chem. Soc. Chem. Commun. *1973*, 853.
[6] *N. Sonoda, K. Kondo, K. Nagano, N. Kambe, F. Morimoto*, Angew. Chem. *92*, 317 (1980); Angew. Chem. Int. Ed. Engl. *19*, 308 (1980).

Photoreduction of Ketones and Aldehydes to Alcohols with Hydrogen Selenide[**]

By *Nobuaki Kambe, Kiyoshi Kondo, Shinji Murai,* and *Noboru Sonoda*[*]

Among the various photoreactions[1] of carbonyl compounds, the photoreduction of aldehydes and ketones is one of the best understood and, with few exceptions[2], usually affords 1,2-dihydroxy compounds[3]. We now wish to report the photoreaction of ketones and aldehydes with hydrogen selenide, H_2Se to give alcohols and selenium [eq. (1)].



$$\text{R, R'}{>}C{=}O + H_2Se \xrightarrow{h\nu} \text{R, R'}{>}C(OH)H + Se \quad (1)$$

Table 1. Reaction times and yields of photoreduction of carbonyl compounds according to eq. (1).

Carbonyl compound	t [h]	Yield [%]
Benzophenone	2	78 [a]
Acetophenone	0.33	98
Benzaldehyde	0.5	92
Cyclohexanone	18	93
Acetone	27	81
Cyclohexanecarbaldehyde	13	80
2-Acetonaphthone	3	70

[a] Accompanied by 7% of 1,1,2,2-tetraphenyl-1,2-ethanediol.

The photoreduction is achieved by irradiation of the substrates in tetrahydrofuran (THF) in a Pyrex reaction tube (15 °C/N_2); yields are good (Table 1).

The reduction of aryl-substituted carbonyl compounds proceeds more rapidly than that of alkyl-substituted carbonyl compounds. The following observations are important in relation to the mechanism of the early stage of this reduction. (i) H_2Se in THF has no absorption band in the 300–800 nm region; (ii) irradiation of H_2Se in the absence of carbonyl compounds in the same reaction apparatus used for the photoreduction causes no apparent change; (iii) acetophenone undergoes much slower photoreduction in the presence of diphenyl as a triplet quencher; (iv) 2-acetonaphthone, which is known to give π-π^* triplet on photoexcitation[2c,4], is reduced by H_2Se to 1-(2-naphthyl)ethanol in 70% yield (Table 1).

[*] Prof. Dr. N. Sonoda [†], N. Kambe, Dr. K. Kondo, Prof. Dr. S. Murai
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)
[†] Author to whom correspondence should be addressed.

[**] Photoreaction of hydrogen selenide, Part 1.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1008 $ 02.50/0

Experimental

1-Phenylethanol: A well-degassed THF solution (3 ml) of acetophenone (30 mg, 0.25 mmol) in a Pyrex reaction tube is irradiated for 20 min by high-pressure mercury lamp (300 W) in the presence of H_2Se (0.45 mmol); selenium starts to deposit immediately. After oxidation of remaining H_2Se by introducing air into the reaction mixtures, metallic selenium is filtered off. The yield of 1-phenylethanol is 98% (GC and ^{1}H-NMR analyses).

Received: June 2, 1980 [Z 625c IE]
German version: Angew. Chem. 92, 1041 (1980)

[1] *N. J. Turro:* Modern Molecular Photochemistry. Benjamin/Cummings Publ. Corp., Menlo Park, California 1978.

[2] a) *W. E. Bachmann*, J. Am. Chem. Soc. *55*, 391 (1933); b) *S. G. Cohen, W. V. Sherman, ibid. 85*, 1642 (1963); c) *G. S. Hammond, P. A. Leermakers, ibid. 84*, 207 (1962).

[3] *G. Ciamician, P. Silber*, Ber. Dtsch. Chem. Ges. *33*, 2911 (1900); *34*, 1530 (1901); *J. N. Pitts, Jr., R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald, R. B. Martin*, J. Am. Chem. Soc. *81*, 1068 (1959); *W. M. Moore, G. S. Hammond, R. P. Foss, ibid. 83*, 2789 (1961); *G. S. Hammond, W. P. Barker, W. M. Moore, ibid. 83*, 2795 (1961); *A. Beckett, G. Porter*, Trans. Faraday Soc. *59*, 2038 (1963); *N. C. Yang, S. Murov*, J. Am. Chem. Soc. *88*, 2852 (1966).

[4] *S. G. Cohen, G. A. Davis, W. D. K. Clark*, J. Am. Chem. Soc. *94*, 867 (1972).

Reduction of Carbonyl Compounds by Aluminum Telluride and H_2O or D_2O

By *Nobuaki Kambe, Kiyoshi Kondo, Satoru Morita, Shinji Murai*, and *Noboru Sonoda*[*]

Our studies on tellurium-catalyzed reaction of amines and carbon monoxide[1] led us to investigate hydrogen telluride as a potential intermediate. We found hydrogen telluride to have unique reducing ability toward carbonyl compounds. Thus reduction of benzaldehyde with hydrogen telluride proceeds at 0 °C under nitrogen to produce benzyl alcohol [eq. (1)].

$$PhCHO + H_2Te \xrightarrow{N_2,\ 0\,^\circ C} PhCH_2OH + Te \qquad (1)$$

Since the use of thermally unstable, air- and light-sensitive, gaseous hydrogen telluride requires troublesome experimental procedures, a convenient method has been developed for its *in situ* generation from aluminum telluride and water [eq. (2), Table 1].

$$\begin{matrix} R \\ \diagdown \\ C{=}O \\ \diagup \\ R' \end{matrix} + 1/3\ Al_2Te_3 + 2\ H_2O \longrightarrow \begin{matrix} R & H \\ \diagdown & \diagup \\ C & \\ \diagup & \diagdown \\ R' & OH \end{matrix} + Te + 2/3\ Al(OH)_3 \qquad (2)$$

Table 1. Isolated yields on reduction of carbonyl compounds with Al_2Te_3/H_2O (D_2O) [a].

Reactant	Product	Yield [%]
Benzaldehyde	Benzyl alcohol	100
Benzaldehyde	α, *O*-Dideuteriobenzyl alcohol	100
o-Methylbenzaldehyde	*o*-Methylbenzyl alcohol	86 [b]
n-Octanal	*n*-Octyl alcohol	50
Cyclohexanone	Cyclohexyl alcohol	51 [c]

[a] Reaction conditions, see *Experimental*. [b] 1 mmol of Al_2Te_3 per mmol of reactant. [c] 6 mmol of Al_2Te_3 per mmol of reactant, 66 °C, 5 h.

[*] Prof. Dr. N. Sonoda, Dr. K. Kondo [+], N. Kambe, S. Morita, Prof. Dr. S. Murai
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)
[+] Author to whom correspondence should be addressed.

The applicability of D_2O as deuterium source in the present reduction system is of vital importance, since all other deuterating reducing agents are extremely expensive. It is noteworthy that the reduction of α,β-unsaturated carbonyl compounds by H_2Te, generated *in situ*, proceeds in a highly selective manner[2] to the CC double bond [eq. (3), Table 2]; no allylic alcohols are detected in the products.

$$PhCH{=}CH{-}\overset{O}{\overset{\|}{C}}{-}R \xrightarrow[H_2O]{Al_2Te_3} PhCH_2{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}R \qquad (3)$$

Table 2. Isolated yields on the reduction of α,β-unsaturated carbonyl compounds with Al_2Te_3/H_2O.

R	Reactant: Al_2Te_3	*T* [°C]	*t* [h]	Yield [%] [a]
H	1:2	−15	0.3	89 (96)
Me	1:2	0	1	75 (90) [b]
Me	1:6	0	5	54 [c]
Ph	1:4	0	6	84

[a] Isolated yields; values in parentheses are yields determined by GLPC. [b] Accompanied by 2% of 4-phenyl-2-butanol (GLPC). [c] Together with 21% of 4-phenyl-2-butanol.

Experimental

A) Reduction of benzaldehyde with H_2Te[3]: H_2Te generated in a separate flask by the addition of a large excess of H_2O (2 ml) to Al_2Te_3 (2.19 g, 5 mmol) at 25 °C is introduced by a gentle stream of nitrogen into the reaction flask containing benzaldehyde (106 mg, 1 mmol) and tetrahydrofuran (THF, 10 ml) at 0 °C. Tellurium begins to deposit immediately. After 5 min, tellurium (0.29 mmol) is recovered by filtration, and the filtrate is shown by GLPC to contain benzyl alcohol (0.33 mmol) and benzaldehyde (0.67 mmol).

B) Reduction of benzaldehyde by Al_2Te_3/D_2O: D_2O (0.22 ml, 12 mmol) is added at −78 °C to a suspension of Al_2Te_3 (876 mg, 2 mmol) in THF (10 ml) containing benzaldehyde (106 mg, 1 mmol) with vigorous stirring. The temperature is raised to 0 °C in 30 min and maintained there for another 2 h. Filtration followed by evaporation of the solvent leaves essentially pure PhCHDOD (110 mg, 1.0 mmol) quantitatively.

Received: March 4, 1980 [Z 625d IE]
German version: Angew. Chem. 92, 1041 (1980)

[1] *N. Kambe, K. Kondo, H. Ishii, S. Murai, N. Sonoda*, Angew. Chem. *91*, 582 (1979); Angew. Chem. Int. Ed. Engl. *18*, 547 (1979).

[2] *L. Mordenti, J. J. Brunet, P. Caubere*, J. Org. Chem. *44*, 2203 (1979); *J. P. Collman, R. G. Finke, P. L. Matloch, R. Wahren, R. G. Komoto, J. I. Brauman*, J. Am. Chem. Soc. *100*, 1119 (1978); *M. F. Semmelhack, R. D. Stauffer, A. Yamashita*, J. Org. Chem. *42*, 3180 (1977); *R. Noyori, I. Umeda, T. Ishigami*, J. Org. Chem. *37*, 1542 (1972).

[3] *L. M. Dennis, R. P. Anderson*, J. Am. Chem. Soc. *36*, 882 (1914).

Reduction of Aromatic Nitro, Nitroso, Hydroxylamino, Azo, and Azoxy Compounds with Hydrogen Telluride from Aluminum Telluride and Water

By *Nobuaki Kambe, Kiyoshi Kondo*, and *Noboru Sonoda*[*]

Reagents for the reduction of aromatic nitro compounds to the corresponding amines by classical methods (catalytic hydrogenation, Clemmensen type reductions, Birch reduction)

[*] Prof. Dr. N. Sonoda [+], N. Kambe, Dr. K. Kondo
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Osaka 565 (Japan)
[+] Author to whom correspondence should be addressed.

have recently been supplemented by selenophenol[1] and transition metal hydrides[2]. Reaction with typical hydride reagents such as $LiAlH_4$[3], $LiAl(OR)_3H$[3], and $NaBH_4$[4] are usually sluggish.

In this paper we wish to report that hydrogen telluride[5] generated *in situ* has a high reducing ability toward nitroarenes [Table 1, eq. (1)].

$$ArylNO_2 + Al_2Te_3 + 4H_2O \rightarrow ArylNH_2 + 2Al(OH)_3 + 3Te \quad (1)$$

Table 1. Yields obtained in the reduction of some aromatic nitrogen compounds with Al_2Te_3/H_2O; for reaction conditions, see *Experimental*.

Reactant	Ar—NH_2 Yield [%]	Ar—NHNH—Ar Yield [%]
$C_6H_5NO_2$	90	trace
$C_6H_5NO_2$	63 [a]	[b]
$C_6H_5NO_2$	45 [c]	[b]
p-$MeC_6H_4NO_2$	92	[b]
m-$MeC_6H_4NO_2$	94	[b]
p-$ClC_6H_4NO_2$	60	[b]
p-$BrC_6H_4NO_2$	47	[b]
p-$MeOC_6H_4NO_2$	60	[b]
C_6H_5NO	16	63
C_6H_5NHOH	98	1
$C_6H_5N{=}NC_6H_5$ [d]	4	96
$C_6H_5N{=}N(O)C_6H_5$ [d]	6	86

[a] $T = 20\,^{\circ}C$. [b] Not determined. [c] $T = -15\,^{\circ}C$. [d] 0.5 mmol of reactant.

It is noteworthy that nitrosobenzene gives hydrazobenzene as a major product while phenylhydroxylamine yields aniline quantitatively. This result might be taken to suggest that nitrosobenzene is not the intermediate in the reduction of nitrobenzene to aniline. Alternatively, however, the intermediacy of nitrosobenzene in the reduction of nitrobenzene is accommodated, if transiently formed nitrosobenzene undergoes rapid further reduction to give phenylhydroxylamine before the condensation[6] with phenylhydroxylamine. The reductions of both azoxybenzene and azobenzene by H_2Te afford good yields of hydrazobenzene, indicating that neither the azo nor the azoxy compound is the probable intermediate in the reduction of nitrobenzene.

Experimental

Powdered Al_2Te_3 (674 mg, 2 mmol), stored under N_2 in the dark, is added to a tetrahydrofuran (10 ml) solution of nitrobenzene (123 mg, 1 mmol) under N_2 at room temperature. Then the temperature is raised to 66 °C. To the vigorously stirred reaction mixture is slowly added an excess of water (0.43 ml, 24 mmol) dropwise by a syringe over a period of 40 min. The reaction mixture is refluxed for another 20 min and worked up. The yield of aniline is 90% (GC, ^{1}H-NMR, and IR).

Received: August 11, 1980 [Z 625e IE]
German version: Angew. Chem 92, 1042 (1980)

[1] *K. Fujimori, H. Yoshimoto, S. Oae*, Tetrahedron Lett. *1979*, 4397.
[2] *K. Cann, T. Cole, W. Slegeir, R. Pettit*, J. Am. Chem. Soc. *100*, 3969 (1978). *A. F. M. Iqbal*, Tetrahedron Lett. *1971*, 3385.
[3] *R. F. Nystrom, W. G. Brown*, J. Am. Chem. Soc. *70*, 3738 (1948); *M. L. Burstall, M. S. Gibson*, J. Chem. Soc. *1958*, 3745; *H. C. Brown, P. M. Weissman*, J. Am. Chem. Soc. *87*, 5614 (1965); *H. C. Brown, P. M. Weissman, N. M. Yoon, ibid. 88*, 1458 (1966); *H. C. Brown, S. Krishnamurthy*, Tetrahedron *35*, 567 (1979).
[4] *R. O. Hutchins, D. W. Lamson, L. Rua, C. Milewski, B. Maryanoff*, J. Org. Chem. *36*, 803 (1971); *J. O. Morley*, Synthesis *1976*, 528.
[5] *N. Kambe, K. Kondo, S. Morita, S. Murai, N. Sonoda*, Angew. Chem *92*, 1041 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1009 (1980).
[6] Nitrosobenzene condenses with phenylhydroxylamine under the present reaction conditions in the absence of H_2Te to azoxybenzene in quantitative yield.

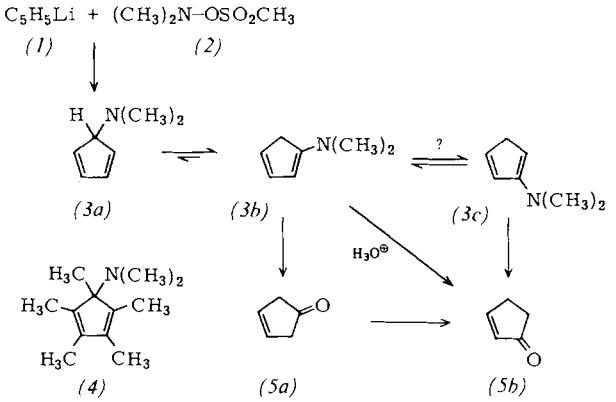
Electrophilic Amination of Cyclopentadienyllithium Compounds[**]

By *Michael Bernheim* and *Gernot Boche*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

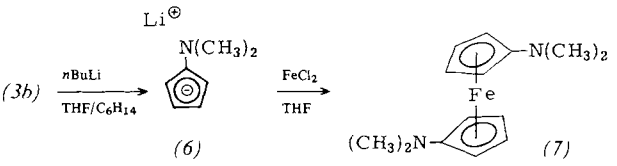
Although cyclopentadienyl compounds have found extraordinarily wide application as ligands of organometallic complexes and as synthons for natural products, *e.g.* prostaglandins, virtually nothing is known about cyclopentadienylamines[1]. We report here on the entry to this class of compounds by electrophilic amination of cyclopentadienyllithium compounds.

Reaction of cyclopentadienyllithium *(1)*[2] with *N,N*-dimethyl-*O*-(methylsulfonyl)hydroxylamine *(2)*[3] in tetrahydrofuran (THF) at −20 °C afforded *N,N*-dimethyl-1,3-cyclopentadienylamine *(3b)* in 47% yield (see Procedure).



From the ^{1}H-NMR spectrum of the $ABCX_2$-type [($CDCl_3$); $\delta = 2.90$ (s; 6H, $N(CH_3)_2$); 3.15 (m; 2H, H^5); 5.12 (mc; 1H, H^2); 5.77 (mc; 1H, H^4); 6.57 (mc; 1H, H^3)] it follows that the primary product of the amination *(3a)* is not present. An analysis of the apparently simple line shapes with the automatic program DAVINS[4] enabled assignment in favor of the isomer with the dienamine constitution *(3b)*[5]. Hydrolysis with a phosphate buffer (pH = 2) confirmed the spectral finding: Whereas *(3c)* should give exclusively 2-cyclopenten-1-one *(5b)*, a 94:6 mixture of 3-cyclopenten-1-one *(5a)* and *(5b)* is formed in 65% yield from *(3b)*[6,9]. It is still unclear whether the *(5b)*-part was formed from *(3b)*, *(3c)*, or by acid-catalyzed isomerization of *(3a)*[7].

Reaction with pentamethylcyclopentadienyllithium[10,2] instead of *(1)* affords *N,N*,1,2,3,4,5-heptamethyl-1,4-cyclo-



[*] Prof. Dr. G. Boche, Dipl.-Chem. M. Bernheim
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)
New address: Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1010 $ 02.50/0

pentadienylamine *(4)* in 40% yield. In contrast to *(3a)*, *(4a)* cannot easily isomerize.

When a solution of *(3b)* in THF is allowed to react with *n*-butyllithium in hexane at −30 °C, the colorless *N,N*-dimethylaminocyclopentadienyllithium *(6)* precipitates out in almost quantitative yield [^{1}H-NMR ([D$_6$]-DMSO): $\delta = 4.90$ (mc; AA'BB' type; 4H, H^2—H^5); 2.40 (s; 6H, N(CH$_3$)$_2$)]. *(6)* is the first amino-substituted cyclopentadienide compound; it can be employed, *e.g.*, for the preparation of metallocenes. Thus, reaction with $FeCl_2$ in THF affords the dark-orange bis(dimethylamino)ferrocene *(7)*, m.p. 63—65 °C, in 55% yield [^{1}H-NMR ($CDCl_3$): $\delta = 2.55$ (s; 12H, N(CH$_3$)$_2$), 3.95 (mc, AA'BB' type; 8H, H^2—H^5, and H$^{2'}$—H$^{5'}$)]. To our knowledge, bis(dimethylamino) compounds of type *(7)* were hitherto unknown. We are currently investigating the chemistry of *(3b)* and *(6)*.

Procedure

A solution of *(2)* (4.17 g, 30.0 mmol) in THF (15 ml) was added at −20 °C to a solution of *(1)* [prepared from cyclopentadiene (2.52 ml, 30 mmol) and *n*-BuLi (20.1 ml, 30 mmol)] in THF (30 ml). After *ca.* 10 min the reaction solution turns cloudy. After 30 minutes' stirring at −20 °C the solvent was removed in a high vacuum at −20 °C and the residue digested with cold pentane. After filtration at −35 °C the pentane solution of *(3b)* was evaporated down in a high vacuum at −20 °C. There remained 1.53 g (47%) of a pale yellow oil. *(3b)* is extremely sensitive towards oxygen and water and decomposes within a few days even in the absence of air and moisture at −30 °C. MS (70 eV, direct sample introduction): $m/e = 109$ (100%, M^+), 108 (43), 94 (39, $M^+ - CH_3$), 58 (57), $(CH_3)_2N{=}CH_2^+$), 44 (74, $N(CH_2)_2^+$).

(6): A solution of *(3b)* (1.35 g, 12.4 mmol) in THF (10 ml) was treated at −30 °C with a solution of *n*-BuLi (10.0 ml, 15.0 mmol) in hexane, whereupon colorless *(6)* precipitated within 2 min. After 1 hours' stirring at −30 °C, *(6)* was filtered off under N_2 at room temperature, washed with pentane and dried in a high vacuum—the product turned light-brown in color. 1.32 g (93%) of *(6)* (dec. point 160 °C) was recovered. It immediately decomposes in air, but can be stored for weeks in a refrigerator in the absence of air.

Received: August 1, 1980 [Z 626 IE]
German version: Angew. Chem. *92*, 1043 (1980)

[1] To our knowledge only two examples have been previously described in the literature: *N*-(3,4-diphenyl-1,3-cyclopentadienyl)pyrrolidine (*H. W. Thompson, B. S. Huegi*, J. Chem. Soc. Perkin Trans. I *1976*, 1603) and a *N,N*-bis(trimethylsilyl)cyclopentadienylamine (*H. Bayer*, Dissertation, Universität München 1979).

[2] *A. Davison, P. E. Rakita*, Inorg. Chem. *9*, 289 (1970).

[3] Instead of *(2)*, m.p. 33—35 °C, also *N,N*-dimethyl-*O*-(diphenylphosphinyl)hydroxylamine, m.p. 128—130 °C, and *N,N*-dimethyl-*O*-(diphenoxyphosphoryl)hydroxylamine, m.p. 45—47 °C, may be used. The three reagents were obtained in analogy to the procedure quoted in *G. Boche, N. Mayer, M. Bernheim, K. Wagner*, Angew. Chem. *90*, 733 (1978); Angew. Chem. Int. Ed. Engl. *17*, 687 (1978).

[4] *D. S. Stephenson, G. Binsch*, Quantum Chem. Prog. Exch. *11*, 378 (1979); J. Magn. Reson. *37*, 395 (1980).

[5] *D. S. Stephenson, M. Bernheim, G. Boche*, Org. Magn. Reson., in press.

[6] The ratio *(5a)*:*(5b)* was determined IR spectroscopically (error +5%). *(5a)*: $\tilde{\nu} = 1750$ cm^{-1} (C=O) [7]; *(5b)*: $\tilde{\nu} = 1710$ cm^{-1} (C=O) [8].

[7] *D. L. Whalen, J. F. Weimaster, A. M. Ross, R. Radhe*, J. Am. Chem. Soc. *98*, 7319 (1976).

[8] *C. J. Pouchert:* The Aldrich Library of Infrared Spectra. Aldrich Chemical Company, Milwaukee, Wisconsin 1970, p. 203.

[9] In the preparation of *(5a)* according to *H. M. Hess, H. C. Brown*, J. Org. Chem. *32*, 4138 (1968), *(5a)* and *(5b)* were formed in the ratio 3:1. Pd-catalyzed synthesis of *(5a)*: *M. Suzuki, Y. Oda, R. Noyori*, J. Am. Chem. Soc. *101*, 1623 (1979).

[10] *R. S. Threlkel, J. E. Bercaw*, J. Organomet. Chem. *136*, 1 (1977).

Chemo- and Diastereoselective Addition of Alkyl- and Aryltitanium(IV) Compounds to Aldehydes and Ketones[**]

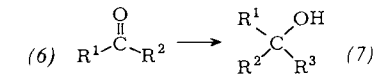
By *Manfred T. Reetz, Rainer Steinbach, Jürgen Westermann*, and *Roland Peter*[*]

The addition of Grignard and alkyllithium reagents to carbonyl compounds is one of the important methods for C—C bond formation. However, it is known that aldehydes and ketones frequently react equally fast, thereby thwarting chemoselectivity[1], and that diastereoselectivity is limited[2]. As part of our studies concerning the use of alkyl- and aryltitanium(IV) compounds in organic synthesis[3], we have discovered that they (i) add smoothly to aldehydes and ketones, (ii) react with aldehydes faster than with ketones, and (iii) show high diastereoselectivity.

The reaction of methyltitanium trichloride *(1)*, dimethyltitanium dichloride *(2)*, methyltitanium triisopropoxide *(3)*, diphenyltitanium dichloride *(4)*, or phenyltitanium triisopropoxide *(5)* with carbonyl compounds *(6)* affords the alcohols *(7)* (Table 1)[4].

CH_3TiCl_3 *(1)* $(CH_3)_2TiCl_2$ *(2)* $CH_3Ti[OCH(CH_3)_2]_3$ *(3)*

(4) $(C_6H_5)_2TiCl_2$ $C_6H_5Ti[OCH(CH_3)_2]_3$ *(5)*



(6) → *(7)*

Table 1. Alcohols *(7)* by addition of titanium reagents *(1)*—*(5)* [4] to aldehydes and ketones *(6)* in dichloromethane.

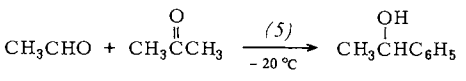
Reactant	R^1	R^2	Titanium reagent [a]	*T* [°C]	*t* [h]	R^3	Product	Yield [%] [b]
(6a)	*n*Pr	H	*(2)*	−40	1	Me	*(7a)*	>90
(6b)	*i*Bu	H	*(1)*	−30	0.5	Me	*(7b)*	>90
(6b)	*i*Bu	H	*(3)*	0	0.5	Me	*(7b)*	>90
(6c)	*c*Hex	H	*(1)*	−40	0.5	Me	*(7c)*	>90
(6c)	*c*Hex	H	*(2)*	−40	1	Me	*(7c)*	≈95 (78)
(6c)	*c*Hex	H	*(3)*	22	0.5	Me	*(7c)*	≈95
(6c)	*c*Hex	H	*(4)*	−78	0.5	Ph	*(7d)*	>90
(6c)	*c*Hex	H	*(5)*	−10	1	Ph	*(7d)*	≈95 (84)
(6d)	—(CH$_2$)$_5$—		*(2)*	−30	0.3	Me	*(7e)*	≈95 (82)
(6e)	Me	*n*Pent	*(3)*	22	48	Me	*(7f)*	0

[a] In the reaction of *(2)* or *(4)* with aldehydes either 1:1 or 0.5:1 mixtures can be used, since both methyl or phenyl groups are transferred. In case of ketones 1:1 ratios are necessary. [b] Not optimized; the numbers given refer to conversion determined by NMR spectroscopy or gas chromatography. The values in brackets refer to isolated products.

Complete chemoselectivity is observed in the reaction of *(1)* or *(3)* with a 1:1 mixture of 3-methylbutyraldehyde *(6b)* and 2-heptanone *(6e)*. In each case the aldehyde adduct *(7b)* is the *sole* product (≈95% conversion). Similarly, *(5)* reacts with a 1:1 mixture of acetaldehyde *(8)* and acetone *(9)* to yield *(10)* (>90%) as the only addition product. In case of phenylmagnesium bromide a 1.5:1 mixture of *(10)* and $(CH_3)_2C(OH)C_6H_5$ is known to arise[5].

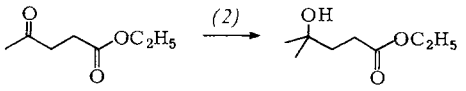
[*] Prof. Dr. M. T. Reetz, Dipl.-Chem. R. Steinbach, Dipl.-Chem. J. Westermann, R. Peter
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.



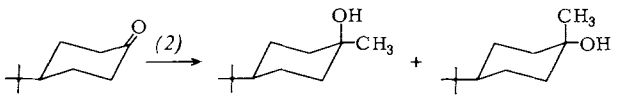
(8) (9) (10)

The reaction of levulinic acid ethyl ester *(11)* with *(2)* affords *(12)* (>90% conversion[6]), demonstrating that in such cases C—C bond formation occurs preferentially at the keto function.



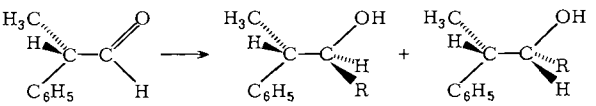
(11) (12)

Initial studies regarding diastereoselectivity in the addition of *(2)* to cyclic ketones were performed with 4-*tert*-butylcyclohexanone *(13)*. At −78 °C a mixture of the axial and equatorial alcohol *(14)* and *(15)* in a ratio of 82:18 (yield 92%) is formed. This is by far the best synthesis of *(14)*, since methylmagnesium bromide[7], dimethylmagnesium[7], and methyllithium[8] afford *(14)* and *(15)* with product ratios of only 60:40, 65:35, and 65:35, respectively.



(13) (14) (15)

The possibility of asymmetric induction in the addition of *(1)*—*(4)* to 2-phenylpropionaldehyde *(16)* was also investigated (Table 2). According to *Cram*, methyl- and phenylmagnesium halide[9] lead to the alcohols *(17a, b)* and *(18a, b)* with product ratios of 66:34 and ≈4:1, respectively[5]. Whereas *(4)* does not lead to an improvement (see Table 2), the diastereoselectivity in the addition of *(1)*, *(2)*, and *(3)* is remarkably high [*(17a)*:*(18a)* as 81:19, 80:20, and 88:12, respectively]. Such high values have not been previously found with any other organometallic compound[2,10]. A switch in solvent from dichloromethane to tetrahydrofuran has essentially no influence on the diastereoselectivity (Table 2).



(16) (17) (18)

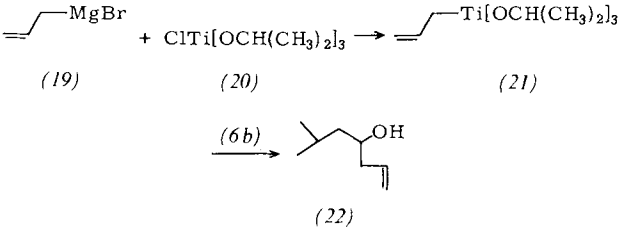
(a), R = CH_3; *(b)*, R = C_6H_5

Table 2. Diastereoselectivity in the addition of titanium reagents *(1)*—*(4)* to 2-phenylpropionaldehyde *(16)* to form the alcohols *(17)* and *(18)*.

Titanium reagent	*T* [°C]	*t* [h]	Solvent	*(17)*:*(18)* [a]	R
(1)	−78	2	CH_2Cl_2	81:19	Me
(2)	−78	1	CH_2Cl_2	80:20	Me
(2)	−96	2	CH_2Cl_2	82:18	Me
(3)	[b]	4	CH_2Cl_2	88:12	Me
(3)	−10	2	CH_2Cl_2	85:15	Me
(3)	0	2	THF	88:12	Me
(4)	−78	0.5	CH_2Cl_2	80:20	Ph

[a] In all reactions, the conversion was >90%. [b] The reaction mixture was gradually allowed to warm up from −40 °C to 0 °C.

Finally, we note that a one-pot procedure starting from Grignard reagents is possible. For example, quenching allylmagnesium bromide *(19)* with chlorotitanium triisopropoxide *(20)* in tetrahydrofuran affords *(21)*[11], which reacts with 3-methylbutyraldehyde to form *(22)* (60% isolated).



(19) (20) (21) (22)

Typical procedure:

A cooled solution (−50 °C) of 2-phenylpropionaldehyde *(16)* (2.7 g, 20 mmol) in 50 ml of dry CH_2Cl_2 is added dropwise within 20 min to a mixture of dimethyltitanium dichloride *(2)*[4] (20 mmol) in CH_2Cl_2 (100 ml). After 1 h the mixture is poured onto ice water and treated with dilute HCl until the precipitate has dissolved. The organic phase is separated and aqueous phase extracted 3 times with CH_2Cl_2. The combined organic phases are dried over magnesium sulfate and the solvent removed. The crude product is studied by gas chromatography [*(17a)*:*(18a)* = 80:20] and distilled with a kugelrohr (80 °C/1 torr): 2.45 g (82%) of *(17a)*/*(18a)*[9].

Received: October 27, 1980 [Z 627 IE]
German version: Angew. Chem. *92*, 1044 (1980)

[1] *K. Nützel* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie. 4th ed., Thieme, Stuttgart 1973, Vol. 13/2a, p. 290.
[2] *J. Morrison, H. S. Mosher:* Asymmetric Organic Reactions, Prentice-Hall, Englewood Cliffs, New Jersey 1971, pp. 84ff.
[3] *M. T. Reetz, J. Westermann, R. Steinbach*, Angew. Chem. *92*, 931, 933 (1980); Angew. Chem. Int. Ed. Engl. *19*, 900, 901 (1980).
[4] *(1)*—*(5)* can be synthesized from the usual organometallic precursors and $TiCl_4$ or chlorotitanium triisopropoxide, respectively: *A. Segnitz* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie. 4th ed., Thieme, Stuttgart Vol. 13/7, 1975, pp. 261ff. In the case of *(1)*, *(2)*, and *(4)* we used Me_2Zn and Ph_2Zn and the corresponding amount of $TiCl_4$ in CH_2Cl_2.
[5] Only one enantiomeric form of the racemate is shown.
[6] Upon distilling a portion of *(12)* is converted in the corresponding lactone.
[7] *H. O. House, W. L. Respess*, J. Org. Chem. *30*, 301 (1965).
[8] *W. J. Houlihan*, J. Org. Chem. *27*, 3861 (1962).
[9] *D. J. Cram, F. A. Abd Elhafez*, J. Am. Chem. Soc. *74*, 5828 (1952); slightly higher values are obtained depending upon the nature of the halogen in the Grignard reagent: *Y. Gault, H. Felkin*, Bull. Soc. Chim. Fr. *1960*, 1342.
[10] Our own experiments using a 1:1 mixture of Me_2Zn and $AlCl_3$ at −50 °C lead to *(17a)*/*(18a)* ratios of only 2:1.
[11] The precise nature of *(21)* in this reaction medium is not known since magnesium salts are present.

Thermal Rearrangement of Tetrakis(phenylimino)cyclobutane and Crystal Structure of Tetraphenylsquaramidine

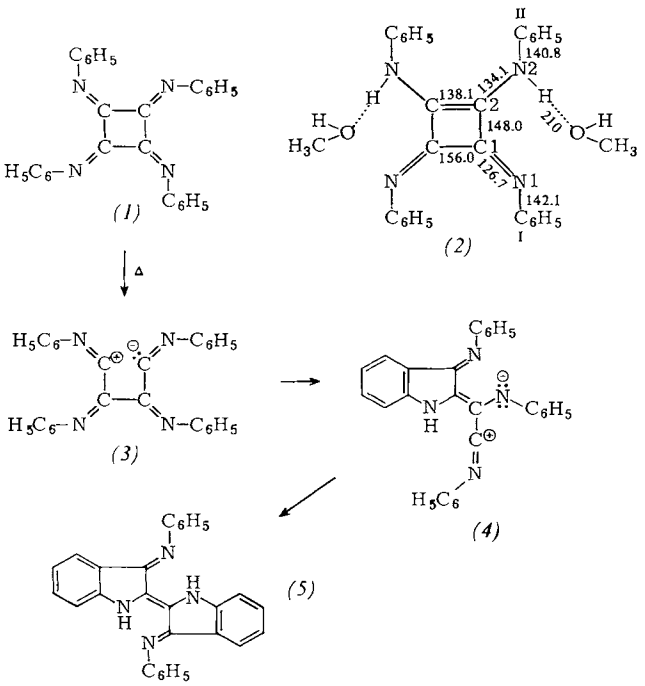
By *Hans Jürgen Bestmann, Eberhard Wilhelm,* and *Günter Schmid*[*]

We recently reported the synthesis and crystal structure of tetrakis(phenylimino)cyclobutane (tetrameric phenyl isocyanide *(1)*[1]), which is readily reduced to tetraphenylsquaramidine *(2)* by alcohols. We have now found that besides polymeric phenyl isocyanide[2], also the blue indigo dianil *(5)*[3]

[*] Prof. Dr. H. J. Bestmann, Dr. E. Wilhelm, Dr. G. Schmid
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1012 $ 02.50/0

(m. p. 296—297 °C (dec.)), is formed on heating *(1)* to 150—200 °C in a high vacuum. One possible mechanism of rearrangement of *(1)* to *(5)* involves initial cleavage of a C—C bond in the cyclobutane ring to give *(3)*, which is then converted by twofold intramolecular, electrophilic aromatic substitution *via* the intermediate *(4)*, describable by several mesomeric forms, to *(5)*[4].



Furthermore, we have found that squaramidine *(2)* crystallizes from methanol with 2 moles of solvent of crystallization. According to X-ray structure analysis[5] the bond lengths and angles in the four-membered ring are comparable with those in other cyclobutene derivatives[6]. The four-membered ring, unlike that in *(1)*, is not completely planar. The greatest distance from the optimum plane is 6 pm for C2. The atom N1 lies 22 pm above, the atom N2 17 pm below this plane. If the nitrogen atoms are included in the calculation of the optimum plane, comparable values are obtained.—The C2—N2 bond is markedly shorter than a C—N single bond (average value 147 pm) and lies in the region of the C—N bond length in pyridine.

The phenyl groups are oriented at angles of 42° (phenyl I) and 34° (phenyl II), respectively, to the optimum plane of the four-membered ring. The two non-equivalent phenyl groups are at an angle of 70° to each other, while the two equivalent phenyl groups are almost parallel.

The two methanol molecules are oriented almost perpendicularly to the plane of the four-membered ring. The distance between H1 and O (210 pm) is indicative of hydrogen bonding. Owing to the C_2 symmetry the tetraphenylsquaramidine·2 methanol molecule has the structure given in Figure 1, suggesting the designation "man on the moon" molecule.

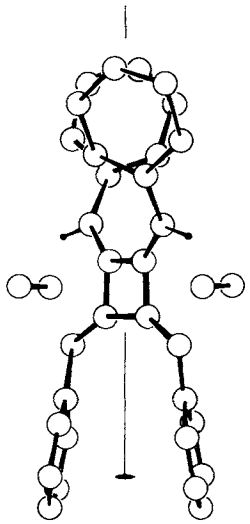


Fig. 1. Structure of *(2)*·CH_3OH in the crystal[5]. Bond lengths [pm], see Formula *(2)*.

Received: July 25, 1980 [Z 628 IE]
German version: Angew. Chem 92, 1045 (1980)

[1] *H. J. Bestmann, G. Schmid, E. Wilhelm,* Angew. Chem. *92*, 134 (1980); Angew. Chem. Int. Ed. Engl. *19*, 136 (1980).
[2] *W. Drenth, R. J. M. Nolte,* Acc. Chem. Res. *12*, 30 (1979).
[3] Elucidation of structure: *C. Grundmann,* Chem. Ber. *91*, 1380 (1958).
[4] For a similar ring-closure reaction see: *H. J. Bestmann, G. Schmid, R. Böhme, E. Wilhelm, H. Burzlaff,* Chem. Ber., in press.
[5] *(2)*·$2CH_3OH$, orange-red crystals from methanol, space group $C2/c\text{-}C_{2h}^6$, $a = 1247.5$, $b = 1384.3$, $c = 1489.3$ pm, $\beta = 90.18°$, $Z = 4$, 1928 structure factors. From $Z = 4$ it follows that the molecule must occupy a special position. In this space group, fourfold special positions are the symmetry centers and the twofold axes, of which the latter are compatible with the expected molecular structure. The structure was solved with the program system CRYSTAN [7] and refined to $R = 0.113$.
[6] *Y. Wang, G. D. Stucky, J. M. Williams,* J. Chem. Soc. Perkin Trans. II *1974*, 35; *D. Belluš, H. C. Mez, G. Rihs, ibid. 1974*, 884; *D. Semmingsen,* Tetrahedron Lett. *1973*, 807; *R. Mattes, S. Schroebler,* Chem. Ber. *105*, 3761 (1972); *C. H. Wong, R. E. Marsh, V. Schomaker,* Acta Crystallogr. *17*, 131 (1964); *I. L. Karle, K. Britts, S. Brenner, ibid. 17*, 1506 (1964); *E. Benedetti, M. R. Ciajolo, J. P. Declercq, G. Germain, ibid. B30*, 2873 (1974).
[7] *H. Burzlaff, R. Böhme, M. Gomm:* CRYSTAN: a crystallographic program system for minicomputers (1977). Institut für Angewandte Physik, Lehrstuhl für Kristallographie, Loewenichstrasse 22, D-8520 Erlangen. We thank Prof. *H. Burzlaff,* who has put the program and the PDP11/45 computer at our disposal.

Synthesis under High Pressure: Michael Addition[**]

By *Kiyoshi Matsumoto*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

The Michael reaction is perhaps one of the most important reactions in the field of organic synthesis due to its wide applicability. However, a variety of systems that do not undergo this condensation are known[1], although many improved methods, for example, employing enamines[2a], organolithium[2b] or organocopper[2c] compounds as carbanion sources and utilizing phase transfer reagents[2d] and organometallic complexes[2e] as catalysts have been reported. The factors responsible for the failure of the Michael condensation have not yet been investigated systematically. However, the presence of many substituents near the reaction center of the donor would appear to hinder both its deprotonation and the addition step[1].

[*] Prof. Dr. K. Matsumoto
College of Liberal Arts and Sciences, Kyoto University
Kyoto 606 (Japan)

[**] Molecular and Reaction Design Based on High Pressure Organic Reactions. Part 2. This work was supported by Research Grants from the Japanese Ministry of Education (Grant-in-aid, No. 284021 and 554146).—Part 1: *K. Matsumoto et al.*, Heterocycles *16*, No. 2, in press (1981).

I now report briefly high pressure assisted Michael addition[3], in which some of these difficulties can be overcome. As shown in Table 1, formerly unsuccessful Michael additions—except that of diethyl phenylmalonate—proceed in good yield when performed under pressure. The present reaction also appears amenable to asymmetric induction[4].

General procedure

Michael acceptor (3 mmol), donor (6 mmol), and triethylamine (0.5 ml) diluted with CH_2Cl_2 are placed in a 10 ml Teflon capsule and kept under hydrostatic pressure (*p* and *t*, see Table 1) at room temperature[5]. After evaporation of solvent and volatile materials at 15 torr, the products are isolated either by vacuum distillation or by chromatography.

Table 1. Reaction conditions and yields of Michael addition under high pressures at room temperature.

Acceptor	Donor	Product		*p* [kbar]	*t* [h]	Isolated yield [%]
$PhCH{=}CHCO_2CH_3$	$CH_3{-}\underset{\displaystyle NO_2}{\underset{\vert}{CH}}{-}CH_3$	$O_2N{-}\overset{\displaystyle PhCHCH_2CO_2CH_3}{\overset{\vert}{C}}(CH_3)_2$	*(1)*	15	91	45 [a]
$CH_2{=}\underset{\displaystyle CH_3}{\underset{\vert}{C}}CO_2CH_3$	$CH_2{-}CH_2{-}CH_3$ $\vert$ NO_2	$O_2N{-}\overset{\displaystyle CH_2CH(CH_3)CO_2CH_3}{\overset{\vert}{C}}HC_2H_5$	*(2)*	15	48	42 [a]
$CH_3CH{=}CHCO_2CH_3$	$CH_2{-}CH_2{-}CH_3$ $\vert$ NO_2	$O_2N{-}\overset{\displaystyle CH_3CHCH_2CO_2CH_3}{\overset{\vert}{C}}HC_2H_5$	*(3)*	15	48	95 [a]
$PhCH{=}CH{-}\underset{\displaystyle O}{\underset{\Vert}{C}}{-}Ph$	$\overset{\displaystyle C_2H_5}{\overset{\vert}{H}}C(CO_2C_2H_5)_2$	$H_5C_2{-}\overset{\displaystyle PhCHCH_2COPh}{\overset{\vert}{C}}(CO_2C_2H_5)_2$	*(4)*	10	70	93 [b]
$PhCH{=}CH{-}\underset{\displaystyle O}{\underset{\Vert}{C}}{-}Ph$	$\overset{\displaystyle nBu}{\overset{\vert}{H}}C(CO_2C_2H_5)_2$	$nBu{-}\overset{\displaystyle PhCHCH_2COPh}{\overset{\vert}{C}}(CO_2C_2H_5)_2$	*(5)*	10	95	67 [b]
$PhCH{=}CH{-}\underset{\displaystyle O}{\underset{\Vert}{C}}{-}Ph$	$\overset{\displaystyle Ph}{\overset{\vert}{H}}C(CO_2C_2H_5)_2$			10 15	96 96	0 [b] 0 [b, c]

[a] Reaction unsuccessful at normal pressure: see *M. C. Kloetzel*, J. Am. Chem. Soc. *70*, 3571 (1948). [b] Reaction unsuccessful at normal pressure: see *R. Connor, D. B. Andrews, ibid. 56*, 2713 (1934). [c] Trace of product isolated.

Table 2. Selected physical data of Michael adducts [a].

(1): M.p. 70—71 °C; IR (KBr): 1730 (C=O), 1535 cm^{-1} (NO_2); ^{13}C-NMR: $\delta = 22.3, 25.6$ (2q, $2CH_3$), 35.0 (t, CH_2), 49.9 (d, *CH*), 51.8 (q, OCH_3), 91.0 (s, CNO_2), 128.0, 128.5, 129.1 (3d, aromatic *CH*), 137.1 (s, aromatic C), 171.3 (*C*=O) [b]

(2): B.p. 95—97 °C/2 torr; IR (neat): 1735 (C=O), 1550 cm^{-1} (NO_2); ^{13}C-NMR: $\delta = 10.1$ (q, CH_3), 16.5, 18.1 (2q, CH_3), 27.4, 27.8 (2t, CH_2), 36.2, 36.3 (2d, *CH*), 36.5, 37.0 (2t, CH_2), 51.9 (q, OCH_3), 87.6, 88.6 (2d, $CHNO_2$), 175.4, 175.8 (2s, C=O) [b, c]

(3): B.p. 80—81 °C/3 torr; IR (neat): 1735 (C=O), 1545 cm^{-1} (NO_2); ^{13}C-NMR: $\delta = 10.6$ (q, CH_3), 15.5, 16.2 (2q, CH_3), 24.2 (t, CH_2), 33.5, 33.6 (2d, *CH*), 37.1, 37.4 (2t, CH_2CO_2), 51.8 (q, OCH_3), 93.6, 94.1 (2d, $CHNO_2$), 172.1 (s, *C*=O) [b, c]

(4): viscous oil; IR (neat): 1685, 1720 cm^{-1} (C=O); ^{13}C-NMR: $\delta = 9.3$ (q, CH_3), 14.1 (q, $2CH_3$), 27.5 (t, CH_2), 42.4 (t, CH_2CO), 44.3 (d, *CH*), 61.6 (t, OCH_2), 62.1 (s, *C*), 127.2, 128.0, 128.2, 128.4, 129.1 (5d, aromatic *CH*), 137.1, 139.3 (2d, aromatic *C*), 170.8, 171.1 (2s, 2*C*=O), 198.0 (s, PhC=O) [b]

(5): viscous oil; IR (neat): 1685, 1725 cm^{-1} (C=O); ^{13}C-NMR: $\delta = 13.8$ (q, CH_3), 14.1 (q, $2CH_3$), 22.9, 26.7, 34.0 (3t, $3CH_2$), 44.3 (d, *CH*), 61.2 (t, $2OCH_2$), 61.6 (s, *C*), 127.1, 128.1, 128.4, 129.1, 132.8 (5d, aromatic *CH*), 137.1, 139.3 (2s, aromatic C), 170.9, 171.3 (s, ester-C=O), 198.0 (s, C=O) [b]

[a] Correct elemental analyses were obtained for all compounds. [b] Solvent: $CDCl_3$/TMS. [c] Diastereomers gave rise to pairs of signals: *C. A. Kingsburgy, R. E. Hutton, D. Durham*, J. Org. Chem. *43*, 4452 (1978).

Received: October 23, 1980 [Z 629 IE]
German version: Angew. Chem *92*, 1046 (1980)

[1] *E. D. Bergmann, D. Ginsberg, R. Pappo*, Org. React. *10*, 179 (1959).

[2] a) *G. Stork, A. Brizzolara, H. Landesman, J. Szmuskovicz, R. Terrell*, J. Am. Chem. Soc. *85*, 207 (1963); b) *R. A. Lee, R. Reusch*, Tetrahedron Lett. *1973*, 969; c) *E. J. Corey, R. H. K. Chen, ibid. 1973*, 1611; d) see *W. P. Weber, G. W. Gokel:* Phase Transfer Catalysis in Organic Chemistry. Springer, Berlin 1977; *E. V. Dehmlow, S. Dehmlow:* Phase Transfer Catalysis. Verlag Chemie, Weinheim 1980; *L. A. Carpino, A. C. Sau*, J. Chem. Soc. Chem. Commun. *1979*, 514; e) *T. Saegusa, Y. Ito, S. Tomita, H. Kinoshita*, Bull. Chem. Soc. Jpn. *45*, 496 (1972); *K. Irie, K. Miyazu, K. Watanabe*, Chem. Lett. *1980*, 353.

[3] Topical reviews of the synthesis of organic compounds under pressure: *W. J. le Noble, H. Kelm*, Angew. Chem. *82*, 887 (1980); Angew. Chem. Int. Ed. Engl. *19*, 841 (1980); *J. Metzger, P. Köll, ibid. 91*, 74 (1979) and *18*, 70 (1979) respectively; *J. A. Gladysz, Y. S. Yu*, J. Chem. Soc. Chem. Commun. *1978*, 599; *J. Jurczak, M. Chemielewski, S. Filipek*, Synthesis *1979*, 41; *H. Kotsuki, H. Nishizawa, S. Kitagawa, M. Ochi, N. Yamasaki, K. Matsuoka, T. Tokoroyama*, Bull. Chem. Soc. Jpn. *52*, 544 (1979).

[4] Michael reactions of chalcone with nitromethane and of methyl vinyl ketone with ethyl 2-oxocyclohexanecarboxylate do not occur in aprotic solvents in the presence of chiral free alkaloids such as quinine; *S. Colonna, H. Hiemstra, H. Wynberg*, J. Chem. Soc. Chem. Commun. *1978*, 238; *K. Hermann, H. Wynberg*, J. Org. Chem. *44*, 2238 (1979). However, at 10—15 kbar at room temperature, these reactions did occur quantitatively in CH_2Cl_2, though in low optical yields (below 5% e.e. at present).

[5] The inexpensive high pressure apparatus employed in the present experiment will be described elsewhere in due course.

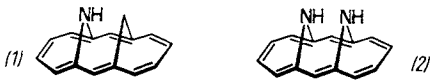
 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1014 $ 02.50/0

syn-1,6-Imino-8,13-methano[14]annulene

By *Emanuel Vogel, Ulrich Brocker,* and *Heinz Junglas*[*]

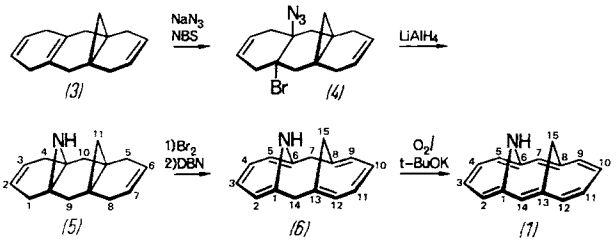
Dedicated to Professor Matthias Seefelder on the occasion of his 60th birthday

The versatile chemistry of 1,6-imino[10]annulene[1], dominated by a delocalized 10π-electron system (formation of substitution products[2]) and an azepine structural unit (production of 1*H*-1-benzoazepines and/or nitrenes[3]), has stimulated us to attempt the synthesis of the NH-bridged-[14]annulenes *syn*-1,6-imino-8,13-methano[14]annulene *(1)* and *syn*-1,6:8,13-bisimino[14]annulene *(2)*. Aromatic character can be predicted for both [14]annulenes, although the steric interaction of the bridges, which occurs in particular in the case of *(1)*, is likely to result in some bending of the annulene ring. The O-analogues of *(1)* and *(2)* have already been prepared[4]; we have now succeeded in synthesizing *(1)*.



(1) *(2)*

Reaction of the 1,4,5,8,9,10-hexahydro-4a,9a-methanoanthracene *(3)*[5] (obtainable by Simmons-Smith cyclopropanation of 1,4,5,8,9,10-hexahydroanthracene) with sodium azide and *N*-bromosuccinimide (Krief reagent)[6] (molar ratio 1:5:1.1) in dimethoxyethane/water at −15 to −20 °C gave a mixture of the *trans*-8aα-azido-10aβ-bromide *(4)*, the structural isomer *trans*-2α-azido-3β-bromide, and the hydrocarbon 1,4,9,10-tetrahydro-4a,9a-methanoanthracene [aromatization product of *(3)*]. Since losses are high in the isolation of *(4)*, the crude mixture was treated at −20 °C in tetrahydrofuran (THF) with $LiAlH_4$ and the reaction product worked-up by chromatography on aluminum oxide, first with hexane (separation of 1,4,9,10-tetrahydro-4a,9a-methanoanthracene) and then with hexane/dichloromethane. In this way an aziridine was obtained which on the basis of NMR spectroscopic and chemical findings proved to be *(5)* [colorless prisms (from ethanol), m.p. 67—68 °C; yield 13%]. The arrangement of the azide- and bromo-substituents in *(4)* conformed with the expectation that the, presumably ionic, addition of the Br/N_3 unit to the tetrasubstituted double bond of *(3)*, effected by the Krief reagent, is sterically controlled by the cyclopropane ring.



(3) *(4)* *(5)* *(6)* *(7)*

Reaction of *(5)* with two equivalents of bromine at −78 °C in dichloromethane afforded almost quantitatively a tetrabromide, which could be dehydrohalogenated with 1,5-diazabicyclo[4.3.0]non-5-ene in THF (room temperature 48 h) to *(6)*. Purification by chromatography on florisil and sublimation in vacuum afforded *(6)* as a lemon yellow, finely-crystalline solid (dec. above 75 °C; yield 26%). From the ^{1}H-NMR spectrum of *(6)* the resonances of the protons of the azepine structural unit—AA'BB'-system at relatively high field [δ = 5.13 and 5.93 (H-2,5 and H-3,4, resp.)] and broad singlet of the imino proton (δ = 3.33)—are underscored, for *(6)* is possibly the first 1*H*-azepine[7] without a substituent on the nitrogen. Attempts to dehydrogenate *(6)* to the NH-bridged annulene *(1)* with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone or noble metal catalysts were unsuccessful, yet such a conversion could be effected with potassium *tert*-butoxide/oxygen in THF (−5 to −10 °C, 30 min). Chromatography on aluminum oxide (hexane/dichloromethane 4:1) and recrystallization from ethanol furnished the air-stable *(1)* as brick red needles; m.p. 149—150 °C, yield 36% (for spectral data of *(1)*, *(5)*, *(6)*, and *(7)* see Table 1).

Table 1. Spectral data of compounds *(1)*, *(5)*, *(6)*, and *(7)*. C- and H atoms in *(7)* were numbered as in *(6)*.

(1): ^{1}H-NMR (CCl_4): δ = −2.07 (br. s, N*H*), −1.52, 2.08 (AX, J_{AX} = 10.2 Hz, H-15$_{exo}$, H-15$_{endo}$), 7.45 (s, H-7,14), 7.23, 7.58 (AA'BB', H-2,3,4,5), 7.23, 7.87 (AA'BB', H-9,10,11,12); UV (EtOH): λ_{max} = 284 nm (ε = 30200), 314 (57100), 375 (9500), 518 (860); IR (CsI): 3330 cm^{-1} (N—H), 3055 (—C—H); MS (80 eV): *m/e* = 207 (*M*$^+$, 100%), 206 (53), 204 (34), 191 (24), 178 (32)

(5): ^{1}H-NMR (CCl_4): δ = 0.12 (br. s, N*H*), 0.24, 1.71 (AX, J_{AX} = 3.0 Hz, H-11$_{exo}$, H-11$_{endo}$), 1.68, 2.16 (AB, J_{AB} = 14.1 Hz, H-9,10), 1.82—2.43 (m, H-1,4,5,8), 5.45 (m, H-2,3,6,7); IR (CCl_4/CS_2): 3290 cm^{-1} (N—H), 1655 (C=C)

(6): ^{1}H-NMR ($CDCl_3$): δ = 1.95, 3.38 (AX, J_{AX} = 12.3 Hz, H-15$_{exo}$, H-15$_{endo}$), 2.93, 3.13 (AB, J_{AB} = 12.6 Hz, H-7,14), 3.33 (br. s, N*H*), 5.13, 5.93 (AA'BB', H-2,3,4,5), 6.03, 6.50 (AA'BB', H-9,10,11,12); UV (*n*-hexane): λ_{max} = 255 nm (sh, ε = 5550), 360 (sh, 170); IR (CsI): 3390 cm^{-1} (N—H), 1648 (C=C)

(7): ^{1}H-NMR ($CDCl_3$): δ = 1.48, 3.40 (AX, J_{AX} = 12.0 Hz, H-15$_{exo}$, H-15$_{endo}$), 3.27, 3.77 (AB, J_{AB} = 16.8 Hz, H-7,14), 3.38 (br. s, N*H*), 5.32, 6.13 (AA'BB', H-2,3,4,5), 6.07, 6.57 (AA'BB', H-9,10,11,12); UV (EtOH): λ_{max} = 269 nm (ε = 3380), 336 (sh, 355); IR (CsI): 3350 cm^{-1} (N—H), 1657 (C=C)

syn-1,6-Imino-8,13-methano[14]annulene *(1)* was recognized by its ^{1}H-NMR spectrum (see Fig. 1) as an aromatic compound. The resonances of the annulene protons—two partially superposing AA'BB' systems and a singlet—appear at relatively low field, while those of the exo CH_2- and the NH-bridge protons are observed at relatively high field. That the *endo*-CH_2-bridge proton is strongly deshielded—the difference in the chemical shifts between the two CH_2-protons is 3.6 ppm!—might be due to a considerable part to its steric interaction with the spatially very close NH-group (van der Waals effect)[8].

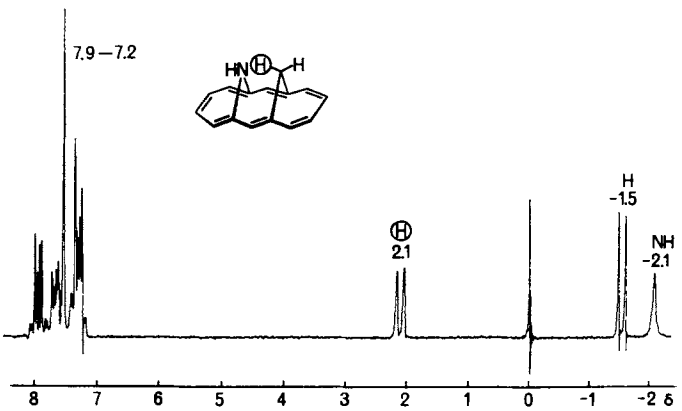
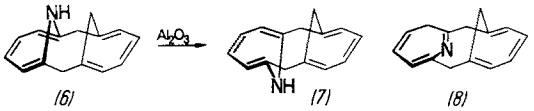


Fig. 1. 90-MHz ^{1}H-NMR spectrum of *syn*-1,6-imino-8,13-methano[14]annulene *(1)* (in CCl_4, TMS as internal standard).

[*] Prof. Dr. E. Vogel, Dr. U. Brocker, Dr. H. Junglas
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

The NH-bridge proton is assigned the *exo* position with a high degree of certainty on the basis of its resonance at relatively high field. If this proton were to be in the *endo* position, then it would not only have to be markedly deshielded as a result of the H—H compression but also show a—not-present—nuclear Overhauser effect. Since the steric arrangement of the NH proton in *(1)* is of topical interest, in view of the much discussed problem of the relative sizes of the free electron pair and the H atom on the trigonal imino nitrogen[9], the assignment should be confirmed by an X-ray structure analysis.

The electronic spectrum of *(1)* has the same form as that of *syn*-1,6:8,13-bismethano[14]annulene, but the short-wave main absorption band shows a splitting, whose cause might be attributed to an interaction of the nitrogen electron pair with the 14π-electron system. Consistent with this explanation, the spectrum of the *N*-acetyl derivative[10] is almost superimposably identical with that of the hydrocarbon.



(6) *(7)* *(8)*

The dihydro[14]annulene *(6)*, characterized by its 1*H*-azepine structural unit, surprisingly isomerizes on chromatography on aluminum oxide (hexane/dichloromethane) to the *anti*-isomer *(7)*, whose structure is proven beyond doubt by the spectral similarity with *(6)* and by an X-ray structure analysis. The obvious idea of a thermal change of conformation can be ruled out, since *(6)* remains completely unchanged even on prolonged heating at 100 °C (in benzene). It may therefore be assumed that the *syn-anti* isomerization of *(6)* is brought about by Al_2O_3-catalyzed prototropic shifts *via* the 3*H*-azepine tautomer *(8)* of *(6)*/*(7)*.

An easy prototropy of *(8)* with formation of *(7)* or regeneration of *(6)*—first example of a reversal of a 1*H*-azepine/3*H*-azepine isomerization[11]—is readily explained by the relatively high strain of *(8)* (violation of the Bredt rule).

Received: July 14, 1980 [Z 630a IE]
German version: Angew. Chem. *92*, 1051 (1980)

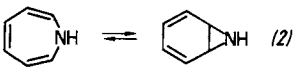
[1] *E. Vogel, W. Pretzer, W. A. Böll*, Tetrahedron Lett. *1965*, 3613.
[2] Bromination of 1,6-imino[10]annulene, like that of 1,6-methano[10]annulene, affords the 2-bromo substitution product (unpublished experiments in collaboration with *F. Schophoff*).
[3] In the flash pyrolysis, *N*-methoxycarbonyl, *N*-methyl-, and *N*-trimethylsilyl-1,6-imino[10]annulene yield the corresponding 1*H*-1-benzazepines, while the *N*-chloro derivative fragments into chloronitrene and naphthalene, already at 50 °C (unpublished experiments in collaboration with *M. Schäfer-Ridder* and *J. Jesse*).
[4] *E. Vogel*, Pure Appl. Chem. *28*, 355 (1971).
[5] *E. Vogel, U. Haberland, J. Ick*, Angew. Chem. *82*, 514 (1970); Angew. Chem. Int. Ed. Engl. *9*, 517 (1970).
[6] *D. Van Ende, A. Krief*, Angew. Chem. *86*, 311 (1974); Angew. Chem. Int. Ed. Engl. *13*, 279 (1974).
[7] Survey *L. A. Paquette* in *J. P. Snyder*: Nonbenzenoid Aromatics. Vol. 1. Academic Press, New York 1969, p. 249. Dimethyl 1*H*-3,4-azepinedicarboxylate, formed according to *R. P. Gandhi, V. K. Chadha* [Indian J. Chem. *9*, 305 (1971)] on photochemical reaction of pyrrole with dimethyl acetylenedicarboxylate, does not appear adequately secured structurally.
[8] Regarding the influence of steric compression on the chemical shift of protons, see *S. Winstein, P. Carter, F. A. L. Anet, A. J. R. Bourn*, J. Am. Chem. Soc. *87*, 5247 (1965); *W. Bremser, H. Günther*, Org. Magn. Reson. *1*, 435 (1969).
[9] *N. L. Allinger, J. A. Hirsch, M. A. Miller*, Tetrahedron Lett. *1967*, 3729; *E. L. Eliel, F. W. Vierhapper*, J. Am. Chem. Soc. *97*, 2424 (1975); *I. D. Blackburne, A. R. Katritzky*, Acc. Chem. Res. *8*, 300 (1975).
[10] This *N*-acetyl derivative, not obtainable directly from *(1)*, could be prepared by transformation of *N*-acetyl-*(5)* into *N*-acetyl-*(6)* by bromination/dehydrobromination, and dehydrogenating this product with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone.
[11] For synthesis of the highly labile 1*H*-azepine and its acid- and base-catalyzed isomerization to 3*H*-azepine, see *E. Vogel, H.-J. Altenbach, J.-M. Drossard, H. Schmickler, H. Stegelmeier*, Angew. Chem. *92*, 1053 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1016 (1980).

1*H*-Azepine: NMR Spectroscopic and Chemical Characterization

By *Emanuel Vogel, Hans-Josef Altenbach, Jakob-Matthias Drossard, Hans Schmickler*, and *Hartmut Stegelmeier*[*]

Dedicated to Professor Ralph A. Raphael on the occasion of his 60th birthday

1*H*-Azepine *(1)*, which was first generated by *Hafner*[1] by hydrolysis of ethyl 1*H*-azepine-*N*-carboxylate with potassium hydroxide and acidification of the resulting potassium salt of the acid *(7)*, has hitherto defied all attempts at detailed characterization owing to its high chemical reactivity[2]. Hence, the assumption, chiefly based on theoretical calculations, that *(1)* is thermodynamically much more favored[3] than the valence-tautomeric benzene imine *(2)* has long been awaiting experimental confirmation.



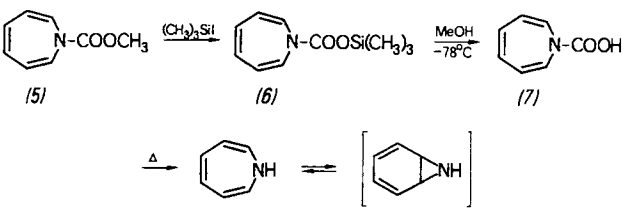
(1) *(2)*

The relative stability of the 1*H*-azepine and benzene imine derivatives *(3)*[4] and *(4)*[5] in neutral medium promted us to attempt the isolation of *(1) via* trimethylsilyl 1*H*-azepine-*N*-carboxylate *(6)*, which is readily accessible by reaction of the ester *(5)* with iodotrimethylsilane[6] in chloroform (room temperature, 24 h; b.p. 63 °C/0.02 torr, yield 71%).



(3) *(4)*

When a solution of *(6)* (3.14 g, 15 mmol) in pentane (10 ml) is treated with methanol (1.2 ml, 30 mmol), the carbamic acid *(7)*[7a] begins to precipitate within a few minutes; after 12 hours precipitation is complete. Subsequent washing with cold ether and drying for 12 h at 0.1 torr affords 1.5 g (74%) of pure *(7)*, a bright-yellow solid which is stable for a several days at −78 °C.



(5) *(6)* *(7)*

(1) *(2)* (<1%)

Decarboxylation of *(7)* in an NMR sample tube under the following conditions yields NMR spectroscopically pure 1*H*-azepine *(1)* (in solution): a solution of *ca.* 25 mg of *(7)* in 0.6 ml $CDCl_3$, prepared at −60 °C, is allowed to warm to

[*] Prof. Dr. E. Vogel, Dr. H.-J. Altenbach, Dipl.-Chem. J.-M. Drossard, Dr. H. Schmickler, Dr. H. Stegelmeier
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

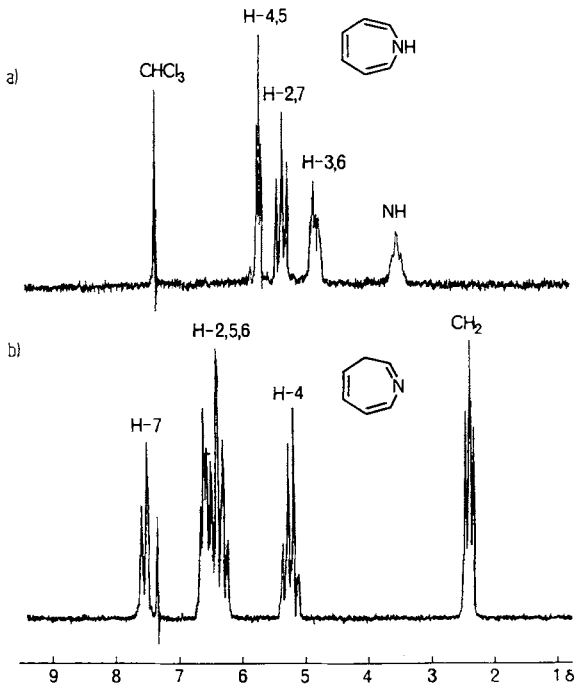
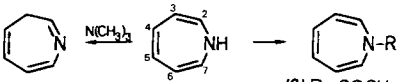


Fig. 1. ^{1}H-NMR spectra (90 MHz) of a) 1*H*-azepine *(1)* (−60 °C) and b) 3*H*-azepine *(8)* (32 °C) (in each case in $CDCl_3$, TMS as internal standard).

room temperature (duration 30—60 s); an intense red coloration is accompanied by gentle evolution of CO_2. The solution is cooled again to low temperature and the NMR spectrum of the sample is measured. Even at −78 °C *(1)* is stable for only a few hours in this solution[8].

Proof of the presence of 1*H*-azepine *(1)*— and of its existence as a seven-membered ring valence tautomer—is based on analysis of the ^{1}H- and ^{13}C-NMR spectra. The ^{1}H-NMR spectrum (Fig. 1), which is temperature independent in the range measured (−120 to −30 °C), and which could be assigned, partly by comparison with the spectrum of *(3)*, partly by double resonance experiments (localization of H-2,7 by irradiation at the frequency of the NH proton) affords the following arguments in favor of *(1)*: i) the chemical shifts of H-2,7 and H-3,6 correspond to those of the α- and β-protons, respectively, in enamines such as *N*-methyl-4,5-dihydro-1*H*-azepine[9a]; ii) the vicinal H—H coupling constants $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ are in good agreement with those of cycloheptatriene. This finding provides useful information, in that $J_{3,4}$ and $J_{4,5}$ change in the same characteristic way on going from *(1)* to *(4)* as in the transition from cycloheptatriene to the norcaradiene model tricyclo[4.3.1.0^{1,6}]deca-2,4-diene[9b].

The ^{1}H-NMR parameters, particularly the vicinal H—H coupling constants, although supporting the presence of *(1)*, are, however, too insensitive to allow detection of less than 10% of *(2)*. More accurate information about the position of the equilibrium *(1)*⇌*(2)* is provided by the likewise temperature independent ^{13}C-NMR spectrum which, in agreement with the symmetry of *(1)* and *(2)*, only comprises three resonance signals. As shown in Table 1, this spectrum is completely analogous to that of oxepin (at −134 °C) and—taking into account the influence of the electronegativity and resonance effect of the N atom on the chemical shifts—also with that of cycloheptatriene. Decisive for the detection of a small equilibrium concentration of *(2)* is the signal of C-2,7, since on the basis of the situation with cycloheptatriene/tricyclo[4.3.1.0^{1,6}]deca-2,4-diene and with oxepin/benzene oxide it may be assumed that *(1)* and *(2)* differ by no less than 80 ppm in the chemical shifts of C-2,7. From the finding that this signal clearly appears in the absorption region of olefinic protons and, on lowering the temperature of measurement to −120 °C, is neither shifted nor shows coalescence phenomena, the maximum amount of *(2)* at equilibrium can be reliably estimated as below 1%. 1*H*-Azepine *(1)* is thus in fact to be regarded, in agreement with prediction, as a practically uniform seven-membered ring valence tautomer.



Characteristic of the chemical behavior of 1*H*-azepine *(1)* is its ready tautomerization, usually accompanied by formation of polymers, by catalytic amounts of acids or bases (preferably trimethylamine) to the colorless 3*H*-azepine *(8)*, whose structure and uniformity is confirmed by the ^{1}H-NMR spectrum (double resonance experiments) (see Fig. 1). 3*H*-Azepine exhibits a somewhat smaller tendency to polymerization than *(1)*, so that it can be distilled in vacuum albeit with high losses[7b]. By reaction of *(1)* with ketene and with methanesulfonyl chloride/triethylamine it was possible to obtain *N*-acetyl-1*H*-azepine *(9)* (yield 20%) and *N*-methanesulfonyl-1*H*-azepine *(10)*, respectively[10] (yield 15%). Reaction with trimethylsilyl trifluoromethanesulfonate afforded the relatively stable, red *N*-trimethylsilyl-1*H*-azepine *(11)*[7c], which became only recently preparatively accessible by pyrolysis of the *N*,*N*′-disilyl derivative of 13,14-diazatricyclo[6.4.1.1^{2,7}]tetradeca-3,5,9,11-tetraene[12].

Received: July 14, 1980 [Z 630b IE]
German version: Angew. Chem 92, 1053 (1980)

[1] *K. Hafner*, Angew. Chem. *75*, 1041 (1963); Angew. Chem. Int. Ed. Engl. *3*, 165 (1964); Reviews: *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew.

Table 1. NMR spectroscopic data of 1*H*-azepine *(1)* and reference compounds. The C and H atoms have been numbered as in *(1)*.

Cpd.		^{1}H-chemical shifts (δ values)			Coupling constants [Hz]			^{13}C-chemical shifts (δ values)		
		H-2,7	H-3,6	H-4,5	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	C-2,7	C-3,6	C-4,5
(1)	1*H*-Azepine	5.22	4.69	5.57	7.97	5.51	10.89	138.0	113.0	132.3
	Cycloheptatriene	5.28	6.12	6.55 [a]	8.58	5.26	10.67 [b]	120.4	126.8	131.0 [c]
	Oxepin							141.8	117.6	130.8 [c]
	Benzene oxide							56.6	128.7	128.7 [c]
(4)	10-Azatricyclo[4.3.1.0^{1,6}]-deca-2,4-diene		6.43	6.01		9.24	6.11 [d]	53.8	129.5	120.9 [d]
	Tricyclo[4.3.1.0^{1,6}]-deca-2,4-diene		6.07	5.71		9.25	5.94 [e]	37.7	128.6	118.8 [f]

[a] Varian catalog of NMR spectra, Vol. 1, No. 158. [b] *J. B. Lambert, L. J. Durham, P. Lepoutere, J. D. Roberts*, J. Am. Chem. Soc. *87*, 3896 (1965). [c] *R. Wehner*, Dissertation, Universität Köln 1975 (measurement of the spectrum of oxepin/benzene oxide at −134 °C). [d] See [5]. [e] See [9b] and *H.-H. Hinrichs*, Dissertation, Universität Köln 1966. [f] *H. Schmickler*, Dissertation, Universität Köln 1974; *H. Günther, T. Keller*, Chem. Ber. *103*, 3231 (1970).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1980* *0570-0833/80/1212-1017 $ 02.50/0*

Chem. Int. Ed. Engl. 6, 402 (1967); *L. A. Paquette, J. P. Snyder* in Nonbenzenoid Aromatics. Vol. 1. Academic Press, New York 1969, p. 249.

[2] Attempts to liberate (1) from (1*H*-azepine)tricarbonyliron [*E. O. Fischer, H. Rühle*, Z. Anorg. Allg. Chem. *341*, 137 (1965)] with trimethylamine oxide led only to difficultly identifiable mixtures of product (*J.-M. Drossard, N. T. Allison, E. Vogel*, unpublished); The reduction of *N*-tosyl-3-azaquadricyclane with sodium in liquid ammonia gave, even below −50 °C, only 3*H*-azepine as isolable product [no physical data given; *H. Prinzbach, H. Babsch*, Heterocycles *11*, 113 (1978)].

[3] According to most recent MINDO/3 calculations of the heats of formation, *(1)* is about 8.5 kcal/mol more stable than *(2)*; corresponding calculations for cycloheptatriene and norcaradiene and for oxepin and benzene oxide gave a thermodynamic preference for the monocyclic valence tautomer of 12.2 and 1.7 kcal/mol, respectively [*D. M. Hayes, S. D. Nelson, W. A. Garland, P. A. Kollman*, J. Am. Chem. Soc. *102*, 1255 (1980)]. For the substituent-determined shifts of the 1*H*-azepine-benzene imine equilibrium in favor of the benzene imine valence tautomer, see *H. Prinzbach, H. Babsch, H. Fritz, P. Hug*, Tetrahedron Lett. *1977*, 1355 (and references cited therein).

[4] *E. Vogel, U. Brocker, H. Junglas*, Angew. Chem. *92*, 1051 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1015 (1980).

[5] The synthesis of (4) was accomplished analogously to that of 10-oxatricyclo[4.3.1.0^{1,6}]deca-2,4-diene [*E. Vogel, H. Günther*, Angew. Chem. Int. Ed. Engl. *6*, 385 (1967)] by dehydrohalogenation of 3,4-dibromo-10-azatricyclo[4.3.1.0^{1,6}]decane with potassium tert-butoxide in tetrahydrofuran; b.p. 28—30 °C/0.5 torr. The *N*-methoxycarbonyl derivative of *(4)* has been described by *L. A. Paquette et al.* [10].

[6] *M. E. Jung, M. A. Lyster*, J. Chem. Soc. Chem. Commun. *1978*, 315; *G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra*, Angew. Chem. *91*, 648 (1979); Angew. Chem. Int. Ed. Engl. *18*, 612 (1979).

[7] a) *(7a)*: ^{1}H-NMR ($CDCl_3$, −60 °C): δ = 5.78 (m, H-3,6), 5.90 (m, H-2,7), 6.25 (m, H-4,5), 12.4 (COO*H*); ^{13}C-NMR ($CDCl_3$, −60 °C): δ = 120.2 (C-3,6), 129.6, 130.6 (C-2,4,5,7), 157.4 (*C*=O); b) *(8)*: Short path distillation at 25 °C/0.1 torr; ^{1}H-NMR ($CDCl_3$): δ = 2.42 (m, 2H-3), 5.25 (m, H-4), 6.20—6.70 (m, H-2,5,6), 7.55 (m, H-7); ^{13}C-NMR ($CDCl_3$): δ = 34.3 (C-3), 113.3, 117.5, 127.3, 136.4, 141.0 (C-2,4,5,6,7); c) *(11)*: ^{1}H-NMR ($CDCl_3$): δ = 0.13 (s, 3 C*H*$_3$), 4.78 (m, H-3,6), 5.03 (m, H-2,7), 5.49 (m, H-4,5); ^{13}C-NMR ($CDCl_3$): δ = 117.6 (C-3,6), 131.8 (C-4,5), 139.1 (C-2,7).

[8] For the synthesis of *(1)* on a preparative scale it proves convenient to decarboxylate 0.5 g of *(7)* in 12 ml of chloroform (also dichloromethane, acetone or ether) according to the procedure given above. The longer reaction time required (1—2 min) results in the formation of *ca.* 10% polymers besides *(1)*. The solution of *(1)* is used immediately for chemical reactions.

[9] a) *J. C. Pommelet, J. Chuche*, Tetrahedron Lett. *1974*, 3897; b) *H. Günther, H.-H. Hinrichs, ibid. 1966*, 787.

[10] *L. A. Paquette, D. E. Kuhla, J. H. Barrett, R. J. Haluska*, J. Org. Chem. *34*, 2866 (1969).

[11] *A. L. Johnson, H. E. Simmons*, J. Am. Chem. Soc. *89*, 3191 (1967).

[12] Unpublished experiments in collaboration with *W. Lange*.

Intramolecular Oxidative Cyclization of 3-Benzyl-1,2,3,4-tetrahydroisoquinolines[**]

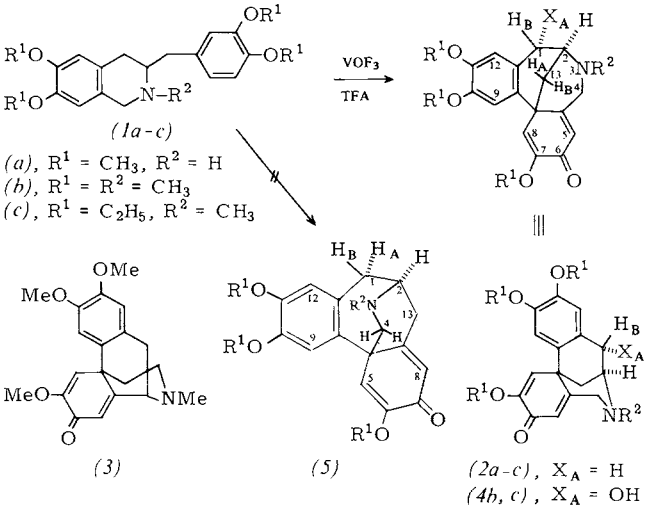
By *Johannes Hartenstein, Theo Heigl,* and *Gerhard Satzinger*[*]

In view of the supreme importance of 1-benzyl-1,2,3,4-tetrahydroisoquinolines for the biosynthesis of alkaloids[1], it is surprising that nature appears to have completely overlooked the 3-benzyl isomers. In the search for such "unnatural" alkaloids we have found that the non-phenolic oxidative coupling of 3-benzyl-1,2,3,4-tetrahydroisoquinolines *(1a—c)*[2] with VOF_3 in trifluoroacetic acid (TFA) at −15 to 0 °C leads smoothly and in high yields (>80%) to the previously unreported 1,2,3,4-tetrahydro-2,8a-methanodibenzo[*c,e*]azocin-6-ones *(2a—c)*[3,4] (Table 1).

The cyclization products *(2)* are closely related to the natural morphinandienones, *e.g. O*-methylflavinantine *(3)*.

The alternative structure *(5)*, the product of a *para*-coupling of the phenyl group with position 8a of the isoquinoline, could be ruled out by analysis of the 360-MHz ^{1}H-NMR spectra. Decoupling experiments with *(2a)* show that a remote coupling of 1 Hz exists only between the vinyl proton H-5 (δ = 6.09) and one of the aliphatic protons (H-4, δ = 3.39). Assuming structure *(5)*, then the demonstrated relation between a vinyl proton and an aliphatic proton by remote coupling would require an unusually large chemical shift of 3.36 for the C-13 methylene group. Also the positions of the signals at 1.91, 2.06 and 1.85 [Table 1, H-13$_B$ for *(2a)*, *(2b)*, and *(2c)*], respectively, would hardly be compatible with the chemical shift of protons of an allylic CH_2-group.

Besides the main products *(2a-c)*, very small amounts (<5%) of products of over oxidation are formed, namely the 3,4-didehydro derivative of *(2a)* in the cyclization of *(1a)*,



and the 1-hydroxy derivatives *(4b, c)* in the cyclization of *(1b, c)*. The hydroxy compounds *(4)* are formed regio- and diastereoselectively from *(2)* in analogy to the hydroxylation of aporphines[5]. Apart from the differences determined by the substituents, the signals for H-2, H-4 and H-13 in *(4)* correspond to those in *(2a—c)*. On the other hand, the ABX system of the H-1 methylene group is absent; instead a somewhat broadened singlet is observed at 4.85. Compatible with a dihedral angle of *ca.* 90° there is practically no coupling between H-1$_B$ and H-2. Moreover, H-12 is shifted downfield by *ca.* 0.2 ppm owing to the proximity of the hydroxy group.

Table 1. Some data of the compounds *(2a—c)*, 3,4-didehydro- *(2a)*, and *(4b)* [a].

(2a), m.p. 186—187 °C (methanol/ether); MS (70 eV): *m/e* 327 (M^+, 12%), 178 (EI, 100), 150 (19); 299 (CI, 100); IR (KBr): 1655, 1633, 1610 cm^{-1}; ^{1}H-NMR [b]: δ = 3.70, 3.73, 3.89 (3 × OCH$_3$), 5.93 (s, H-8), 6.09 (s, H-5), 6.50 (s, H-9), 6.74 (s, H-12); [c] 1.91 (ddd, H-13$_B$, J_{AB} = 12.5, $J_{B\ H1B}$ = 1.5, $J_{B\ H2}$ = 4.0), 2.37 (dd, H-13$_A$, J_{AB} = 12.5, $J_{A\ H2}$ = 1.8), 3.02 (br. d, H-1$_B$, J_{AB} = 18, $J_{B\ H2}$ < 1), 3.37 (dd, H-1$_A$, J_{AB} = 18, $J_{A\ H2}$ = 6.5), 3.33 (d, H-4$_B$, J_{AB} = 14, $J_{B\ H5} \approx 0$), 3.39 (dd, H-4$_A$, J_{AB} = 14, $J_{A\ H5}$ = 1), 3.62 (br., H-2); UV (hydrochloride, ethanol); $\lambda_{max}(\varepsilon)$ = 238 (17200), 275 (6000) nm

(2b), m.p. 168.5—170 °C (methanol); ^{1}H-NMR [b]: δ = 2.54 (s, N—CH$_3$), 3.72, 3.77, 3.88 (3 × OCH$_3$), 5.94 (s, H-8), 6.15 (s, H-5), 6.50 (s, H-9), 6.77 (s, H-12); [c] 2.06 (ddd, H-13$_B$), 2.26 (dd, H-13$_A$), 2.97 (dd, H-1$_B$), 3.11 (s, 2 × H-4), 3.20 (d, H-1$_A$), 3.35 (br., H-2)

(2c), m.p. 158—159 °C (methanol); ^{1}H-NMR [b]: δ = 1.4, 4.0 (m, 3 × OC$_2$H$_5$), 2.52 (N—CH$_3$), 5.89 (s, H-8), 6.10 (s, H-5), 6.50 (s, H-9), 6.72 (s, H-12)

3,4-Didehydro-(2a), m.p. = 188—189 °C (methanol/ether)

(4b), m.p. 188—189 °C (methanol/ether); ^{1}H-NMR [b]: δ = 2.54 (N—CH$_3$), 3.69, 3.74, 3.87 (3 × OCH$_3$), 4.85 (br. s, H-1), 5.93 (s, H-8), 6.07 (s, H-5), 6.47 (s, H-9), 7.01 (s, H-12); [c] 1.85 (dd, H-13$_B$), 2.53 (dd, H-13$_A$), 2.96 (d, H-4$_B$), 3.03 (d, H-4$_A$), 3.24 (br., H-2)

[a] Mass, IR, and UV spectra are in agreement with the given structures. Satisfactory (±0.2%) elemental analyses (C, H, Cl, N) were obtained for the hydrochlorides of *(2a—c)*. [b] 60 MHz, $CDCl_3$, TMS int. [c] 360 MHz, $CDCl_3$, TMS int., *J* in Hz.

[*] Dr. J. Hartenstein [+], Dipl.-Phys. T. Heigl, Dr. G. Satzinger
Gödecke Forschungsinstitut, Arzneimittelforschung
Mooswaldallee 1—9, D-7800 Freiburg (Germany)

[+] Author to whom correspondence should be addressed.

[**] We thank *G. Pohlmann* for valuable assistance with the experiments.

Procedure

(±)-*(2b)*: 2-Methyl-6,7-dimethoxy-3-veratryl-1,2,3,4-tetrahydroisoquinoline *(1b)* (5.63 g, 15.74 mmol) is dissolved in TFA (60 ml) cooled with ice-water, and the stirred solution treated dropwise within 5 min at −15 to −10 °C under N_2 in the absence of moisture with a solution of VOF_3 (4.20 g, 2.5 equivalents) in TFA (200 ml). Stirring is continued for a further 1 h and then the solvent is removed at 20 °C/100 torr. The residue is treated with water and extracted with chloroform. The combined chloroform extracts are washed with semiconcentrated aqueous ammonia. Subsequent drying, removal of solvent, and crystallization of the residue from methanol furnishes 4.55 g (85%) of (±)-*(2b)*.

Received: March 17, 1980 [Z 631 IE]
German version: Angew. Chem. 92, 1055 (1980)

[1] Cf. *D. R. Dalton:* The Alkaloids. M. Dekker, New York 1979, pp. 216f.
[2] *J. Knabe, J. Kubitz,* Arch. Pharm. (Weinheim) *297*, 129 (1964); *J. Knabe, N. Ruppenthal, ibid. 297*, 268 (1964); *J. Knabe, H. Powilleit, ibid. 304*, 52 (1971).
[3] *J. Hartenstein, G. Satzinger,* DOS 2849 472.6 (1978), Gödecke AG.
[4] The reactions were carried out with the racemic compounds. In the formulas the second enantiomer has been omitted.
[5] *J. Hartenstein, G. Satzinger,* Angew. Chem. *89*, 739 (1977); Angew. Chem. Int. Ed. Engl. *10*, 730 (1977).

Total Reversibility of the Addition and Transylidation of Trialkyl(alkylidene)phosphoranes to Metal-Coordinated Carbon Monoxide[**]

By *Herbert Blau* and *Wolfgang Malisch*[*]

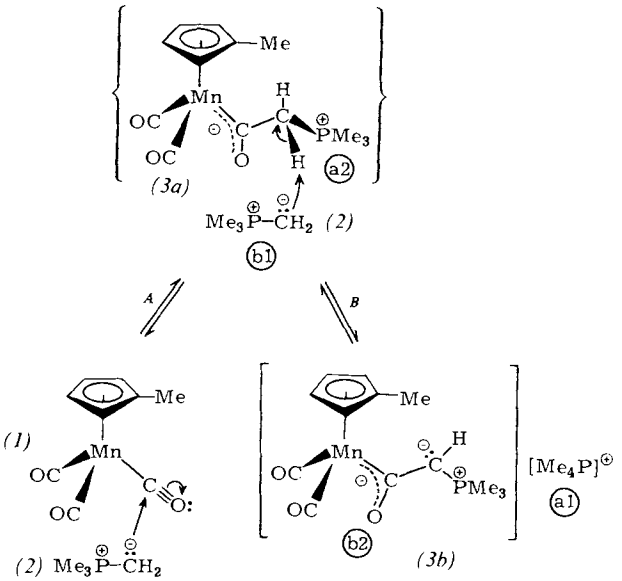
Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday

Nucleophilic phosphorus ylides add to the carbonyl carbon of carbonylmetal compounds that do not contain any ligands other than CO[1]. However, when trialkyl(alkylidene)phosphoranes[2] are used the reaction does not stop at the stage of the 1:1 adduct; instead, a rapid transylidation (with further phosphorane) takes place to give phosphorus ylide-substituted phosphoniummetal acylates[3].

We have now found for the first time that reaction of a carbonyl(cyclopentadienyl)metal compound, $MeC_5H_4Mn(CO)_3$ *(1)*, with trimethyl(methylene)phosphorane *(2)* in the molar ratio 1:2 leads, as with carbonylmetal compounds, in a two-step reaction to formation of phosphorus ylide substituted phosphoniummetal acylates, having quite novel and unusual properties. Thus, the product *(3b)*—an egg-yellow, extremely pyrophoric substance—obtained from *(1)* and *(2)* in pentane by addition and transylidation, completely regenerates the educts *(1)* and *(2)* on dissolution in tetrahydrofuran, or an ample amount of benzene, or pentane.

Consequently, *(3b)* can only be identified by IR spectroscopy (by two low-wavelength νCO bands, indicating the anionic character of the metal acylate), by analysis, and by secondary reactions[5].

Decisive evidence for the structure of *(3b)* is obtained from the product *(5)*, formed in the same fashion from $Et_3P{=}CHMe$ *(4)* and *(1)*; even in pure form, *(5)* is a non-crystallizable oil and can thus be measured NMR spectroscopically[6a].



Dissociation (on dissolution) and regeneration (on concentration of the solution) of *(3b)* and *(5)* can be repeated unlimitedly. Addition of the phosphorus ylide *(2)* to the carbonyl carbon of *(1)* (step A) and deprotonation of the adduct *(3a)* at the CH_2-bridge by further ylide *(2)* (step B) are accordingly completely reversible processes.

$$2\ Et_3P{=}CHMe + MeC_5H_4Mn(CO)_3 \longrightarrow$$
(4) *(1)*

$$[Et_4P][(Mn)\text{–}C(O)\text{–}MeC{=}PEt_3]$$
(5)

$(Mn) = \eta^5\text{-}MeC_5H_4(CO)_2Mn$

Decisive for an understanding of this unusual phenomenon is the fact that in step B a transylidation equilibrium[7] is established between the corresponding acid/base pairs:

$[Me_4P]^{\oplus}$ (acid (a1))/Me_3PCH_2 *(2)* (base (b1))

and

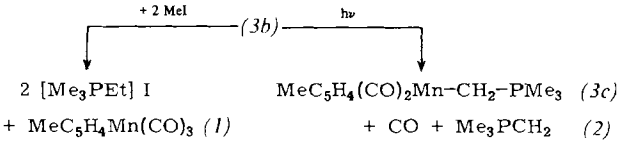
$MePCH_2C(O)\text{–}(Mn)$ *(3a)* (acid (a2))/$[Me_3PCHC(O)\text{–}(Mn)]$ (base (b2))

The shift of equilibrium to the left on dissolution of *(3b)* begins with the deprotonation of the cation (a1) by the anion (b2) and is strongly favored, because the regenerated ylide adduct *(3a)* is extremely labile and is already spontaneously cleaved into *(1)* and *(2)* by the solvent. Since the reversibility of addition and transylidation is not observed in the case of metal systems bearing only CO[1,3] ligands, it has to be ascribed chiefly to the higher σ-donor/π-acceptor ratio of the methylcyclopentadienyl ligand in comparison to CO. It causes a) a lower electrophilicity of the carbonyl carbon and hence a lower stability of the primary product *(3a)*, b) a high electron density on the manganese, which increases the basicity of the ylide function in the metal acylate to such an extent that it can deprotonate the $[Me_4P]^{\oplus}$ counterion[8].

[*] Prof. Dr. W. Malisch, Dipl.-Chem. H. Blau
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Presented in part at the Chemiedozententagung 1979 (Darmstadt), Referateband B47, and the IX. International Conference on Organometallic Chemistry 1979 (Dijon), Abstracts of Papers P32T. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

The reversibility of formation of *(3b)* rationalizes its smooth transformation into the ylide complex *(3c)*[6b] on irradiation and into $[Me_3PEt]^{\oplus}I^{\ominus}$ and *(1)* on reaction with methyl iodide[9].



In both cases the products are formed from free *(1)* and *(2)*, which are generated from *(3b) via* steps B and A during the reaction.

Procedure

(3b): A solution of *(2)* (721 mg, 8.0 mmol) in pentane (15 ml) is added dropwise with vigorous stirring to a solution of *(1)* (872 mg, 4.0 mmol) in pentane (30 ml). A voluminous egg-yellow precipitate immediately separates out. After cooling the reaction mixture to 0 °C for 15 min, the precipitate is collected on a frit, washed with 20 ml ice-cold pentane, and briefly dried in a high vacuum at 25 °C; yield: 1.45 g (91%) *(3b)*. Above 114 °C *(3b)* is converted, with melting, into the educts[4].

(5): Pure *(4)* (1169 mg, 4.0 mmol) is added dropwise at 25 °C to liquid *(1)* (872 mg, 4.0 mmol). The reaction mixture immediately thickens to an orange-brown oil[6a].

(3c): A suspension of *(3b)* (1588 mg, 3.99 mmol) in benzene (60 ml) is irradiated until dissolution of *(3b)* (evolution of CO) and, after concentration of the solution to 30 ml, *(3c)* is precipitated with pentane (60 ml); yield: 994 mg (89%) of golden yellow, crystalline *(3c)*, m.p. 72—74 °C[6b].

Received: April 2, 1980 [Z 632a IE]
German version: Angew. Chem. 92, 1063 (1980)

[1] *W. C. Kaska, D. K. Mitchell, R. F. Reichelderfer, W. D. Korte*, J. Am. Chem. Soc. *96*, 2847 (1974); *L. Knoll*, Chem. Ber. *111*, 814 (1978); *W. Malisch, H. Blau, S. Voran*, Angew. Chem. *90*, 827 (1978); Angew. Chem. Int. Ed. Engl. *17*, 780 (1978).

[2] *H. Schmidbaur, W. Tronich*, Chem. Ber. *101*, 595 (1968).

[3] *W. Malisch, H. Blau*, unpublished results.

[4] IR (nujol): $\nu CO = 1834, 1784\ cm^{-1}$. The acyl band cannot be located since it is shifted into the region of the CH deformation vibrations.

[5] *W. Malisch, H. Blau, U. Schubert*, Angew. Chem. *92*, 1065 (1980); Angew. Chem. Int. Ed. Eng. *19*, 1020 (1980).

[6] a) *(5)*: $^{13}C\{^1H\}$-NMR (neat, TMS ext.): $\delta = 103.9, 83.7, 83.3$, and 14.4 (ring-C-1, -C-2,5, -C-3,4, and $-CH_3$), 259.8 (br., acyl-C), 226.5 (CO), 62.9 (C–P, $J_{CP} = 74.3$ Hz), 27.9 (CCH_3); $^{31}P\{^1H\}$-NMR (neat, H_3PO_4 ext.): $\delta = 40.11$ ($P^{\oplus}$, broadened by proton exchange with *(4)* which is present in small amounts), 6.45 (P–C); IR (film): $\nu CO = 1845, 1760\ cm^{-1}$; b) *(3c)*: ^1H-NMR (C_6D_6, TMS int.): $\delta = 4.4$ (m, 4 ring-H), 1.95 (ring-CH_3), 0.87 (d, $P(CH_3)_3$, $^2J_{HCP} = 13.0$ Hz), −0.39 (d, CH_2, $^2J_{HPC} = 12.4$); $^{13}C\{^1H\}$-NMR (C_6D_6, TMS int.): $\delta = 240.1$ (CO), 98.3, 83.5, 82.3, and 14.2 (Ring-C-1, -C-2,5, -C-3,4, and $-CH_3$), 14.1 (d, PCH_3, $J_{CP} = 55.9$ Hz), −15.1 (d, CH_2, $J_{CP} = 33.8$ Hz); $^{31}P\{^1H\}$-NMR (C_6D_6, H_3PO_4 ext.): $\delta = 29.2$; IR (C_6H_6): $\nu CO = 1871, 1790\ cm^{-1}$.

[7] Phosphonium salts can be regarded as Brønsted acids, alkylidenephosphoranes as the corresponding bases: cf. *H. J. Bestmann*, Angew. Chem. *77*, 609, 651, 850 (1965); Angew. Chem. Int. Ed. Engl. *4*, 583, 645, 830 (1965).

[8] We have meanwhile observed this effect on several carbonyl (cyclopentadienyl) and carbonyl(cyclopentadienyl)nitrosylmetal complexes; *W. Malisch, H. Blau*, Z. Naturforsch., in press.

[9] Analogous results are obtained in the case of reactions with $C_5H_5Mn(CO)_3$ instead of *(1)*. The ring substituent accordingly has no influence on the formation and reactivity of the compounds analogous to *(3b)* $[C_5H_5(CO)_2Mn—C(O)CHPMe_3][Me_4P]$; m.p. (with back dissociation) = 140 °C; photolysis affords $C_5H_5(CO)_2Mn—CH_2—PMe_3$, m.p. 110 °C.

Phosphorus Ylide Carbene Complexes of Manganese—Synthesis and Structure[***]

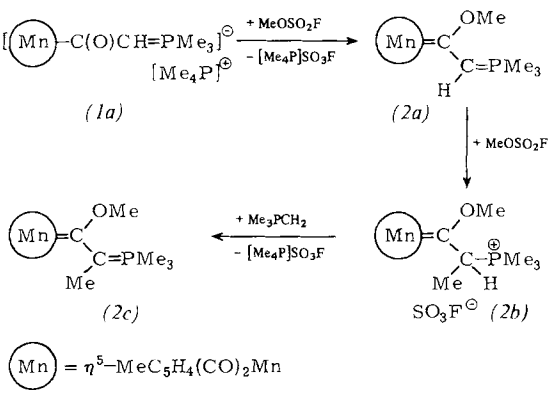
By *Wolfgang Malisch, Herbert Blau,* and *Ulrich Schubert*[*]

Dedicated to Professor Alfred Roedig on the occasion of his 70th birthday

The pronounced tendency of phosphorus ylide-substituted tetraalkylphosphoniummanganese acylates

$R_4P[(Mn)—C(O)CR'=PR_3]$ *(1)* [*(1a)*, R = Me, R' = H; *(1b)*, R = Et, R' = Me] to regenerate phosphorus ylide and (Mn)-CO determines the products in the photoreaction of *(1)* and in its reaction with alkyl halides[1]. Reactions in which the manganeseacyl-phosphorus ylide skeleton remains intact can be realized with the *hard* alkylating reagent $MeOSO_2F$[2], but proceed in a complex fashion since *(1a)* has, with its acyl oxygen and ylide carbon two potentially nucleophilic centers. Moreover, even on reaction in substance or in a small amount of solvent *(1a)* affords $MePCH_2$[1], which interferes in the reaction.

Reaction of *(1a)* and an equimolar amount of $MeOSO_2F$ generates, *via* elimination of $[Me_4P][SO_3F]$[3], a mixture of the ylide-carbene complexes *(2a)* and *(2c)*.



Mechanistically this product formation can be interpreted in terms of the ambifunctional anion of *(1a)* being initially methylated at the *hard* oxygen[4], which bears most of the negative charge. *(2a)* then reacts partially with further alkylating agent to give the phosphoniumcarbene complex *(2b)*, which is only a short-lived intermediate in this reaction since it is immediately deprotonated to *(2c)* by Me_3PCH_2 [formed from *(1a)*]. *(2b)* is obtained in pure form on reaction of excess $MeOSO_2F$ with *(1a)*[5]. In a separate reaction with $MePCH_2$, *(2b)* can be converted quantitatively into *(2c)*, which can be protonated once again with ethereal HCl selectively at the ylide function to give

$[(Mn)—C(OMe)CHMePMe_3]Cl$, m.p. 120 °C.

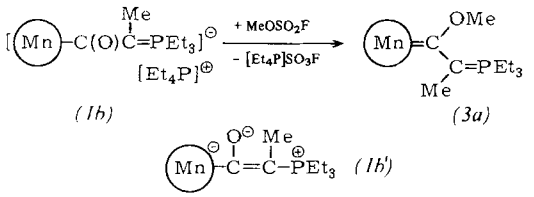
On the other hand, it is not possible to control the successive methylation of the acyl oxygen [in *(1a)*] and ylide function [in *(2a)*] by $MeOSO_2F$ in such a way that the oxygen is

[*] Prof. Dr. W. Malisch, Dipl.-Chem. H. Blau
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)
Dr. U. Schubert [**]
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] X-ray structure analysis.

[***] Presented in part at the Chemiedozententagung 1979 (Darmstadt) Referatband B47, and the XI. International Conference on Organometallic Chemistry 1979 (Dijon), Abstracts of Papers P32T. This work was supported by the Fonds der Chemischen Industrie.

exclusively methylated. Such a reaction is realized only with the triethyl(ethylidene) homologue *(1b)*, which smoothly affords the *O*-alkylated product *(3)* as shiny golden yellow crystals, m.p. 84 °C.



(1b) *(3a)*

(1b')

This reaction tendency can be attributed to a steric hindrance of *C*-alkylation by the methyl ligands on the ylide carbon and/or to an increase in the electron density on the acyl oxygen by its donor activity and that of the ethyl groups on the phosphorus. For the anion of *(1b)* the resonance structure *(1b')* should be strongly favored[6].

Table 1. Spectroscopic data of the carbene-manganese complexes *(2a—c)* [a].

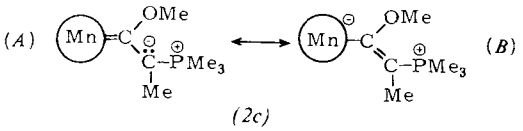
(2a): ^{1}H-NMR (C_6D_6): $\delta = 4.44$ (m, 4 ring-H), 1.96 (s, ring-CH_3), 4.73 (d, HC—P, $^2J_{HCP} = 34$ Hz), 4.04 (s, OCH_3), 0.74 (d, $P(CH_3)_3$, $^2J_{HPC} = 13.6$ Hz); IR (C_6H_6): $\nu CO = 1897$ vs, 1827 vs cm^{-1} [measured in admixture with *(2b)*]

(2b): ^{1}H-NMR (CD_3CN): $\delta = 4.93$ (m, 4 ring-H), 1.93 (s, ring-CH_3), 4.36 (s, OCH_3), 1.7 (dq, HCP, $^3J_{HCCH} = 7.6$ Hz, $^2J_{HCP} = 12.2$ Hz), 1.33 (dd, CH_3CP, $^3J_{HCCP} = 23$ Hz), 1.72 (d, $P(CH_3)_3$, $^2J_{HCP} = 14.2$ Hz); ^{31}P-NMR ([D_6]-DMSO): $\delta = 29.9$; IR (THF): $\nu CO = 1960$ vs, 1895 vs cm^{-1}

(2c): ^{1}H-NMR (C_6D_6): $\delta = 4.44$ (m, 4 ring-H), 1.94 (s, ring-CH_3), 2.28 (d, CH_3C, $^3J_{HCCP} = 16.2$ Hz), 4.00 (s, OCH_3), 0.80 (d, $P(CH_3)_3$, $^2J_{HCP} = 13.2$ Hz); ^{13}C-NMR (C_6D_6): $\delta = 236.19$ (CO), 257.6 (d, C—Mn, $^2J_{CP} = 7.77$ Hz), 101.9, 82.5, 81.1 and 14.4 (ring-C-1, -C-2,5, -C-3,4 and -CH_3), 58.14 (H_3CO), 17.81 (d, CH_3C, $^2J_{CCP} = 18.87$ Hz), 13.01 (d, CH_3P, $J_{CP} = 52.16$ Hz), 90.61 (d, C—P, $J_{CP} = 69.9$ Hz); ^{31}P-NMR (C_6D_6): $\delta = -4.49$; IR (C_6H_6): $\nu CO = 1898$ vs, 1830 vs cm^{-1}

[a] δ Values rel. TMS int. (^{1}H, ^{13}C) and H_3PO_4 ext. (^{31}P). ^{13}C- and ^{31}P-NMR ^{1}H-decoupled.

The composition and structure of *(2a—c)* and *(3)* are confirmed by elemental analysis and by IR and NMR spectra (cf. Table 1). In the case of *(2c)* its constitution was also confirmed by an X-ray structure analysis (cf. Fig. 1)[7]. This shows that the bonding in *(2c)* is best described by two resonance forms.



(A) *(B)*

(2c)

Fig. 1. Structure of *(2c)* in the crystal (important bond lengths in [pm]). Bond angles: Mn—C10—O10 123.5(7), Mn—C10'C11 129.0(8), O10—C10'C11 107.6(9), C10—C11—P 117.7(8)° [7].

(2c) differs from the $C_5H_5(CO)_2Mn$-carbene complexes known so far (resonance form A)[8] in that the length of the Mn—$C_{carbene}$ bond is extended by 7—10 pm, that of the $C_{carbene}O$ bond by 7—8 pm, and that the methyl group on O10 is no longer located in the coordination plane of the carbene carbon. The carbene carbon is electronically stabilized according to resonance form B, mainly by the ylide function; the methoxy group no longer participates[8]. Accordingly, the C10—C11 bond has strong double bond character, while the P—C11 bond (176.6 pm) is markedly longer than the corresponding bonds in phosphorus ylides. For comparison: The P—C_{sp^2} bond lengths in $[(Me_3P)_3C]I_2$ are 175 pm (formal bond order: 1.33)[9].

Procedure

(2b): *(1a)*, formed on reaction of $MeC_5H_4Mn(CO)_3$ (1.31 g, 6 mmol) with Me_3PCH_2 (1.08 g, 12 mmol) in pentane (15 ml) at 0 °C[1], is cooled, together with the solvent, to −78 °C. After addition of $MeOSO_2F$ (1.37 g, 12 mmol) and warming to room temperature the pale-yellow crystalline precipitate of *(2b)*, $[Me_4P]SO_3F$ and $[EtPMe_3]SO_3F$ is filtered off, washed with 3 × 5 ml benzene, and dried in a vacuum. Recrystallization from THF/CH_3CN (20 ml) affords 0.92 g (35%) of yellow *(2b)*, m.p. 99—100 °C.

(2c): A suspension of the above mixture of salts in benzene (40 ml) is treated dropwise at 8 °C with a solution of Me_3PCH_2 (0.45 g, 6 mmol) in benzene (10 ml). After 30 minutes' stirring the insoluble $[EtPMe_3]SO_3F$ and $[Me_4P]SO_3F$ are filtered off on a frit; the clear reaction solution is then evaporated down to 15 ml. After addition of pentane (30 ml) and cooling to 0 °C, 1.10 g (54%) of golden-yellow *(2c)*, m.p. 115—117 °C (dec.), crystallizes.

Received: April 2, 1980 [Z 632b IE]
German version: Angew. Chem. 92, 1065 (1980)

[1] $[MeP]SO_3F$ is contaminated with $[Me_3PEt]SO_3F$, which is formed by reaction of Me_3PCH_2 with $MeOSO_2F$.

[2] *R. Gompper, H.-H. Wagner*, Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976); *B. G. Pearson, J. Songstad*, J. Org. Chem. *32*, 2899 (1967).

[3] Me_3PCH_2 is immediately removed from the reaction mixture as $[Me_3PEt]SO_3F$.

[4] The ethyl groups guarantee high stabilization of the phosphonium moiety.

[5] Space group $Pca2_1$; $a = 1770(1)$, $b = 795.4(3)$, $c = 1187.7(6)$; $Z = 4$; $V = 1672 \times 10^6$ pm^3; ρ (calc) = 1.34 g/cm^3. Syntex $P2_1$/XTL, $Mo_{K\alpha}$-radiation (graphite monochromator, $\lambda = 71.069$ pm), 1077 structure factors ($F_0 \geq 3.90$), $R_1 = R_2 = 0.066$.

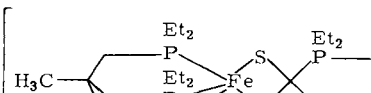
[6] *U. Schubert*, J. Organomet. Chem. *185*, 373 (1980).

[7] *B. Zimmer-Gasser, D. Neugebauer, U. Schubert, H. H. Karsch*, Z. Naturforsch. *B34*, 1267 (1979).

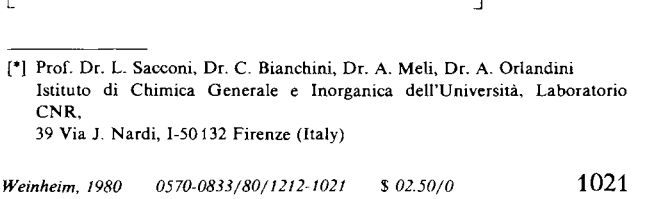
Metal-Assisted Reaction of Carbon Disulfide with the "Etriphos" Phosphane Ligand: Synthesis and Structure of $[(Etriphos)Fe\{S_2C(Et_2PCH_2)_2CMe_2\}](BF_4)_2$

By *Claudio Bianchini, Andrea Meli, Annabella Orlandini,* and *Luigi Sacconi*[*]

By reaction of CS_2 with hydrated iron(II) tetrafluoroborate in the presence of (neopentanetriyltris(diethylphosphane) ("Etriphos") *(1)*, we have obtained the iron(II) complex $[(Etriphos)FeZ](BF_4)_2$ *(2)*, where Z is the unprecedented six-membered heterocyclic zwitterion 1,1,3,3-tetraethyl-5,5-dimethyl-1,3-diphosphonia-2,2-cyclohexanedithiolate.



(1), etriphos



(2)

[*] Prof. Dr. L. Sacconi, Dr. C. Bianchini, Dr. A. Meli, Dr. A. Orlandini
Istituto di Chimica Generale e Inorganica dell'Università, Laboratorio CNR,
39 Via J. Nardi, I-50132 Firenze (Italy)

An X-ray structural investigation[1] on compound *(2)* (Fig. 1) has shown that the iron atom is five-coordinated by the three phosphorus atoms of the Etriphos ligand and by the two sulfur atoms of the zwitterion in a distorted square pyramid.

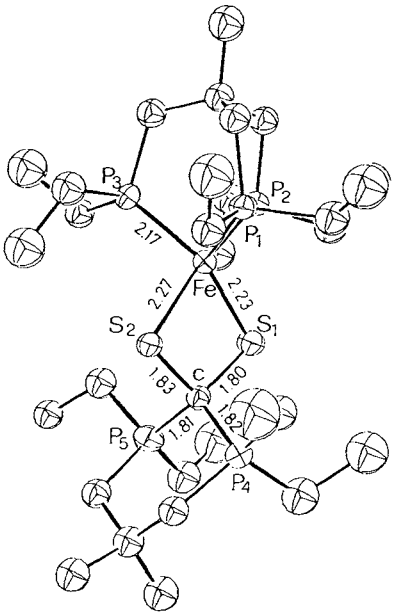


Figure 1. Perspective view of the complex cation $[(Etriphos)FeZ]^{2+}$ *(2)* (ORTEP diagram). Important bond lengths and bond angles: Fe—P(1—3) = 2.149—2.191(5) Å, S1—Fe—P3 = 150.1(2), S2—Fe—P2 = 163.7(2), S1—Fe—S2 = 77.8(2), S1—C—S2 = 101.7(9)° [1].

Some metal complexes with disulfido ligands containing *only one* quaternary phosphonium atom have already been reported[2], but no ring closure within the zwitterion has previously been observed. Definite conclusions have not been reached about the cleavage of a carbon-phosphorus bond in the third chain of the Etriphos rest.

The title compound *(2)* seems to be the first example of a five-coordinate iron(II) complex lying in a singlet ground state. Its diamagnetism can be ascribed to the very high $\sum n^0$ value of the P_3S_2 donor set[3], even higher than that of the P_4Br set in the complex $[Fe(P_4)Br]BPh_4$, which shows a singlet-triplet spin state equilibruim[4].
($P_4 = Ph_2P(CH_2)_2PPh(CH_2)_2PPh(CH_2)_2PPh_2$)

Procedure

All operations are performed under N_2 and with oxygen-free solvents. CS_2 is bubbled for 30 min through a hot mixture of *(1)*[5] (2 mmol) in dichloromethane (40 ml) and $Fe(BF_4)_2 \cdot 6H_2O$ (1 mmol) in ethanol (30 ml). The reaction mixture is maintained at reflux temperature for one hour. The resulting dark green solution is concentrated to give green crystals which are recrystallized from dichloromethane/ethanol; yield 40%.

Received: May 13, 1980 [Z 633 IE]
German version: Angew. Chem. *92*, 1055 (1980)

[1] Philips PW 1100 automatic diffractometer. Crystallographic data for the complex: $a = 18.964(7)$, $b = 18.016(7)$, $c = 14.033(5)$ Å, $\beta = 109.1(1)°$, monoclinic, space group $P2_1/c$, $Z = 4$. The structure was refined from 1936 observed reflections with $I \geq 3\sigma(I)$ to $R = 0.074$ and $R_W = 0.073$ respectively.

[2] *T. V. Ashworth, E. Singleton, M. Laing*, J. Chem. Soc. Chem. Commun. *1976*, 875; *G. R. Clark, T. J. Collins, S. M. James, W. R. Roper, K. G. Town, ibid. 1976*, 475; *P. V. Yaneff*, Coord. Chem. Rev. *23*, 183 (1977).

[3] *F. Basolo, R. G. Pearson:* Mechanisms of Inorganic Reactions. Wiley, New York 1967.

[4] *M. Bacci, S. Midollini, P. Stoppioni, L. Sacconi*, Inorg. Chem. *12*, 1801 (1973).

[5] *W. Hewertson, H. R. Watson*, J. Chem. Soc. *1962*, 1490.

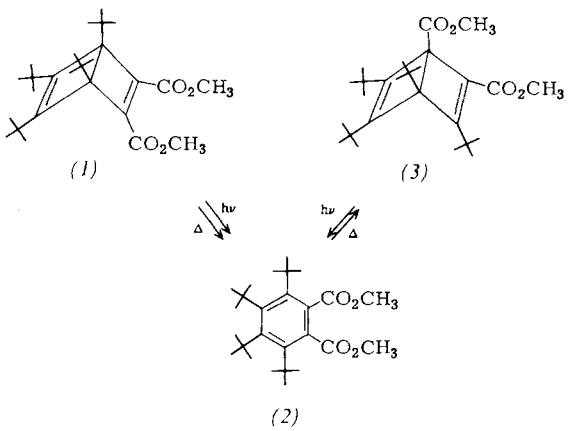
Reversal of Stability in the Benzene/Dewar-Benzene System[1]

By *Günther Maier* and *Klaus-Albert Schneider*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 70th birthday

In all previously investigated cases[2] the valence isomers of benzene and its derivatives under normal conditions[3] are higher in energy than the aromatic parent molecules. We have now found that crowding of very bulky groups can make the Dewar-benzene isomer more stable than the partner with an intact benzene ring.

Despite the great steric hindrance, tetra-*tert*-butylcyclobutadiene[4] reacts smoothly with acetylenedicarboxylate, even at room temperature, to give the symmetric Dewar-phthalate *(1)* (colorless crystals, m.p. 94—97 °C, 83%).



When *(1)* is heated to 120 °C a new, unsymmetrical Dewar-benzene isomer *(3)* is formed (colorless crystals, m.p. 98—100 °C, 51%) with another arrangement of the substituents. The structures assigned to *(1)* and *(3)* follow from the spectra (see Table 1) and the finding that both bicycles are

Table 1. Spectral data of the compounds *(1)*, *(2)*, and *(3)*. IR [cm^{-1}]; UV [nm], $\lambda_{max}(\varepsilon)$ in cyclohexane; NMR: δ values rel. to TMS (p = primary, q = quaternary).

(1): IR (CCl_4): 1730, 1715 (C=O), 1627 (C=C); UV: 256 (2500); MS: *m/e* = 418.3083 (calc.), 418.3079 (obs.); ^{1}H-NMR ($CDCl_3$): 1.37 (18H), 1.39 (18H), 3.78 (6H); ^{13}C-NMR (CD_2Cl_2): 32.4 (p), 32.7 (p), 33.5 (q), 34.6 (q), 51.6 (p), 78.4 (q), 152.3 (q), 158.7 (q), 165.0 (C=O)

(2): IR (Film): 1730, 1715 (C=O); UV: 305 (4050), 265 (14600) [5]; MS: *m/e* = 418.3083 (calc.), 418.3063 (obs.); ^{1}H-NMR (CD_2Cl_2): 1.44 (18H), 1.47 (18H), 3.64 (6H); ^{13}C-NMR (CD_2Cl_2): 34.8 (p), 36.2 (p), 41.0 (q), 46.5 (q), 52.0 (p), 129.2 (q), 142.6 (q), 160.1 (q), 171.1 (C=O)

(3): IR (CCl_4): 1734, 1720 (C=O), 1620 (C=C); UV: 235 (1650); MS: *m/e* = 418.3083 (calc.), 418.3120 (obs.); ^{1}H-NMR ($CDCl_3$): 1.18 (9H [a]), 1.30 (9H), 1.33 (9H), 1.37 (9H), 3.68 (3H), 3.85 (3H); ^{13}C-NMR ($C_2D_2Cl_4$): 29.5 (p [b]), 30.2 (p), 30.4 (p), 32.2 (p), 32.7 (q), 34.1 (q), 34.6 (q), 34.8 (q), 51.1 (p), 51.7 (p), 59.4 (q), 75.9 (q), 136.0 (q), 153.9 (q), 156.3 (q), 165.8 (q), 171.0 (C=O), 173.4 (C=O)

[a] At room temperature broad, at 120 °C in $C_2D_2Cl_4$ sharp. [b] At room temperature scarcely visible, at 100 °C sharp.

[*] Prof. Dr. G. Maier, Dipl.-Chem. K.-A. Schneider
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

converted into dimethyl 3,4,5,6-tetra-*tert*-butylphthalate *(2)* [oil; from *(1)*: 24%; from *(3)*: 43%] on irradiation with 254-nm light.

The thermally induced rearrangement *(1)*→*(3)* is without precedent, and could proceed *via* a sort of $[{}_{\pi}2_a + {}_{\pi}2_a + {}_{\sigma}2_s]$-sigmatropic shift[6]. The interim appearance of the NMR signals of *(2)*, however, would rather suggest that *(1)* first of all opens to give *(2)*, which then cyclizes to *(3)*. This would indicate that the Dewar-benzene derivative *(3)* must be thermodynamically more favored than the benzene derivative *(2)*. This is in fact so. Compound *(2)* rearranges at 120 °C into *(3)* in 90% yield. The eclipsed position of the bulky substituents in *(2)*, the first benzene derivative with four directly adjacent *tert*-butyl groups, and their more favorable staggered orientation in the Dewar-benzene derivative *(3)* effect reversal of the usual order of stability.

Received: October 22, 1980 [Z 634 IE]
German version: Angew. Chem. *92*, 1056 (1980)

[1] Valence Isomerizations, Part 15. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 14: *G. Maier, I. Fuss, M. Schneider*, Tetrahedron Lett. *1970*, 1057.

[2] Summaries: *G. Maier:* Valenzisomerisierungen. Verlag Chemie, Weinheim 1972, p. 165; *A. Greenberg, J. F. Liebmann:* Strained Organic Molecules. Organic Chemistry. Vol. 38. Academic Press, New York 1978, p. 232.

[3] Only in the case of hexakis(pentafluoroethyl)benzene is the Dewar-benzene derivative energetically more favorable above 278 °C for entropy reasons.

[4] *G. Maier, S. Pfriem, U. Schäfer, R. Matusch*, Angew. Chem. *90*, 552 (1978); Angew. Chem. Int. Ed. Engl. *17*, 520 (1978).

[5] Dimethyl 3,4,6-tri-*tert*-butylphthalate absorbs at $\lambda = 277$ ($\varepsilon = 8800$) and 218 nm (33100), the 3,4,5-isomer at 284 (8500) and 230 nm (17650) (*G. Maier, F. Bosslet*, unpublished).

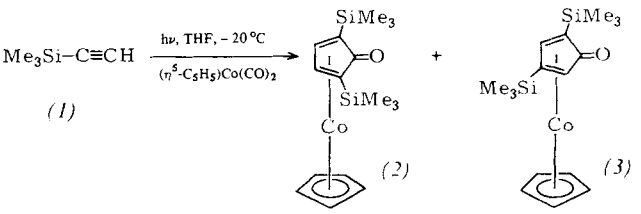
[6] Such a reaction has been postulated for a bicyclo[3.2.0]heptadienone: *T. Miyashi, M. Nitta, T. Mukai*, J. Am. Chem. Soc. *93*, 3441 (1971).

Cobalt Mediated [2+2+2]-Cycloadditions: A Simple Route to Substituted Cyclopentadienones[**]

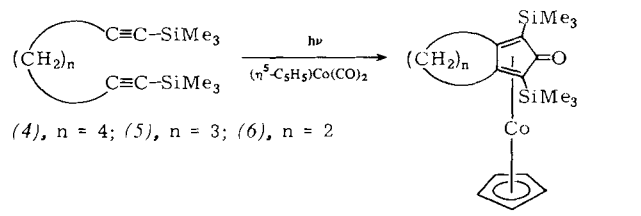
By *Ernst R. F. Gesing, Jeffrey P. Tane*, and *K. Peter C. Vollhardt*[*]

Five-membered ring construction *en route* to cyclopentanoid natural products is an area of intensive current research effort[1]. Cyclopentadienones[2] have played no role in it due to their high reactivity in Diels-Alder reactions, avoidable only by introduction of synthetically disadvantageous bulky substituents, typically *tert*-butyl and phenyl. An attractive way to generate and stabilize the cyclopentadienone nucleus is by the transition metal-mediated cyclization of two alkynes with one molecule of carbon monoxide[3], but application of this method to organic synthesis has been hampered by low yields due to poor selectivity, the necessity for the presence of specific substituents or expensive metals, and the absence of mild demetalation methods.

We have found that irradiation of $(\eta^5\text{-}C_5H_5)Co(CO)_2$ in the presence of trimethylsilylacetylene *(1)* in tetrahydrofuran at −20 °C furnishes the dark red complexes *(2)* and *(3)* with pronounced chemo-[4] and regioselectivity (ratio 3:1) in good yield (Table 1). Higher temperatures lead to increasing alkyne trimer formation.



Interestingly, the more bulky η^5-$[C_5(CH_3)_5]Co(CO)_2$ reverses the product ratio (1:3.7) of the corresponding pentamethyl-analogs of *(2)* and *(3)*, an observation which might become valuable in synthetic applications.



(4), n = 4; *(5)*, n = 3; *(6)*, n = 2

(7), n = 4; *(8)*, n = 3; *(9)*, n = 2

Similar reaction with α,ω-diynes *(4)* and *(5)* yield the annelated cyclopentadienones *(7)* and *(8)*, whereas *(6)* requires different reaction conditions (irradiation with a GE projection lamp, 120 V, 250 W; refluxing *o*-xylene; syringe pump addition) to give the theoretically interesting[6] strained *(9)* in low yield (Table 1).

Table 1. Physical data of compounds *(2)*, *(3)*, *(7)*—*(18)*. All new compounds gave satisfactory analytical data and mass spectra. ^{1}H-NMR: δ values; IR: ν_{CO}; UV: λ_{max} (log ε), in cyclohexane.

(2): 53%, m.p. 180 °C; ^{1}H-NMR (C_6D_6): 4.80 (s, 2H), 4.60 (s, 5H), 0.40 (s, 18H); IR (CCl_4): 1580 cm^{-1}

(3): 17%; m.p. 88 °C; ^{1}H-NMR (C_6D_6): 4.94 (d, J = 1 Hz, 1H), 4.72 (s, 5H), 4.36 (d, J = 1 Hz, 1H), 0.46 (s, 9H), 0.19 (s, 9H); IR (CCl_4): 1591 cm^{-1}

(7): 73%; m.p. 236 °C; ^{1}H-NMR (C_6D_6): 4.53 (s, 5H), 2.20 (m, 4H), 1.93 (m, 4H), 0.53 (s, 18H); IR ($CHCl_3$): 1567, 1544 cm^{-1}

(8): 61%, m.p. 256 °C; ^{1}H-NMR (C_6D_6): 4.53 (s, 5H), 2.40—1.83 (m, 6H), 0.60 (s, 18H); IR ($CHCl_3$): 1566, 1544 cm^{-1}

(9): 6%; m.p. 238 °C; ^{1}H-NMR (C_6D_6): 4.60 (s, 5H), 2.92 (AA'BB'm, 4H), 0.53 (s, 18H); IR ($CHCl_3$): 1559, 1536 cm^{-1}

(10): yellow crystals; $T_{dimerization} = 37$ °C; ^{1}H-NMR (CD_2Cl_2): 7.27 (s, 2H), 0.14 (s, 18H); IR (CCl_4): 1698 cm^{-1}; UV (C_6H_{12}): 387 (2.88), 405 sh (2.83), 435 sh (2.58) nm

(11): yellow needles; m.p. 74 °C; ^{1}H-NMR (C_6D_6): 2.53 (m, 4H), 1.40 (m, 4H), 0.52 (s, 18H); IR ($CHCl_3$): 1678 cm^{-1}; UV (C_6H_{12}): 441 (2.86), 444 sh (2.70)

(12): yellow needles; m.p. 27 °C; ^{1}H-NMR (C_6D_6): 2.30 (t, J = 6 Hz, 4H), 1.67 (quin, J = 6 Hz, 2H), 0.50 (s, 18H); IR ($CHCl_3$): 1683 cm^{-1}; UV (C_6H_{12}): 396 (2.91)

(13): fluorescing yellow oil; ^{1}H-NMR (C_6D_6): 2.90 (s, 4H), 0.43 (s, 18H); IR ($CHCl_3$): 1681 cm^{-1}; UV (C_6H_{12}): 393 (3.12)

(14): colorless crystals; m.p. 84 °C; ^{1}H-NMR (CCl_4): 7.08 (d, J = 3 Hz, 1H), 6.03 (d, J = 6 Hz, 1H), 5.71 (d, J = 6 Hz, 1H); 3.07 (d, J = 3 Hz, 1H), 0.25 (s, 9H), 0.18 (s, 9H), 0.08 (s, 9H), 0.02 (s, 9H); IR (CCl_4): 1750, 1675 cm^{-1}

(15): red orange crystals; m.p. 52 °C; ^{1}H-NMR ($CDCl_3$): 5.15 (s, 5H), 5.08 (AA'm, 2H), 4.49 (BB'm, 2H), 2.38 (s, 2H); IR (NaCl): 3407 (ν_{OH}), 1528 cm^{-1}

(16): carmine red crystals; m.p. 82 °C; ^{1}H-NMR ($CDCl_3$): 4.80 (s, 5H), 4.20 (s, 2H), 2.27 (m, 4H), 1.77 (m, 4H); IR ($CHCl_3$): 3696 (ν_{OH}), 1570 cm^{-1}

(17): carmine red crystals; m.p. 182 °C; ^{1}H-NMR ($CDCl_3$): 4.90 (s, 5H), 4.43 (s, 2H), 2.30 (s, 2H), 2.40 (m, 6H); IR ($CHCl_3$): 3672 (ν_{OH}), 1562 cm^{-1}

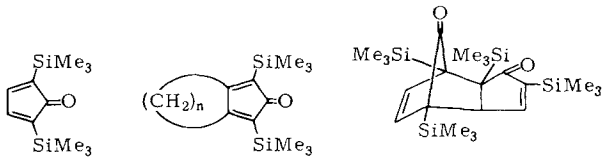
(18): carmine red crystals; m.p. 134 °C; ^{1}H-NMR ($CDCl_3$): 5.03 (s, 5H), 4.53 (s, 2H), 3.25 (m, 4H); IR ($CHCl_3$): 1568 cm^{-1}

α-Silyl-substituted enones have been shown to be excellent Michael acceptors[6]. Thus, the ligands encountered in *(2)*,

[*] Dr. E. R. F. Gesing, J. P. Tane, Prof. Dr. K. P. C. Vollhardt
Department of Chemistry, University of California, Berkeley;
Materials and Molecular Research Division
Lawrence Berkeley Laboratory
Berkeley, California 94720 (USA)

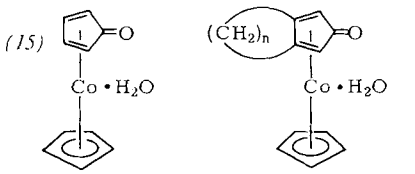
[**] This work was supported by the NIH (GM22479). We appreciate preliminary experiments by Mr. *R. L. Brainard*. *E. R. F. G.* thanks the NATO/DAAD for a research fellowship (1979—1980). *K. P. C. V.* is a Fellow of the A. P. Sloan Foundation (1976—1980) and a Camille and Henry Dreyfus Teacher Scholar (1978—1983).

(7), and *(8)* constitute potentially valuable organic synthons, if decomplexation without dimerization were possible. The latter is achieved in nearly quantitative yields using ceric ammonium nitrate in a two-phase solvent system (CH_3CN/*n*-C_5H_{12}) to give *(11)*—*(13)* (Table 1). Under the same conditions at −20 °C, *(2)* yields the volatile *(10)* (11%) and its dimer *(14)* (54%) assigned the *exo*-configuration[7]. Dimerization of *(10)* occurs readily at 37 °C, but the monomer may be quantitatively regenerated by flash pyrolysis at 550 °C (10^{-4}—10^{-5} torr) (Table 1). This compound constitutes the first useful monomeric cyclopentadienone synthon.



(10) *(11)*, n = 4; *(12)*, n = 3; *(13)*, n = 2 *(14)*

The parent cycloalkane-annelated cyclopentadienones *(2)* and *(7)*—*(9)* were unknown. Their synthesis is of synthetic and theoretical interest since one may predict their respective rates of dimerization *to decrease* due to the increasing strain associated with the respective Diels-Alder adducts. Treatment of *(2)* and *(7)*—*(9)* with benzyltrimethylammonium fluoride (THF, 2 equiv. ethanol, reflux) gave the hydrated complexes *(15)*—*(18)* (Table 1) in 70—80% yield. Oxidation of *(16)* and *(17)* under the conditions employed in the preparation of *(10)*—*(13)*, gave ligand dimers, whereas in the case



(16), n = 4
(17), n = 3
(18), n = 2

of *(18)* a 1:1 adduct with acetonitrile of as yet unknown structure was obtained. This confirms that uncomplexed bicyclo[3.2.0]hepta-1(5),4-dien-3-one is reluctant to dimerize but is otherwise highly reactive.

Procedure

η^4-Cyclopentadienone-(η^5-C_5H_5)Co complexes *(2)*, *(3)*, *(7)*, *(8)*: 17 mmol of alkyne *(1)*, 6 mmol of *(4)* or 6 mmol of *(5)* and 3 mmol of (η^5-C_5H_5)$Co(CO)_2$ were irradiated in dry, degassed, THF (250 ml) at −20 °C with a Hanovia Hg medium pressure lamp (679 A36) for 5.5 h. The solvent was evaporated and the crude residue chromatographed (neutral Al_2O_3, Alfa CAMAG 95+%, −60 mesh, deactivated with 4.5% H_2O) to recover excess alkyne (elution with *n*-pentane) and subsequently the products (elution with ether). Recrystallization from ether/pentane, yields pure products.

Oxidative demetalations to form *(10)*—*(13)*: A 2.5×10^{-2} M solution of complexes *(2)*, *(7)*, *(8)*, or *(9)* in acetonitrile at 0 °C was covered with an equal volume of *n*-pentane and reacted with $(NH_4)_2Ce(NO_3)_6$ (1.5 equiv.) with stirring. After 30 min the yellow pentane layer was decanted, more cold pentane added, and the procedure repeated until the hydrocarbon layer stayed colorless. The solvent was removed and the product sublimed (10 °C/0.025 torr; −10 °C cold finger) or recrystallized (*n*-pentane).

Received: September 22, 1980 [Z 635 IE]
German version: Angew. Chem. *92*, 1057 (1980)

[1] *R. A. Ellison*, Synthesis *1973*, 397; *P. Prempree, T. Siwapinyoyos, C. Thebtaranonth, Y. Thebtaranonth*, Tetrahedron Lett. *1980*, 1169; *A. E. Greene, J.-P. Deprés*, J. Am. Chem. Soc. *101*, 4003 (1979); *B. M. Trost, D. M. T. Chan, ibid. 101*, 6429 (1979), and references therein.

[2] *M. A. Ogliaruso, M. G. Romanelli, E. J. Becker*, Chem. Rev. *65*, 261 (1965); *G. Maier, R. Boßlett*, Tetrahedron Lett. *1972*, 1025; *O. L. Chapman, C. L. McIntosh*, Chem. Commun. *1971*, 770.

[3] *W. Hübel* in *I. Wender, P. Pino:* Organic Syntheses via Metal Carbonyls. Wiley, New York 1968. Vol. I, p. 273; *P. Pino, G. Braca* in Vol. II (1977), p. 419.

[4] Depending on conditions (η^5-C_5H_5)$Co(CO)_2$ reacts with alkynes chemoselectively to give cyclotrimers, biscarbyne clusters, η^4-cyclohexadiene-, and η^4-cyclobutadiene complexes, respectively: *R. L. Funk, K. P. C. Vollhardt*, J. Am. Chem. Soc. *102*, 5245, 5253 (1980); *E. D. Sternberg, K. P. C. Vollhardt, ibid. 102*, 4839 (1980); *J. R. Fritch, K. P. C. Vollhardt*, Angew. Chem. *92*, 570 (1980); Angew. Chem. Int. Ed. Engl. *19*, 559 (1980); *K. P. C. Vollhardt, M. J. Winter*, to be published.

[5] *R. Breslow, M. Oda, T. Sugimoto*, J. Am. Chem. Soc. *96*, 1639 (1974); *R. S. Macomber*, J. Org. Chem. *38*, 816 (1973).

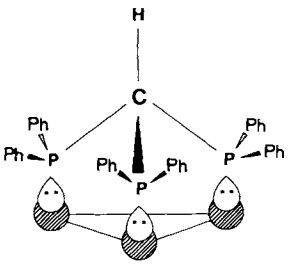
[6] *G. Stork, B. Ganem*, J. Am. Chem. Soc. *95*, 6152 (1973); *R. K. Boeckman, ibid. 95*, 6867 (1973); *96*, 6179 (1974); *G. Stork, T. Singh, ibid. 96*, 6181 (1974).

[7] *R. Y. S. Tan, R. A. Russell, R. N. Warrener*, Tetrahedron Lett. *1979*, 5031.

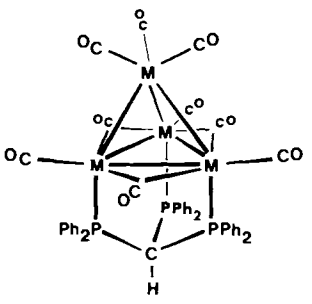
Polymetallic Complexes: Complexation of the Triangular Faces of Clusters by the Tripod Ligand, $HC(PPh_2)_3$[**]

By *Anita A. Arduini, Ali A. Bahsoun, John A. Osborn,* and *Christian Voelker*[*]

Strategies for the synthesis of multimetallic complexes are of great interest but have not been widely developed[1]. We have sought therefore to bind several metal atoms in close proximity by use of suitably designed polydentate ligands. For the stabilization of triangular arrays of metal atoms of which metal cluster frameworks are mainly constructed, we have synthesized and studied the family of tripod ligands, $RC(L^1L^2L^3)$, where L^1, L^2, L^3 are donor functions such as PR_2, AsR_2, SR[2]. Models show the bite angle to favor the simultaneous binding of *three* metal atoms to the tripod ligand *(1)*, rather than chelation about one metal as found typically for other tripod ligands[3]. We illustrate here that the easily prepared[4], archetypal member of this ligand family, $HC(PPh_2)_3$, *(1)* (or tripod) can indeed complex three metal atoms on a cluster surface: This unusual binding mode can also be utilized for the stepwise synthesis of clusters[5].



(1)



(2), (3), (5), (7)

[*] Prof. J. A. Osborn, Dr. A. A. Arduini, Dr. A. A. Bahsoun, C. Voelker
Laboratoire de Chimie Inorganique Moléculaire et de Catalyse
Institut Le Bel, Université Louis Pasteur
4, rue Blaise Pascal, F-67000 Strasbourg (France)

[**] This work was supported by the Centre National de la Recherche Scientifique (ERA 721) and A.T.P. N° 4095 (Catalyse Homogène).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1024 $ 02.50/0

Tetrahedral clusters of the type $M_4(CO)_{12}$ were chosen to test the complexation properties of *(1)* since no stereochemical problems on substitution were anticipated[6]. This expectation is borne out by experiment since reactions of *(1)* with $M_4(CO)_{12}$ clusters proceed cleanly to yield nearly quantitative yields of products *(2)*—*(7)* (Table 1). C_{3v} structures are proposed for these complexes, the tripod ligand complexing a carbonyl-bridged triangular face as shown for *(2)*, *(3)*, *(5)*, and *(7)*, whereas in *(4)* and *(6)* all carbonyls are terminal.

Table 1. Some spectroscopic properties of the complexes $M_4(CO)_9$(tripod) [a].

	M_4	Color	IR (ν_{CO} [cm^{-1}], CH_2Cl_2)	$^{31}P\{^1H\}$-NMR δ (rel. H_3PO_4)
(2)	Co_4	green	2050 s, 2000 s, 1975 s, 1780 m	44.3 (s)
(3)	Rh_4	deep red	2060 s, 2010 vs, 1990 s, 1805 s	18.0 (l, m), 14.4 (l, m), $J_{Rh\ P}$ = 133 Hz
(4)	Ir_4	yellow	2060 s, 2010 vs, 1970 s, 1950 m	−39.1 (s)
(5)	Co_2Rh_2	violet	2040 s, 2005 vs, 1985 s, 1845 w, 1805 m, 1785 m	33.0 (l, br), 29.0 (l, d), 25.2 (l, d), $J_{Rh\ P}$ = 137 Hz
(6)	H_4Ru_4	deep red	2065 s, 2015 s, 2000 s, 1960 w, br, 1940 w, br	35.9 (s)
(7)	$HFeCo_3$	deep violet	2045 s, 2035 s, 2010 vs, 1970 w, 1930 m, 1810 s, 1780 s	44.5 (br)

[a] Satisfactory elemental analyses were obtained for all the new compounds.

Several points are of note: a) The ^{13}C-NMR spectrum of *(3)* at 70 °C shows no sign of carbonyl exchange processes (merry-go-round or other)[7a], whereas the parent $Rh_4(CO)_{12}$ shows a limiting spectrum only at −65 °C[7b]. However, the exchange of ^{13}CO with *(3)* shows statistical incorporation to occur, indicating that intramolecular exchange is fast on a chemical time scale; b) in the reactions producing *(5)* and *(7)* the tripod ligand has selected only one of the two different faces to complex, *e.g.* for *(5)* the $CoRh_2$ face is complexed preferentially to the Co_2Rh face; c) these constrained clusters appear more resistant to fragmentation than the parent compounds, a property which may be useful if multimetal site catalysis is to be observed[8]. For example, refluxing *(2)* in toluene produces (π-toluene)$Co_4(CO)_6$(tripod)[9] in quantitative yield with no special precautions[10]. Also both *(2)* and *(3)* undergo no change in toluene at 100 °C under CO (30 bar) over 18 h whereas under such conditions the parent carbonyls (or their phosphane-substituted derivatives) are unstable[11].

Experimental

(1) (0.30 g, 0.53 mmol) in toluene (30 ml) was added dropwise with vigorous stirring to $Rh_4(CO)_{12}$ (0.38 g, 0.51 mmol) dissolved in hexane (80 ml) over 1 h. The solution then was stirred under a slow stream of argon for *ca.* 6 h. The deep red precipitate of *(3)* was filtered off, washed with hexane (2 × 25 ml), and dried *in vacuo*. Recrystallization from CH_2Cl_2/hexane gives *(3)* (0.50 g, 80%) as deep red crystals.

Received: August 4, 1980 [Z 636a IE]
German version: Angew. Chem. *92*, 1058 (1980)

[1] For a recent review, see *H. Vahrenkamp*, Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978). For a rare example of designed cluster synthesis, see *F. Richter, H. Vahrenkamp, ibid. 91*, 566 (1979) and *18*, 531 (1979), respectively.

[2] See also *J. J. de Boer, J. A. van Doom, C. Masters*, J. Chem. Soc. Chem. Commun. *1978*, 1005; *H. H. Karsch, U. Schubert, D. Neugebauer*, Angew. Chem. *91*, 518 (1979); Angew. Chem. *18*, 484 (1979).

[3] See for example *P. Dapporto, S. Midollini, A. Orlandini, L. Sacconi*, Inorg. Chem. *15*, 2768 (1976); *K. D. Tan, R. Uriarte, T. J. Mazanec, D. W. Meek, J. Am. Chem. Soc. 101*, 6614 (1979).

[4] *K. Issleib, H. P. Abicht*, J. Prakt. Chem. *312*, 456 (1970); we have characterized *(1)* more completely, *e.g.* by mass spectrum [parent ion, *m/e* = 568] and NMR spectroscopy [in toluene, $^{31}P\{^1H\}$, δ = −9.4 ppm (from H_3PO_4)].

[5] *J. A. Osborn, G. Stanley*, Angew. Chem. *92*, 1059 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1025 (1980).

[6] *Masters et al.* [2] using an analogous ligand, $(CH_3)Si(PnBu_2)_3$, and we, using *(1)*, have found that reactions with $Ru_3(CO)_{12}$ gave only poor yields of capped products. This we attribute mainly to the observation that in these triangular complexes, $M_3(CO)_{12}$ (M = Fe, Ru), substitution occurs generally at the equatorial site whereas the capped product derives from axial substitution.

[7] a) *E. Band, E. L. Muetterties*, Chem. Rev. *78*, 639 (1978); b) *J. Evans, B. F. G. Johnson, J. Lewis, J. R. Norton, F. A. Cotton*, Chem. Commun. *1973*, 807.

[8] *E. L. Muetterties, T. N. Rhodin, E. Band, C. F. Brucker, W. R. Pretzer*, Chem. Rev. *79*, 91 (1979).

[9] An X-ray structure of (π-toluene)$Co_4(CO)_6$(tripod) has been carried out which confirms the structure proposed here (*J. J. Bonnet*, to be published).

[10] *G. Bor, G. Sbrignadello, F. Marcati*, J. Organomet. Chem. *46*, 357 (1972); *I. V. Khand, G. R. Know, P. L. Pauson, W. E. Watts*, J. Chem. Soc. Perkin Trans. *1973*, 975; *I. Sisak, C. Sisak, F. Ungvary, G. Palyi, L. Marko*, J. Organomet. Chem. *90*, 77 (1975).

[11] *R. Whyman*, J. Chem. Soc. Dalton Trans. *1972*, 1375.

Template Synthesis of Clusters using the Tripod Ligand $HC(PPh_2)_3$ $Ni_3(CO)_6$(tripod)[**]

By *J. A. Osborn* and *George G. Stanley*[*]

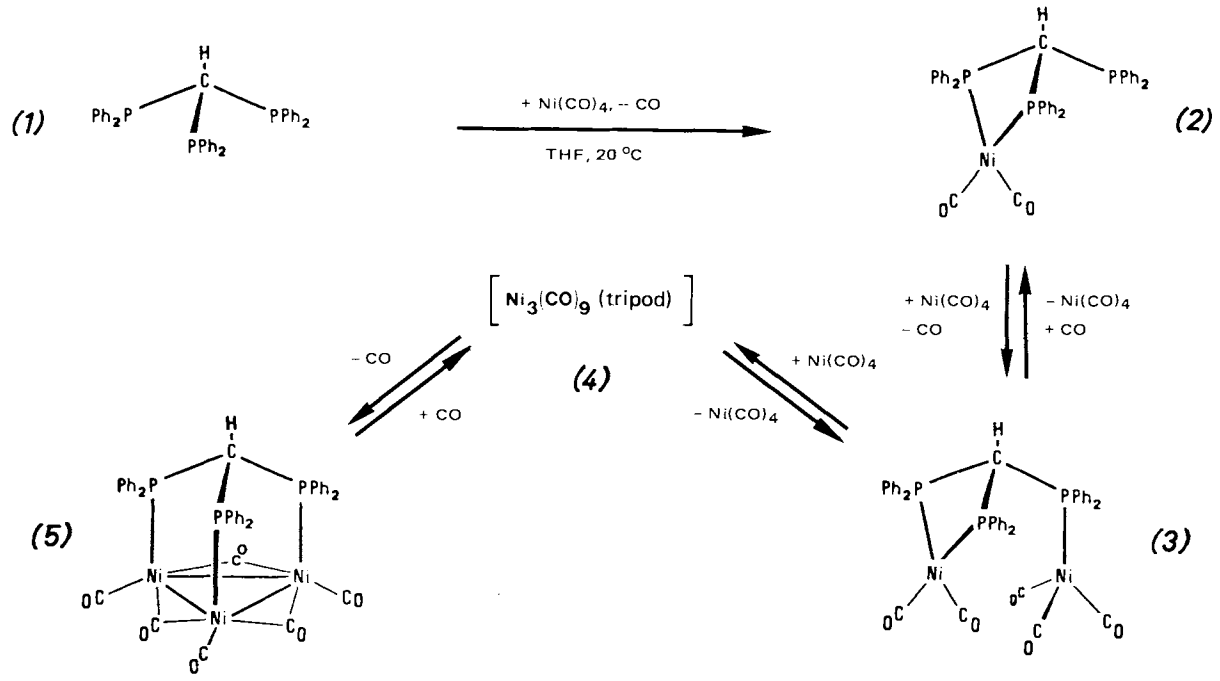
We have shown[1] that the ligand $HC(PPh_2)_3$, *(1)*, (tripod) belongs to an unusual class of ligands which will bind three metals simultaneously in a triangular array. Here we illustrate how this property can be used for the construction of trinuclear clusters from mononuclear starting materials.

When *(1)* is reacted with an excess of $Ni(CO)_4$, a yellow solution is obtained, which on evaporation *in vacuo* turns orange and precipitates the light orange solid, $Ni_3(CO)_6$(tripod) *(5)*[2]. This compound has been characterized by elemental analysis and molecular weight measurements as well as infrared and ^{31}P-NMR spectroscopy (Table 1). Compound *(5)* has C_{3v} symmetry and is the first known nickel(0) trimer, the only other well characterized Ni(0) clusters being $Ni_4(CO)_6[P(CH_2CH_2CN)_3]_4$[3a] and $Ni_4(CNR)_7$[3b].

The mechanism of formation of *(5)* has been monitored by IR and ^{31}P-NMR studies. On addition of excess $Ni(CO)_4$ to *(1)*, only two tripod-containing species are initially observed: $Ni(CO)_2$(tripod) *(2)*[2] and a small amount of $Ni_2(CO)_5$(tripod) *(3)*[2]. In the mononuclear species *(2)*, which has been prepared separately, tripod functions as a bidentate ligand on one metal center[4]. The dimer *(3)*, which is formed by attack of $Ni(CO)_4$ on the free PPh_2 of *(2)*, has not been isolated[2]. Characteristically, the IR spectrum of *(3)* shows a simple superposition of nickel dicarbonyl and tricarbonyl moieties, consistent with the expected lack of a Ni—Ni bonding interaction. However, no trimer is observed in solution until vacuum evacuation to remove, paradoxically, the excess $Ni(CO)_4$ as well as the CO liberated. The explanation is that the presence of CO liberated in forming *(2)* and *(3)* disfavors the formation of trimer in the equilibrium and also inhibits the dissociation of $Ni(CO)_4$ to form $Ni(CO)_3$. This

[*] Prof. J. A. Osborn, Dr. G. G. Stanley
Laboratoire de Chimie Inorganique Moléculaire et de Catalyse
Institut Le Bel, Université Louis Pasteur
4, rue Blaise Pascal, F-67000 Strasbourg (France)

[**] This work was supported by the Centre National de la Recherche Scientifique (ERA 721) and ATP N° 4095 (Catalyse Homogène). Support from GRECO (CO) is also gratefully acknowledged. *G. G. S.* is a recipient of a NATO Postdoctoral Fellowship.



latter reactive species is needed to open the chelate in *(3)* to form the trinuclear species *(4)*[5]. Decarbonylation of *(4)* occurs rapidly *in vacuo* to form three M—M bonds, yielding the trinuclear species *(5)*. We find that treatment of *(5)* with CO (1 bar) regenerates *(2)* and $Ni(CO)_4$; similar behavior has been observed with the related anionic nickel carbonyl clusters[6].

Hence *(1)* can act as a template for the stepwise formation of trinuclear clusters.

Experimental

All manipulations were performed under nitrogen. *(1)* (2.5 g, 4.4 mmol) dissolved in THF (160 ml) was added to $Ni(CO)_4$ (22 g, 130 mmol) in THF (30 ml) at 25 °C. The solution immediately turns light yellow with CO evolution. *(2)* can be isolated at this stage as a light yellow powder by precipitation with hexane. Alternatively, on evaporation of the original solution *in vacuo*[7] at 25 °C, the solution becomes deep orange and an orange precipitate of *(5)* forms at *ca.* half volume. Recrystallization of *(5)* from CH_2Cl_2/hexane yields orange crystals (2.0 g, 50%).

Received: August 4, 1980 [Z 636b IE]
German version: Angew. Chem. 92, 1059 (1980)

[1] *A. A. Arduini, A. A. Bahsoun, J. A. Osborn, C. Voelker*, Angew. Chem. *92*, 1058 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1024 (1980).

[2] *(2)*: pale yellow solid; IR (CH_2Cl_2): 1998 s, 1939 s, ν_{CO}; $^{31}P\{^1H\}$: $\delta = -21.8$ (t, 1P), +30.5 (d, 2P, $J_{P\ P} = 20$ Hz); *(3)*: IR (CH_2Cl_2): 2070 m, 2040 m, 2000 s, 1940 s cm^{-1}, ν_{CO}; $^{31}P\{^1H\}$: $\delta = +34.3$ (t, 1P), +43.8 (d, 2P, $J_{P\ P} = 4$ Hz); *(5)*: IR (CH_2Cl_2): 2040 m, 2010 s, 1855 m, 1830 m cm^{-1}; ν_{CO}; $^{31}P\{^1H\}$: $\delta = 31.7$ (s).

[3] a) *M. J. Bennett, F. A. Cotton, B. H. Winguist*, J. Am. Chem. Soc. *89*, 5306 (1967); b) *E. L. Muetterties, E. Band, A. Kokorin, W. R. Pretzer, M. G. Thomas*, Inorg. Chem. *19*, 1552 (1980).

[4] The ν_{CO} vibrations in the IR spectrum of *(2)* are almost identical with those observed for $Ni(CO)_2(Ph_2PCH_2PCH_2)$; cf. *G. R. Van Hecke, W. Horrocks*, Inorg. Chem. *5*, 1960 (1966).

[5] A pale yellow complex can be precipitated out of concentrated reaction mixtures but it cannot be obtained pure. The IR spectrum in the solid state shows terminal carbonyl bands at 2060 and 1970 cm^{-1}, but on dissolving in CH_2Cl_2 to give an orange solution, these bands disappear to be replaced by those of *(2)*, *(5)*, and *(3)* and $Ni(CO)_4$. These observations indicate this species to be the trimer *(4)* formed before closure to *(5)* occurs and hence of formula $Ni_3(CO)_n$(tripod) where $n = 8$ or 9.

[6] *G. Longoni, M. Manassero, M. Sansoni*, J. Organomet. Chem. *174*, C41 (1979).

[7] The vacuum-evaporated $Ni(CO)_4$ is trapped in a liquid N_2 cooled cold trap in which Br_2 has previously been frozen. On warming $NiBr_2 + CO$ are formed. This reaction is very exothermic and for large amounts of $Ni(CO)_4$ appropriate precautions should be taken.

Novel Photocycloadditions of Dibromomaleimides to 1,3-Dimethyl-6-azauracil[**]

By *Géza Szilágyi* and *Heinrich Wamhoff*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

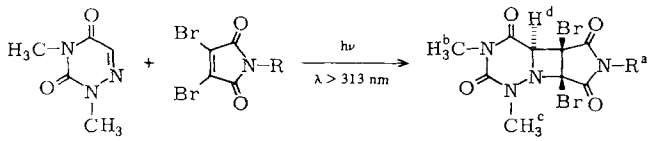
Photoreactions of cyclophilic molecules with pyrimidine bases and their aza analogues have great importance as model reactions for photochemotherapy[2]. So far, very few examples of photocycloadditions to the moderately reactive C=N double bond of heterocycles have been reported in the literature[3]. Dihalomaleic imides and anhydrides react photochemically with 1,3-dimethyluracil with $[_\pi 2_s + _\pi 2_s]$-cycloaddition and with 5-mono- and 5,5'-disubstitution, respectively[4]; we now report the surprisingly smooth photoaddition of the dibromomaleimides *(2a, b)* with 1,3-dimethyl-6-azauracil *(1)*.

After long-wave UV irradiation (Pyrex filter, $\lambda > 313$ nm) of *(1)*[5] with equimolar amounts of *(2a, b)* in various solvents, the [2+2]-cycloadducts *(3a, b)* can be isolated in high yields; photoalkylation products are not formed (Table 1), acetone serving both as solvent and as sensitizer.

The stereochemistry of the fusion of *(3a, b)* follows from the ^1H-NMR spectra (Table 2). The H^d resonance at $\delta = 5.23$ to 5.26 indicates a *cis-anti-cis* coupling, as is found in the cor-

[*] Prof. Dr. H. Wamhoff, Dr. G. Szilágyi
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] Photochemistry of Heterocycles, Part 10. This work was supported by the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung des Landes Nordrhein-Westfalen, and the Fonds der Chemischen Industrie. *G. Sz.* thanks the Alexander-von-Humboldt Stiftung for a fellowship.—Part 9: [1].



(1) (2a, b) (3a, b)

(a), R = CH_3; (b), R = H

Table 1. Preparative yields of *(3a)* and *(3b)* in dependence of solvent and sensitizer.

Reactand	Solvent (Sens. = benzophenone)	*t* [h]	Yield [%]
(2a)	Acetone	15	70
(2b)	Acetone	15	45
(2a)	Acetonitrile/Sens.	68	20
(2a)	Dioxane/Sens.	24	11
(2a)	Tetrahydrofuran/Sens.	72	0

responding 1,3-dimethyluracil adduct[4]. The absorption at relatively high field is due to the near vicinity of a carbonyl group[6].

Table 2. Some physical data of *(3a)*, *(3b)*, *(4)*, *(5)*, and *(6)*. NMR spectra in [D_6]DMSO/TMS. All products gave correct CHN analyses and characteristic IR and mass spectra.

(3a), m.p. 206—207 °C; IR (KBr): 1780, 1710 (imide), 1730, 1660 cm^{-1} (C=O); ^{1}H-NMR: δ = 3.16 (s, 3H^c), 2.93, 2.91 (2 s, 3H^a and 3H^b), 5.23 (s, H^d); ^{13}C-NMR: 26.15 (C-10), 27.16 (C-4), 36.90 (C-2), 55.12 (C-7), 70.66 (C-6), 80.92 (C-8), 150.48 (C-3), 165.04 (C-5), 165.34 (C-9), 165.56 (C-11)

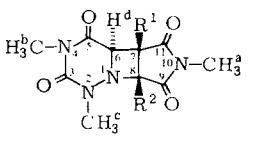
(3b), m.p. 184—187 °C; IR (KBr): 3450 (N—H), 1775, 1705 cm^{-1} (imide), 1735, 1660 cm^{-1} (C=O); ^{1}H-NMR: δ = 2.93 (s, 3H^b), 3.13 (s, 3H^c), 5.26 (s, H^d), ~12 (s, H^a)

(4), m.p. 215—216 °C; ^{1}H-NMR: δ = 3.18 (s, 3H^c), 2.93 (s, 3H^b), 2.91 (s, 3H^a), 5.26 (d, H^d), 4.48 (d, H$^{e'}$)

(5), m.p. 203—205 °C; ^{1}H-NMR: δ = 3.07 (s, 3H^c), 2.91 (s, 3H^b), 2.84 (s, 3H^a), 5.10 (s, H^d), 4.82 (s, H^e)

(6), m.p. 215—217 °C

Products following the photoreaction of *(1)* with *(2a)* are *(4)* and *(3)* (in dioxane, yields 0.3% and 6%, resp.), and *(6)* (in tetrahydrofuran (THF), yield 11%). *(4)* are *(5)* (Table 2) are formed by Br/H exchange with the solvent; *(6)* is obtained by acetone-sensitized substitution of THF[7]. The constitution and coupling of *(6)* are supported by ^{1}H- and ^{13}C-NMR data. Especially informative is the absence of a C-6,7,12 long range doublet splitting ($^3J_{CCC\cdots H}$-coupling); instead, a simple doublet is found for C-6 (64.1).



(4), R^1 = H$^{e'}$, R^2 = Br
(5), R^1 = Br, R^2 = H^e
(6), R^1 = Br, R^2 = 

Procedure

To a solution of *(1)* (10 mmol) and *(2a, b)* (10 mmol) in the solvent (200 ml) is added the sensitizer (in THF: 15 ml of acetone or 20 mg of benzophenone) and the is mixture irradiated with a Hg high-pressure lamp (Philips HPK 125). The course of the reaction is monitored by thin-layer chromatography (benzene/methanol 85:15). After the reaction in acetone the product *(3a, b)* is filtered off; in all other cases, the solvent is removed by evaporation and the residual oil chromatographed on silica gel in systems of increasing polarity (petroleum ether 60—90/acetone 10:1, 10:2, 10:3) and recrystallized from ethanol (see Table 2).

Received: December 21, 1979 [Z 637 IE]
revised: November 7, 1980
German version: Angew. Chem. *92*, 1066 (1980)

[1] *K. Wald, A. A. Nada, G. Szilágyi, H. Wamhoff*, Chem. Ber. *113*, 2884 (1980).
[2] *G. Weber:* Photochemotherapie. Thieme, Stuttgart 1978; *D. Vella Briffa, A. P. Warin*, J. Roy. Soc. Med. *72*, 440 (1979); *M. A. Pathak et al.:* Sunlight and Man. University of Tokyo Press, Tokyo 1974. As synthons of bacterial DNA, 6-azathymine and 6-azauracil and their ribonucleosides increase resistance towards UV radiation owing to their comparative inertness toward cycloaddition; cf. *J. S. Swenton, J. A. Hyatt*, J. Am. Chem. Soc. *96*, 4879 (1974), and references cited therein.
[3] Cf. *A. Padwa*, Chem. Rev. *77*, 37 (1977), and references cited therein.
[4] *G. Szilágyi, H. Wamhoff, P. Sohár*, Chem. Ber. *107*, 1265 (1974).
[5] *J. Gut, M. Prystas, J. Jonas, F. Šorm*, Collect. Czech. Chem. Commun. *26*, 974 (1961).
[6] *G. Steffan*, Chem. Ber. *101*, 3688 (1968).
[7] For the biacetyl-sensitized photoalkylation of THF and dioxane with dihalomaleimides, cf. *K. R. Stahlke, W. Hartmann*, DOS 2352216 (1975), Bayer; Chem. Abstr. *83*, P79950e (1975).

A Photochemical Route to (±)-Estrone[**]

By *Gerhard Quinkert, Wolf-Dietrich Weber, Ulrich Schwartz*, and *Gerd Dürner*[*]

Dedicated to Professor Rolf Sammet on the occasion of his 60th birthday

Estrone *(1)*, R = H, is an attractive synthetic target compound. The pathways leading to this goal are appealing if they open up uncharted areas of methodology. We now report[1] a convergent steroid synthesis based on the approach A + D → AD → ABCD (Scheme 1).

The phototransient *rac-(5)* plays a pivotal role in this concept. It undergoes intramolecular [4+2]-cycloaddition[2] to give the steroid *rac-(3)*, which forms *rac-(1)*, R = H, by dehydration, hydrogenation, and ether cleavage. The kinetically unstable *o*-quinodimethane derivative *rac-(5)* is accessible by regioselective electronic excitation and photoenolization[3] of the key compound *rac-(10)*. The Michael adduct *rac-(10)* (Table 1) is formed smoothly[4], from the inexpensive chemicals *m*-cresol methyl ether, dimethyl malonate *(6)*, R = CH_3, and (*E*)-1,4-dibromo-2-butene.

In order to prepare the achiral A ring building block, *m*-cresol methyl ether is allowed to react at 0 °C (in the presence of iron filings) with bromine in CCl_4 to give *(4)* (93%)[5]. The Grignard compound obtained *in situ* from *(4)* reacts at < −20 °C with dimethylformamide in tetrahydrofuran (THF) to give *(7)* (75%). The aldehyde *(7)* is transformed, by treatment with the Grignard compound obtained from 1-bromovinyl(trimethyl)silane[6] in THF at *ca.* 50 °C, into *(9)* (98%) which can be oxidized with chromic acid in a two-phase system, affording *(12)* (80%).

The synthesis of the racemic D ring component (2Ξ,3*RS*)-*(13)* begins with reaction of *(6)*, R = CH_3, at 55 °C with (*E*)-1,4-dibromo-2-butene in methanol containing sodium methoxide. The resulting dimethyl *rac*-2-vinylcyclopropane-1,1-

[*] Prof. Dr. G. Quinkert, Dr. W.-D. Weber, Dr. U. Schwartz, Dr. G. Dürner
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

[**] Light-Induced Reactions, Communication 21. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Hoechst AG. *Marlies Dürr* and *Gabriele Stracke* contributed greatly to optimization of the various reaction steps.—Communication 20: *G. Quinkert, F. Cech, E. Kleiner, D. Rehm*, Angew. Chem. *91*, 585 (1979); Angew. Chem. Int. Ed. Engl. *18*, 557 (1979).

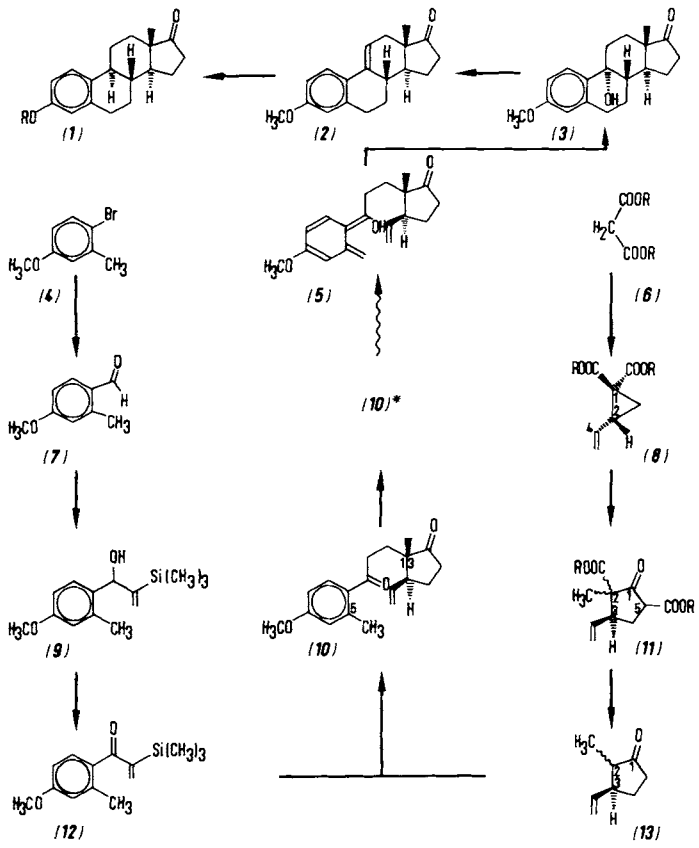


Table 1. Selected physical data of the identified achiral compounds. All new compounds and those synthesized by new methods showed satisfactory analytical data and were characterized by IR and ^{1}H-NMR spectra, and in some cases also by UV and ^{13}C-NMR spectra.

rac-(1), R = H: m.p. 254 °C (ethanol)

rac-(1), R = CH_3: m.p. 142—144 °C (Methanol)

rac-(2): m.p. 150—152 °C (methanol); UV (methanol): $\lambda_{max}(\varepsilon) = 262$ (19400), 296 sh nm (3350); IR (KBr): 3020 (w, C=C—H), 1740 (s, CO), 1620 (w, C=C), 1610, 1575, 1500 cm^{-1} (each m, benzene ring); ^{1}H-NMR ($CDCl_3$): $\delta = 0.93$ (s, CCH_3), 1.23—3.07 (m, 12H), 3.78 (s, OCH_3), 6.13 (m, 11-H), 6.55—6.86 and 7.42—7.65 (each m, 1-, 2-, and 4-H); ^{13}C-NMR ($CDCl_3$): $\delta = 14.43$ (q, C-18), 22.49 (t, C-15), 27.75 (t, C-7), 29.90 (t, C-6), 33.92 (t, C-12), 36.13 (t, C-16), 38.21 (d, C-8), 46.14 (s, C-13), 47.77 (d, C-14), 55.11 (q, OCH_3), 112.69 (d, C-2), 113.28 (d, C-4), 116.59 (d, C-11), 125.24 (d, C-1), 126.99 (s, C-9), 135.31 (s, C-10), 137.32 (s, C-5), 158.51 (s, C-3), 221.23 (s, C-17)

rac-(3): m.p. 172—174 °C (dichloromethane/ether, dec.)

(7): b.p. 90 °C/0.3 torr

rac-(8), R = CH_3: b.p. 55 °C/0.05 torr

(9): UV (cyclohexane): $\lambda_{max}(\varepsilon) = 233$ (8600), 278 (1340), 284 nm (1290)

rac-(10): b.p. 190 °C/0.2 torr; UV (*n*-hexane): $\lambda_{max}(\varepsilon) = 264$ (17200), 224 sh (12800), 290 sh (1600), 310 sh nm (230); IR (Film): 1738 (s, five-membered ring ketone), 1677 (s, aryl ketone), 1644 (w, C=C), 1605, 1580, 1503 (s, s and w, benzene ring), 998, 920 (each m, vinyl group), 867, 817 cm^{-1} (each w, 1,2,4-trisubst. benzene ring); ^{1}H-NMR ($CDCl_3$): $\delta = 0.91$ (s, CH_3 on C-13), 1.71—3.1 (m, 9 aliphatic H), 2.53 (s, CH_3 on C-5), 3.84 (s, OCH_3), 5.12—5.19 and 5.76—5.89 (each m, 2 bzw. 1 olefinic H), 6.76 and 7.73 (each m, 2 and 1 aromatic H); ^{13}C-NMR ($CDCl_3$): $\delta = 17.41$ (q, C-18), 22.36 (q, C-6), 24.31 (t, C-12), 30.54 (t, C-15), 35.48 (t, C-11/C-16), 36.78 (t, C-16/C-11), 48.48 (d, C-14), 50.82 (s, C-13), 55.11 (q, CH_3 an O), 110.48 (d, C-2), 116.59 (t, C-7), 117.50 (d, C-4), 129.85 (s, C-10), 131.67 (d, C-1), 137.13 (d, C-8), 141.67 (s, C-5), 161.69 (s, C-3), 200.95 (s, C-9), 221.36 (s, C-17)

(12), b.p. 105 °C/0.2 torr

rac-cis-(13): ^{1}H-NMR ($CDCl_3$): $\delta = 0.98$ (d, CH_3), 1.85—2.00 (m, 1 aliphatic H), 2.00—2.15 (m, 1 aliphatic H), 2.23—2.31 (m, aliphatic H), 2.36 (4q, 2-H), 2.96 (m, 1 aliphatic H), 5.04—5.17 (m, 2 olefinic H), 5.61—5.78 (m, 1 olefinic H)

rac-trans-(13): ^{1}H-NMR ($CDCl_3$): $\delta = 1.05$ (d, CH_3), 1.58—1.74 (m, 1 aliphatic H), 1.87 (4-sextet, 2-H), 2.04—2.44 (m, 4 aliphatic H), 5.04—5.20 (m, 2 olefinic H), 5.73—5.89 (m, 1 olefinic H)

rac-(14): m.p. 124—128 °C (ether/pentane)

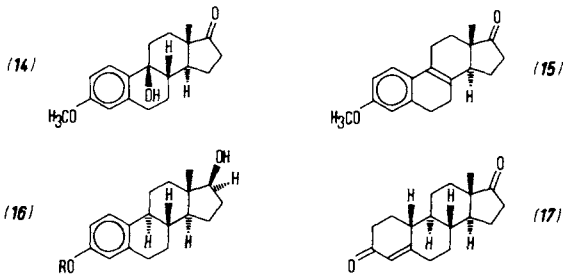
rac-(15): m.p. 120—123 °C (methanol/ether/pet. ether)

rac-(16), R = H: m.p. 198 °C (chloroform)

dicarboxylate *(RS)-(8)*, R = CH_3[7] (65%) affords, on treatment with dimethyl methylmalonate in methanol containing sodium methoxide (to which hexamethylphosphoric triamide has been added), the racemates of *(2Ξ,3RS,5Ξ)-(11)*, R = CH_3 (67%). The mixture of stereoisomers (no separation necessary) undergoes hydrolysis (10 h under reflux in aqueous/methanolic sodium hydroxide) and decarboxylation at pH ≈ 4.5 to form *(2Ξ,3RS)*-2-methyl-3-vinylcyclopentanone *(2Ξ,3RS)-(13)* (75%).

The A and D ring components *(12)* and *(2Ξ,3RS)-(13)* (no separation of isomers necessary) react at room temperature in a mixture of *tert*-butyl alcohol and ether containing sodium *tert*-butoxide to furnish *rac*-6,7;8,9-diseco-3-methoxy-1,3,5(10),7-estratetraene-9,17-dione *rac-(10)* [>60% relative to *(12)* or reacted *(2Ξ,3RS)-(13)*].

Irradiation [24 h for 1 g of *rac-(10)*] of a methylcyclohexane solution containing *rac-(10)*, pyridine, and mesitol, at 98 °C with UV light of $\lambda > 340$ nm yields a product consisting mainly of *rac-(3)*, and also containing *rac-(14)*[8]. The mixture left on removal of solvent is dissolved in benzene and the solution is refluxed for 20 min after addition of oxalic acid. The dehydration product obtained is a mixture of 95% *rac-(2)* (Table 1) and 5% *rac-(15)*[9]. It is isolated in 61% yield based on *rac-(10)* and does not have to be separated regardless of whether *rac*-estrone *rac-(1)*, R = H[10], *rac*-estradiol-17β *rac-(16)*, R = H[11], or *rac*-19-nor-4-androstene-3,17-dione *rac-(17)*[12] is the synthetic target compound.



The total steroid synthesis presented in this communication has the following characteristic features:

- it contains a photochemical key step;
- it starts from inexpensive chemicals;
- it proceeds with extremely high regio- and diastereoselectivity, and considerable overall yield[13];
- it can be directed asymmetrically to naturally occurring (+)-estrone *(1)*, R = H [and to *(16)*, R = H and *(17)*][1b]

Received: October 6, 1980 [Z 638a IE]
German version: Angew. Chem. *92*, 1060 (1980)

[1] a) Cf. *G. Quinkert*, Afinidad *34*, 42 (1977); Chimia *31*, 225 (1977); b) for the asymmetric synthesis of (+)-estrone, see *G. Quinkert, U. Schwartz, H. Stark, W.-D. Weber, H. Baier, F. Adam, G. Dürner*, Angew. Chem. *92*, 1062 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1029 (1980).

[2] *o*-Quinodimethane derivatives, albeit obtained by thermal routes from isomeric benzocyclobutene or corresponding sulfone derivatives, play an important part in the synthesis of estrone and its derivatives: *W. Oppolzer, K. Bättig, M. Petrzilka*, Helv. Chim. Acta *61*, 1945 (1978); *T. Kametani, H. Matsumoto, H. Nemoto, K. Fukumoto*, J. Am. Chem. Soc. *100*, 6218 (1978); *R. L. Funk, K. P. C. Vollhardt, ibid. 101*, 215 (1979); *P. A. Grieco, T. Takigama, W. J. Schillinger*, J. Org. Chem. *45*, 2247 (1980); *K. C. Nicolaou, W. E. Barnette, P. Ma, ibid. 45*, 1463 (1980).

[3] *P. G. Sammes*, Tetrahedron *32*, 405 (1976); *P. J. Wagner*, Pure Appl. Chem. *49*, 259 (1977); *R. Haag, J. Wirz, P. J. Wagner*, Helv. Chim. Acta *60*, 2595 (1977); *K. Uji-Ie, K. Kikuchi, H. Kokubun*, J. Photochem. *10*, 145 (1979); *P. K. Das, M. V. Encines, R. D. Small, Jr., J. C. Scaiano*, J. Am. Chem. Soc. *101*, 6965 (1979).

[4] Under the conditions chosen *(vide infra)*, the thermodynamically more stable of the two enolate anions of the D ring component adds, in extremely regioselective manner, to *(12)*. The $(CH_3)_3Si$ ligand ensures that the reaction also produces *rac-(10)* in extremely high stereoselectivity.

[5] *m*-Cresol methyl ether (3-methylanisole) is brominated analogously to 3-ethylanisole: *D. J. Nelson, E. A. Uschak*, J. Org. Chem. *42*, 3308 (1977).

[6] *A. Ottolenghi, M. Friedkin, A. Zilkha*, Can. J. Chem. *41*, 2977 (1963).

[7] *rac-(8)*, $R = C_2H_5$, was synthesized by *R. W. Kierstead, R. P. Linstead, B. C. L. Weedon*, J. Chem. Soc. *1952*, 3613; we adopted to procedure of *J. M. Stewart, G. K. Pagenkopf*, J. Org. Chem. *34*, 7 (1969), but used *(6)*, $R = CH_3$. Concerning nucleophilic ring opening of cyclopropane derivatives activated by electron acceptors, see *S. Danishefsky*, Acc. Chem. Res. *12*, 66 (1979).

[8] The diastereomer of *rac-(5)* having Z-configurated 9,10-double bond traverses mainly that transition structure in which the dienophilic vinyl group approaches the *o*-quinonoid dienic moiety from the β-side, from the *exo* orientation: this affords *rac-(3)*. A competition reaction, of admittedly subordinate proportions, proceeds *via* that transition structure in which the vinyl group approaches the diene unit from the α-side, from the *endo* orientation: this gives *rac-(14)*. *rac-(3)* and *rac-(14)* are separated only for identification.

[9] *rac-(2)* and *rac-(15)* are separated only for identification.

[10] The mixture *rac-(2)* + *rac-(15)* is reduced by potassium in liquid ammonia in the presence of aniline and then oxidized by chromic acid to give *rac-(1)*, $R = CH_3$: *G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, H. Smith*, J. Chem. Soc. *1963*, 5072. *rac-(1)*, $R = CH_3$, is transformed, on heating with pyridine hydrochloride to 210 °C, into *rac-(1)*: *W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, L. V. Chinn*, J. Am. Chem. Soc. *74*, 2832 (1952).

[11] The mixture *rac-(2)* + *rac-(15)* is reduced by potassium in liquid ammonia in the presence of aniline and then treated with diisobutylaluminum hydride *rac-(16)*; R = H: *J.-C. Hilscher*, DBP 2409991 (1976); Schering; Chem. Abstr. *84*, 59862v (1976).

[12] The mixture *rac-(2)* + *rac-(15)* is converted by Birch reduction into *rac-(17)* [by analogy with the procedure of *W. S. Johnson, W. A. Vredenburgh, J. E. Pike*, J. Am. Chem. Soc. *82*, 3409 (1960)].

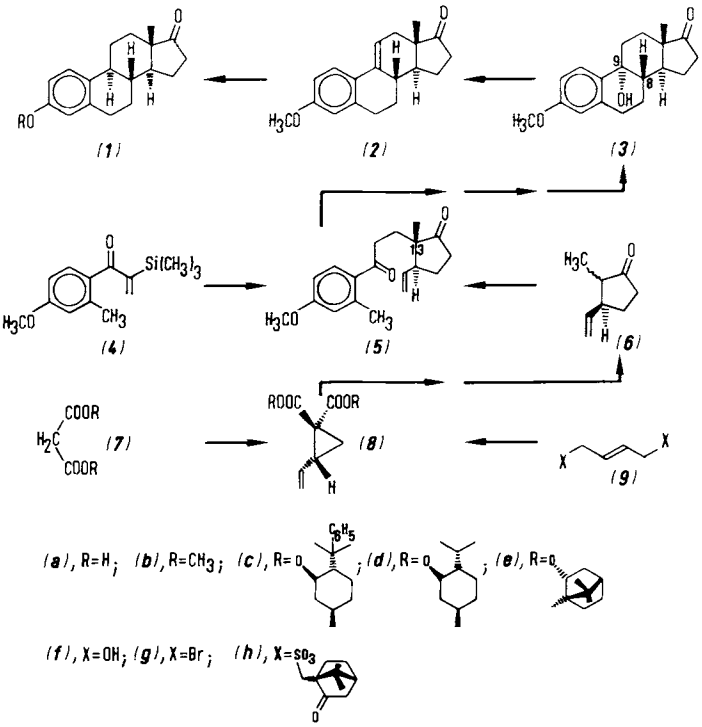
[13] Since *rac-(10)* undergoes at least 61% conversion into [*rac-(2)* + *rac-(15)*], the overall yield of this mixture is 22% for *m*-cresol methyl ether and 12% for (*E*)-1,4-dibromo-2-butene or dimethyl malonate.

Asymmetric Total Synthesis of (+)-Estrone[**]

By *Gerhard Quinkert, Ulrich Schwartz, Herbert Stark, Wolf-Dietrich Weber, Helmut Baier, Friedheld Adam*, and *Gerd Dürner*[*]

Dedicated to Professor Rolf Huisgen on the occasion of his 60th birthday

We have reported a steroid total synthesis which can be directed towards various racemic synthetic target compounds in considerable overall yield[1]. This synthesis contains a photochemical key reaction, starts from inexpensive chemicals, and proceeds largely regio- and stereoselectively. Of the four asymmetric C atoms of the title compound *(1a)*, three have been introduced with high diastereoselectivity: C-13 by a Michael addition, leading to the photo-enolizable key compound *rac-(5)*, C-8 and C-9 *via* an *o*-quinodimethanoid phototransient whose intramolecular Diels-Alder reaction[2] completes the steroid skeleton [of *rac-(3)*]. If the chiral dextrorotatory D ring component is used instead of the racemate (2Ξ,3*RS*)-*(6)*, then stereoselection is complete: natural (+)-estrone *(1a)* and its relatives thus become accessible by enantiomer selection (Scheme 1).

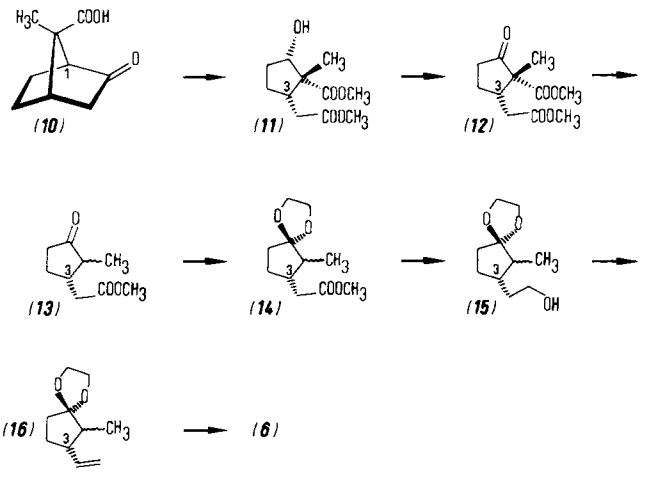


Scheme 1

The chiral, dextrorotatory D ring component has been obtained in three ways:

- According to Scheme 1, by ring expansion of the dextrorotatory three-membered ring compound *(R)-(8b)*, which is accessible from *(RS)-(8a)* by resolution with brucine[3,4];
- according to Scheme 2, by ring opening of the levorotatory bicyclic compound *(1S)-(10)*, obtained from *(1RS)-(10)* by resolution with (+)-1-phenylethylamine[5];
- according to Scheme 1, by ring expansion of the three-membered ring enantiomers *(R)-(8b)*/*(S)-(8b)* = 9:1, which are obtainable in this composition by asymmetric induction during diastereoselective cyclopropanation of *(7c)* and subsequent transesterification[6].

Table 1 indicates the extent of asymmetric induction, and shows (i) that the chiral substituent R greatly influences the



Scheme 2

[*] Prof. Dr. G. Quinkert, Dr. U. Schwartz, Dipl.-Chem. H. Stark, Dr. W.-D. Weber, Dipl.-Chem. H. Baier, Dipl.-Chem. F. Adam, Dr. G. Dürner
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50

[**] Light Induced Reactions, Communication 22. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and Hoechst AG. We are indebted to Prof. *R. Wiechert*, Schering AG, for kindly supplying large amounts of valuable steroids. *Marlies Dürr, Gabriele Stracke*, and *Sabine Beck* contributed greatly to optimization of the various reaction steps.—Communication 21: [1].

transformation of the malonic diesters *(7c)*, *(7d)*, and *(7e)* into products of type *(8)* and (ii) that the diastereoselective-asymmetric step of the synthesis is superior to the enantioselective-asymmetric alkylation [of *(7b)* by chiral *(9h)*[7] or by achiral *(9g)* in the presence of a chiral phase transfer catalyst[8]].

Table 1. Extent of asymmetric induction in the synthesis of *(8b)*.

Synthesis	Asymm. induction [%]
Diastereoselectively asymmetric	
(7c) + *(9g)*	76—80
(7d) + *(9g)*	52—54
(7e) + *(9g)*	39
Enantioselectively asymmetric	
(7b) + *(9h)*	13
(7b) + *(9g)*	<2

(*R*)-*(8b)* and (1*S*)-*(10)*, both obtained by resolution of racemates, represent reference compounds for the corresponding species from the chiral branch; *(5)* and *(2)*[9], which are obtained after introduction of (*R*)-*(8b)* and (1*S*)-*(10)* into the synthetic procedure (Scheme 1), are reference compounds for the corresponding species from the chiral trunk.

Table 2 shows that the optical yield of the diastereoselective-asymmetric synthesis is 80% on use of *(7c)*.

Table 2. Optical yield of the diastereoselectively asymmetric synthesis of *(2)* and intermediates [starting from *(7c)*] relative to reference compounds.

Opt. act. cpd.	$[\alpha]_D$ From the diastereoselectively asymmetric synthesis	Reference cpd.	Opt. yield [%]
(2)	+231.8 (dioxane)	+288.6	80
(5)	+ 21.2 ($CHCl_3$)	+ 27.1	80
(6)	+112.7 (CH_2Cl_2)	+149.0	76
(8b)	+ 43.9 (CCl_4)	+ 55.0	80

Table 3 contains some selected physical data of the compounds discussed above.

Table 3. Selected physical data of the identified chiral compounds. All formerly undescribed compounds and those synthesized by new methods exhibit correct molecular compositions and were characterized by IR and ^{1}H-NMR spectra.

(1a): m.p. 259 °C (ethanol); $[\alpha]_D^{20} = 164.8$ ($c = 0.501$ in dioxane)
(2): m.p. 143—144 °C (pentane); $[\alpha]_D^{20} = 288.6$ ($c = 0.506$ in dioxane).—*(2)* and *rac-(2)* [1] have similar IR spectra (KBr) but identical UV (methanol) and ^{1}H-NMR spectra ($CDCl_3$)
(5): $[\alpha]_D^{20} = 27.1$ ($c = 1.007$ in $CHCl_3$).—UV- (*n*-hexane), IR- (Film) and ^{1}H-NMR spectra ($CDCl_3$) of *(5)* and *rac-(5)* [1] were identical
cis-(6) + *trans-(6)* (8:92): $[\alpha]_D^{20} = 149.0$ ($c = 0.963$ in CH_2Cl_2)
(8b): $[\alpha]_D^{25} = 55.0$ ($c = 0.96$ in CCl_4)
(1*S*)-*(10)*: m.p. 206 °C (acetone, dec.); $[\alpha]_D^{20} = -76.1$ ($c = 0.992$ in ethanol)
(3*S*)-*(11)*: b.p. 120 °C/0.09 torr; $[\alpha]_D^{20} = -20.7$ ($c = 1.016$ in $CHCl_3$)
(3*S*)-*(12)*: b.p. 120 °C/0.06 torr; $[\alpha]_D^{20} = 67.9$ ($c = 0.960$ in $CHCl_3$)
(3*S*)-*(13)*: b.p. 90 °C/0.07 torr; $[\alpha]_D^{20} = 78.3$ ($c = 0.937$ in $CHCl_3$)
(3*S*)-*(14)*: b.p. 90 °C/0.05 torr; $[\alpha]_D^{20} = -38.1$ ($c = 1.004$ in $CHCl_3$)
(3*S*)-*(15)*: $[\alpha]_D^{20} = -49.5$ ($c = 1.000$ in $CHCl_3$)
(3*S*)-*(16)*: b.p. 90 °C/14 torr; $[\alpha]_D^{20} = -24.1$ ($c = 0.947$ in $CHCl_3$)

Received: October 6, 1980 [Z 638 b IE]
German version: Angew. Chem. 92, 1062 (1980)

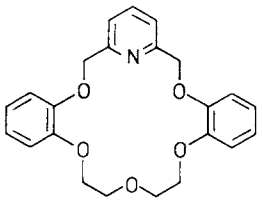
[1] *G. Quinkert, W.-D. Weber, U. Schwartz, G. Dürner*, Angew. Chem. 92, 1060 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1027 (1980).
[2] Review: *R. G. Carlson*, Annu. Rep. Med. Chem. 9, 270 (1974); *W. Oppolzer*, Angew. Chem. *89*, 10 (1977); Angew. Chem. Int. Ed. Engl. *16*, 10 (1977); *W. Oppolzer*, Synthesis *1978*, 793; *R. L. Funk, K. P. C. Vollhardt*, Chem. Soc. Rev. 9, 41 (1980); *G. Brieger, J. N. Bennett*, Chem. Rev. *80*, 63 (1980).
[3] *S. Danishefsky, G. Rovnyak*, J. Chem. Soc. Chem. Commun. *1972*, 821: $[\alpha]_D = +55.2$ for *(8b)* in CCl_4; *N. A. Abraham*, Tetrahedron Lett. *1974*, 1393: $[\alpha]_D = -54.7$ for *ent-(8b)* in CCl_4; *F. Adam*, unpublished: $[\alpha]_D^{25} = +55.0$ for *(8b)* in CCl_4.
[4] Assuming the configuration at C-2 to invert on ring expansion and on the basis of the conversion into (+)-*(1a)*, *R* chirality is assigned to (+)-*(8b)*.
[5] Since the chirality center C-4 is unaffected on transformation of (−)-*(10)* into (2Ξ,3*S*)-*(6)* and because (−)-*(10)* can be converted into (+)-*(1a)*, *S* chirality is assigned to C-4.
[6] In fact, the compound was first hydrolyzed to the dicarboxylic acid (*R*)-*(8a)* and then esterified with diazomethane to give (*R*)-*(8b)*.
[7] *G. Quinkert, K. R. Schmieder, G. Dürner, K. Hache, A. Stegk, D. H. R. Barton*, Chem. Ber. *110*, 3582 (1977), see Section 5.2.1.3.
[8] (−)-*N,N*-Dimethylephedrinium bromide was used as chiral phase transfer catalyst; see *H. B. Kagan, J. C. Fiaud*, Top. Stereochem. *10*, 236 (1978); *E. V. Dehmlow*, Angew. Chem. *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *16*, 493 (1977), see Section 4.8.
[9] *(2)* has also been obtained by dehydrogenation of *(1b)* according to *C. G. Pitt, D. H. Rector, C. E. Cook, M. C. Wani*, J. Med. Chem. *22*, 966 (1979), the crude product contains, in addition to 97% of *(2)*, the isomer 3-methoxy-1,3,5(10),8-estratetraen-17-one, which was removed by preparative HPLC.

Selective Inclusion of Alcohols with a New Pyridino Crown[**]

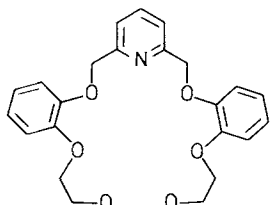
By *Edwin Weber* and *Fritz Vögtle*[*]

Dedicated to Professor David Ginsburg on the occasion of his 60th birthday

Although several host/guest complexes of crown compounds with CH- and NH-acidic neutral molecules such as acetonitrile, nitromethane, and dimethyl sulfone have already been described[1], alcohols have so far defied all attempts at inclusion by compounds of this kind. Spurred on by the surprising complexation of uncharged guest molecules by the hexadentate dibenzopyridino crown *(1)*[1], our systematic study has now culminated in the discovery of the heptadentate tribenzopyridino crown *(2)* as a new host substance of this type. It is the first crown to form inclusion compounds—selectively—with aliphatic alcohols. Alcohol inclusion compounds of any kind were formerly very rare[2].



(1)



(2)

Our synthesis of *(2)* started from pyrocatechol monobenzyl ether *(3)*[3]; cyclization *(7)* + *(8)* → *(2)* could be accomplished by the dilution principle[4].

Compound *(2)* is obtained as a complex of exact 2:1 stoichiometry (ligand:guest) with *methanol* on recrystallization

[*] Prof. Dr. F. Vögtle, Dr. E. Weber
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] Part 8 of Complexes between Neutral Molecules.—Part 7: [1].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1980 0570-0833/80/1212-1030 $ 02.50/0

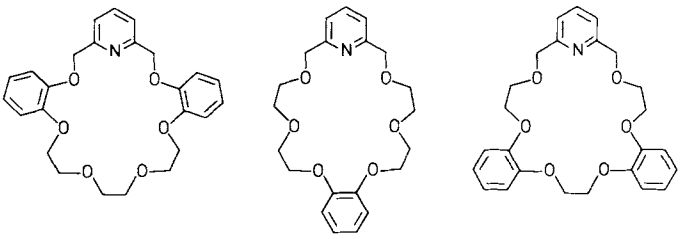
from this solvent[5]. The complex is so stable that it loses no methanol even on standing for weeks under normal conditions, or on drying for 1 d at 25 °C/15 torr. Heating to 48 °C leads to melting and slow decomposition with evaporation of the methanol, this process being complete at *ca.* 70 °C[5]. The melt then resolidifies. Renewed melting is observed at 102—104 °C—the melting point of the free ligand *(2)*.

The new ligand *(2)* binds not only *methanol* but also other alcohols to various extents, as is seen from the melting point, ^{1}H-NMR spectrum, and elemental analysis: while *ethanol* likewise gives a 2:1 complex, and is bound preferentially on recrystallization from a 1:1 *methanol/ethanol* mixture, the branched alcohols *isopropyl, isobutyl,* and *sec-butyl alcohol* do not give complexes but instead the free ligand.

In the homologous series of unbranched alcohols from *1-propanol* to *1-hexanol* complexes of various stability are obtained, some of which decompose already at 25 °C/0.2 torr. 1-Octanol no longer gives a complex. Maximum complexation is observed with ethanol and the limit lies at 1-heptanol. The 1-propanol complex is significantly less stable than those of ethanol and 1-butanol: it decomposes on standing under normal conditions.

The observed host/guest binding is thus selective with regard to chain length and branching of the guest molecule. The selectivity appears to be more pronounced than with trio-thymotide (TOT) which still includes cetyl alcohol[6a]. We assume that the guest molecules are accommodated, as in some TOT clathrates[6b]—and hence in contrast to crown complexes of acetonitrile[1], nitromethane[1], dimethyl sulfone[7], in which bonding is mainly by C—H···O interaction—in not particularly large *inter*molecular cavities of the crystal. However, since *(2)* does not include longer-chain alcohols, the host lattice appears to form only cages, and not cages *and* channels as in TOT[6b]. In contrast to the situation in the alcohol clathrates of the donorless TOT, the guest molecules in *(2)* are probably oriented since the OH group can form a hydrogen bond to the pyridine nitrogen[8].

Crown ethers such as *(2)* and *(1)*, and particularly the pyridino crowns which are symmetrically stiffened in TOT-like manner with aromatic rings[2a,9a], could possibly prove to be a treasure trove for systematically accessible new host molecules showing wide flexibility with respect to ring size, number of donors, and substitution, and capable of selectively complexing not only cations but also neutral organic molecules. The neutral host *(2)* is so far unique in that the structurally related heptadentate benzopyridino crowns *(9)*[1], *(10)* (m.p. 66—67 °C), and *(11)* (m.p. 99—100 °C)[4], also synthesized for the first time for purposes of comparison, do not form analogous alcohol inclusion compounds.

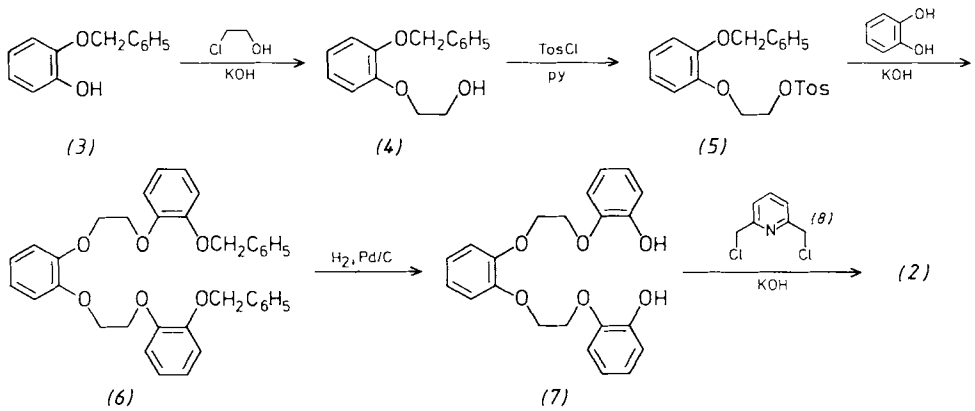


(9) *(10)* *(11)*

Procedure[4]

(4): KOH (14.0 g, 250 mmol) in boiling ethanol (250 cm^3) is stirred for 30 min with 2-benzyloxyphenol *(3)*[3] (50.0 g, 250 mmol); the temperature is maintained and ethylene chlorohydrin (20.1 g, 250 mmol) is then added dropwise. After 6 h under reflux the reaction mixture is filtered, the solvent removed in *in vacuo,* and the residue is dissolved in chloroform, washed with 0.2 N NaOH, and dried over Na_2SO_4. Distillation gives 29.3 g (48%) of colorless oil which crystallizes on standing; b.p. 167 °C/0.5 torr, n_D^{20} 1.5815, m.p. 40—41 °C (*n*-heptane).

(5): Compound *(4)* (24.4 g, 100 mmol) in pyridine is reacted under the usual conditions with toluenesulfonyl chloride (21.0 g, 110 mmol): 33.4 g (84%) colorless crystals, m.p. 44—46 °C (*n*-heptane).



(6): Catechol (4.40 g, 40 mmol), KOH (4.50 g, 80 mmol), and *(5)* (31.8 g, 80 mmol) are reacted as described for *(4)*. The solid residue is crystallized from ethanol: m.p. 91—93 °C, 65% yield.

(7): Compound *(6)* (14.0 g, 25 mmol) is hydrogenated in ethyl acetate for 4 h at room temperature under 3 bar H_2 over Pd/activated charcoal (10%). Yield 9.5 g (91%), colorless crystals, m.p. 116—118 °C (*n*-heptane).

Cyclization to (2): Compound *(7)* (7.65 g, 20 mmol) in dimethylformamide (250 cm^3), 2,6-bis(chloromethyl)pyridine *(8)*[9b] (3.52 g, 20 mmol) in *n*-butanol (250 cm^3), and KOH (2.25 g, 40 mmol) in ethanol (250 cm^3) are reacted under dilution principle conditions in boiling *n*-butanol (1000 cm^3). Evaporation *in vacuo,* washing with H_2O, dissolution in chloroform and chromatography (Al_2O_3, Woelm, basic, activity grade I) affords a glassy product which crystallizes immediately upon addition of methanol. Yield 2.43 g (26%), colorless scales of methanol adduct, m.p. 48 °C (incipient decomposition) to 60 °C; the melt generally solidifies at *ca.* 70 °C and remelts at 102—104 °C. ^{1}H-NMR ($CDCl_3$, TMS int. ref.): 5.12 (benzylic CH_2).

Received: August 5, 1980 [Z 644 IE]
German version: Angew. Chem. 92, 1067 (1980)

[1] *cf. F. Vögtle, W. M. Müller, E. Weber*, Chem. Ber. *113*, 1130 (1980).
[2] a) *D. D. MacNicol, J. J. McKendrick, D. R. Wilson*, Chem. Soc. Rev. *7*, 65 (1978); b) *K. Pollmer*, Z. Chem. *19*, 81 (1979).
[3] *J. H. Jones, G. T. Young*, J. Chem. Soc. *C 1968*, 436.
[4] The compounds gave satisfactory elemental analyses and appropriate spectra.
[5] Analogous stoichiometry and similar decomposition ranges are observed with tri-*o*-thymotide clathrates: cf. *W. Baker, B. Gilbert, W. D. Ollis*, J. Chem. Soc. *1952*, 1443.
[6] a) *D. Lawton*, J. Chem. Soc. *1958*, 2339; b) *D. J. Williams, D. Lawton*, Tetrahedron Lett. *1975*, 111.
[7] We thank Prof. Dr. *M. R. Truter*, Cambridge, for communication of the structure of [18]crown-6·dimethyl sulfone complex. The CH_3 hydrogen atoms of the guest form H bonds with the oxygens of the host crown.
[8] Analogous OH···N bonds exist in bipyridine · resorcinol adducts. We thank Prof. Dr. *W. H. Watson*, Texas Christian University, for communication this result prior to publication; cf. *G. Oepen, F. Vögtle*, Justus Liebigs Ann. Chem. *1979*, 2114.
[9] a) *G. Allegra, M. Farina, A. Immirzi, A. Colombo, U. Rossi, R. Broggi, G. Natta*, J. Chem. Soc. *B 1967*, 1020, 1028; b) *W. Baker, K. M. Buggle, J. F. W. McOmie, D. A. M. Watkins, ibid. 1958*, 3594.

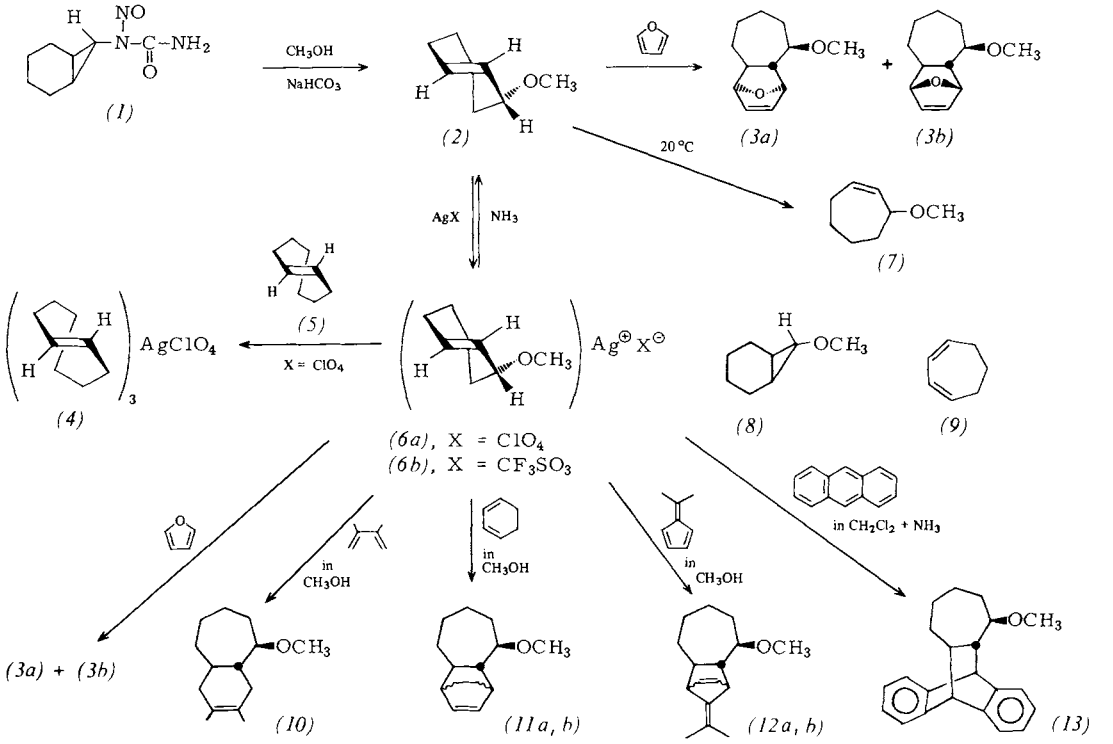
Cycloadditions with Silver Ion-Stabilized (2*RS*,3*RS*)-3-Methoxy-*trans*-Cycloheptene[**]

By *Heiner Jendralla*[*]

While compounds having a *trans* double bond in an eight-membered ring are as a rule stable at room temperature, no stable *trans*-cycloheptene or a corresponding bridgehead olefin could be prepared despite continued efforts[1]. Trapping experiments on photochemically generated *trans*-cycloheptene revealed that its lifetime at $-10\,^{\circ}C$ is 23 minutes[2].

"Normal" deamination of the nitrosourea *(1)* in weakly basic methanol led to the unstabilized title compound *(2)* as intermediate together with *(8)* as primary product[3]. Though *(2)* rapidly isomerizes to the *cis*-olefin *(7)* at room temperature[4], it can be trapped to the extent of 95% in the form of the cycloadducts *(3a)* and *(3b)* on deamination of *(1)* in methanol/furan[3].

On addition of silver perchlorate or trifluoromethanesulfonate (triflate) to a methanolic solution of *(1)* the deamination proceeds without the necessity of a base. If the reaction product is partitioned between ether and water, the ether extracts contain a mixture of the products *(7)*, *(8)*, and small amounts of *(9)*. If ammonia is now passed through the aqueous solution and the extraction is repeated, practically only *(7)* with small amounts of *(9)* and no *(8)* are found in the extract. Since the *cis*-olefin *(7)* forms no water-soluble silver perchlorate complex under the reaction conditions, this experiment indicates the reversible stabilization of the *trans*-olefin *(2)* as the water-soluble silver(I) complex *(6)*[5]. Removal of water *in vacuo* affords *(6)* as a colorless, thermally stable and moderately light-sensitive powder. The triflate complex could be isolated analytically pure by recrystallization (ethyl acetate/pentane/$-30\,^{\circ}C$)[6]. Elemental analysis gave an olefin/silver ratio of 1:1[9]. The *trans*-configuration of the double bond and the configuration of the methoxy group follow from the identical ^{1}H-NMR spectra of *(6a)* and *(6b)*. 1-H ($\delta = 5.80$) and 2-H (5.50) form an AB system; the large coupling constant $J_{1,2} = 17.9$ Hz confirms their *trans* orientation. 2-H also couples with 3-H ($J_{2,3} = 7.9$ Hz), whilst 1-H couples differently with the two protons on C-7 ($J_{1,7} = 9.2$ Hz, $J_{1,7'} = 4.3$ Hz). The magnitude of $J_{2,3}$ confirms the (2*RS*, 3*RS*)-configuration of *(2)*[7] previously deduced[3] from the adducts *(3a)* and *(3b)*. The very good agreement of the proton coupling constants of *(6a)* and *(6b)* with those of 3-methoxy-*trans*-cyclooctene[7] would suggest that the homologous olefins have a similar conformation. If one assumes that the olefin in *(6)* has the crown conformation ("eight-shaped loop") already demonstrated in the case of *trans*-cyclooctene[8], C-5 is found to be located exactly "behind" the double bond, *i.e.* should lie centrally in the shielding cone of anisotropism. The ^{13}C-NMR spectra of *(6a)* and *(6b)* contain four triplets. C-5 is shielded by about the same amount



[*] Dr. H. Jendralla
Institut für Organische Chemie, FB 9
Gesamthochschule, D-5600 Wuppertal 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Zentrale Verfügungsfonds der GH Wuppertal. I am indebted to Dr. *W. Dietrich* (Universität Bochum), who kindly recorded the ^{13}C-NMR spectra.

(8 ppm) compared to C-4 and C-6 as C-7 is deshielded due to its allylic position[9]. An X-ray structure analysis of *(6b)* is in progress.

The silver complex *(6a)* reacts with dienes at room temperature to give the corresponding cycloadducts *(3)* and *(10)*—*(13)*. Gas chromatographically, the sole impurity found in all cases was the *cis*-olefin *(7)* (2—13%). The following diastereomeric ratios *a/b* were determined by capillary gas chromatography: *(3)*: 4.4:1; *(11)*: 2.0:1; *(12)*: 2.4:1. The ratio *a/b* = 4.4:1 of the furan adducts *(3)* differs drastically from that found in the trapping of free *trans*-olefin *(2)* (*a/b* = 0.95:1)[3] and suggests that part of the cycloaddition takes place in the ligand sphere of the silver ion. The insolubility of *(6a)* in solvents suitable for anthracene hinders cycloaddition of the complex. However, *(13)* (m.p. 122 °C) was obtained when ammonia was passed into the stirred suspension of *(6a)* in the saturated anthracene solution in dichloromethane. Reaction of *(6a)* with *trans*-cyclooctene *(5)* gave tris(*trans*-cyclooctene)silver perchlorate *(4)*, m.p. 197 °C (decomp.). Preliminary experiments show that *cis,trans*-cycloheptadienes can also be stabilized as silver complexes.

Received: January 4, 1980 [Z 645 IE]
supplemented: April 15, 1980
German version: Angew. Chem. *92*, 1068 (1980)

[1] *J. F. Liebman, A. Greenberg*, Chem. Rev. *76*, 311 (1976); *E. J. Corey, F. A. Carey, R. A. E. Winter*, J. Am. Chem. Soc. *87*, 934 (1965).
[2] *J. Inoue, S. Takamuku, H. Sakurai*, J. Chem. Soc. Perkin Trans. II *1977*, 1635.
[3] *W. Kirmse, H. Jendralla*, Chem. Ber. *111*, 1857 (1978).
[4] No cycloadducts can be detected if furan is added after 3 h.
[5] A similar stabilization of photochemically generated *trans*-cycloheptene by copper(I) triflate was recently reported: *J. Th. M. Evers, A. Mackor*, Recl. Trav. Chim. Pays-Bas *98*, 423 (1979); Tetrahedron Lett. *1980*, 415.
[6] *(6a)* could not be crystallized. A rough purification was achieved by salting-out *(6a)* from a saturated solution with $NaNO_3$.
[7] *Whitham* and *Wright*, J. Chem. Soc. *C 1971*, 883, prepared the diastereomers of 3-methoxy-(1*E*)-cyclooctene *via* a stereochemically unambiguous route. They found for the (2*RS*.3*SR*)-isomer $J_{2,3} = 2.1$ Hz, for the (2*RS*,3*RS*)-isomer $J_{2,3} = 9.0$ Hz. They also quoted $J_{1,8} = 9.1$ Hz, $J_{1,8'} = 3.55$ Hz.
[8] *O. Ermer*, Angew. Chem. *86*, 672 (1974); Angew. Chem. Int. Ed. Engl. *13*, 604 (1974).
[9] All the new compounds gave satisfactory ^{1}H-NMR spectra. *(6a)*: m.p. 157—159 °C (dec.) [6], ^{1}H-NMR (D_2O, TMS ext.): $\delta = 5.80$ (ddd, 1-H, $J_{1,2} = 17.9$ Hz, $J_{1,7} = 9.2$ Hz, $J_{1,7'} = 4.3$ Hz), 5.50 (dd, 2-H, $J_{1,2} = 17.9$ Hz, $J_{2,3} = 7.9$ Hz), 4.20 (m, 3-H), 3.50 (s, OCH_3), 2.73—1.30 (m, 8H); ^{13}C-NMR (D_2O, TMS ext.): $\delta = 123.0$ (d, C-1), 120.6 (d, C-2), 81.7 (d, C-3), 57.5 (q, OCH_3), 39.2 (t, C-7), 31.3 (t), and 31.1 (t) (C-4, C-6), 23.0 (t, C-5); essentially in agreement with MS of *(7)*. *(6b)*: m.p. 142—143 °C (dec.), ^{1}H-NMR: as *(6a)*; ^{13}C-NMR (D_2O/TMS ext.): $\delta = 121.7$ (d, $J_{CH} = 161.6$ Hz, C-1), 120.9 (q, $J_{CF} = 317.7$ Hz, CF_3), 119.9 (d, $J_{CH} = 161.6$ Hz, C-2), 81.3 (d, $J_{CH} = 150.4$ Hz, C-3), 57.2 (q, $J_{CH} = 142.6$ Hz, OCH_3), 38.9 (t, $J_{CH} = 129.4$ Hz, C-7), 31.0 and 30.7 (t, C-4, C-6), 22.6 (t, C-5).

$Li_{12}Si_7$, a Compound Having a Trigonal Planar Si_4 Cluster and Planar Si_5 Rings

By *Hans Georg von Schnering, Reinhard Nesper, Jan Curda,* and *Karl-Friedrich Tebbe*[*]

In a renewed study of the lithium-silicon system we were able to show[1] that the long-known violet compound "Li_2Si" actually has the composition $Li_{14}Si_6$ ($Li_{2.33}Si$). The metallic gray compound immediately adjacent on the silicon-rich side has now been identified as $Li_{12}Si_7$. This is the silicon-richest phase in the Li/Si system; it was formerly described as $Li_{13}Si_7$[2]. Preparation of the pure compound from the elements was accomplished in well baked-out, sealed tantalum ampoules at 1270 K. Syntheses under various conditions, thermal analysis, and coulometric titration demonstrate that $Li_{12}Si_7$ coexists in equilibrium with Si and $Li_{14}Si_6$. The compound has a almost negligible phase width ($1.69 \leq Li/Si \leq 1.71$); it melts congruently at 890 K and is extraordinarily sensitive to moisture and oxygen.

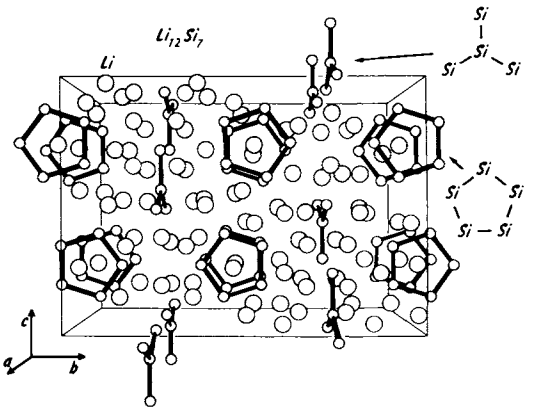


Fig. 1. Crystal structure of $Li_{12}Si_7$; projection of the unit cell along the *a* axis (Li, large circles; Si, small circles). Space group Pnma (No. 62); $a = 861.0(2)$, $b = 1973.8(4)$, $c = 1434.1(4)$ pm; 8 formula units in the unit cell; 2190 reflections *hkl*, $Mo_{K\alpha}$ radiation, $R = 0.035$ (anisotropic). None of the atoms shows anomalous coefficients U_{ij} or occupation densities. Subsequent ΔF synthesis is without notable contours [6].

$Li_{12}Si_7$ is unequivocally a semiconductor with a band gap of $E_G = 0.6$ eV and a specific conductivity at room temperature of $\sigma(298) = 10^{-6}\ \Omega^{-1}\ cm^{-1}$. The compound is diamagnetic with a considerably greater susceptibility than silicon ($\chi_{mol} = -23 \times 10^{-6}\ cm^3\ mol^{-1}$ for $Li_{1.714}Si$). These physical properties are important for an understanding of the bonding because they are indicative of a normal valence compound. The structure should therefore fulfil the rules of *Zintl* and *Klemm*[3] and of *Mooser* and *Pearson*[4].

$Li_{12}Si_7$ forms orthorhombic crystals (Fig. 1) with a surprising new kind of anionic Si_n cluster: Planar Si_5 rings—analogues are already known in the germanide $Li_{11}Ge_6$[5]—are accompanied by hitherto unknown star-shaped trigonal planar Si_4 clusters of 3/m-D_{3h} symmetry. The bond lengths d(Si-Si) in the Si_5 ring vary between 235.6 and 238.1 pm ($\bar{d} = 236.8$ pm) and those in the Si_4 star between 236.5 and 239.3 pm ($\bar{d} = 238.0$ pm); they are only slightly longer than the interatomic distance of a Si—Si single bond (235.1 pm).

Attempts to describe this structure in terms of the model of formal ions run into difficulties: for $Li_{24}Si_{14} \hat{=} (Li^+)_{24}(Si_4^{x-})(Si_5^{y-})_2$, the expression $x + 2y = 24$ would apply. The formal charge assigned to silicon (Si^{2-}) owing to the homonuclear divalency of the Si atoms in the Si_5 ring gives $y = 10$ as solution. However, this leads directly to Si_4^{4-}, a 20 e system normally found for the tetrahedrane structure of the isoelectronic P_4 molecule. Is the Si_4^{4-} star an excited tetrahedrane state then? Assuming an ($sp^2 + p$) configuration for all four Si atoms, a plausible description can be formulated with three three-center bonds and seven nonbonding electron pairs. Another remarkable variant results with the solution $x = y = 8$. The polyanion Si_4^{8-} would be isoelectronic with the carbonate anion CO_3^{2-} and the polyanion Si_5^{8-} with cyclopentene. We hope that this interesting structure will rouse the interest of theoreticians. The isostructural compound $Li_{12}Ge_7$ has likewise been prepared.

Received: July 28, 1980 [Z 639 IE]
German version: Angew. Chem. *92*, 1070 (1980)

[*] Prof. Dr. H. G. von Schnering [*], Dr. R. Nesper, Dipl.-Ing. J. Curda
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
Prof. Dr. K.-F. Tebbe
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)
[*] To whom correspondence should be addressed.

[1] *H. G. v. Schnering, R. Nesper, K.-F. Tebbe, J. Curda*, Z. Metallkde. *71*, 357 (1980).
[2] *H. Axel, H. Schäfer, A. Weiss*, Z. Naturforsch. *B 20*, 1302 (1965).
[3] *E. Zintl*, Angew. Chem. *52*, 1 (1939); *W. Klemm*: Festkörperprobleme, Vol. III. Vieweg, Braunschweig 1963; cf. also *H. Schäfer, B. Eisenmann, W. Müller*, Angew. Chem. *85*, 742 (1973); Angew. Chem. Int. Ed. Engl. *12*, 694 (1973).
[4] *E. Mooser, W. B. Pearson*, Prog. Semicond. *5*, 103 (1960).
[5] *U. Frank, W. Müller*, Z. Naturforsch. *B 30*, 313 (1975).
[6] *H. G. v. Schnering et al.*, Z. Kristallogr., in press.

Planar Four-Coordinated Silicon?

By *Jack D. Dunitz*[*]

The announcement by *Meyer* and *Nagorsen*[1] that the bis(*o*-phenylenedioxy)silane molecule *(1)* is planar in the crystalline state is sufficiently novel and provocative that it can hardly avoid drawing critical attention to the evidence on which it is based. In the absence of a detailed X-ray analysis this evidence consists of a crystallographic symmetry argument: X-ray rotation and Weissenberg photographs led to a monoclinic unit cell with dimensions $a = 10.56$, $b = 5.60$, $c = 10.96$ Å, $\beta = 122°$, space group $P2_1/c$; with two molecules of $(C_6H_4O_2)_2Si$ per cell each silicon atom must occupy a crystallographic inversion center and hence must lie in a common plane with its four bonded oxygen atoms.

There are two weak points in this argument. In the first place, with a short *b* axis it may be dangerous to eliminate the alternative space group P2/c on the basis of a few systematically absent ($0k0$; $k = 2n+1$) reflections. If this space group is admitted as a possibility the silicon atoms could sit on twofold rotation axes instead of inversion centers and the symmetry argument for the planarity of the SiO_4 grouping would lose its force. In the second place, even if the space group $P2_1/c$ is accepted, the method of assigning molecular symmetry from space group arguments is not infallible because the molecular arrangement in the crystal may be disordered. There are many cases where molecular symmetries assigned in this way would obviously be in error. Perhaps the most famous case is that of azulene ($P2_1/a$, $Z = 2$)[2].

There is still another serious flaw in the experimental evidence: the chemical identity of the crystalline compound that was actually examined by X-ray diffraction is by no means proven. In fact the cell dimensions cited by *Meyer* and *Nagorsen* have a suspicious resemblance to those of catechol[3], a compound that might well be produced from *(1)* in the presence of traces of water.

In summary, the experimental evidence by *Meyer* and *Nagorsen*[1] is insufficient to establish *(1)* as the first compound with planar four-coordinated silicon. The theoretical arguments[1,4] of course retain whatever significance they had.

Received: March 21, 1980 [Z 640a IE]
German version: Angew. Chem. *92*, 1070 (1980)

[*] Prof. Dr. J. D. Dunitz
Organic Chemistry Laboratory
Swiss Federal Institute of Technology (ETH), ETH-Zentrum
CH-8092 Zürich (Switzerland)

[1] *H. Meyer, G. Nagorsen*, Angew. Chem. *91*, 587 (1979); Angew. Chem. Int. Ed. Engl. *18*, 551 (1979).
[2] *J. M. Robertson, H. M. M. Shearer, G. A. Sim, D. G. Watson*, Acta Crystallogr. *15*, 1 (1962). For some other examples see *J. D. Dunitz*, X-ray Analysis and the Structure of Organic Molecules, Cornell University Press, 1979, pp. 103—106.
[3] *H. Wunderlich, D. Mootz*, Acta Crystallogr. *B 27*, 1684 (1971); $a = 10.082$, $b = 5.518$, $c = 10.943$ Å, $\beta = 118.53°$ or after axis transformation, $a' = 10.771$ Å, $\beta' = 124.68°$. Slightly different values are given by *C. J. Brown*, Acta Crystallogr. *21*, 170 (1966).
[4] *E. U. Würthwein, P. v. R. Schleyer*, Angew. Chem. *91*, 588 (1979); Angew. Chem. Int. Ed. Engl. *18*, 553 (1979).

Planar Four-Coordinated Silicon—A Reply

By *Günter Nagorsen* and *Heinrich Meyer*[*]

The criticism leveled by *Dunitz*[1] at our communication[2] is partly justified. However, we had ourselves already emphasized that the space group determination is based on the absence of a few reflections and is hence not entirely compelling.

From 1975 to 1979 it proved impossible to again obtain suitable single crystals of the extremely sensitive monomeric bis(*o*-phenylenedioxy)silane *(1)*, and experimental results were therefore published only after supporting evidence had been obtained from model calculations[2,3].

The similarity between the lattice data of catechol and *(1)* appears remarkable at first sight, although *"a"* is significantly different. On closer examination, though, it actually provides powerful support for our structural model: for the H bond system linking two catechol molecules in *planar* fashion merely has to be replaced by silicon in a planar coordination, and the similarity in cell dimensions become entirely plausible.

Pure catechol melts at a temperature 8 °C lower than our substance and is stable to atmospheric moisture. Some of our (few) single crystals were hydrolyzed; catechol was identified alongside a gel of silicic acid. Within seconds of exposure to air, the lustrous crystals had become covered with a gel. Our identification of *(1)* was also based on mass spectrometry under the conditions of crystal growth.

We consider a possible disorder of the molecules in the crystal of *(1)* to be hardly applicable, since most of the cases cited by *Dunitz*[1] are (almost) planar, somewhat asymmetric systems whose disorder is explicable. Rather, it was precisely the lack of an isostructural relationship with the orthocarbonic ester that drew our attention to this structural problem.

Received: September 25, 1980 [Z 640b IE]
German version: Angew. Chem. *92*, 1071 (1980)

[1] *J. D. Dunitz*, Angew. Chem. *92*, 1070 (1980); Angew. Chem. Int. Ed. Engl. *19*, 1034 (1980).
[2] *H. Meyer, G. Nagorsen*, Angew. Chem. *91*, 587 (1979); Angew. Chem. Int. Ed. Engl. *18*, 551 (1979).
[3] *E. U. Würthwein, P. v. R. Schleyer*, Angew. Chem. *91*, 588 (1980); Angew. Chem. Int. Ed. Engl. *18*, 553 (1979).

[*] Prof. Dr. G. Nagorsen, Dr. H. Meyer
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1980. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar*, **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors Dr. *Helmut Grünewald* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany, Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

AUTHOR INDEX

G.E. = Reference to Volume *92* (1980) of the German Edition of Angewandte Chemie. References are given for Review Articles and Short Communications only.—No "G.E." reference is given for a Book Review.

ABELE, R. 477 [G.E. 493]
Adam, F. 1029 [G.E. 1062]
Adam, W. 48, 762 [G.E. 54, 815]
Adamiak, D. A. 549 [G.E. 578]
Adams, H.-N. 404 [G.E. 411]
Adiwidjaja, G. 563 [G.E. 559]
Agrifoglio, G. 641 [G.E. 645]
Aigner, H. 136 [G.E. 133]
Albert, A. 310 [G.E. 319]
Albright, T. A. 728 [G.E. 747]
Ali, Sk. A. 557 [G.E. 573]
Alper, H. 315 [G.E. 321]
Alscher, A. 638 [G.E. 654]
Altenbach, H.-J. 1016 [G.E. 1053]
Alwani, Z. 623 [G.E. 633]
Aly, A. A. M. 71 [G.E. 66]
Amble, E. 629 [G.E. 643]
Amstutz, R. 53 [G.E. 59]
Anastassiou, A. G. 43, 393, 639 [G.E. 53, 402, 657]
Andres, K. 571 [G.E. 563]
Angst, C. 140, 141, 143 [G.E. 139, 141, 143]
Appel, R. 213, 556 [G.E. 206, 578]
Arduini, A. A. 1024 [G.E. 1058]
Ashkenazi, P. 933, 936 [G.E. 970, 972]
Atwood, J. L. 931 [G.E. 964]
Au, G. von 824 [G.E. 843]
Aznar, F. 146 [G.E. 132]

BACCOUCHE, M. 322 [G.E. 320]
Badri, R. 639 [G.E. 657]
Bahsoun, A. A. 1024 [G.E. 1058]
Baier, H. 1029 [G.E. 1062]
Balci, M. 48, 301 [G.E. 54, 316]
Ball, F. 718 [G.E. 742]
Banks, R. E. 230
Barth, J. 725 [G.E. 753]
Bartholomé, E. 148, 838
Bartkowiak, F. 198 [G.E. 201]
Bartlett, N. 944 [G.E. 956]
Bartmann, W. 819 [G.E. 850]
Bartoli, J. F. 909 [G.E. 938]
Bats, J. W. 125 [G.E. 122]
Baumgartner, E. 550 [G.E. 564]
Becher, G. 469 [G.E. 490]
Beck, G. 819 [G.E. 850]
Beck, W. 834 [G.E. 863]
Becker, F. S. 227 [G.E. 226]
Becker, G. 741 [G.E. 756]
Becker, W. 321 [G.E. 304]
Beckhaus, H.-D. 429 [G.E. 417]
Beckmann, L. 303 [G.E. 305]
Benn, R. 44 [G.E. 45]
Ben-Zvi, Z. 543 [G.E. 577]
Berke, H. 225 [G.E. 224]
Bernal, I. 641 [G.E. 645]
Berndt, A. 57 [G.E. 64]
Bernheim, M. 1010 [G.E. 1043]
Berstermann, H.-M. 564 [G.E. 555]
Besenhard, J. O. 491 [G.E. 476]
Bestmann, H. J. 136, 475, 822, 1012 [G.E. 134, 492, 856, 1045]
Bianchini, C. 405, 1021 [G.E. 412, 1055]
Biekert, E. 148, 838
Biffar, W. 56, 58 [G.E. 63, 65]
Bindewald, R. 394 [G.E. 394]
Binsch, G. 411 [G.E. 445]
Birkhan, M. 741 [G.E. 756]
Bittler, K. 190 [G.E. 187]
Blanck, K. 650 [G.E. 655]
Blank, H. 128 [G.E. 124]
Blank, N. E. 44 [G.E. 45]
Blaschke, G. 13 [G.E. 14]
Blau, H. 1019, 1020 [G.E. 1063, 1065]
Bliefert, C. 943 [G.E. 957]
Bloch, R. 928 [G.E. 969]
Boche, G. 1010 [G.E. 1043]
Bock, H. 51, 147, 209, 834 [G.E. 56, 136, 213, 863]
Bogdanović, B. 622, 817, 818 [G.E. 633, 844, 845]
Bögge, H. 654 [G.E. 665]
Böhle, C. 746 [G.E. 758]
Böhme, M. 473 [G.E. 474]
Boldhaus, M. 943 [G.E. 957]
Bolleter, M. 708 [G.E. 734]
Bolz, P.-R. 227 [I.E. 220]
Bonnet, J.-J. 551 [G.E. 572]
Borgarello, E. 646 [G.E. 663]
Boross, L. 331
Bosse, D. 130 [G.E. 138]
Bosshardt, H. 303 [G.E. 302]
Bott, K. 171 [G.E. 169]
Bovey, F. A. 657
Bratos, S. 76
Brauer, D. J. 836 [G.E. 859]
Braun, A. M. 675 [G.E. 712]
Braun, H. 400 [G.E. 407]
Braun, S. 621 [G.E. 635]
Breitmaier, E. 816, 924 [G.E. 841, 957]
Bringmann, G. 460 [G.E. 483]
Brink, K. 943 [G.E. 957]
Brinker, U. H. 304, 631 [G.E. 314, 641]
Brocker, U. 1015 [G.E. 1051]
Brokatzky, J. 47 [G.E. 48]
Brönneke, A. 625 [G.E. 637]
Brossmer, R. 208 [G.E. 200]
Brown, G. H. 330
Bruder, H. 396 [G.E. 395]
Brunner, H. 641 [G.E. 645]
Brüntrup, G. 465 [G.E. 469]
Buckingham, A. D. 76
Bünsch, A. 902 [G.E. 929]
Bünzel, M. 322 [G.E. 320]
Bürger, H. 836 [G.E. 859]
Burger, K. 810 [G.E. 836]
Bursill, L. A. 745 [G.E. 755]
Bussas, R. 732, 737 [G.E. 748, 750]
Butler, J. D. 330
Butters, T. 926 [G.E. 952]

CASTRO, B. 742 [G.E. 761]
Cavagna, F. 129; 132 [G.E. 126, 127]
Chandrasekhar, J. 485 [G.E. 488]
Chappuis, G. 742 [G.E. 761]
Chottard, J.-C. 909 [G.E. 938]
Christl, M. 457, 458 [G.E. 465, 466]
Chu-Tao-pen 66, 67 [G.E. 49, 51]
Cielusek, G. 70 [G.E. 60]
Clauss, K. 131 [G.E. 138]
Clegg, W. 134, 943 [G.E. 130, 959]
Cook, R. 324 [G.E. 310]
Cordier, G. 324 [G.E. 310]
Costa, T. 555 [G.E. 557]
Cotton, F. A. 875 [G.E. 921]
Creswick, M. W. 641 [G.E. 645]
Cromie, E. R. 316 [G.E. 323]
Curda, J. 1033 [G.E. 1070]

DAHLHOFF, W. V. 546, 547, 548 [G.E. 552, 553, 553]
Dartmann, M. 654 [G.E. 665]
Day, P. 290 [G.E. 290]
Dean Wilson, W. 478 [G.E. 494]
Deger, H. M. 41, 913, 921 [G.E. 43, 943, 944]
Dehnicke, K. 220 [G.E. 211]
Delay, F. 726 [G.E. 764]
De Lucchi, O. 762 [G.E. 815]
de Meijere, A. 138, 387 [G.E. 135, 387]
Denis, J. M. 928 [G.E. 969]
Denis, J.-N. 1006 [G.E. 1039]
DesMarteau, D. D. 643 [G.E. 659]
Dialer, K. 407 [G.E. 389]
Di Varia, M. 405 [G.E. 412]
Dixon, K. R. 931 [G.E. 964]
Doll, K.-H. 479 [G.E. 487]
Domesle, R. 489 [G.E. 499]
Dorio, M. M. 330
Dormoy, J. R. 742 [G.E. 761]
Dräger, M. 923 [G.E. 950]
Dresow, B. 321, 321 [G.E. 303, 304]
Drossard, J.-M. 1016 [G.E. 1053]
du Mont, W.-W. 553, 554 [G.E. 561, 562]
Dunand, A. 310 [G.E. 319]
Dunitz, J. D. 53, 1033 [G.E. 59, 1070]
Dürner, G. 1027, 1029 [G.E. 1060, 1062]
Dürr, H. 648 [G.E. 647]

EADIE, D. T. 931 [G.E. 964]
Ebel, S. 229
Eberbach, W. 47 [G.E. 48]
Eberle, H.-J. 73 [G.E. 70]
Ebert, K. H. 333 [G.E. 331]
Eckert-Maksić, M. 807 [G.E. 833]
Eckhardt, G. 459 [G.E. 463]
Ederer, H. J. 333 [G.E. 331]
Effenberger, F. 151 [G.E. 147]
Efraty, A. 633 [G.E. 649]
Eggerer, H. 136 [G.E. 133]
Eisenmann, B. 490 [G.E. 480]
Elstner, E. F. 473 [G.E. 474]
Eltz, H. von der 628 [G.E. 639]
Endres, H. 653 [G.E. 644]
Engel, W. D. 659 [G.E. 684]
Engelmann, M. 710 [G.E. 738]
Enkelmann, V. 912 [G.E. 941]
Ennen, J. 328 [G.E. 321]
Erden, I. 387 [G.E. 387]
Ernst, H. 827 [G.E. 861]
Eschenmoser, A. 140, 141, 143 [G.E. 139, 141, 143]
Eujen, R. 836 [G.E. 859]

FACHINETTI, G. 404 [G.E. 411]
Fahr, E. 829 [G.E. 858]
Faix, W. G. 197 [G.E. 194]
Fecher, P. 829 [G.E. 858]
Fehlhammer, W. P. 480 [G.E. 478]
Feigel, M. 396 [G.E. 395]
Feinstein, I. 633 [G.E. 649]
Felcht, U.-H. 132 [G.E. 127]
Fenske, D. 492 [G.E. 477]
Feser, R. 940 [G.E. 960]
Feuerherd, K.-H. 201 [G.E. 197]
Fischer, E. O. 205, 643 [G.E. 206, 662]
Fischer, G. 407 [G.E. 389]
Fischer, Hans 724 [G.E. 766]
Fischer, Hartmut 301 [G.E. 316]
Fitzer, E. 375 [G.E. 375]
Fleischhauer, I. 304 [G.E. 314]
Flippen-Anderson, J. L. 906 [G.E. 936]
Flohr, G. 460 [G.E. 483]
Föhles, J. 394 [G.E. 394]
Follmann, R. 303 [G.E. 305]
Francis, C. G. 402 [G.E. 409]
Franck, B. 460, 461 [G.E. 483, 484]
Francke, W. 630 [G.E. 640]
Frank, R. M. 318 [G.E. 306]
Franke, W. 485 [G.E. 488]
Freed, J. H. 330
Freitag, G. 457 [G.E. 465]
Friebolin, H. 208 [G.E. 200]
Fries, S. 831, 832, 833 [G.E. 848, 848, 849]
Fritch, J. R. 559 [G.E. 570]
Fritschi, U. S. 742 [G.E. 761]
Fritz, H. 47, 214, 567 [G.E. 48, 216, 575]
Fröhlich, C. 145 [G.E. 131]

Frolow, F. 326, 633 [G.E. 324, 649]
Fryer, J. R. 148
Fuess, H. 125 [G.E. 122]
Fuhrhop, J.-H. 322, 550 [G.E. 320, 564]
Füllmann, H. 714 [G.E. 742]
Fuss, A. 49 [G.E. 55]

GÄB, S. 474 [G.E. 483]
Galantai, E. 653 [G.E. 644]
Garvey, D. S. 557 [G.E. 573]
Gasteiger, J. 495 [G.E. 503]
Gdaniec, M. 549 [G.E. 578]
Gebler, W. 722 [G.E. 767]
Gehrken, H.-P. 461 [G.E. 484]
George, M. V. 907, 973 [G.E. 939, 1005]
Gesing, E. R. F. 1023 [G.E. 1057]
Giese, B. 207, 835 [G.E. 215, 864]
Giesemann, W. 136 [G.E. 133]
Ginsburg, D. 933, 936 [G.E. 970, 972]
Gleiter, R. 715 [G.E. 768]
Glemser, O. 408, 833, 944 [G.E. 393, 904, 956]
Gollnick, K. 831, 832, 833 [G.E. 848, 848, 849]
Gompper, R. 216, 217, 463 [G.E. 207, 208, 468]
Goth, H. 810 [G.E. 836]
Grätzel, M. 646, 675 [G.E. 663, 712]
Greenberg, A. 75
Grimme, W. 307 [G.E. 307]
Grob, C. A. 708 [G.E. 734]
Grogg, P. 742 [G.E. 761]
Gross, J. 491, 809 [G.E. 476, 835]
Groth, U. 212 [G.E. 205]
Gruehn, R. 505 [G.E. 531]
Grüter, H.-W. 714 [G.E. 735]
Guggolz, E. 651 [G.E. 660]
Günther, D. 130 [G.E. 138]
Günther, Harald 301, 921 [G.E. 316, 944]
Günther, Horst 563 [G.E. 559]

HAAS, H. J. 648 [G.E. 647]
Haenel, M. W. 44, 636 [G.E. 45, 653]
Haesslein, J.-L. 1005 [G.E. 1038]
Hafner, K. 199, 621 [G.E. 202, 635]
Halász, I. 24 [G.E. 25]
Halberstadt, I. K. 814 [G.E. 840]
Hammer, R. 809 [G.E. 835]
Hanack, M. 392 [G.E. 391]
Hanko, R. 625 [G.E. 637]
Harder, R. 564 [G.E. 555]
Harms, K. 134 [G.E. 130]
Hartenstein, J. 1018 [G.E. 1055]
Härter, P. 225 [G.E. 224]
Hartwig, P. 74 [G.E. 72]
Hartwig, W. 212 [G.E. 205]
Hauer, J. 945 [G.E. 955]
Hasselmann, D. 634 [G.E. 651]
Hatz, R. 656
Haubrich, G. 213 [G.E. 206]
Haupt, H. 87 [G.E. 83]
Hebel, P. 913, 921 [G.E. 943, 944]
Hehre, W. J. 485 [G.E. 488]
Heigl, T. 1018 [G.E. 1055]
Heiker, F. R. 904 [G.E. 930]
Heimbach, P. 569, 570 [G.E. 567, 569]
Heinemann, U. 216, 217 [G.E. 207, 208]
Heintz, A. 223 [G.E. 209]
Heitz, W. 718 [G.E. 742]
Hellfeldt, K. 396 [G.E. 395]
Hellmann, H. 148, 838
Helmreich, E. J. M. 441 [G.E. 429]
Hemminger, W. 838
Henkel, G. 709, 710 [G.E. 737, 738]
Henning, R. 645 [G.E. 664]
Hensel, F. 593 [G.E. 598]
Herbert, R. 457 [G.E. 465]
Herrera, A. 927 [G.E. 951]
Herrmann, W. A. 651, 927 [G.E. 660, 961]
Hertenstein, U. 127 [G.E. 123]
Hess, H. 650 [G.E. 655]
Heublein, A. 49 [G.E. 55]
Heumann, K. G. 406 [G.E. 406]
Higuchi, T. 399 [G.E. 405]
Himmele, W. 184, 178 [G.E. 176, 182]
Hintzer, K. 471 [G.E. 473]
Hirashima, T. 1007 [G.E. 1040]
Hirotsu, K. 399 [G.E. 405]
Hirsch, E. 813 [G.E. 839]
Hirsch, H. L. 475 [G.E. 492]
Hoberg, H. 145, 146, 927 [G.E. 131, 132, 951]
Höcker, H. 219 [G.E. 212]
Hoffmann, H. M. R. 827 [G.E. 861]
Hoffmann, R. W. 218 [G.E. 218]
Hofmann, P. 494, 728 [G.E. 496, 747]
Hoggard, R. 632 [G.E. 650]
Höhne, G. 838
Hopf, H. 389 [G.E. 388]
Hoppe, D. 303, 625 [G.E. 305, 637]
Hoppe, R. 110, 489 [G.E. 106, 499]
Hossain, M. B. 309 [G.E. 326]
Hotzel, A. 739 [G.E. 751]
Houghton, R. P. 656
Houriet, R. 905 [G.E. 934]
Hub, H.-H. 938 [G.E. 962]
Hubbuch, A. 394 [G.E. 394]
Huber, H. X. 402 [G.E. 409]
Huber, W. 624 [G.E. 636]
Huck, H.-M. 558 [G.E. 580]
Huisgen, R. 202, 906, 947 [G.E. 198, 936, 979]
Hull, W. E. 924 [G.E. 957]
Hünig, S. 747
Hunkler, D. 567 [G.E. 575]
Hunter, G. 316 [G.E. 323]
Hupfer, B. 938 [G.E. 962]
Hürter, H.-U. 481 [G.E. 479]

IDELMANN, P. 546, 547 [G.E. 552, 553]
Iler, R. K. 230
Immirzi, A. 721 [G.E. 744]
Inamoto, N. 399 [G.E. 405]
Ippen, J. 66, 67 [G.E. 49, 51]
Irngartinger, H. 211 [G.E. 214]
Isbarn, G. 333 [G.E. 331]
Isenberg, W. 943 [G.E. 959]

JACOB, E. 227 [G.E. 226]
Jagow, G. von 659 [G.E. 684]
Jansen, M. 386 [G.E. 386]
Jayaraman, A. 587 [G.E. 626]
Jendralla, H. 1032 [G.E. 1068]
Jochum, C. 495 [G.E. 503]
Johansen, J. E. 141 [G.E. 141]
Jonas, K. 520 [G.E. 513]
Jostes, R. 654, 875 [G.E. 665, 921]
Jünemann, W. 388 [G.E. 390]
Jung, G. 712 [G.E. 739]
Junglas, H. 1015 [G.E. 1051]
Jutzi, P. 484 [G.E. 496]

KAIM, W. 911 [G.E. 940]
Kajiwara, M. 140 [G.E. 139]
Kalck, P. 551 [G.E. 572]
Kambe, N. 308, 1007, 1008, 1009, 1009 [G.E. 317, 1040, 1041, 1041, 1042]
Kaminsky, W. 390 [G.E. 396]
Karl, A. 484 [G.E. 496]
Karle, I. 906 [G.E. 936]
Käs, H. H. 386 [G.E. 386]
Kasmai, H. S. 43, 393, 639 [G.E. 53, 402, 657]
Katritzky, A. R. 306 [G.E. 315]
Katryniok, D. 645 [G.E. 646]
Kauffmann, Th. 328, 723 [G.E. 321, 746]
Kaupp, G. 243, 714 [G.E. 245, 735]
Kawamoto, K. 928 [G.E. 974]
Keilich, G. 208 [G.E. 200]
Kelker, H. 656
Kelm, H. 841 [G.E. 887]
Kerkmann, T. 466 [G.E. 470]
Kessler, H. 411 [G.E. 445]
Khalifa, M. H. 712 [G.E. 739]
Khouzami, F. 640 [G.E. 658]
Kiedrowski, G. von 134 [G.E. 130]
Kimmel, Y. 543 [G.E. 577]
Kinne, R. 540 [G.E. 547]
Kira, M. 620 [G.E. 632]
Kisch, H. 317, 645 [G.E. 303, 664]
Kitschke, B. 566 [G.E. 556]
Kiwi, J. 646 [G.E. 663]
Kleemann, A. 627 [G.E. 640]
Klein, H.-F. 362, 491, 809 [G.E. 362, 476, 835]
Klein, H. W. 441 [G.E. 429]
Klein, J. 44 [G.E. 45]
Kleiner, H.-J. 133 [G.E. 129]
Kleiner, N. 923 [G.E. 950]
Kleinschroth, J. 389 [G.E. 388]
Klessinger, M. 908 [G.E. 937]
Klöter, G. 942 [G.E. 954]
Kluth, J. 569, 570 [G.E. 567, 569]
Kniep, R. 645 [G.E. 646]
Knolle, J. 819 [G.E. 850]
Koch, H. 938 [G.E. 962]
Koelle, U. 640 [G.E. 658]
Köhler, F. H. 479 [G.E. 487]
Kojima, H. 538 [G.E. 550]
Kokel, B. 716 [G.E. 754]
Köksal, Y. 472 [G.E. 486]
Kolb, M. 725 [G.E. 753]
Kolthoff, I. M. 149
Kondo, K. 308, 1007, 1007, 1008, 1009, 1009 [G.E. 317, 1040, 1040, 1041, 1041, 1042]
König, H. 749 [G.E. 802]
König, K.-H. 201 [G.E. 197]
König, W. A. 910 [G.E. 935]
Kopanski, L. 459 [G.E. 463]
Koppenhagen, V. B. 321, 321 [G.E. 303, 304]
Koppenhoefer, B. 471 [G.E. 473]
Koray, A. R. 44 [G.E. 45]
Korte, F. 474 [G.E. 483]
Köser, H. G. 307 [G.E. 307]
Köster, R. 546, 546, 548 [G.E. 552, 553, 553]
Koszinowski, J. 202 [G.E. 198]
Kratky, C. 141 [G.E. 141]
Krauth-Siegel, L. R. 397 [G.E. 403]
Krebs, B. 481, 709, 710 [G.E. 479, 737, 738]
Kreher, R. 320 [G.E. 309]
Kremmer, T. 331
Kresze, G. 732, 737 [G.E. 748, 750]
Krief, A. 1006 [G.E. 1039]
Krieger, C. 66 [G.E. 49]
Krimmer, H.-P. 199 [G.E. 202]
Krivan, V. 197 [G.E. 194]
Kröhnke, C. 912 [G.E. 941]
Krüger, C. 520, 571, 746, 817 [G.E. 513, 563, 758, 844]
Kubo, K. 545 [G.E. 566]
Kunkely, H. 221, 717 [G.E. 228, 745]
Künstlinger, M. 924 [G.E. 957]
Kunz, H. 932 [G.E. 953]
Kunz, W. 708 [G.E. 734]
Kunze, U. 220 [G.E. 227]

L'ABBÉ, G. 276 [G.E. 277]
Lander, N. 543 [G.E. 577]
Lang, R. 457 [G.E. 465]
Lange, H. 401 [G.E. 408]
Lange, M. 909 [G.E. 938]
L'Annunziata, M. F. 573
Lappert, M. F. 656
Lattmann, R. 143 [G.E. 143]
Lee, W.-B. 835 [G.E. 864]
Lefferts, J. L. 309 [G.E. 326]
Leibfritz, D. 396 [G.E. 395]
Leininger, H. 458 [G.E. 466]
Le Noble, W. 841 [G.E. 887]
Lenoir, D. 318 [G.E. 306]
Leuchtenberger, W. 627 [G.E. 640]
Leupold, E. I. 126 [G.E. 125]
Lex, J. 41, 913 [G.E. 43, 943]
Ley, H. 148, 838
Lhotak, H. 328 [G.E. 321]
Liao, S. 818 [G.E. 845]
Lichtenthaler, R. N. 223 [G.E. 209]
Liebelt, W. 220 [G.E. 211]
Liebenow, H. 713 [G.E. 740]
Liebman, J. F. 75
Lin, J.-T. 540 [G.E. 547]
Lindner, E. 73, 824 [G.E. 70, 843]
Lindner, H. J. 566 [G.E. 556]
Lingens, F. 828 [G.E. 855]
Linkies, A. 129 [G.E. 126]
Lippert, E. 76
Lloyd, J. M. 306 [G.E. 315]
Loosen, K. 634 [G.E. 651]
Lorenz, K. 932 [G.E. 953]
Lorke, M. 45 [G.E. 46]
Luck, W. A. P. 28 [G.E. 29]
Lüdemann, H.-D. 945 [G.E. 955]
Lumb, M. D. 75

MACFARLANE, R. D. 933, 936 [G.E. 970, 972]
Madach, T. 226 [G.E. 225]
Mahajan, M. P. 907 [G.E. 939]
Maier, G. 51, 52, 209, 211, 1022 [G.E. 56, 58, 213, 214, 1056]
Maier, T. 137 [G.E. 128]
Malisch, W. 1019, 1020 [G.E. 1063, 1065]
Malsch, K.-D. 211 [G.E. 214]
Mangold, D. 222 [G.E. 196]
Mannschreck, A. 469 [G.E. 490]
Mansuy, D. 909 [G.E. 938]
Manzo, R. H. 306 [G.E. 315]
Mark, H. F. 228
Märkl, G. 747
Markó, L. 226 [G.E. 225]
Markó-Monostory, B. 226 [G.E. 225]
Marosi, L. 743 [G.E. 756]
Martens, J. 627 [G.E. 640]
Martin, H.-D. 807 [G.E. 833]
Masamune, S. 557 [G.E. 573]
Masana, J. 929 [G.E. 968]
Massa, W. 741 [G.E. 756]
Matsumoto, K. 1013 [G.E. 1046]
Mayer, B. 807 [G.E. 833]
Mayr, A. J. 632 [G.E. 650]
Mayr, H. 814 [G.E. 840]
Mazur, Y. 1004 [G.E. 1037]
Mealli, C. 931 [G.E. 967]
Mechoulam, R. 543 [G.E. 577]
Meixner, J. 207 [G.E. 215]
Meli, A. 405, 1021 [G.E. 412, 1055]
Mertin, W. 505 [G.E. 531]
Mews, R. 408, 883 [G.E. 393, 904]
Meyer, H. 1034 [G.E. 1071]
Michel, J. 731 [G.E. 763]
Midollini, S. 931 [G.E. 967]
Mihm, G. 52 [G.E. 58]
Mildenberger, H. 137 [G.E. 128]
Milewski-Mahrla, B. 555 [G.E. 557]
Mintas, M. 469 [G.E. 490]
Mintzer, J. 147 [G.E. 136]
Mitra, A. 973 [G.E. 1005]
Miyata, T. 1007 [G.E. 1040]
Moderhack, D. 45 [G.E. 46]
Molloy, K. C. 309 [G.E. 326]
Moneti, S. 931 [G.E. 967]
Mootz, D. 483, 552 [G.E. 481, 559]
Morimoto, F. 308, 1040 [G.E. 317, 1040]
Morita, S. 1009 [G.E. 1041]
Mueller-Westerhoff, U. T. 638 [G.E. 654]
Mülhaupt, R. 857 [G.E. 869]
Müllen, K. 624 [G.E. 636]
Müller, A. 72, 654, 875 [G.E. 69, 665, 921]
Müller, K. 1 [G.E. 1]
Müller, M. 621 [G.E. 635]
Mulzer, J. 465, 466 [G.E. 469, 470]
Murad, A. F. 389 [G.E. 388]
Murai, S. 928, 1007, 1008, 1009 [G.E. 974, 1040, 1041, 1041]
Murata, I. 543, 545 [G.E. 565, 566]
Musco, A. 721 [G.E. 744]
Mynott, R. 636 [G.E. 653]

NAAB, P. 143 [G.E. 143]
Nachmansohn, D. 573
Nagano, K. 308 [G.E. 317]
Nagorsen, G. 1034 [G.E. 1071]
Naithani, K. 394 [G.E. 394]
Nakadaira, Y. 620 [G.E. 632]
Nakajima, T. 811, 812 [G.E. 837, 838]
Nakazawa, T. 543, 545 [G.E. 565, 566]
Neidlein, R. 204, 739 [G.E. 199, 751]
Nesper, R. 1033 [G.E. 1070]
Neudeck, H. 308 [G.E. 318]
Neudert, B. 553 [G.E. 561]
Neugebauer, F. A. 724 [G.E. 766]
Neumann, H. 55 [G.E. 62]
Niecke, E. 709, 710 [G.E. 737, 738]
Niemann, K. 636 [G.E. 653]
Niimoto, Y. 545 [G.E. 566]
Noltemeyer, M. 943 [G.E. 959]
Nöth, H. 56, 58, 482 [G.E. 63, 65, 481]
Nonhebel, D. C. 229

OERTLING, W. A. 933, 936 [G.E. 970, 972]
Öfele, K. 538 [G.E. 550]
Offermann, W. 464 [G.E. 471]
Offord, R. E. 838
Ohta, A. 202 [G.E. 198]
Olabishi, O. 494
Olah, G. A. 811, 812 [G.E. 837, 838]
Olgemöller, B. 834 [G.E. 863]
Opgenorth, H.-J. 388 [G.E. 390]
Orlandini, A. 1021 [G.E. 1055]
Osborn, J. A. 1024, 1025 [G.E. 1058, 1059]
Ostertag, W. 190 [G.E. 187]
Ostoja Starzewski, K.-H. 316 [G.E. 323]
Othmer, D. F. 228
Overberger, C. G. 228
Ozin, G. A. 402 [G.E. 409]

PALM, J. 41 [G.E. 43]
Pandey, B. 907 [G.E. 939]
Pankiewicz, K. 549 [G.E. 578]
Pannell, K. H. 632 [G.E. 650]
Paske, D. 456 [G.E. 464]
Patel, R. C. 306 [G.E. 315]
Paul, W. 713 [G.E. 740]
Paulsen, H. 902, 904 [G.E. 929, 930]
Paulus, E. F. 132 [G.E. 127]
Pelizzetti, E. 646 [G.E. 663]
Peter, R. 1011 [G.E. 1044]
Pettersen, R. C. 632 [G.E. 650]
Pfleiderer, W. 473 [G.E. 474]
Pickardt, J. 70, 325 [G.E. 60, 313]
Pietsch, H. 129 [G.E. 126]
Pilet, O. 1003 [G.E. 1036]
Pino, P. 857 [G.E. 869]
Piovesana, O. 561 [G.E. 579]
Pittman, C. U. 478 [G.E. 494]
Plank, J. 651, 937 [G.E. 660, 961]
Platz, H. 475 [G.E. 492]
Poilblanc, R. 551 [G.E. 572]
Pommer, E.-H. 184 [G.E. 176]
Pommerening, H. 56, 482 [G.E. 63, 481]
Power, P. P. 656
Prakash, G. K. S. 811, 812 [G.E. 837, 838]
Prauser, G. 407 [G.E. 389]
Pregosin, P. S. 316, 721 [G.E. 323, 744]
Prince, T. L. 315 [G.E. 321]
Prinzbach, H. 214, 567 [G.E. 216, 575]
Pritzkow, H. 942 [G.E. 954]
Prössdorf, W. 479 [G.E. 487]
Puttkamer, H. von 921 [G.E. 944]

QUAST, H. 49 [G.E. 55]
Quinkert, G. 1027, 1029 [G.E. 1060, 1062]

RABENAU, A. 74 [G.E. 72]
Rabinovich, D. 326 [G.E. 324]
Raddatz, P. 472 [G.E. 486]
Rankin, D. W. H. 316 [G.E. 323]
Ratzenhofer, M. 317 [G.E. 303]
Rautenstrauch, V. 726 [G.E. 764]
Redlich, H. 630 [G.E. 640]
Reetz, M. T. 900, 901, 1011 [G.E. 931, 933, 1044]
Reichert, U. 830 [G.E. 832]
Reinsch, U. 72 [G.E. 69]
Reisenauer, H. P. 52, 566 [G.E. 58, 556]
Reissenweber, G. 222 [G.E. 196]
Reissig, H.-U. 813, 906 [G.E. 839, 936]
Reitel, Ch. 201 [G.E. 197]
Rensing, A. 328 [G.E. 321]
Rentzea, C. N. 199 [G.E. 195]
Reuschling, D. 129 [G.E. 126]
Rheinwald, M. 475 [G.E. 492]
Richardson, T. J. 944 [G.E. 956]
Richter, F. 65 [G.E. 66]
Richter, U.-B. 636 [G.E. 653]
Richter, W. J. 473 [G.E. 474]
Riedel, D. 937 [G.E. 961]
Riegler, N. 211 [G.E. 214]
Rieke, R. D. 538 [G.E. 550]
Rieker, A. 712 [G.E. 739]
Riesner, D. 231 [G.E. 233]
Riffel, H. 650 [G.E. 655]
Ringsdorf, H. 938 [G.E. 962]
Ringshandl, R. 456 [G.E. 464]
Robeson, L. M. 494
Roesky, H. W. 125, 943 [G.E. 122, 959]
Röll, W. 205 [G.E. 206]
Rösch, L. 55 [G.E. 62]
Rosmus, P. 51 [G.E. 56]
Roth, B. 209 [G.E. 213]
Roth, G. 829 [G.E. 858]
Röttele, H. 207 [G.E. 204]
Rüchardt, C. 429 [G.E. 417]
Rücker, Ch. 214 [G.E. 216]
Rupp, R. H. 819 [G.E. 850]
Russow, J. 147 [G.E. 136]
Rustemeier, K. 816 [G.E. 841]
Ryan, R. C. 478 [G.E. 494]

SAALFRANK, R. W. 713 [G.E. 740]
Sacconi, L. 405, 931, 1021 [G.E. 412, 967, 1055]
Saenger, W. 344 [G.E. 343]
Sakurai, H. 620 [G.E. 632]
Salcher, O. 828 [G.E. 855]
Sander, J. 131 [G.E. 138]
Sanger, A. R. 656
Satzinger, G. 1018 [G.E. 1055]
Sauer, J. 456, 747, 779 [G.E. 464, —, 773]
Saunders, M. 485 [G.E. 488]
Schade, G. 822 [G.E. 856]
Schäfer, H. 324, 490 [G.E. 310, 480]
Schäfer, K. 223 [G.E. 209]
Schäfer-Stahl, H. 477, 729 [G.E. 493, 761]
Schal, H.-P. 567 [G.E. 575]
Schang, P. 715 [G.E. 768]
Schanne, L. 636 [G.E. 653]
Schaper, K.-J. 572
Scheffold, R. 629 [G.E. 643]
Schenkluhn, H. 569, 570 [G.E. 567, 569]
Scherer, O. J. 571 [G.E. 563]
Scheuermann, H. 388 [G.E. 390]
Schiefer, H.-P. 406 [G.E. 406]
Schiffer, R. 202 [G.E. 198]
Schimanski, U. 654 [G.E. 665]
Schlamann, W. 645 [G.E. 664]
Schleyer, P. v. R. 485 [G.E. 488]
Schlingmann, G. 321, 321 [G.E. 303, 304]
Schlögl, K. 308 [G.E. 318]
Schlosser, M. 303, 487 [G.E. 302, 497]
Schlüter, K. 57 [G.E. 64]
Schmickler, H. 1016 [G.E. 1053]
Schmid, G. (Erlangen) 136, 822, 1012 [G.E. 134, 856, 1045]
Schmid G. (Essen) 54 [G.E. 61]
Schmidbaur, H. 71, 555 [G.E. 66, 557]
Schmidpeter, A. 650, 722, 825 [G.E. 655, 767, 860]
Schmidt, A. 463 [G.E. 468]
Schmidt, R. R. 731 [G.E. 763]
Schmidt, U. 198 [G.E. 201]
Schneider, G. M. 575 [G.E. 585]
Schneider, K.-A. 211, 1022 [G.E. 214, 1056]
Schneider, O. 392 [G.E. 391]
Schnering, H. G. von 1033 [G.E. 1070]
Schnöckel, H. 323 [G.E. 310]
Schöllhorn, R. 492, 983 [G.E. 477, 1015]
Schöllkopf, U. 212 [G.E. 205]
Schomburg, D. 825 [G.E. 860]
Schramm, W. 492 [G.E. 477]
Schröder, G. 207 [G.E. 204]
Schubert, U. 555, 643, 809, 1020 [G.E. 557, 662, 835, 1065]
Schulz, E. 739, 740 [G.E. 751, 752]
Schulz, G. 219 [G.E. 212]
Schulz, R. 69, 821 [G.E. 52, 846]
Schulze, J. 54 [G.E. 61]
Schulze, K. 197 [G.E. 194]
Schulze, U. 910 [G.E. 935]
Schulze, W. 397 [G.E. 403]
Schumann, H. 70 [G.E. 60]
Schurig, V. 471 [G.E. 473]
Schwartz, U. 1027, 1029 [G.E. 1060, 1062]
Schwarz, H. 485, 905 [G.E. 488, 934]
Schweig, A. 69, 739, 740, 821 [G.E. 52, 751, 752, 846]
Schweizer, B. 53 [G.E. 59]
Schwertfeger, W. 126 [G.E. 123]
Schwick, H.-G. 87 [G.E. 83]
Schwickardi, M. 818 [G.E. 845]
Seaborg, G. T. 228
Seebach, D. 53 [G.E. 59]
Seelinger, R. 203 [G.E. 223]
Seiler, P. 53 [G.E. 59]
Seki, Y. 928 [G.E. 974]
Sellner, I. 456 [G.E. 464]
Seltzer, H. 474 [G.E. 483]
Seppelt, K. 643, 942 [G.E. 659, 954]
Seppelt, W. 214 [G.E. 216]
Seydel, J. K. 572
Shanzer, A. 326, 327 [G.E. 324, 325]

Shaw, M. T. 494
Sheldrick, G. 134, 943 [G.E. 130, 959]
Sheldrick, W. S. 321, 321, 722, 825 [G.E. 303, 304, 767, 860]
Shima, I. 399 [G.E. 405]
Shochet, N. 326 [G.E. 324]
Sialom, B. 1004 [G.E. 1037]
Sichert, H. 456 [G.E. 464]
Siebert, W. 746 [G.E. 758]
Siegel, H. 178 [G.E. 182]
Siegemund, G. 126 [G.E. 123]
Sievers, S. 910 [G.E. 935]
Sikorsky, P. 818 [I.E. 845]
Sinn, H. 390 [G.E. 396]
Smyth, W. F. 409
Snitman, D. L. 557 [G.E. 573]
Solladié-Cavallo, A. 1005 [G.E. 1038]
Solouki, B. 51 [G.E. 56]
Sombroek, J. 41 [G.E. 43]
Sonoda, N. 308, 928, 1007, 1007, 1008, 1009, 1009 [G.E. 317, 974, 1040, 1040, 1041, 1041, 1042]
Spliethoff, B. 622, 818 [G.E. 633, 845]
Srivastava, R. C. 656
Staab, H. A. 66, 67 [G.E. 49, 51]
Stahl, I. 408 [G.E. 393]
Stähle, M. 303, 487 [G.E. 302, 497]
Stanley, G. G. 1025 [G.E. 1059]
Stark, H. 1029 [G.E. 1062]
Starker, B. 66, 67 [G.E. 49, 51]
Stec, W. J. 549 [G.E. 578]
Steckhan, E. 46 [G.E. 47]
Steffan, B. 459 [G.E. 463]
Steffen, M. 483 [G.E. 481]
Stegelmeier, H. 1016 [G.E. 1053]
Steglich, W. 459 [G.E. 463]
Steidel, J. 325 [G.E. 313]
Stein, U. 834 [G.E. 863]
Steinbach, R. 900, 901, 1011 [G.E. 931, 933, 1044]
Steinseifer, F. 328, 723 [G.E. 321, 746]
Stenlake, J. B. 409
Steudel, R. 325 [G.E. 313]
Stobart, S. R. 931 [G.E. 964]
Strähle, J. 404 [G.E. 411]
Streu, J. 631 [G.E. 641]
Stühler, G. 469 [G.E. 490]
Stühler, H.-O. 468 [G.E. 475]
Suckling, C. J. 839
Suckling, C. W. 839
Suckling, K. E. 839
Suffert, J. 1005 [G.E. 1038]
Sukumaran, K. B. 973 [G.E. 1005]
Sundermeyer, W. 203 [G.E. 223]
Supp, M. 208 [G.E. 200]
Sustmann, R. 779 [G.E. 773]
Swaid, I. 575 [G.E. 585]
Szilágyi, G. 1026 [G.E. 1066]

TAGLIAFERRI, E. 566 [G.E. 556]
Takeshita, K. 928 [G.E. 974]
Talbiersky, J. 198 [G.E. 201]
Tamir, I. 543 [G.E. 577]
Tane, J. P. 1023 [G.E. 1057]
Tebbe, K.-F. 1033 [G.E. 1070]
Tedder, J. M. 229
Thétaz, C. 566 [G.E. 556]
Thies, H. 485 [G.E. 488]
Thomas, J. M. 745 [G.E. 755]
Tietze, L.-F. 134, 830 [G.E. 130, 832]
Tobita, H. 620 [G.E. 632]
Toda, F. 926 [G.E. 952]
Tödheide, K. 606 [G.E. 612]
Tölle, H.-G. 654 [G.E. 665]
tom Dieck, H. 396 [G.E. 395]
Tompkins, F. C. 76
Tran-Viet, D. 628 [G.E. 639]
Tsay, Y.-H. 571 [G.E. 563]
Turro, N. J. 675 [G.E. 712]

UGI, I. 495 [G.E. 503]
Uhl, W. 741 [G.E. 756]
Use, G. 320 [G.E. 309]

VAHRENKAMP, H. 65, 226 [G.E. 66, 225]
Van der Helm, D. 309 [G.E. 326]
van Pée, K.-H. 828 [G.E. 855]
van Wasen, U. 575 [G.E. 585]
Vega, J. C. 929 [G.E. 968]
Veith, H. J. 540 [G.E. 548]
Veith, M. 401 [G.E. 408]
Venanzi, L. M. 721 [G.E. 744]
Viehe, H. G. 716 [G.E. 754]
Visca, M. 646 [G.E. 663]
Voelker, C. 1024 [G.E. 1058]
Vogel, E. 41, 913, 921, 1015, 1016 [G.E. 43, 943, 944, 1051, 1053]
Vogel, P. 1003 [G.E. 1036]
Vogler, A. 221, 717 [G.E. 228, 745]
Vogtel, P. 24 [G.E. 25]
Vögtle, F. 464, 1030 [G.E. 471, 1067]
Völkel, G. 945 [G.E. 955]
Vollhardt, K. P. C. 559, 1023 [G.E. 570, 1057]
Vollmann, H. W. 99 [G.E. 95]
Vollmer, H.-J. 390 [G.E. 396]
Voss, J. 563 [G.E. 559]
Vostrowsky, O. 475 [G.E. 492]

WACKERLE, L. 633 [G.E. 649]
Wagner, A. 41 [G.E. 43]
Wald, K. M. 933, 936 [G.E. 970, 972]
Walde, A. 303 [G.E. 302]
Walker, G. 485 [G.E. 488]
Walton, A. 229
Walton, J. C. 229
Wamhoff, H. 933, 936, 1026 [G.E. 970, 972, 1066]
Weber, E. 1030 [G.E. 1067]
Weber, R. 471 [G.E. 473]
Weber, W. 138, 387 [G.E. 135, 387]
Weber, W.-D. 1027, 1029 [G.E. 1060, 1062]
Wegner, G. 912 [G.E. 941]
Weidenhammer, K. 44 [G.E. 45]
Weigel, H. 627 [G.E. 640]
Weigert, W. M. 148, 838
Weimann, B. 569, 570 [G.E. 567, 569]
Weinberger, B. 481 [G.E. 478]
Weinges, K. 628 [G.E. 639]
Weise, E. 148, 838
Weiss, B. 648 [G.E. 647]
Weissermel, K. 79 [G.E. 75]
Weller, F. 220 [G.E. 211]
Wellmann, J. 46 [G.E. 47]
Wennerström, O. 624 [G.E. 636]
Wentrup, C. 564, 566, 720, 821 [G.E. 555, 556, 743, 846]
Weppner, W. 74 [G.E. 72]
Wermeckes, B. 817 [G.E. 844]
Werner, H. 940 [G.E. 960]
Werner, K. v. 128 [G.E. 124]
Westerhaus, A. 556 [G.E. 578]
Westermann, J. 900, 901, 1011 [G.E. 931, 933, 1044]
Wichelhaus, W. 74 [G.E. 72]
Wieghardt, K. 558 [G.E. 580]
Wiessler, M. 400 [G.E. 407]
Wild, J. 198 [G.E. 201]
Wilemon, G. M. 478 [G.E. 494]
Wilhelm, E. 136, 1012 [G.E. 134, 1045]
Wilke, G. 622 [G.E. 633]
Winslow, F. H. 657
Winter, H.-W. 564, 566, 720, 821 [G.E. 555, 556, 743, 846]
Winter, W. 220, 926 [G.E. 227, 952]
Winterfeldt, E. 472 [G.E. 486]
Wissmann, H. 133 [G.E. 129]
Witt, M. 943 [G.E. 959]
Wittmann, D. 643 [G.E. 662]
Wittmann, J. 147 [G.E. 136]
Woldt, R. 390 [G.E. 396]
Wolken, J. J. 330
Wolmershäuser, G. 571 [G.E. 563]
Woltermann, A. 328 [G.E. 321]
Wright, R. E. 717 [G.E. 745]
Wunder, F. A. 126 [G.E. 125]
Wussow, H.-G. 563 [G.E. 559]
Wüstenfeld, P. 829 [G.E. 858]

YAMAMURA, K. 543 [G.E. 565]
Yoshifuji, M. 399 [G.E. 405]

ZADOK, E. 1004 [G.E. 1037]
Zahn, H. 394 [G.E. 394]
Zamankhan, H. 125 [G.E. 122]
Zanazzi, P. F. 561 [G.E. 579]
Zass, E. 140 [G.E. 139]
Zaworotko, M. D. 931 [G.E. 964]
Zeidler, M. D. 697 [G.E. 700]
Zeiner, H. 204 [G.E. 199]
Zeiss, H.-J. 218 [G.E. 218]
Zeiss, W. 825 [G.E. 860]
Ziegler, D. 208 [G.E. 200]
Ziegler, M. L. 44, 397, 651 [G.E. 45, 403, 660]
Zippel, M. 465 [G.E. 469]
Zorn, H. 709, 710 [G.E. 737, 738]
Züchner, K. 944 [G.E. 956]
Zuckerman, J. J. 306 [G.E. 326]
Zummack, W. 905 [G.E. 934]
Zwaschka, F. 722 [G.E. 767]

SUBJECT INDEX

FP = Full paper (review article) SC = Short communication
G.E. = Reference to Volume 92 (1980) of the German Edition of Angewandte Chemie
References are given for Review Articles and Short Communications only.

ABSOLUTE configuration of the cancerostatic S(−)-isophosphamide (SC) 549 [G.E. 578]

Acetals, Phosphorus triiodide and diphosphorus tetraiodide, new reagents for deprotection of ~ and ketals (SC) 1006 [G.E. 1039]

Acetylene, Photochemically induced 1,2-bis(dialkylalumination) of diphenyl-~ (SC) 146 [G.E. 132]

Adamantane structure, $P_4(N\text{-}i\text{-}C_3H_7)_6$, a P_4X_6 molecule with and without ~ (SC) 571 [G.E. 563]

Addition, Total reversibility of ~ and transylidation of trialkyl(alkylidene)phosphoranes to metal-coordinated carbon monoxide (SC) 1019 [G.E. 1063]
Chemo- and diastereoselective ~ of alkyl- and aryl-titanium compounds to aldehydes and ketones (SC) 1011 [G.E. 1044]

Adenosine triphosphate, Structure and function of the energy-converting system of mitochondria (FP) 659 [G.E. 684]

Affinity gel, Phlorizin polymer as ~ for sugar-binding proteins (SC) 540 [G.E. 547]

Air pollution chemistry (Book Review) 330

Acetaldehyde as main product of the oxidation of ethylene oxide on a silver catalyst (SC) 407 [G.E. 389]

Alcohols, Photoreduction of ketones and aldehydes to ~ with selane (SC) 1008 [G.E. 1041]
Selective inclusion of ~ with a new pyridino crown (SC) 1030 [G.E. 1067]

Aldehydes, Coupling of solvolysis and C—C linkage: Promising synthetic route to functionalized carboxylic acids, ~, and ketones (FP) 171 [G.E. 169]
Photoreduction of ketones and ~ to alcohols with selane (SC) 1008 [G.E. 1041]
Reduction of carbonyl compounds by aluminum telluride and H_2O or D_2O (SC) 1009 [G.E. 1041]

Aldol condensation, Highly stereoselective ~ using an enantioselective chiral enolate (SC) 557 [G.E. 573]

Alkali metals, Catalytic graphite-intercalation with ~ in solution (SC) 491 [G.E. 476]

Alkali metal titanium sulfides, Nonstoichiometric ~ with channel structure (SC) 492 [G.E. 477]

Alkali metal-transition metal π-complexes (FP) 520 [G.E. 513]

Alkaloids, Intramolecular oxidative cyclization of 3-benzyl-1,2,3,4-tetrahydroisoquinolines (SC) 1018 [G.E. 1055]

Alkanes, Influence of isomerism of ~ on the thermodynamic properties of cyclohexane/alkane mixtures (SC) 223 [G.E. 209]

Alkanethiols, Addition of ~ to diketene (SC) 127 [G.E. 123]

1-Alkenes, Cycloadditions of diazoalkanes to ~ (SC) 202 [G.E. 198]

Alkylideneammonium ions, Collision induced fragmentation of ~ (SC) 541 [G.E. 548]

Alkyne cleavage, Biscarbyne clusters by ~: A general reaction (SC) 559 [G.E. 570]

Allenes, Acylated ketenimines and ~ from oxazol-5(4H)-ones and furan-2(3H)-ones (SC) 564 [G.E. 555]

Allenyl cations, Competing [3+4] and [2+4] cycloadditions of ~ (SC) 814 [G.E. 840]

Allyl cations, Synthesis of norbornenes from cyclopentadiene and allyl alcohols in an acidic two phase system (SC) 827 [G.E. 861]

Allylic compounds of magnesium, lithium and potassium: σ- or π-structures? (SC) 487 [G.E. 497]

Alumination, Photochemically induced 1,2-bis(dialkyl-~) of diphenylacetylene (SC) 146 [G.E. 132]

Aluminum compounds, First "small ring" in fluorometalates: $Ba_6F_4(F_4AlF_{2/2})_4$ = "$Ba_3Al_2F_{12}$" (SC) 489 [G.E. 476]

Aluminum telluride, Reduction of carbonyl compounds by ~ and H_2O or D_2O (SC) 1009 [G.E. 1041]
Reduction of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with hydrogen telluride from ~ and water (SC) 1009 [G.E. 1042]

Ambiphilicity of 1,1-diethoxy-4,4,4-trifluoro-3-(trifluoromethyl)-1,2-butadiene (SC) 713 [G.E. 740]

Amide rotation, Influence of ionic and polar solutes upon $\Delta G^{\neq}$ and $\Delta V^{\neq}$ of the ~ in aqueous solutions of dimethylacetamide (SC) 945 [G.E. 955]

Amides, Metal and metalloid ~ (Book Review) 656

N-(Amidosulfonyl)hydroxylamine, H_2NSO_2NHOH (SC) 943 [G.E. 957]

Amines, Mechanism of pyrylium/pyridinium ring interconversion. Mild preparative conditions for conversion of ~ into pyridinium ions (SC) 306 [G.E. 315]
Asymmetric synthesis of ~ by carbon-carbon coupling in α-position to nitrogen (SC) 725 [G.E. 753]
Selenium-catalyzed reduction of aromatic nitro compounds to ~ by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
Reduction of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with hydrogen telluride from aluminum telluride and water (SC) 1009 [G.E. 1042]
New arene(dicarbonyl)chromium chelates: Use in the asymmetric synthesis of ~ (SC) 1005 [G.E. 1038]

Aminoacetylenes, N-Ethynylamines of the type R—NH—C≡C—H (SC) 720 [G.E. 743]

Amino acids, Enantioselective synthesis of α-methylserines (SC) 212 [G.E. 205]

4-Aminobutyramide, New preparation of ~ (SC) 627 [G.E. 640]

3-(2-Amino-3-chlorophenyl)pyrrole, Formation of pyrrolnitrin and ~ from 7-chlorotryptophan (SC) 828 [G.E. 855]

Aminooxophosphane, $(R_2NPO)_3$: Novel heterocycle with λ^3-phosphorus by trimerization of an ~ (SC) 709 [G.E. 737]
Complex-stabilization of ~ (phosphinidene oxide) (SC) 710 [G.E. 738]

Amino-protecting group for use in peptide synthesis which can be introduced electrochemically (SC) 712 [G.E. 739]

Aminopyridines (SC) 388 [G.E. 390]

Ammonium ions, Collision induced fragmentation of alkylidene-~ (SC) 541 [G.E. 548]

Amphoterism, New variant of ~ of tin(II) hydroxide: $Sn(OH)_2$ as stannio complex ligand (SC) 553 [G.E. 561]

Analytical chemistry, Treatise on ~, Part I: Theory and practice (Book Review) 149

Analytical methods, Chromatographic resolution of racemates (FP) 13 [G.E. 14]
Kinetic and mechanistic evaluation of NMR spectra (FP) 411 [G.E. 445]
Physiochemical principles and applications of supercritical fluid chromatography (SFC) (FP) 575 [G.E. 585]

Annulenes, Synthesis of CH_2-Bridged [4n+2]-~ by a building-block approach (SC) 41 [G.E. 43]
syn-1,6-Ethano-8,13-methano[14]annulene (SC) 913 [G.E. 943]
Structure and dynamic behavior of syn-1,6-ethano-8,13-methano[14]annulene (SC) 921 [G.E. 944]
Mixed oligomers of propellanes and bridged ~ with bis(maleimides) and bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 936 [G.E. 972]
Cyclic oligomers of propellanes and bridged ~ with bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 933 [G.E. 970]
syn-1,6-Imino-8,13-methano[14]annulene (SC) 1015 [G.E. 1051]

Antimony compounds, Novel selenoantimonate(III) anions in $Na_4Sb_4Se_{11}$ (SC) 324 [G.E. 310]
Dimerization of S_6O to $S_{12}O_2$: Crystal structure analysis of $S_{12}O_2 \cdot 2SbCl_5 \cdot 3CS_2$ (SC) 325 [G.E. 313]

Anthracenemagnesium, Catalytic synthesis of magnesium hydride under mild conditions (SC) 818 [G.E. 845]

Arenes, Photochemical rearrangements and fragmentations of benzene derivatives and annelated ~ (FP) 243 [G.E. 245]

Aromaticity, syn-1,6-Ethano-8,13-methano[14]annulene (SC) 913 [G.E. 943]
Structure and dynamic behavior of syn-1,6-ethano-8,13-methano[14]annulene (SC) 921 [G.E. 944]

Arsenic compounds, Zintl phases with complex anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$ (SC) 490 [G.E. 480]

Asymmetric catalysis, Conformational analysis of 1-phenylethyl substituents in metal complexes and their importance for ~ (SC) 641 [G.E. 645]

Asymmetric induction, Enhancement of 1,2-~ on C—C linkage by use of chiral 2-butenylboronic esters (SC) 218 [G.E. 218]

Asymmetric synthesis of amines by carbon-carbon coupling in the α-position to nitrogen (SC) 725 [G.E. 753]
New arene(dicarbonyl)chromium chelates: Use in the ~ of amines (SC) 1005 [G.E. 1038]
~ of (+)-estrone (SC) 1029 [G.E. 1062]

Aza[14]annulenes (SC) 207 [G.E. 204]

2-Azabarrelenone and 3-methoxy-2-azabarrelene (SC) 463 [G.E. 468]

Δ^3-1,2-Azaboroline, Preparation of 1-tert-butyl-3-methyl-2-phenyl-~ and utilization of its anion as a complex ligand analogous to cyclopentadienyl (SC) 54 [G.E. 61]

2-Aza-1,3-butadienes, 1,3-Bis-(dimethylamino)-~ from 1-alkyl-2-azavinamidinium salts (SC) 217 [G.E. 208]

6-Azauracil, New photocycloadditions of dibromomaleimides to 1,3-dimethyl-~ (SC) 1026 [G.E. 1066]

1H-Azepine: NMR spectroscopic and chemical characterization (SC) 1016 [G.E. 1053]

3H-Azepine, 1H-Azepine: NMR spectroscopic and chemical characterization (SC) 1016 [G.E. 1053]

Azides, Iminium-activated ~—New reagents for transfer of diazonium or diazo groups (SC) 716 [G.E. 754]

2-Azidopyrimidine, ^{15}N-NMR spectroscopic detection of the tetrazolo[1,5-a]pyrimidine/2-~ equilibrium (SC) 924 [G.E. 957]

Azoalkanes, Synthesis of unusual organic mo-

lecules from ~ (FP) 762 [G.E.] 815
β-Azolyl-α,α-dicarbonyl compounds (SC) 137 [G.E. 128]
Azomethine imine, Trimerization of an ~ by three successive 1,3-dipolar cycloaddition reactions (SC) 906 [G.E. 936]
Azulenesulfonium salts, Synthesis and rearrangement (SC) 621 [G.E. 635]

BARRELENE, 2-Azabarrelenone and 3-methoxy-2-aza-~ (SC) 463 [G.E. 468]
Benzene, Photochemical rearrangements and fragmentations of ~ derivatives and annelated arenes (FP) 243 [G.E. 245]
9,10-Benzotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9,11-tetraene—A Diels-Alder adduct of ~ and naphthalene (SC) 307 [G.E. 307]
Reversal of stability in the ~/Dewar ~ system (SC) 1022 [G.E. 1056]
Benzodicyclobutadiene, Complexation of a ~ with $Fe_2(CO)_9$ (SC) 926 [G.E. 952]
Benzophenonedilithium as complex with tetrahydrofuran and tetramethylethylenediamine (SC) 817 [G.E. 844]
9,10-Benzotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9,11-tetraene—A Diels-Alder adduct of benzene and naphthalene (SC) 307 [G.E. 307]
4,5-Benzotricyclo[4.1.0.0^{1,3}]hept-4-ene (SC) 631 [G.E. 641]
Benzotropylium tetrafluoroborate, Synthesis and intramolecular charge-transfer interaction in 1,4-dihydro-1,4-ethano-~ (SC) 545 [G.E. 566]
1,4-Benzoxazines, Oxidation of isatins to isatoic anhydrides and 2,3-dioxo-~ (SC) 222 [G.E. 196]
Benzvalene, Relation between orbital character and reaction product in the reaction of ~ and homobenzvalene with thiophenol (SC) 457 [G.E. 465]
Oxidation reactions of ~: Ozonolysis, cis-hydroxalation, epoxidation, and singlet oxygen addition (SC) 458 [G.E. 466]
Benzyl ligand, (1,2,5,6-η-1,5-Cyclooctadiene)(1,2,7-η-7-methylbenzyl)(7,8-η-styrene)rhodium(I)—Antarafacial fluctuation of the ~ and temperature-dependent-coordination of styrene (SC) 468 [G.E. 475]
3-Benzyl-1,2,3,4-tetrahydroisoquinolines, Intramolecular oxidative cyclization of 3-benzyl-1,2,3,4-tetrahydroisoquinolines (SC) 1018 [G.E. 1055]
Bicycloconjugation, Question of ~ in naphtho-fused 9-heterobicyclo[4.2.1]nona-2,4,7-trienes as examined by ^{13}C-NMR spectroscopy (SC) 639 [G.E. 657]
Bicyclo[3.2.0]hept-6-ene, New C_8H_{10} isomers: 2-Methylene-~[3.2.0]hept-6-ene and 3-methylenetricyclo[4.1.0.0^{2,7}]heptane—thermal and metal-catalyzed rearrangements (SC) 634 [G.E. 651]
Bicyclopropylidene, Three variants of the [2+2]-cycloadditions of ~ (SC) 387 [G.E. 387]
Biscarbyne clusters by alkyne cleavage: A general reaction (SC) 559 [G.E. 570]
1,3-Bis(dialkylamino)-1,3-butadiene from 1-methylvinamidinium salts (SC) 216 [G.E. 207]
1,2-Bis(dialkylalumination), Photochemically induced ~ of diphenylacetylene (SC) 146 [G.E. 132]
1,3-Bis(dimethylamino)-2-aza-1,3-butadienes from 1-alkyl-2-azavinamidinium salts (SC) 217 [G.E. 208]
Bis(maleimides), Mixed oligomers of propellanes and bridged annulenes with ~ and bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 963 [G.E. 972]
Bismuthanes, Diphenylbismuthyl group—A potential new auxiliary group in organic synthesis (SC) 723 [G.E. 746]
Bis(o-phenylenedioxy)silane, Planar tetracoordinated silicon? (SC) 1033 [G.E. 1070]
Planar tetracoordinated silicon—A reply (SC) 1034 [G.E. 1071]
Bis(triazolinediones), Cyclic oligomers of propellanes and bridged annulenes with studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 933 [G.E. 970]
Mixed oligomers of propellanes and bridged annulenes with bis(maleimides) and ~ studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 936 [G.E. 972]
Bituminous coal, ^{13}C-NMR spectroscopic studies on ^{13}C-methylated ~ (SC) 636 [G.E. 653]
Blood plasma, Chemistry and function of human plasma proteins (FP) 87 [G.E. 83]
Borates, Tetrakis(trimethylsilyl)borate and other trimethylsilyl-~ (SC) 58 [G.E. 65]
Boron compounds, Preparation of 1-tert-butyl-3-methyl-2-phenyl-Δ^3-1,2-azaboroline and utilization of its anion as a complex ligand analogous to cyclopentadienyl (SC) 54 [G.E. 61]
Stabilization of diborane(4) derivatives by tert-butyl groups: the first tetraalkyldiborane (4) (SC) 56 [G.E. 63]
Persistent tetraalkyldiboranes (4) (SC) 57 [G.E. 64]
Exceedingly mild desulfurization of thiols by sodium triethylhydroborate and transition metal chlorides (SC) 315 [G.E. 321]
Hexakis(dimethylamino)cyclohexaborane, a boron(I) compound without electron deficiency (SC) 482 [G.E. 481]
Boronic esters, Enhancement of 1,2-asymmetric induction on C—C linkage by use of chiral 2-butenyl-~ (SC) 218 [G.E. 218]
Boron sulfides, B_8S_{16}—An "inorganic porphine" (SC) 481 [G.E. 479]
Boron trifluoride: Crystal structure of a metastable phase (SC) 483 [G.E. 481]
Brefeldin, Novel entry to ~ A (SC) 472 [G.E. 486]
Bromination, Heterogeneously catalyzed gas-phase ~ of trifluoromethane (SC) 147 [G.E. 136]
~ with N-bromosuccinimide: solvent and selectivity (SC) 464 [G.E. 471]
N-Bromosuccinimide, Brominations with ~: solvent and selectivity (SC) 464 [G.E. 471]
1,2-Butadiene, Ambiphilicity of 1,1-diethoxy-4,4,4-trifluoro-3-(trifluoromethyl)-~ (SC) 713 [G.E. 740]
2-Butenylboronic esters, Enhancement of 1,2-asymmetric induction on C—C linkage by use of chiral ~ (SC) 218 [G.E. 218]
2-tert-Butyl-2H-isoindole: A partner for reactions with electrophiles (SC) 320 [G.E. 309]
Butyramide, New preparation of 4-amino-~ (SC) 627 [G.E. 640]

CAFFEINE, Photoreactions of stilbene with ~: Known, and new types of reactions (SC) 714 [G.E. 735]
Cage molecules, Cubane-type Sn_4N_3O cage (SC) 401 [G.E. 408]
Calcium isotope separation on an exchange resin having cryptand anchor groups (SC) 406 [G.E. 406]
Calorimetry, Grundlagen der Kalorimetrie (Book Review) 838
Cancerostatic, Absolute configuration of the ~ S(−)-isophosphamide (SC) 549 [G.E. 578]
Cannabinoids, Stereocontrolled intramolecular Diels-Alder reaction of heterodienes; studies on the synthesis of ~ (SC) 134 [G.E. 130]
Captodative substituent effects and the chromophoric system of indigo (SC) 908 [G.E. 937]
Carbamates, Lithiated allyl N,N-dialkyl-~ as homoenolate equivalents: Synthesis of protected 4-oxoalkanoates (SC) 625 [G.E. 637]
Carbamoyl halides, Synthesis of α-haloalkyl-~ (SC) 201 [G.E. 197]
Carbene-carbene rearrangement, 1,5-Dihydropentalene by tandem ~ (SC) 304 [G.E. 314]
Carbenecarbonylmetal complexes, Electrochemical oxidation of dicarbene complexes of the type (carbene)$_2$MoL(CO)$_3$: interconversion among three isomers via electrochemical redox process (SC) 538 [G.E. 550]
Carbene complexes, Structure of $[(CO)_5CrNEt_2]BF_4$, a key organometallic compound; reaction to give the carbene complex $(CO)_5CrC(AsPh_2)NEt_2$ (SC) 643 [G.E. 662]
Carbocations, Coupling of solvolysis and C—C linkage: A promising synthetic route to functionalized carboxylic acids, aldehydes, and ketones (FP) 171 [G.E. 169]
Carbocycles, Synthesis of cyclic compounds from triphenyl(phenyliminovinylidene)-phosphorane and carboxylic acids (SC) 822 [G.E. 856]
Carbodiimides, Cyclic ~ in nitrene rearrangements (SC) 566 [G.E. 556]
Carbodiphosphoranes, Ring-strained ~ (SC) 555 [G.E. 557]
Carbohydrates, L-Gulose or D-gluco-hexodialdose from D-glucurono-6,3-lactone by controlled reductions (SC) 546 [G.E. 552]
Pure D-gulose from D-gulono-1,4-lactone (SC) 547 [G.E. 553]
Simple new method for the synthesis of 2-deoxy-aldehydo-hexoses (SC) 548 [G.E. 553]
Synthesis of the pentasaccharide chain of the Forssman antigen (SC) 902 [G.E. 929]
Synthesis of chiral valienamine (SC) 904 [G.E. 930]
Carbon, Thermal degradation of polymers to polymeric ~—An approach to the synthesis of new materials (FP) 375 [G.E. 375]
Carbonates, Metal-catalyzed synthesis of cyclic ~ from carbon dioxide and oxiranes (SC) 317 [G.E. 302]
~ and poly-~ from urea and alcohol (SC) 718 [G.E. 742]
Carbon-carbon bond, Towards an understanding of the ~ (FP) 429 [G.E. 417]
Carbon-carbon coupling, Asymmetric synthesis of amines by ~ in the α-position to nitrogen (SC) 725 [G.E. 753]
Carbon disulfide, Metal-assisted reaction of ~ with "Etriphos" phosphane ligand: synthesis and structure of $[(Etriphos)Fe\{S_2C(EtPCH_2)_2CMe_2\}](BF_4)_2$ (SC) 1021 [G.E. 1055]
Carbon dioxide, Metal-catalyzed synthesis of cyclic carbonates from ~ and oxiranes (SC) 317 [G.E. 302]
Solubility of nonvolatile biochemical substances in compressed ~ (SC) 623 [G.E. 633]
Carbon disulfide, Nucleophilic addition of triphenylstannyllithium to ~ (SC) 220 [G.E. 227]
Carbon monoxide, ~/water as a reducing agent: formation of selane from selenium (SC) 308 [G.E. 317]
First insertion reaction of ~ into a rhenium-carbon σ-bond (SC) 824 [G.E. 843]
UV irradiation of nucleic acids and their components in the presence of air (SC) 829 [G.E. 858]
Carbon skeleton isomerization, Experimental and theoretical study of the degenerate ~ of the cyclopentyl cation in the gas phase (SC) 485 [G.E. 488]
Carbonyl groups, Distribution of terminal and bridging ~ in an anionic carbonylmetal cluster as a result of ion-pair formation. Crystal and molecular structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$ (SC) 404 [G.E. 441]
Carbonyl ylides, Intramolecular cycloadditions of ~ (SC) 47 [G.E. 48]
Carboxylic acids, Coupling of solvolysis and C—C linkage: A promising synthetic route to functionalized ~, aldehydes, and ketones (FP) 171 [G.E. 169]
Carbyne complexes, Double addition of a nucleophile to carbyne and carbonyl C-atom: S-phenyl 2-phenyl-2-(phenylthio)thioacetate from trans-bromotetracarbonyl(phenylcarbyne)chromium and thiophenolate (SC) 205 [G.E. 206]
Biscarbyne clusters by alkyne cleavage: A general reaction (SC) 559 [G.E. 570]

Catalysis, Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for homogeneous ~ (FP) 362 [G.E. 362]
Conformational analysis of 1-phenylethyl substituents in metal complexes and their importance for asymmetric ~ (SC) 641 [G.E. 645]
Catalysts, Catalysis of hydroformylation by $Co_4(CO)_{8-x}(\mu_2\text{-}CO)_2(PPh_3)_x(\mu_4\text{-}PPh)_2$, x = 0 or 2: clusters as ~ (SC) 478 [G.E. 494]
Dimerization of propylene with ~ exhibiting activities like highly-active enzymes (SC) 622 [G.E. 633]
Characterization by Mössbauer spectroscopy of iron carbide phases in a highly active carbon matrix catalyst for medium pressure Fischer-Tropsch synthesis (SC) 729 [G.E. 761]
Dehydroxylation of hydrogen zeolites: Conditions for the preparation of thermally stable ~ (SC) 743 [G.E. 759]
Metalloporphyrin-catalyzed hydroxylation of cyclohexane by alkyl hydroperoxides: Pronounced efficiency of iron-porphyrins (SC) 909 [G.E. 938]
Catechol, Planar tetracoordinated silicon? (SC) 1033 [G.E. 1070]
Planar tetracoordinated silicon—A reply (SC) 1034 [G.E. 1071]
CC bond formation, Chemo- and diastereoselective addition of alkyl- and aryltitanium compounds to aldehydes and ketones (SC) 1011 [G.E. 1044]
Cell models, Polymerizable phospholipid analogues—New stable biomembrane models and ~ (SC) 938 [G.E. 962]
^{252}Cf-Plasma desorption mass spectrometry, Mixed oligomers of propellanes and bridged annulenes with bis(maleimides) and bis(triazolinediones) studied by ~ (SC) 936 [G.E. 972]
Cyclic oligomers of propellanes and bridged annulenes with bis(triazolinediones) studied by ~ (SC) 933 [G.E. 970]
Chalcogran, Optically active ~ (2-ethyl-1,6-dioxaspiro[4.4]nonane) (SC) 630 [G.E. 640]
Chalcone, "Synthetic enzymes"-Highly stereoselective epoxidation of ~ in a triphasic toluene-water-poly[(S)-alanine] system (SC) 929 [G.E. 968]
Charge-transfer interaction, 1,4-Dihydro-1,4-bis(dicyanomethylene) triptycenes. Synthesis and intramolecular ~ (SC) 543 [G.E. 565]
Synthesis and intramolecular ~ in 1,4-dihydro-1,4-ethanobenzotropylium tetrafluoroborate (SC) 545 [G.E. 566]
Chemical distance, Principle of minimum ~ (PMCD) (FP) 495 [G.E. 503]
Chemisorption of gases on metals (Book Review) 76
Chemoreceptors, Differentiation between chiral pheromone analogues by ~ (SC) 475 [G.E. 492]
Chiral recognition, Separation of the enantiomers of 2-hydroxycarboxylic acids on optically active stationary phases (SC) 910 [G.E. 935]
Chloroformamidinium chlorides, Synthesis of carbocyclic and heterocyclic π-electron systems with pentafulvenoid ~ (SC) 199 [G.E. 202]
7-Chlorotryptophan, Formation of pyrrolnitrin and 3-(2-amino-3-chlorophenyl)pyrrole from 7-chlorotryptophan (SC) 828 [G.E. 855]
Chromatography, Chromatographic resolution of racemates (FP) 13 [G.E. 14]
Determination of morphological properties of swellable solids by size exclusion ~ (FP) 24 [G.E. 25]
Physicochemical principles and applications of super-critical fluid ~ (SFC) (FP) 575 [G.E. 585]
Liquid ~ of enantiomers: Determination of enantiomeric purity in spite of extensive peak overlap (SC) 469 [G.E. 490]
Phlorizin polymer as affinity gel for sugar-binding proteins (SC) 540 [G.E. 547]
Chromium, Ultratrace analysis: Determination of ~, Fe, and Co in the ppb and ppt range for checking the preparation of high-purity niobium (SC) 197 [G.E. 194]
Chromium complexes, Structural investigations on (η^{12}-[3.3]paracyclophane)chromium(0) and its cation in (η^{12}-[3.3]paracyclophane)chromium(I) triiodide (SC) 44 [G.E. 45]
Double addition of a nucleophile to carbyne and carbonyl C-atom: S-Phenyl 2-phenyl-2-(phenylthio)thioacetate from trans-bromotetracarbonyl(phenylcarbyne)-chromium and thiophenolate (SC) 205 [G.E. 206]
Complex stabilization of 3-oxopropadienylidene (C_3O) with pentacarbonylchromium(0) (SC) 225 [G.E. 224]
Structure of $[(CO)_5CrNEt_2]BF_4$, a key organometallic compound; reaction to give the carbene complex $(CO)_5CrC(AsPh_2)NEt_2$ (SC) 643 [G.E. 662]
Chromium compounds, Chromium(II)-catalyzed electrochemical dehalogenation of β-hydroxyhalides—convenient entry to deoxynucleosides (SC) 46 [G.E. 47]
Transition-metal complexes with pyrazolyl bridging ligands between very different metal centers (SC) 931 [G.E. 931]
New arene(dicarbonyl)chromium chelates: Use in the asymmetric synthesis of amines (SC) 1005 [G.E. 1038]
Chromophoric system, Captodative substituent effects and the ~ of indigo (SC) 908 [G.E. 937]
Citrate synthase reaction, (3R,S)-3,4-Dicarboxy-3-hydroxybutyl coenzyme A, an inhibitor of the ~ (SC) 136 [G.E. 133]
Citreoviridins from Aspergillus terreus (SC) 461 [G.E. 484]
Clusters, First optically active ~: resolution of enantiomers and absolute configuration of $SFeCoMoCp(CO)_8$ (SC) 65 [G.E. 66]
Activation and sulfur-atom transfer reaction of cluster-bonded S_2^{2-}-bridge ligands: synthesis of the new cluster $[Mo_3^{IV}S_4(CN)_9]^{5-}$ from $[Mo_3^{IV}S(S_2)_6]^{2-}$ and CN^- (SC) 72 [G.E. 69]
Trinuclear ~ of the early transition elements (SC) 875 [G.E. 921]
Polymetal complexes: Complexation of cluster triangular faces by the tripod ligand, $HC(PPh_2)_3$ (SC) 1024 [G.E. 1058]
Template synthesis of ~ using the tripod ligand $HC(PPh_2)_3$: $Ni_3(CO)_6$(tripod) (SC) 1025 [G.E. 1059]
Coal, ^{13}C-NMR spectroscopic studies on ^{13}C-methylated bituminous ~ (SC) 636 [G.E. 653]
Cobalt, Ultratrace analysis: Determination of Cr, Fe, and ~ in the ppb and ppt range for checking the preparation of high-purity niobium (SC) 197 [G.E. 194]
Cobalt clusters, Catalysis of hydroformylation by $Co_4(CO)_{8-x}(\mu_2\text{-}CO)_2(PPh_3)_x(\mu_4\text{-}PPh)_2$, x = 0 or 2: Clusters as catalysts (SC) 478 [G.E. 494]
Cobalt complexes, Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for homogeneous catalysis (FP) 362 [G.E. 362]
Distribution of terminal and bridging CO-Groups in an anionic carbonyl metal cluster as a result of ion-pair formation. Crystal and molecular structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$ (SC) 404 [G.E. 441]
Theoretical investigation of the diethynylcyclobutadiene(cyclopentadienyl)cobalt rearrangement (SC) 728 [G.E. 747]
Olefin-insertion into cobalt (d^8) complexes—Structure of ethylene(phenyl)tris(trimethylphosphane)cobalt (SC) 809 [G.E. 835]
Cobalt compounds, First optically active cluster: resolution of enantiomers and absolute configuration of $SFeCoMoCp(CO)_8$ (SC) 65 [G.E. 66]
Direct synthesis of the perfluoroalkanesulfinates of iron(II), cobalt(II), and nickel(II): SO_2-assisted addition of alkyl halides to transition metals (SC) 128 [G.E. 124]
Cobalt-mediated [2+2+2]-cycloadditions: A simple route to substituted cyclopentadienones (SC) 1023 [G.E. 1057]
Coenzyme A, (3R,S)-3,4-Dicarboxy-3-hydroxybutyl ~, an inhibitor of the citrate synthase reaction (SC) 136 [G.E. 133]
Complexes, Polarized low-temperature crystal spectra of inorganic ~ (FP) 290 [G.E. 290]
Compressed solutions, Chemistry in ~ (FP) 841 [G.E. 887]
Conformation, Rigid phenyl-group ~ in complexes (SC) 396 [G.E. 395]
Conformational analysis of 1-phenylethyl substituents in metal complexes and their importance for asymmetric catalysis (SC) 641 [G.E. 645]
Conjugation, Diagonal interaction in the four-membered ring. Experimental demonstration of a dominating circumannular ~: 5,6-Dimethylenebicyclo[2.1.1]hexane (SC) 807 [G.E. 833]
Coordination, Upright unsymmetrical ~ in a cyclopropenylnickel complex: Synthesis and structure of $[(C_3Ph_3)Ni(PPh_3)_2]PF_6$ (SC) 931 [G.E. 967]
Copolymerization parameters, Correlation between radical reactivities and ~ (SC) 206 [G.E. 215]
Copper complexes, MoS_4^{2-} and $MoOS_3^{2-}$ as structurally versatile and biochemically interesting ligands in crystalline multinuclear Cu- and Fe-complexes (SC) 654 [G.E. 665]
Corrinoids, Structure of metal-free ~ from Rhodopseudomonas sphaereoides (SC) 321 [G.E. 303]
Structure of yellow metal-free and yellow cobalt-containing ~ (SC) 321 [G.E. 304]
Crown ethers, Calcium isotope separation on an exchange resin having cryptand anchor groups (SC) 406 [G.E. 406]
Selective inclusion of alcohols with a new pyridino crown (SC) 1030 [G.E. 1067]
Crystal spectra, Polarized low-temperature ~ of inorganic complexes (FP) 290 [G.E. 290]
Cyanogen, Syntheses with ~—A simple route to 4,5-dichloroimidazoles (SC) 130 [G.E. 138]
Cyanophosphinidene, The ≡PCN group as a pseudochalcogen; ~-substituted heterocycles (SC) 722 [G.E. 767]
Cyclization, 1,5-Electrocyclizations—An important principle of heterocyclic chemistry (FP) 947 [G.E. 979]
Thermal and photochemical transformations of hetero-1,3,5-hexatrienes into five-membered rings—Possible pericyclic reactions (FP) 973 [G.E. 1005]
Cycloaddition, Mechanistic aspects of Diels-Alder reactions: A critical survey (FP) 779 [G.E. 773]
Intramolecular ~ of carbonyl ylides (SC) 47 [G.E. 48]
~ of diazoalkanes to 1-alkenes (SC) 202 [G.E. 198]
Three variants of the [2+2]-~ of bicyclopropylidene (SC) 387 [G.E. 387]
Competing [3+4] and [2+4] ~ of allenyl cations (SC) 814 [G.E. 840]
Double ~ yielding a tricyclic diphosphorane (SC) 825 [G.E. 860]
Thermal ~ of dimethyl acetylenedicarboxylate to cyclic enol ethers and thioenol ethers (SC) 832 [G.E. 848]
Thermal [2+2]-cycloadditions of tetracyanoethylene to cyclic thioenol ethers (SC) 831 [G.E. 848]
Cobalt-mediated [2+2+2]-~: A simple route to substituted cyclopentadienones (SC) 1023 [G.E. 1057]
~-s with silver ion stabilized (2RS,3RS)-3-methoxy-trans-cycloheptene (SC) 1032 [G.E. 1068]
Cyclobutadiene, Tetraphenyl-~-cycloalkene-nickel(0) complexes (SC) 145 [G.E. 131]

Theoretical investigation of the diethynylcyclobutadiene(cyclopentadienyl)cobalt rearrangement (SC) 728 [G.E. 747]
Cyclobutane, Tetrakis(phenylimino)-~ (tetrameric phenyl isocyanide) (SC) 136 [G.E. 134]
Cyclobutane derivatives, Thermal [2+2]-cycloadditions of tetracyanoethylene to cyclic thioenol ethers (SC) 831 [G.E. 848]
Cyclodextrin inclusion compounds in research and industry (FP) 344 [G.E. 343]
Cyclodimer distribution, Ligand-property control in the nickel(0)/butadiene/P-ligand catalytic system: "Electronic" factors in the control of ~ (SC) 570 [G.E. 569]
2,4,6-Cycloheptatriene-1-carbaldehyde, Dynamic behavior (SC) 301 [G.E. 316]
Cycloheptatriene trioxides, Stereospecific syntheses (SC) 48 [G.E. 54]
trans-Cycloheptene, Cycloadditions with silver ion-stabilized (2RS,3RS)-3-methoxy-~ (SC) 1032 [G.E. 1068]
Cyclohexane, Influence of isomerism of alkanes on the thermodynamic properties of ~(alkane mixtures (SC) 233 [G.E. 209]
Metalloporphyrin-catalyzed hydroxylation of ~ by alkyl hydroperoxides: Pronounced efficiency of iron-porphyrins (SC) 909 [G.E. 938]
Cyclopentadienones, Cobalt-mediated [2+2+2]-cycloadditions: A simple route to substituted ~ (SC) 1023 [G.E. 1057]
Cyclopentadienylamines, Electrophilic amination of cyclopentadienyllithium compounds (SC) 1010 [G.E. 1043]
Cyclopentyl cation, An experimental and theoretical study of the degenerate carbon skeleton isomerization of the ~ in the gas phase (SC) 485 [G.E. 488]
Cyclophanes, Structural investigations on (η^{12}-[3.3]paracyclophane]chromium(0) and its cation in (η^{12}-[3.3]paracyclophane)chromium(I) triiodide (SC) 44 [G.E. 45]
Tetrathiafulvalenopara-~ (SC) 66 [G.E. 49]
~ as diene components in Diels-Alder reactions (SC) 389 [G.E. 388]
Cyclopropanes, Heterocyclic analogues of methylene-~ (FP) 276 [G.E. 277]
Tetrachlorovinylcarbene from tetrachlorocyclopropene; facile synthesis of vinyl-~ (SC) 138 [G.E. 135]
Cyclopropane derivatives, Donor-acceptor substituted cyclopropanes: Synthesis and ring opening to 1,4-dicarbonyl compounds (SC) 813 [G.E. 839]
Cyclopropanimines by photolysis of pyrazolinimines: thermal reaction of an excited state (SC) 49 [G.E. 55]
Cyclopropenylnickel complex, Upright unsymmetrical coordination in a ~: Synthesis and structure of $[(C_3Ph_3)Ni(PPh_3)_2]PF_6$ (SC) 931 [G.E. 967]
Cyclopropyl ketone oximes, Rearrangement to 5,6-dihydro-4H-1,2-oxazines (SC) 199 [G.E. 195]
Cycloreversions, cis-/trans-Tris-[2.1.1]-σ-homobenzenes; synthesis and stereochemistry of [„2+„2+„2]-~ (SC) 567 [G.E. 575]
Cyclotri(phosphazenes) complexes with P-coordinated PdX_2 and PtX_2 (SC) 650 [G.E. 655]

DECARBOXYLATION, Thermal ~ of β-lactones: Steric hindrance of mesomerism as indication of a zwitterionic intermediate (SC) 465 [G.E. 469]
Decathiacyclotetradecane-6,7,13,14-tetraone, Synthesis and crystal structure analysis (SC) 125 [G.E. 122]
Dehalogenation, Chromium(II)-catalyzed electrochemical ~ of β-hydroxyhalides—convenient entry to deoxynucleosides (SC) 46 [G.E. 47]
Dehydroxylation of hydrogen zeolites: Conditions for preparation of thermally stable catalysts (SC) 743 [G.E. 759]
2-Deoxy-aldehydo-hexoses, Simple new synthesis (SC) 548 [G.E. 553]
Deoxynucleosides, Chromium(II)-catalyzed electrochemical dehalogenation of β-hydroxyhalides—convenient entry to ~ (SC) 46 [G.E. 47]
Depsipeptides, Synthesis of alternating ~ with the 4-methylthiophenoxycarbonyl group as protecting and activating group for the amino function (SC) 932 [G.E. 953]
Dermatoses, Photochemistry of sulfonamides and sulfonylureas: A contribution to the problem of light-induced ~ (SC) 648 [G.E. 647]
Desulfurization, Exceedingly mild ~ of thiols by sodium triethylhydroborate and transition metal chlorides (SC) 315 [G.E. 321]
Deuterium compounds, Reduction of carbonyl compounds by aluminum telluride and H_2O or D_2O (SC) 1009 [G.E. 1041]
Dewar benzene, Reversal of stability in the benzene/~ system (SC) 1022 [G.E. 1056]
Diacylphosphanes, Lithium dibenzoylphosphide·1,2-dimethoxyethane—A new 2-phospha-1,3-dionate (SC) 741 [G.E. 756]
Diagonal interaction in the four-membered ring. Experimental demonstration of a dominating circumannular conjugation: 5,6-dimethylenebicyclo[2.1.1]hexane (SC) 807 [G.E. 833]
Diastereoselective addition, Chemo- and ~ of alkyl- and aryl-titanium compounds to aldehydes and ketones (SC) 1011 [G.E. 1044]
Diazoalkanes, Cycloadditions to 1-alkenes (SC) 202 [G.E. 198]
Diazonium group transfer, Iminium-activated azides—New reagents for transfer of diazonium or diazo groups (SC) 716 [G.E. 754]
Dibenz[b,g]oxocinide ion, Direct observation of the ~; A non-aromatic (4n+2) species (SC) 393 [G.E. 402]
cis-1,2-Dibenzoylalkenes, Alkali metal-induced transformations of ~: Transformation of 11,12-dibenzoyl-9,10-dihydro-9,10-ethenoanthracene (SC) 907 [G.E. 939]
11,12-Dibenzoyl-9,10-dihydro-9,10-ethenoanthracene, Alkali metal-induced transformations of cis-1,2-dibenzoylalkenes: Transformation of ~ (SC) 907 [G.E. 939]
Diborane(4) derivatives, Stabilization by tert-butyl groups: the first tetraalkyldiborane(4) (SC) 56 [G.E. 63]
Persistent tetraalkyldiboranes(4) (SC) 57 [G.E. 64]
Dicarbamates, Syntheses with metalloid derivatives: Preparation of macrocyclic ~ (SC) 326 [G.E. 324]
1,4-Dicarbonyl compounds, Donor-acceptor substituted cyclopropanes: synthesis and ring opening to ~ (SC) 813 [G.E. 839]
1,2-Dichloroacenaphthylene, Ozonolysis (SC) 474 [G.E. 483]
4,5-Dichloroimidazoles, Syntheses with cyanogen—Simple route to ~ (SC) 130 [G.E. 138]
(3R,S)-3,4-Dicarboxy-3-hydroxybutyl coenzyme A, an inhibitor of the citrate synthase reaction (SC) 136 [G.E. 133]
Dicyanoketene, Direct detection in the gas phase (SC) 739 [G.E. 751]
Dicyanothioketene, Direct detection in the gas phase (SC) 740 [G.E. 752]
Dicyclobutabenzene, Complexation of a benzodicyclobutadiene with $Fe_2(CO)_9$ (SC) 926 [G.E. 952]
L-3,4-Didehydroproline, Direct method for synthesis of N-Boc-~ (SC) 742 [G.E. 761]
Diels-Alder adduct, 9,10-Benzotricyclo[6.2.2.$0^{2,7}$]dodeca-3,5,9,11-tetraene—A ~ of benzene and naphthalene (SC) 307 [G.E. 307]
Diels-Alder reactions, Mechanistic aspects: A critical survey (FP) 779 [G.E. 773]
Stereocontrolled intramolecular ~ of heterodienes; studies on the synthesis of cannabinoids (SC) 134 [G.E. 130]
Cyclophanes as diene components (SC) 389 [G.E. 388]
Nitrile function of tetracyanoethylene as dienophile (SC) 810 [G.E. 836]
Diene components, Cyclophanes as ~ in Diels-Alder reactions (SC) 389 [G.E. 388]
Dienophile, Nitrile function of tetracyanoethylene as ~ in Diels-Alder reactions (SC) 810 [G.E. 836]
Difluorosulfur imides, New aspects of reaction of ~ with fluorine (SC) 408 [G.E. 393]
5,6-Dihydro-4H-1,2-oxazines, Rearrangement of cyclopropyl ketones oximes to ~ (SC) 199 [G.E. 195]
1,5-Dihydropentalene by tandem carbene-carbene rearrangement (SC) 304 [G.E. 314]
Diisocyanide ligands, Template polymerization of rhodium(I) with rigid bent ~ (SC) 633 [G.E. 649]
Diketene, Addition of alkanethiols to ~ (SC) 127 [G.E. 123]
Dimethylacetamide, Influence of ionic and polar solutes upon $\Delta G^{\neq}$ and $\Delta V^{\neq}$ of the amide rotation in aqueous solutions of dimethylacetamide (SC) 945 [G.E. 955]
1,3-Dimethyl-6-azauracil, New photocycloadditions of dibromomaleimides to ~ (SC) 1026 [G.E. 1066]
5,6-Dimethylenebicyclo[2.1.1]hexane, Diagonal interaction in the four-membered ring. Experimental demonstration of a dominating circumannular conjugation: ~ (SC) 807 [G.E. 833]
1,4-Dioxanes with four fluorine and/or trifluoromethyl substituents on C^2 and C^3 from vicinal perfluorodicarbonyl compounds (SC) 126 [G.E. 123]
1,6-Dioxaspiro[4.4]nonane, Quantitative separation of the enantiomer pairs of the pheromone 2-ethyl-~ by complexation chromatography on an optically active metal complex (SC) 471 [G.E. 473]
Optically active chalcogran (2-Ethyl-~) (SC) 630 [G.E. 640]
Diphenylacetylene, Photochemically induced 1,2-bis(dialkylalumination) (SC) 146 [G.E. 132]
Diphenylbismuthyl group—A potential new auxiliary group in organic synthesis (SC) 723 [G.E. 746]
Diphosphoranes, Ring-strained carbo-~ (SC) 555 [G.E. 557]
Diphosphorus tetraiodide, Phosphorus triiodide and ~, new reagents for deprotection of acetals and ketals (SC) 1006 [G.E. 1039]
1,3-Dipolar cycloaddition, Trimerization of an azomethine imine by three successive ~ reactions (SC) 906 [G.E. 936]
Disaccharides, Facile synthesis of α- and β-O-glycosyl imidates; preparation of glycosides and ~ (SC) 731 [G.E. 763]
Distance, Principle of minimum chemical ~ (PMCD) (FP) 495 [G.E. 503]
Disulfenes, Perfluoro- and perchloro-~ (SC) 203 [G.E. 223]
1,2-Dithiacycloalkanes, One-electron oxidation of 1,2-dithiacycloalkanes (SC) 834 [G.E. 863]
1,3,2-Dithiaplumbocanes—Heterocycles with lead(IV)—sulfur bonds (SC) 923 [G.E. 950]
1,3-Dithietane 1,1,3,3-tetraoxide, Perfluoro- and perchlorodisulfenes 203 [G.E. 223]
Dithiolenes, Photolysis of water catalyzed by transition metal ~ (SC) 645 [G.E. 664]
Dithiomalonaldehyde, Transition-metal complexes of malonaldehyde and ~ (SC) 638 [G.E. 654]
Donor-acceptor substitution, Donor-acceptor substituted cyclopropanes: Synthesis and ring opening to 1,4-dicarbonyl compounds (SC) 813 [G.E. 839]
Drugs, Pharmaceutical chemistry today—Changes, problems, and opportunities (FP) 749 [G.E. 802]
Synthetische Arzneimittel (Synthetic ~) (Book Review) 229
Double cycloaddition yielding a tricyclic diphosphorane (SC) 825 [G.E. 860]
Dynamic NMR spectroscopy, Kinetic and mechanistic evaluation of NMR spectra (FP) 411 [G.E. 445]

ELECTROCHEMICAL oxidation of dicarbene complexes of type (carbene)$_2$MoL(CO)$_3$: Interconversion among three isomers via electrochemical redox process (SC) 538 [G.E. 550]
Electrochemistry, Chromium(II)-catalyzed electrochemical dehalogenation of β-hydroxyhalides—convenient entry to deoxynucleosides (SC) 46 [G.E. 47]
1,5-Electrocyclizations—An important principle of heterocyclic chemistry (SC) 947 [G.E. 979]
Electrolytes, Lithium nitride halides—New solid ~ with high Li^+ ion conductivity (SC) 74 [G.E. 72]
Electron acceptors, 1,2,3,5,6,7-s-Hydrindacenehexone and 1,2,3,6,7,8-pyrenehexone—Two new strong ~ (SC) 715 [G.E. 768]
Electron/ion transfer, Reversible topotactic redox reactions of solids by ~ (SC) 983 [G.E. 1015]
Electron microscopy, High-resolution transmission ~ re-examined as a tool in solid state chemistry (FP) 505 [G.E. 531]
Chemical applications of transmission ~ (Book Review) 148
Electron resonance spectroscopy, Multiple ~ (Book Review) 330
Electron transfer, Structure and function of the energy-converting system of mitochondria (FP) 659 [G.E. 684]
Outer sphere ~ reactions: A novel linear relationship between the selectivity and the normal potential of the reducing agents (SC) 558 [G.E. 580]
Electrophilic amination of cyclopentadienyllithium compounds (SC) 1010 [G.E. 1043]
Electrophilic reagents—Recent developments and their preparative application (FP) 151 [G.E. 147]
Enantiomers, Liquid chromatography of ~: Determination of enantiomeric purity in spite of extensive peak overlap (SC) 469 [G.E. 490]
Quantitative separation of the enantiomeric pairs of the pheromone 2-ethyl-1,6-dioxaspiro[4.4]nonane by complexation chromatography on an optically active metal complex (SC) 471 [G.E. 473]
Separation of ~ of 2-hydroxycarboxylic acids on optically active stationary phases (SC) 910 [G.E. 935]
Energy conversion, Structure and function of the energy-converting system of mitochondria (FP) 659 [G.E. 684]
Energy hypersurfaces, Reactions paths on multidimensional ~ (FP) 1 [G.E. 1]
Encyclopedia of chemical technology, Kirk-Othmer: ~ (Book Review) 228
Enethiolates, α-Carbamoyloxymethyl-substituted lithium ~ from 1-(N,N-dimethylcarbamoylthio)-2-methyl-1-propenyllithium (SC) 303 [G.E. 305]
Enol ethers, Thermal cycloadditions of dimethyl acetylenedicarboxylate to cyclic ~ and thioenol ethers (SC) 832 [G.E. 848]
Enophile, N-Sulfinylnonafluorobutanesulfonamide—A super-~ (SC) 732, 840 [G.E. 748]
Enzymes, Dimerization of propylene with catalysts exhibiting activities like highly-active ~ (SC) 622 [G.E. 633]
Epoxidation, Oxidation reactions of benzvalene: Ozonolysis, cis-hydroxylation, ~, and singlet oxygen addition (SC) 458 [G.E. 466]
"Synthetic enzymes". Highly stereoselective ~ of chalcone in a triphasic toluene-water-poly[(S)-alanine] system (SC) 929 [G.E. 968]
Ergochrome, Sequence analysis of ~—Biosynthesis by competitive incorporation (SC) 460 [G.E. 483]
Estrone, A photochemical route to (±)-~ (SC) 1027 [G.E. 1060]
Asymmetric total synthesis of (+)-estrone (SC) 1029 [G.E. 1062]
syn-1,6-Ethano-8,13-methano[14]annulene, Structure and dynamic behavior (SC) 921 [G.E. 944]
3-Ethoxyacroleins, Oxopropenylation of Grignard compounds with ~ (SC) 816 [G.E. 841]
Ethylene, Selective pathway from methanol to ~ and propene (SC) 126 [G.E. 125]
Unusually rapid cis-trans isomerization of a tetrasilylated ~: Generation of free radicals during rotation (SC) 620 [G.E. 632]
Ethylene(hydrido)iridium(III) complex, Cationic ~ (SC) 834 [G.E. 863]
Ethylene oxide, Acetaldehyde as main product of oxidation of ~ on a silver catalyst (SC) 407 [G.E. 389]
Ethylene(phenyl)tris(trimethylphosphane)cobalt, Olefin-insertion into cobalt (d^8) complexes—Structure of ~ (SC) 809 [G.E. 835]
N-Ethynylamines of the type R—NH—C≡C—H (SC) 720 [G.E. 743]
Etriphos, Metal-assisted reaction of carbon disulfide with "~" phosphane ligand: Synthesis and structure of $[(\sim)Fe\{S_2C(EtPCH_2)_2CMe_2\}](BF_4)_2$ (SC) 1021 [G.E. 1055]
Euglenapterin—An unusual new natural pteridine derivative from Euglena gracilis (SC) 473 [G.E. 474]

FISCHER-Tropsch synthesis, Characterization by Mössbauer spectroscopy of iron carbide phases in a highly active carbon matrix catalyst for medium pressure ~ (SC) 729 [G.E. 761]
Flash vacuum pyrolysis, 2-Vinylidene-2H-indene (SC) 821 [G.E. 846]
Fluctuating ligands, (1,2,5,6-η-1,5-Cyclooctadiene)(1,2,7-η-7-methylbenzyl)(7,8-η-styrene)rhodium(I)—Antarafacial fluctuation of the benzyl ligand and temperature-dependent coordination of styrene (SC) 468 [G.E. 475]
Fluid chromatography, Physicochemical principles and applications of supercritical ~ (SFC) (FP) 575 [G.E. 585]
Fluorine chemicals, Organo-~ and their industrial applications (Book Review) 230
Fluorine compounds, 1,4-Dioxanes with four fluorine and/or trifluoromethyl substituents on C^2 and C^3 from vicinal perfluorodicarbonyl compounds (SC) 126 [G.E. 123]
Direct synthesis of the perfluoroalkanesulfinates of iron(II), cobalt(II), and nickel(II): SO_2-assisted addition of alkyl halides to transition metals (SC) 128 [G.E. 124]
New aspects of the reaction of difluorosulfur imides with fluorine (SC) 408 [G.E. 393]
Ambiphilicity of 1,1-diethoxy-4,4,4-trifluoro-3-(trifluoromethyl)-1,2-butadiene (SC) 713 [G.E. 740]
N-Sulfinylnonafluorobutanesulfonamide—A superenophile (SC) 732 [G.E. 748]
The pentafluoropyridine cation $C_5F_5N^+$ (SC) 944 [G.E. 956]
N-Fluoroiminosulfur tetrafluoride, F—N=SF_4 (SC) 643 [G.E. 659]
Fluorometalates, The first "small ring" in ~: $Ba_6F_4(F_4AlF_{2/2})_4$ = "$Ba_3Al_2F_{12}$" (SC) 489 [G.E. 476]
Fluorophosphane ligands, General method for preparation of multidentate ~ (SC) 316 [G.E. 323]
Forssman antigen, Synthesis of the pentasaccharide chain of the ~ (SC) 902 [G.E. 929]
Fragmentation, Photochemical rearrangements and ~ of benzene derivatives and annelated arenes (FP) 243 [G.E. 245]
Collision induced ~ of alkylideneammonium ions (SC) 541 [G.E. 548]
Inductive, CC-hyperconjugative, and frangomeric effects in solvolytic ~ (SC) 708 [G.E. 734]
Fluoride-induced ~ of trimethylsilyloxysulfonates to form cis-coupled hexahydroazulenones (SC) 830 [G.E. 832]
Frangomeric effects, Inductive, CC-hyperconjugative, and ~ in solvolytic fragmentation reactions (SC) 708 [G.E. 734]
Free-energy relationships, Significance of isoselective temperatures for the existence of linear ~ (SC) 835 [G.E. 864]
6-Fulveneselone (SC) 69 [G.E. 52]
Fulvalenoparacyclophanes, Tetrathia-~ (SC) 66 [G.E. 49]
Fulvalenophanes, [2.2]- and [3.3]-tetrathia-~ (SC) 67 [G.E. 51]
Fungicides, 3-Phenylpropylamines. New class of systemic ~ (FP) 184 [G.E. 176]
Furan, Proton and hydrogen affinity of ~ and the site of protonation in the gas phase (SC) 905 [G.E. 934]
Furan derivatives, Thermal cycloadditions of dimethyl acetylenedicarboxylate to cyclic enol ethers and thioenol ethers (SC) 832 [G.E. 848]
Furan-2(3H)-ones, Acylated ketenimines and allenes from oxazol-5(4H)-ones and ~ (SC) 564 [G.E. 555]

GALLIUM compounds, Synthesis and properties of the first organosilyl-~ (SC) 55 [G.E. 62]
Gas chromatography, Separation of the enantiomers of 2-hydroxycarboxylic acids on optically active stationary phases (SC) 910 [G.E. 935]
Gas phase, Computer simulation of kinetics of complicated ~ reactions (FP) 333 [G.E. 331]
Gas-phase protonation, Proton and hydrogen affinity of furan and the site of (SC) 905 [G.E. 934]
Gel chromatography, theory, methodology, application (Book Review) 331
Germanium compounds, The $(Ph_4C_4GeMe)Fe(CO)_3$ cation: Synthesis, structure, and bonding (SC) 484 [G.E. 496]
Zintl phases with complex anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$ (SC) 490 [G.E. 480]
(Trifluoromethyl)fluorogermanates (SC) 836 [G.E. 859]
α-D-Glucuronides of 1-(N-alkyl-N-nitrosoamino)alkyl alcohols (SC) 400 [G.E. 407]
D-Glucurono-6,3-lactone, L-Gulose or D-gluco-hexodialdose from ~ by controlled reductions (SC) 546 [G.E. 552]
Glycogen phosphorylases, Role of pyridoxal phosphate in catalysis of ~ (FP) 441 [G.E. 429]
Glycosides, Facile synthesis of α- and β-O-glycosyl imidates; preparation of ~ and disaccharides (SC) 731 [G.E. 763]
O-Glycosyl imidates, Facile synthesis of α- and β-~; preparation of glycosides and disaccharides (SC) 731 [G.E. 763]
Gold complexes, Synthesis and reaction of diorganophosphinite ~ (SC) 71 [G.E. 66]
Gold(I) dithioacetate, Gold(I)-gold(I) interactions. Tetrameric ~ (SC) 561 [G.E. 579]
Gold(I)-gold(I) interactions. Tetrameric gold(I) dithioacetate (SC) 561 [G.E. 579]
Graphite-intercalation, Catalytic ~ with alkali metals in solution (SC) 491 [G.E. 476]
Grignard compounds, Oxopropenylation of ~ with 3-ethoxyacroleins (SC) 816 [G.E. 841]
D-Gulono-1,4-lactone, Pure D-gulose from ~ (SC) 547 [G.E. 553]
Gulose, L-~ or D-gluco-hexodialdose from D-glucurono-6,3-lactone by controlled reductions (SC) 546 [G.E. 552]
Pure D-~ from D-gulono-1,4-lactone (SC) 547 [G.E. 553]

β-HALOETHYL groups, Vitamin B_{12} and a vitamin B_{12} model compound as catalysts of reductive removal of protecting ~ from acids (SC) 629 [G.E. 643]
Heme, A pyrazine-bridged ~ dimer absorbing at 800 nm (SC) 322 [G.E. 320]
Hericenes, 2,3,5,6,7,8-Hexakis(methylene)bicyclo[2.2.2]octane (SC) 1003 [G.E. 1036]
9-Heterobicyclo[4.2.1]nona-2,4,7-trienes, Question of bicycloconjugation in naphtho-fused ~ as examined by ^{13}C-NMR spectroscopy (SC) 639 [G.E. 657]

Heterocycles, 1,5-Electrocyclizations—An important principle of heterocyclic chemistry (FP) 947 [G.E. 979]
Thermal and photochemical transformations of hetero-1,3,5-hexatrienes into five-membered rings—Possible pericyclic reactions (FP) 973 [G.E. 1005]
Syntheses with metalloid derivatives. Preparation of ~ (SC) 327 [G.E. 325]
Synthesis of cyclic compounds from triphenyl(phenyliminovinylidene)phosphorane and carboxylic acids (SC) 822 [G.E. 856]
Hetero-1,3,5-hexatrienes, Thermal and photochemical transformations of ~ into five-membered rings—Possible pericyclic reactions (FP) 973 [G.E. 1005]
Hexaazabenzene, Photochemical reductive cis-elimination in cis-diazidobis(triphenylphosphane)platinum(II). Evidence of formation of bis(triphenylphosphane)platinum(0) and ~ (SC) 717 [G.E. 745]
Hexahydroazulenones, Fluoride-induced fragmentation of trimethylsilyloxysulfonates to form cis-coupled ~ (SC) 830 [G.E. 832]
1,2,3,7,8,20-Hexahydroporphyrin, an easily formed ligand system isomeric to porphyrinogens (SC) 141 [G.E. 141]
2,3,5,6,7,8-Hexakis(methylene)bicyclo[2.2.2]octane (SC) 1003 [G.E. 1036]
D-gluco-Hexodialdose, L-Gulose or ~ from D-glucurono-6,3-lactone by controlled reductions (SC) 546 [G.E. 552]
High temperature technology, Physical chemistry of ~ (Book Review) 946
History of science, Stereospecific polymerization of propylene: An outlook 25 years after its discovery (FP) 857 [G.E. 869]
German-Jewish pioneers in science 1900—1933 (Book Review) 573
Homobenzenes, cis-/trans-Tris-[2.1.1]-σ-~; synthesis and stereochemistry of [„2+„2+„2]-cycloreversions (SC) 567 [G.E. 575]
Homobenzvalene, Relation between orbital character and reaction product in reaction of benzvalene and ~ with thiophenol (SC) 457 [G.E. 465]
Homoenolate equivalents, Lithiated allyl N,N-dialkylcarbamates as ~: synthesis of protected 4-oxoalkanoates (SC) 625 [G.E. 637]
Homogeneous catalysis, Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for ~ (FP) 362 [G.E. 362]
Homotropone, "α,α,α"-, "α,β,α"-, and "α,α,β"-Trioxa-tris-σ-~ (SC) 214 [G.E. 216]
1,2,3,5,6,7-s-Hydrindacenehexone and 1,2,3,6,7,8-pyrenehexone—Two new strong acceptors (SC) 715 [G.E. 768]
Hydrido complex, Cationic ethylene(hydrido)iridium(III) complex (SC) 834 [G.E. 863]
Hydroformylation, Synthesis of intermediates by rhodium-catalyzed ~ (FP) 178 [G.E. 182]
Catalysis of ~ by $Co_4(CO)_{8-x}(\mu_2\text{-}CO)_2(PPh_3)_x(\mu_4\text{-}PPh)_2$, x = 0 or 2: Clusters as catalysts (SC) 478 [G.E. 494]
Hydrogen bonds, OH clusters with homodromic circular arrangement of ~ (SC) 398 [G.E. 404]
Novel proton-ordered, two-dimensional cross-linking of water molecules in pyridine trihydrate (SC) 552 [G.E. 559]
Hydrogen telluride, Reduction of carbonyl compounds by aluminum telluride and H_2O or D_2O (SC) 1009 [G.E. 1041]
Reduction of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with ~ from aluminum telluride and water (SC) 1009 [G.E. 1042]
Hydrogen zeolites, Dehydroxylation of ~: Conditions for preparation of thermally stable catalysts (SC) 743 [G.E. 759]
2-Hydroxycarboxylic acids, Separation of the enantiomers of ~ on optically active stationary phases (SC) 910 [G.E. 935]
β-Hydroxyhalides, Chromium(II)-catalyzed electrochemical dehalogenation of ~—convenient entry to deoxynucleosides (SC) 46 [G.E. 47]
Hydroxylamine derivatives, N-(Amidosulfonyl)hydroxylamine, H_2NSO_2NHOH (SC) 943 [G.E. 957]
Hydroxylation, Oxidation reactions of benzvalene: ozonolysis, cis-~, epoxidation, and singlet oxygen addition (SC) 458 [G.E. 466]
Metalloporphyrin-catalyzed ~ of cyclohexane by alkyl hydroperoxides: Pronounced efficiency of iron-porphyrins (SC) 909 [G.E. 938]

syn-1,6-IMINO-8,13-METHANO[14]ANNULENE (SC) 1015 [G.E. 1051]
4-Imino-1,2-oxazetidines, Stable ~ from N-neopentylidene-tert-butylamine N-oxide and isocyanides (SC) 45 [G.E. 46]
Inclusion compounds, Cyclodextrin ~ in research and industry (FP) 344 [G.E. 343]
Selective inclusion of alcohols with a new pyridino crown (SC) 1030 [G.E. 1067]
Inclusion reactions, Reversible topotactic redox reactions of solids by electron/ion transfer (FP) 983 [G.E. 1015]
Indigo, Captodative substituent effects and the chromophoric system of ~ (SC) 908 [G.E. 937]
Indole pigments from the fruiting bodies of the slime mold Arcyria denudata (SC) 459 [G.E. 463]
Industrial chemistry, Ullmanns Encyklopädie der technischen Chemie (Book Review) 838
Insertion, Olefin-~ into cobalt (d^8) complexes—Structure of ethylene(phenyl)-tris(trimethylphosphane)cobalt (SC) 809 [G.E. 835]
First insertion reaction of carbon monoxide into a rhenium-carbon σ-bond (SC) 824 [G.E. 843]
Intercalation complexes of metallocenes in iron oxide chloride (SC) 477 [G.E. 493]
Catalytic graphite intercalation with alkali metals in solution (SC) 491 [G.E. 476]
Iodine compounds, New dinuclear iridium(II) complexes arising by oxidative addition of I_2 to $Ir_2(\mu\text{-}StBu)_2(CO)_2L_2$ (SC) 551 [G.E. 572]
Iodomethyl(phosphane)complex, Conversion of an ~ into a methylenephosphorane-complex: Example of a nucleophile-catalyzed isomerization reaction (SC) 940 [G.E. 960]
Ion cyclotron resonance spectroscopy, Proton and hydrogen affinity of furan and the site of protonation in the gas phase (SC) 905 [G.E. 934]
Ion exchange, Calcium isotope separation on an exchange resin having cryptand anchor groups (SC) 406 [G.E. 406]
Ion pair formation, Distribution of terminal and bridging CO-groups in an anionic carbonylmetal cluster as a result of ~. Crystal and molecular structure of $LiCo_3(CO)_{10}\cdot i\text{-}Pr_2O$ (SC) 404 [G.E. 441]
Iridium complexes, New dinuclear iridium(II) complex arising by oxidative addition of I_2 to $[Ir_2(\mu\text{-}StBu)_2(CO)_2L_2]$ (SC) 551 [G.E. 572]
New dihydrido-bridged binuclear platinum-~ (SC) 721 [G.E. 744]
Cationic ethylene(hydrido)iridium(III) complex (SC) 834 [G.E. 863]
Iron, Ultratrace analysis: Determination of Cr, ~, and Co in the ppb and ppt range for checking the preparation of high-purity niobium (SC) 197 [G.E. 194]
Iron carbide phases, Characterization by Mössbauer spectroscopy of ~ in a highly active carbon matrix catalyst for medium pressure Fischer-Tropsch synthesis (SC) 729 [G.E. 761]
Iron complexes, Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for homogeneous catalysis (FP) 362 [G.E. 362]
First fixation of the unstable species sulfur monoxide in a cluster: Synthesis and structure of $Fe_3(CO)_9(S)SO$ (SC) 226 [G.E. 225]
Phthalocyaninatoiron with pyrazine as a bidentate bridging ligand (SC) 392 [G.E. 391]
The $(Ph_4C_4GeMe)Fe(CO)_3$ cation: Synthesis, structure, and bonding (SC) 484 [G.E. 496]
MoS_4^{2-} and $MoOS_3^{2-}$ as structurally versatile and biochemically interesting ligands in crystalline multinuclear Cu- and Fe-complexes (SC) 654 [G.E. 665]
Bis(η-cyclopentadienyliron-μ,η-thiadiborolene)iron—structure of a $\eta\text{-}C_5H_5$ tetradecker sandwich complex (SC) 746 [G.E. 758]
Iron compounds, First optically active cluster: resolution of enantiomers and absolute configuration of $SFeCoMoCp(CO)_8$ (SC) 65 [G.E. 66]
Direct synthesis of the perfluoroalkanesulfinates of iron(II), cobalt(II), and nickel(II): SO_2-assisted addition of alkyl halides to transition metals (SC) 128 [G.E. 124]
Metal-assisted reaction of carbon disulfide with "etriphos" phosphane ligand: Synthesis and structure of $[(Etriphos)Fe\{S_2C(EtPCH_2)_2CMe_2\}](BF_4)_2$ (SC) 1021 [G.E. 1055]
Iron oxide chloride, Intercalation complexes of metallocenes in ~ (SC) 477 [G.E. 493]
Isatins, Oxidation to isatoic anhydrides and 2,3-dioxo-1,4-benzoxazines (SC) 222 [G.E. 196]
Isatoic anhydrides, Oxidation of isatins to ~ and 2,3-dioxo-1,4-benzoxazines (SC) 222 [G.E. 196]
Isobacteriochlorin, Mutual interconversion of the chromophoric system of porphyrinogen and ~ (SC) 140 [G.E. 139]
Synthesis and transformation of 5-cyano-2,2,8,8,12,13,17,18-octamethyl-~ (SC) 143 [G.E. 143]
Isocyanates, Synthesis of α-haloalkylcarbamoyl halides (SC) 201 [G.E. 197]
Isocyanides, Stable 4-imino-1,2-oxazetidines from N-neopentylidene-tert-butylamine N-oxide and ~ (SC) 45 [G.E. 46]
Template polymerization of rhodium(I) with rigid bent diisocyanide ligands (SC) 633 [G.E. 649]
N-Isocyanoiminotriphenylphosphorane: Synthesis, coordination chemistry, and reactions at the metal (SC) 480 [G.E. 478]
2H-Isoindole, 2-tert-Butyl-~: A partner for reactions with electrophiles (SC) 320 [G.E. 309]
Isomerism, Influence of ~ of alkanes on the thermodynamic properties of cyclohexane/alkane mixtures (SC) 223 [G.E. 209]
Isomerization, Experimental and theoretical study of the degenerate carbon skeleton ~ of the cyclopentyl cation in the gas phase (SC) 485 [G.E. 488]
Base-catalyzed conversion of an equatorial into an axial methoxycarbonyl group due to a 1,5-long-range substituent effect (SC) 543 [G.E. 577]
Unusually rapid cis-trans ~ of a tetrasilylated ethylene: Generation of free radicals during rotation (SC) 620 [G.E. 632]
Conversion of an iodomethyl(phosphane)-into a methylenephosphorane complex: Example of a nucleophile-catalyzed ~ reaction (SC) 940 [G.E. 960]
Isophosphamide, Absolute configuration of the cancerostatic S(−)-~ (SC) 549 [G.E. 578]
Isoselective temperatures, Significance of ~ for existence of linear free-energy relationships (SC) 835 [G.E. 864]
Isotope separation, Calcium ~ on an exchange resin having cryptand anchor groups (SC) 406 [G.E. 406]

KETALS, Phosphorus triiodide and diphosphorus tetraiodide, new reagents for deprotection of acetals and ~ (SC) 1006 [G.E. 1039]

Ketenes, Direct detection of dicyanoketene in the gas phase (SC) 739 [G.E. 751]
Ketenimines, Acylated ~ and allenes from oxazol-5(4H)-ones and furan-2(3H)-ones (SC) 564 [G.E. 555]
Ketones, Coupling of solvolysis and C—C linkage: A promising synthetic route to functionalized carboxylic acids, aldehydes and ~ (FP) 171 [G.E. 169]
Functionalization of α-methylene ~ (SC) 131 [G.E. 138]
Photoreduction of ~ and aldehydes to alcohols with selane (SC) 1008 [G.E. 1041]
Reduction of carbonyl compounds by aluminum telluride and H_2O or D_2O (SC) 1009 [G.E. 1041]
Kinetics, Computer simulation of ~ of complicated gas phase reactions (FP) 333 [G.E. 331]

β-LACTAMS, Pyrrolizidines by rearrangement of ~ (SC) 129 [G.E. 126]
β-Lactones, Thermal decarboxylation of ~: Steric hindrance of mesomerism as indication of a zwitterionic intermediate (SC) 465 [G.E. 469]
2-Thietanimines from α-deprotonated ~ and phenyl isothiocyanate—A novel four-membered ring/four-membered ring recyclization (SC) 466 [G.E. 470]
Language, Symbolic ~ of the chemist (FP) 110 [G.E. 106]
Lead compounds, 1,3,2-Dithiaplumbocanes—heterocycles with lead(IV)—sulfur bonds (SC) 923 [G.E. 950]
Ligand-property control, ~ in the nickel(0)/butadiene/P-ligand catalytic system: Dominance of "steric" factors in the control of oligomer distribution (SC) 569 [G.E. 567]
~ in the nickel(0)/butadiene/P-ligand catalytic system: "Electronic" factors in the control of cyclodimer distribution (SC) 570 [G.E. 569]
Ligands, Coupling of well-established organotransition metal chemistry donor groups to multielectron ~ (SC) 328 [G.E. 321]
Rigid phenyl-group conformation in complexes (SC) 396 [G.E. 395]
Liposomes, Polymerizable phospholipid analogues—New stable biomembrane and cell models (SC) 938 [G.E. 962]
Liquid crystals, Handbook of ~ (Book Review) 656
Liquid metals and liquid semiconductors (FP) 593 [G.E. 598]
Liquids, Structure of simple molecular ~ (FP) 697 [G.E. 700]
Organic ~: structure, dynamics, and chemical properties (Book Review) 76
2-Lithio-2-methyl-1,3-dithiane, Crystal structure of ~·tetramethylethylenediamine (SC) 53 [G.E. 59]
Lithium compounds, Enantioselective synthesis of α-methylserines (SC) 212 [G.E. 205]
1,3-Bis(1-lithio-3-methyl-1-phenylpentyl)benzene, an organodilithium compound soluble in aromatic hydrocarbons (SC) 219 [G.E. 212]
Nucleophilic addition of triphenylstannyllithium to carbon disulfide (SC) 220 [G.E. 227]
Lithium bis(trimethylsilyl)methylene diphenylphosphoranide, a building block for the synthesis of bis(methylenephosphoranes) (SC) 243 [G.E. 206]
Distribution of terminal and bridging CO-groups in an anionic carbonylmetal cluster as a result of ion-pair formation. Crystal and molecular structure of $LiCo_3(CO)_{10}$·i-Pr_2O (SC) 404 [G.E. 441]
Allylic compounds of magnesium, lithium and potassium: σ- or π-structures? (SC) 487 [G.E. 497]
Lithiated allyl N,N-dialkylcarbamates as homoenolate equivalents: Synthesis of protected 4-oxoalkanoates (SC) 625 [G.E. 637]
Tripropylcarbazoyllithium (SC) 762 [G.E. 764]
Lithium compounds, $Li_{12}Si_7$, a compound having trigonal planar Si_4 cluster and planar Si_5 rings (SC) 1033 [G.E. 1070]
Lithium dibenzoylphosphide·1,2-dimethoxyethane—A new 2-phospha-1,3-dionate (SC) 741 [G.E. 756]
Lithium enethiolates, α-Carbamoyloxymethyl-substituted ~ from 1-(N,N-dimethylcarbamoylthio)-2-methyl-1-propenyllithium (SC) 303 [G.E. 305]
Lithium nitride halides—new solid electrolytes with high Li^+ ion conductivity (SC) 74 [G.E. 72]
Living polymers on polymerization with extremely productive Ziegler catalysts (SC) 390 [G.E. 396]
Luminescence spectroscopy (Book Review) 75

MACROMOLECULES. An introduction to polymer science (Book Review) 657
Magnesium compounds, Allylic compounds of magnesium, lithium, and potassium: σ- or π-structures? (SC) 487 [G.E. 497]
Magnesium hydride, Catalytic synthesis under mild conditions (SC) 818 [G.E. 845]
Malonaldehyde, Transition-metal complexes of ~ and dithio-~ (SC) 638 [G.E. 654]
Manganese compounds, Nucleophilic elimination-cycloaddition of α,ω-alkanediyl bis(triflates), a novel method for the synthesis of metallacycles with reactive metal-carbon bonds (SC) 73 [G.E. 70]
Total reversibility of addition and transylidation of trialkyl(alkylidene)phosphoranes to metal-coordinated carbon monoxide (SC) 1019 [G.E. 1063]
Phosphorus ylide carbene complexes—Synthesis and structure (SC) 1020 [G.E. 1065]
Mass spectrometry, Collision induced fragmentation of alkylideneammonium ions (SC) 541 [G.E. 548]
Matrix catalyst, Characterization by Mössbauer spectroscopy of iron carbide phases in a highly active carbon ~ for medium pressure Fischer-Tropsch synthesis (SC) 729 [G.E. 761]
Membrane, Vesicles with a monolayer, redox-active ~ (SC) 550 [G.E. 564]
Membrane models, Polymerizable phospholipid analogues—New stable biomembrane and cell models (SC) 938 [G.E. 962]
Mercaptocarbenium ion, ^{13}C-NMR study of protonated thioketones in superacidic media: Significance of ~ contributions (SC) 811 [G.E. 837]
Metal complexes in organic chemistry (Book Review) 656
Metallacycles, Nucleophilic elimination-cycloaddition of α,ω-alkanediyl bis(triflates), a novel method for the synthesis of ~ with reactive metal-carbon bonds (SC) 73 [G.E. 70]
Metallocenes, Intercalation complexes of ~ in iron oxide chloride (SC) 477 [G.E. 493]
Permethylated electron-excess ~ (SC) 640 [G.E. 658]
Metalloid derivatives, Syntheses with ~: Preparation of macrocyclic dicarbamate (SC) 326 [G.E. 324]
Syntheses with ~. Preparation of heterocycles (SC) 327 [G.E. 325]
Metalloporphyrin catalysts, Metalloporphyrin-catalyzed hydroxylation of cyclohexane by alkyl hydroperoxides: Pronounced efficiency of iron-porphyrins (SC) 909 [G.E. 938]
Metal polymers, Synthesis of organotrimetal polymers using trimetal vapor-fluid matrix techniques (SC) 402 [G.E. 409]
Metal-to-metal bonds, Simple method of forming ~ (SC) 937 [G.E. 961]
Methanol, Selective pathway from ~ to ethylene and propene (SC) 126 [G.E. 125]
Methoxycarbonyl group, Base-catalyzed conversion of an equatorial into an axial ~ due to a 1,5-long-range substituent effect (SC) 543 [G.E. 577]
(2RS,3RS)-3-Methoxy-trans-cycloheptene, Cycloadditions with silver ion-stabilized ~ (SC) 1032 [G.E. 1068]
Methylation, Geminal dialkylation of ketones with Grignard compounds and methyltitanium(IV) chlorides (SC) 901 [G.E. 931]
Chemoselective and position specific ~ of tert-alkyl halides with methyltitanium(IV) chlorides (SC) 901 [G.E. 933]
μ-Methylene complex, Synthesis of the first methylidyne-rhodium cluster by proton-induced H_2/CH_4-elimination from a ~ (SC) 651 [G.E. 660]
Methylenecyclopropanes, Heterocyclic analogues of ~ (FP) 276 [G.E. 277]
α-Methylene ketones, Functionalization (SC) 131 [G.E. 138]
Methylenephosphorane, $Ph(Me_3Si)C{-}P{-}Cl$, the first P-halofunctionalized ~ (SC) 556 [G.E. 578]
Methylenephosphorane-complex, Conversion of an iodomethyl(phosphane)- into a ~: Example of a nucleophile-catalyzed isomerization reaction (SC) 940 [G.E. 960]
Methylidyne-rhodium cluster, Synthesis of the first ~ by proton-induced H_2/CH_4-elimination from a μ-methylene complex (SC) 651 [G.E. 660]
Methyl ketones, Are α-oxothioacyl chlorides formed in the reaction of ~ with thionyl chloride? (SC) 563 [G.E. 559]
α-Methylserines, Enantioselective synthesis (SC) 212 [G.E. 205]
4-Methylthiophenoxycarbonyl group, Synthesis of alternating depsipeptides with the ~ as protecting and activating group for the amino function (SC) 932 [G.E. 953]
Methyltitanium(IV) chlorides, Geminal dialkylation of ketones with Grignard compounds and ~ (SC) 901 [G.E. 931]
Chemoselective and position specific methylation of tert-alkyl halides with ~ (SC) 901 [G.E. 933]
Micellar systems, Photophysical and photochemical processes in ~ (FP) 675 [G.E. 712]
Michael addition, Synthesis under high pressure: ~ (SC) 1013 [G.E. 1046]
Minimum chemical distance, Principle of ~ (PMCD) (FP) 495 [G.E. 503]
Mitochondria, Structure and function of the energy-converting system of ~ (FP) 659 [G.E. 684]
Models, Molecular and crystal structure ~ (Book review) 229
Chemistry through ~ (Book Review) 839
Molecular liquids, Structure of simple ~ (FP) 697 [G.E. 700]
Molten salts, Influence of density and temperature on properties of pure ~ (FP) 606 [G.E. 612]
Molybdenum compounds, First optically active cluster: resolution of enantiomers and absolute configuration of $SFeCoMoCp(CO)_8$ (SC) 65 [G.E. 66]
Activation and sulfur-atom transfer reaction of cluster-bonded S_2^{2-}-bridge ligands: synthesis of the new cluster $[Mo_3^{IV}S_4(CN)_9]^{5-}$ from $[Mo_3^{IV}S(S_2)_6]^{2-}$ and CN^- (SC) 72 [G.E. 69]
Electrochemical oxidation of dicarbene complexes of type $(carbene)_2MoL(CO)_3$: Interconversion among three isomers via electrochemical redox process (SC) 538 [G.E. 550]
MoS_4^{2-} and $MoOS_3^{2-}$ as structurally versatile and biochemically interesting ligands in crystalline multinuclear Cu- and Fe-complexes (SC) 654 [G.E. 665]
Morphological properties, Determination of ~ of swellable solids by size exclusion chromatography (FP) 24 [G.E. 25]
Multielectron ligands, Coupling of well-established organotransition metal chemistry donor groups to ~ (SC) 328 [G.E. 321]
Mutarotation, ^1H-NMR investigations on ~ rotation of N-acetyl-D-neuraminic acid (SC) 208 [G.E. 200]

NAPHTHALENE, 9,10-Benzotricyclo[6.2.2.0^{2,7}]dodeca-3,5,9,11-tetraene—A Diels-Alder adduct of benzene and ~ (SC) 307 [G.E. 307]
(+)-(2R)-5,5′-Dimethyl-2,2′-spirobi(2,3-dihydro-1H-cyclopenta[a]-~)—A chiral spirohydrocarbon containing orthogonal ~ units (SC) 308 [G.E. 318]
Neuraminic acid, ^{1}H-NMR investigations on mutarotation of N-acetyl-D-~ (SC) 208 [G.E. 200]
Nickelacyclopentene derivatives from nickel(0), carbon monoxide, and alkyne (SC) 927 [G.E. 951]
Nickel complexes, Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for homogeneous catalysis (FP) 362 [G.E. 362]
Tetraphenylcyclobutadienecycloalkenenickel(0) complexes (SC) 145 [G.E. 131]
Photooxidation of the ligands of bis(o-semiquinonediimine)nickel(II) and -platinum(II) (SC) 221 [G.E. 228]
Ligand-property control in the nickel(0)/butadiene/P-ligand catalytic system: Dominance of "steric" factors in the control of oligomer distribution (SC) 569 [G.E. 567]
Ligand-property control in the nickel(0)/butadiene/P-ligand catalytic system: "Electronic" factors in the control of cyclodimer distribution (SC) 570 [G.E. 569]
Nickel compounds, Direct synthesis of the perfluoroalkanesulfinates of iron(II), cobalt(II), and nickel(II): SO_2-assisted addition of alkyl halides to transition metals (SC) 128 [G.E. 124]
Upright unsymmetrical coordination in a cyclopropenylnickel complex: Synthesis and structure of $[(C_3Ph_3)Ni(PPh_3)_2]PF_6$ (SC) 931 [G.E. 967]
Template synthesis of clusters using the tripod ligand $HC(PPh_2)_3$: $Ni_3(CO)_6$(tripod) (SC) 1025 [G.E. 1059]
Niobium, Ultratrace analysis: Determination of Cr, Fe, and Co in the ppb and ppt range for checking the preparation of high-purity ~ (SC) 197 [G.E. 194]
Nitrenes, Cyclic carbodiimides in nitrene rearrangements (SC) 566 [G.E. 556]
μ-Nitrido complex, $(AsPh_4)W_2NCl_{10}$, a ~ containing tungsten(V) and tungsten(VI) (SC) 220 [G.E. 211]
Nitroarenes, Selenium-catalyzed reduction of aromatic nitro compounds to amines by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
Reduction of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with hydrogen telluride from aluminum telluride and water (SC) 1009 [G.E. 1042]
Nitrogen compounds, Novel SN-ligand: Structure of $PtCl(S_4N_3)$ (SC) 653 [G.E. 644]
Reduction of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with hydrogen telluride from aluminum telluride and water (SC) 1009 [G.E. 1042]
Nitrosamines, α-D-Glucuronides of 1-(N-alkyl-N-nitrosoamino)alkyl alcohols (SC) 400 [G.E. 407]
Nitroso compounds, α-D-Glucuronides of 1-(N-alkyl-N-nitrosoamino)alkyl alcohols (SC) 400 [G.E. 407]
NMR spectroscopy, Kinetic and mechanistic evaluation of NMR spectra (FP) 411 [G.E. 445]
Extreme ^{13}C-NMR data as information on organometal radicals (SC) 479 [G.E. 487]
^{13}C-NMR spectroscopic studies on ^{13}C-methylated bituminous coal (SC) 636 [G.E. 653]
The question of bicycloconjugation in naphtho-fused 9-heterobicyclo[4.2.1]nona-2,4,7-trienes as examined by ^{13}C-NMR spectroscopy (SC) 639 [G.E. 657]
^{13}C-NMR study of protonated thioketones in superacidic media: Significance of mercaptocarbenium ion contributions (SC) 811 [G.E. 837]
Thiobenzoyl cations (SC) 812 [G.E. 838]
^{15}N-NMR spectroscopic detection of the tetrazolo[1,5-a]pyrimidine/2-azidopyrimidine equilibrium (SC) 924 [G.E. 957]
Norbornenes, Synthesis of ~ from cyclopentadiene and allyl alcohols in an acidic two phase system (SC) 827 [G.E. 861]
Normal potential, Outer sphere electron transfer reactions. Novel linear relationship between selectivity and ~ of reducing agents (SC) 558 [G.E. 580]
Nucleic acids, Viroids: A class of subviral pathogens (FP) 231 [G.E. 233]
UV irradiation of ~ and their components in the presence of air (SC) 829 [G.E. 858]
Nucleobases, UV irradiation of nucleic acids and their components in the presence of air (SC) 829 [G.E. 858]

OLEFIN-insertion into cobalt (d^8) complexes—Structure of ethylene(phenyl)-tris(trimethylphosphane)cobalt (SC) 809 [G.E. 835]
Oligomer distribution, Ligand-property control in the nickel(0)/butadiene/P-ligand catalytic system: Dominance of "steric" factors in the control of ~ (SC) 569 [G.E. 567]
Oligomers, Cyclic ~ of propellanes and bridged annulenes with bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectronomy (SC) 933 [G.E. 970]
Mixed ~ of propellanes and bridged annulenes with bis(maleimides) and bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectronomy (SC) 936 [G.E. 972]
One-electron oxidation of 1,2-dithiacycloalkanes (SC) 834 [G.E. 863]
Organic metals, Radical cation salts of simple arenes—A new family of "organic metals" (SC) 912 [G.E. 941]
Organisches Praktikum, Integriertes ~ (Book review) 747
Organofluorine chemicals and their industrial applications (Book Review) 230
Organometal radicals, Extreme ^{13}C-NMR data as information on ~ (SC) 479 [G.E. 487]
3-Oxabicyclo[4.3.0]non-1-en-9-one, (6R,7R)-(−)-7-Hydroxy-~. A readily accessible and highly versatile intermediate (SC) 628 [G.E. 639]
3-Oxa-ene reactions of N-sulfinylnonafluorobutanesulfonamide with alkanones—General synthesis of 2-oxoalkanesulfinic acid derivatives (SC) 737 [G.E. 750]
1,2-Oxazetidines, Stable 4-imino-~ from N-neopentylidene-tert-butylamine N-oxide and isocyanides (SC) 45 [G.E. 46]
Oxazines, Rearrangement of cyclopropyl ketone oximes to 5,6-dihydro-4H-1,2-~ (SC) 199 [G.E. 195]
Oxazol-5(4H)-ones, Acylated ketenimines and allenes from ~ and furan-2(3H)-ones (SC) 564 [G.E. 555]
Oxidation, Structural changes on ~: Flattening of the C_4-cluster of tetrahedrane (SC) 209 [G.E. 213]
Oxygen atoms produced by microwave discharge: Reactions with arenes (SC) 1004 [G.E. 1037]
Oxidative addition, New dinuclear iridium(II) complexes arising by ~ of I_2 to $[Ir_2(\mu\text{-}StBu)_2(CO)_2L_2]$ (SC) 551 [G.E. 572]
Oxiranes, Synthesis of monosubstituted (S)-~ in high optical purity (SC) 198 [G.E. 201]
Metal-catalyzed synthesis of cyclic carbonates from carbon dioxide and ~ (SC) 317 [G.E. 302]
2-Oxoalkanesulfinic acid, 3-Oxa-ene reactions of N-sulfinylnonafluorobutanesulfonamide with alkanones—General synthesis of ~ derivatives (SC) 737 [G.E. 750]
4-Oxoalkanoates, Lithiated allyl N,N-dialkylcarbamates as homoenolate equivalents: Synthesis of protected ~ (SC) 625 [G.E. 637]
3-Oxopropadienylidene, Complex stabilization of ~ (C_3O) with pentacarbonylchromium(0) (SC) 225 [G.E. 224]
Oxopropenylation of Grignard compounds with 3-ethoxyacroleins (SC) 816 [G.E. 841]
α-Oxothioacetyl chlorides, Are ~ formed in the reaction of methyl ketones with thionyl chloride? (SC) 563 [G.E. 559]
6-Oxoverdazyls (SC) 724 [G.E. 766]
Oxygen atoms produced by microwave discharge: Reactions with arenes (SC) 1004 [G.E. 1037]
Ozonolysis, Oxidation reactions of benzvalene: ~, cis-hydroxylation, epoxidation, and singlet oxygen addition (SC) 458 [G.E. 466]
~ of 1,2-dichloroacenaphthylene (SC) 474 [G.E. 483]

[2$_4$]-PARACYCLOPHANETETRAENE, Dianion and tetraanion of ~—New unusual perimeter systems (SC) 624 [G.E. 636]
Pentafluoropyridine cation, $C_5F_5N^+$ (SC) 944 [G.E. 956]
Pentasaccharide chain, Synthesis of ~ of the Forssman antigen (SC) 902 [G.E. 929]
Peptide synthesis, New ~ (SC) 133 [G.E. 129]
4-Sulfobenzyl, a new carboxy protecting group (SC) 394 [G.E. 394]
An amino-protecting group for use in ~ which can be introduced electrochemically (SC) 712 [G.E. 739]
Pericyclic reactions, Thermal and photochemical transformations of hetero-1,3,5-hexatrienes into five-membered rings—Possible ~ (FP) 973 [G.E. 1005]
PE spectroscopy, 2-Vinylidene-2H-indene (SC) 821 [G.E. 846]
One-electron oxidation of 1,2-dithiacycloalkanes (SC) 834 [G.E. 863]
Pharmaceutical chemistry today—Changes, problems, and opportunities (FP) 749 [G.E. 802]
Pharmacology, Foundation of molecular ~, Vol. 1 and 2 (Book Review) 409
Phenols, Oxygen atoms produced by microwave discharge: Reactions with arenes (SC) 1004 [G.E. 1037]
1-Phenylethyl substituents, Conformational analysis of ~ in metal complexes and their importance for asymmetric catalysis (SC) 641 [G.E. 645]
Phenyl-group conformation, Rigid ~ in complexes (SC) 396 [G.E. 395]
Phenyl groups, A very crowded molecule: X-Ray crystallographic analysis of bis(2,4,6-tri-tert-butylphenyl)phosphinic chloride (SC) 399 [G.E. 405]
Phenyl isocyanide, Tetrakis(phenylimino)cyclobutane (tetrameric ~) (SC) 136 [G.E. 134]
3-Phenylpropylamines. A new class of systemic fungicides (FP) 184 [G.E. 176]
Pheromone analogues, Differentiation between chiral ~ by chemoreceptors (SC) 475 [G.E. 492]
Pheromones, Quantitative separation of the enantiomer pairs of the pheromone 2-ethyl-1,6-dioxaspiro[4.4]nonane by complexation chromatography on an optically active metal complex (SC) 471 [G.E. 473]
Phlorizin polymer as affinity gel for sugar-binding proteins (SC) 540 [G.E. 547]
2-Phospha-1,3-dionate, Lithium dibenzoylphosphide·1,2-dimethoxyethane—A new ~ (SC) 741 [G.E. 756]
Phosphanes, General method for preparation of multidentate fluorophosphane ligands (SC) 316 [G.E. 323]
Metal-assisted reaction of carbon disulfide with "Etriphos" phosphane ligand: Synthesis and structure of $[(Etriphos)Fe\{S_2C(EtPCH_2)_2CMe_2\}](BF_4)_2$ (SC) 1021 [G.E. 1055]
Polymetal complexes: Complexation of cluster triangular faces by the tripod ligand, $HC(PPh_2)_3$ (SC) 1024 [G.E. 1058]

Template synthesis of clusters using the tripod ligand $HC(PPh_2)$: $Ni_3(CO)_6$(tripod) (SC) 1025 [G.E. 1059]
Phosphazenes, Cyclotri(phosphazene) complexes with P-coordinated PdX_2 and PtX_2 (SC) 650 [G.E. 655]
Phosphinidene oxide, Complex-stabilization of an aminooxophosphane (~) (SC) 710 [G.E. 738]
Phosphinite complexes, Synthesis and reaction of diorgano-~ of gold (SC) 71 [G.E. 66]
Phosphinous anhydride, Bis(di-tert-butylphosphino)tellurium(II). A derivative of ~ exhibiting umpolung (SC) 554 [G.E. 562]
Phospholane 1-oxides, Synthesis and structure of 3-chloro-4-hydroxy- and 3,4-epoxy-~ (SC) 132 [G.E. 127]
Phospholipid analogues, Polymerizable ~—New stable biomembrane and cell models (SC) 938 [G.E. 962]
Phosphonic anhydrides, New peptide synthesis (SC) 133 [G.E. 129]
Phosphorane, Lithium bis(trimethylsilyl)methylene diphenylphosphoranide, a building block for the synthesis of bis(methylenephosphoranes) (SC) 243 [G.E. 206]
N-Isocyanoiminotriphenyl-~: Synthesis, coordination chemistry, and reactions at the metal (SC) 480 [G.E. 478]
Synthesis of cyclic compounds from triphenyl(phenyliminovinylidene)-~ and carboxylic acids (SC) 822 [G.E. 856]
Double cycloaddition yielding a tricyclic di-~ (SC) 825 [G.E. 860]
Total reversibility of addition and transylidation of trialkyl(alkylidene)phosphoranes to metal-coordinated carbon monoxide (SC) 1019 [G.E. 1063]
Phosphorus compounds, A very crowded molecule: X-ray crystallographic analysis of bis(2,4,6-tri-tert-butylphenyl)phosphinic chloride (SC) 399 [G.E. 405]
Triple-decker sandwich complexes of 4d and 5d metals with cyclo-triphosphorus as μ,η^3-ligand: Structural and magnetic properties (SC) 405 [G.E. 412]
$Ph(Me_3Si)C{=}P{-}Cl$, the first P-halofunctionalized methylenephosphorane (SC) 556 [G.E. 578]
$P_4(N\text{-}i\text{-}C_3H_7)_6$, a P_4X_6 molecule with and without adamantane structure (SC) 571 [G.E. 563]
$(R_2NPO)_3$: Novel heterocycle with λ^3-phosphorus by trimerization of an aminooxophosphane (SC) 709 [G.E. 737]
Phosphorus triiodide and diphosphorus tetraiodide, new reagents for deprotection of acetals and ketals (SC) 1006 [G.E. 1039]
Phosphorylases, Role of pyridoxal phosphate in catalysis of glycogen ~ (FP) 441 [G.E. 429]
Photochemical degradation, UV irradiation of nucleic acids and their components in the presence of air (SC) 829 [G.E. 858]
Photochemical processes, Photophysical and ~ in micellar systems (FP) 675 [G.E. 712]
Photochemistry, Photochemical rearrangements and fragmentations of benzene derivatives and annelated arenes (FP) 243 [G.E. 245]
Cyclopropanimines by photolysis of pyrazolinimines. Thermal reaction of an excited state (SC) 49 [G.E. 55]
~ of sulfonamides and sulfonylureas: A contribution to the problem of light-induced dermatoses (SC) 648 [G.E. 647]
Photoreactions of stilbene with caffeine: Known, and new types of reactions (SC) 714 [G.E. 735]
Photochemotherapy, New photocycloadditions of dibromomaleimides to 1,3-dimethyl-6-azauracil (SC) 1026 [G.E. 1066]
Photocycloadditions, New ~ of dibromomaleimides to 1,3-dimethyl-6-azauracil (SC) 1026 [G.E. 1066]
Photolysis, Direct ~ of uranium hexafluoride as a preparatively utilizable endothermic reaction (SC) 227 [G.E. 226]
~ of water catalyzed by transition metal dithiolenes (SC) 645 [G.E. 664]
Cyclic water cleavage by visible light: Drastic improvement of yield of H_2 and O_2 with bifunctional redox catalysts (SC) 646 [G.E. 663]
Photooxidation of the ligands of bis(o-semiquinonediimine)nickel(II) and -platinum(II) (SC) 221 [G.E. 228]
Photoreduction of ketones and aldehydes to alcohols with selane (SC) 1008 [G.E. 1041]
Phthalocyaninatoiron with pyrazine as a bidentate bridging ligand (SC) 392 [G.E. 391]
Pigments, Developments in the field of inorganic ~ (FP) 190 [G.E. 187]
Plasma proteins, Chemistry and function of human ~ (FP) 87 [G.E. 83]
Platinum, Water gas shift reaction with the aid of selenium/~ catalyst (SC) 1007 [G.E. 1040]
Platinum complexes, Photooxidation of the ligands of bis(o-semiquinonediimine)nickel(II) and -platinum(II) (SC) 221 [G.E. 228]
^{195}Pt-NMR spectroscopy of catalytically active complexes. Extremely large spin-spin coupling between platinum and tin (SC) 316 [G.E. 323]
Photochemical reductive cis-elimination in cis-diazidobis(triphenylphosphane)platinum(II). Evidence of the formation of bis(triphenylphosphane)platinum(0) and hexaazabenzene (SC) 717 [G.E. 745]
Novel SN-ligand: Structure of $PtCl(S_4N_3)$ (SC) 653 [G.E. 644]
Platinum compounds, Transition-metal complexes with pyrazolyl bridging ligands between very different metal centers (SC) 931 [G.E. 931]
Platinum-indium complexes, New dihydrido-bridged binuclear ~ (SC) 721 [G.E. 744]
Polarography of molecules of biological significance (Book Review) 409
Polycarbonates and carbonates from urea and alcohol (SC) 718 [G.E. 742]
Polyethylene, "Living polymers" on polymerization with extremely productive Ziegler catalysts (SC) 390 [G.E. 396]
Polymerization, Stereospecific ~ of propylene: An outlook 25 years after its discovery (FP) 857 [G.E. 869]
Template ~ of rhodium(I) with rigid bent diisocyanide ligands (SC) 633 [G.E. 649]
Polymer-polymer miscibility (Book Review) 494
Polymers, Raw material-polymer interrelationships—Today and tomorrow (FP) 79 [G.E. 75]
Thermal degradation of ~ to polymeric carbon—An approach to the synthesis of new materials (FP) 375 [G.E. 375]
"Living ~" on polymerization with extremely productive Ziegler catalysts (SC) 390 [G.E. 396]
Synthesis of organotrimetal ~ using trimetal vapor-fluid matrix techniques (SC) 402 [G.E. 409]
Polypropylene, Stereospecific polymerization of ~: An outlook 25 years after its discovery (FP) 857 [G.E. 869]
Porphine analogues, B_8S_{16}—An "inorganic porphine" (SC) 481 [G.E. 479]
Porphyrinogen, Mutual interconversion of the chromophoric system of ~ and isobacteriochlorin (SC) 140 [G.E. 139]
1,2,3,7,8,20-Hexahydroporphyrin, an easily formed ligand system isomeric to ~-s (SC) 141 [G.E. 141]
Porphyrins, Metalloporphyrin-catalyzed hydroxylation of cyclohexane by alkyl hydroperoxides: Pronounced efficiency of iron-~ (SC) 909 [G.E. 938]
Potassium compounds, Allylic compounds of magnesium, lithium, and potassium: σ- or π-structures? (SC) 487 [G.E. 497]
Pressure, Chemistry in compressed solutions (FP) 841 [G.E. 887]
Synthesis under high ~: Michael addition (SC) 1013 [G.E. 1046]
Principle of minimum chemical distance (PMCD) (FP) 495 [G.E. 503]
Printing forms, New technologies for the filmless manufacture of ~ (FP) 99 [G.E. 95]
Propellanes, Cyclic oligomers of ~ and bridged annulenes with bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 933 [G.E. 970]
Mixed oligomers of ~ and bridged annulenes with bis(maleimides) and bis(triazolinediones) studied by ^{252}Cf-plasma desorption mass spectrometry (SC) 936 [G.E. 972]
Propene, Selective pathway from methanol to ethylene and ~ (SC) 126 [G.E. 125]
Prostacyclin analogues, New ~ (SC) 819 [G.E. 850]
Protecting group, 4-Sulfobenzyl, a new carboxy ~ (SC) 394 [G.E. 394]
Vitamin B_{12} and a vitamin B_{12} model compound as catalysts of reductive removal of β-haloethyl ~-s from acids (SC) 629 [G.E. 643]
Synthesis of alternating depsipeptides with the 4-methylthiophenoxycarbonyl group as protecting and activating group for the amino function (SC) 932 [G.E. 953]
Phosphorus triiodide and diphosphorus tetraiodide, new reagents for deprotection of acetals and ketals (SC) 1006 [G.E. 1039]
Proteins, Chemistry and function of human plasma ~ (FP) 87 [G.E. 83]
Phlorizin polymer as affinity gel for sugar-binding ~ (SC) 540 [G.E. 547]
Semisynthetic ~ (Book Review) 838
Propylene, Dimerization of ~ with catalysts exhibiting activities like highly-active enzymes (SC) 622 [G.E. 633]
Pseudochalcogen, The PCN group as ~: Cyanophosphinidene-substituted heterocycles (SC) 722 [G.E. 767]
Pteridines, Euglenapterin—An unusual new natural pteridine derivative from Euglena gracilis (SC) 473 [G.E. 474]
Pyrazine, A ~-bridged heme dimer absorbing at 800 nm (SC) 322 [G.E. 320]
Phthalocyaninatoiron with ~ as a bidentate bridging ligand (SC) 392 [G.E. 391]
Pyrazolinimines, Cyclopropanimines by photolysis of ~ thermal reaction of an excited state (SC) 49 [G.E. 55]
Pyrazolyl bridges, Transition-metal complexes with ~ between very different metal centers (SC) 931 [G.E. 931]
1,2,3,6,7,8-Pyrenehexone, 1,2,3,5,6,7-s-Hydrindacenehexone and ~—Two new strong acceptors (SC) 715 [G.E. 768]
Pyridine trihydrate, Novel proton-ordered, two-dimensional cross-linking of water molecules in ~ (SC) 552 [G.E. 559]
Pyridines, Amino-~ (SC) 388 [G.E. 390]
Pyridinium ions, Mechanism of the pyrylium/pyridinium ring interconversion. Mild preparative conditions for conversion of amines into ~ (SC) 306 [G.E. 315]
Pyridino crown ethers, Selective inclusion of alcohols with a new pyridino crown (SC) 1030 [G.E. 1067]
Pyridoxal phosphate, Role of ~ in the catalysis of glycogen phosphorylases (FP) 441 [G.E. 429]
Pyrolysis, Short-path ~: silabenzene (SC) 51 [G.E. 56]
Pyrrolizidines by rearrangement of β-lactams (SC) 129 [G.E. 126]
Pyrylium/pyridinium ring interconversion, Mechanism of ~. Mild preparative conditions for conversion of amines into pyridinium ions (SC) 306 [G.E. 315]
Pyrrolnitrin, Formation of ~ and 3-(2-amino-3-chlorophenyl)pyrrole from 7-chlorotryptophan (SC) 828 [G.E. 855]

RACEMATES, Chromatographic resolution of ~ (FP) 13 [G.E. 14]
Radical anion, Alkali metal-induced transformations of cis-1,2-dibenzoylalkenes: Transformation of 11,12-dibenzoyl-9,10-dihydro-9,10-ethenoanthracene (SC) 907 [G.E. 939]

Radical cation salts of simple arenes—A new family of "organic metals" (SC) 912 [G.E. 941]
Radical ions, Isoelectronic ~ and redox systems (SC) 911 [G.E. 940]
Radical reactivities, Correlation between ~ and copolymerization parameters (SC) 206 [G.E. 215]
Radicals, Unusually rapid cis-trans isomerization of a tetrasilylated ethylene: Generation of free ~ during rotation (SC) 620 [G.E. 632]
~ (Book Review) 229
Radionuclides, Radiotracers in agricultural chemistry (Book Review) 573
Raw materials-polymer interrelationships—Today and tomorrow (FP) 79 [G.E. 75]
Reaction paths on multidimensional energy hypersurfaces (FP) 1 [G.E. 1]
Reactions, Computer simulation of the kinetics of complicated gas phase ~ (FP) 333 [G.E. 331]
Rearrangement, Photochemical ~-s and fragmentations of benzene derivatives and annelated arenes (FP) 243 [G.E. 245]
Theoretical investigation of the diethynylcyclobutadiene(cyclopentadienyl)cobalt ~ (SC) 728 [G.E. 747]
Thermal rearrangement of tetrakis(phenylimino)cyclobutane and crystal structure of tetraphenylsquaramidine (SC) 1012 [G.E. 1045]
Recyclization, 2-Thietanimines from α-deprotonated β-lactones and phenyl isothiocyanate—A novel four-membered ring/four-membered ring ~ (SC) 466 [G.E. 470]
Redox reactions, Reversible topotactic ~ of solids by electron/ion transfer (FP) 983 [G.E. 1015]
Redox systems, Isoelectronic radical ions and ~ (SC) 911 [G.E. 940]
Reducing agent, Carbon monoxide/water as ~: Formation of selane from selenium (SC) 308 [G.E. 317]
Outer sphere electron transfer reactions. A novel linear relationship between selectivity and normal potential of ~-s (SC) 558 [G.E. 580]
Reduction, Selenium-catalyzed ~ of aromatic nitro compounds to amines by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
~ of carbonyl compounds by aluminum telluride and H_2O or D_2O (SC) 1009 [G.E. 1041]
~ of aromatic nitro, nitroso, hydroxylamino, azo, and azoxy compounds with hydrogen telluride from aluminum telluride and water (SC) 1009 [G.E. 1042]
Rhenium compounds, First insertion reaction of carbon monoxide into a rhenium-carbon σ-bond (SC) 824 [G.E. 843]
Rhodium clusters, Synthesis of the first methylidyne-~ by proton-induced H_2/CH_4-elimination from a μ-methylene complex (SC) 651 [G.E. 660]
Simple method of forming metal-to-metal bonds (SC) 937 [G.E. 961]
Rhodium complexes, μ-Arylthio- and μ-arylthio-μ-chlorodicarbonylbis(tri-tert-butylphosphane)dirhodium: dinuclear ~ with different bridging ligands (SC) 70 [G.E. 60]
(1,2,5,6-η-1,5-Cyclooctadiene)(1,2,7-η-7-methylbenzyl)(7,8-η-styrene)rhodium(I)—Antarafacial fluctuation of the benzyl ligand and temperature-dependent coordination of styrene (SC) 468 [G.E. 475]
Rhodium compounds, Synthesis of intermediates by rhodium-catalyzed hydroformylation (FP) 178 [G.E. 182]
Template polymerization of rhodium(I) with rigid bent diisocyanide ligands (SC) 633 [G.E. 649]
Ribonucleic acid, Viroids: A class of subviral pathogens (FP) 231 [G.E. 233]
Ring contraction, (8→5)Contraction of the eight-membered ring of $S_4N_4O_2$ (SC) 943 [G.E. 959]
Rotation, Unusually rapid cis-trans isomerization of a tetrasilylated ethylene: Generation of free radicals during ~ (SC) 620 [G.E. 632]
Ruthenium catalysts, $Ru_3(CO)_{12}$-catalyzed synthesis of vinylsilanes from olefins and hydrosilanes (SC) 928 [G.E. 974]

SALTS, Influence of density and temperature on the properties of pure molten ~ (FP) 606 [G.E. 612]
Sandwich complexes, Triple-decker ~ of 4d and 5d metals with cyclo-triphosphorus as μ,η^3-ligand: Structural and magnetic properties (SC) 405 [G.E. 412]
Bis(η-cyclopentadienyliron-μ,η-thiadiborolene)iron—Structure of a η-C_5H_5 tetradecker sandwich complex (SC) 746 [G.E. 758]
Selane, Carbon monoxide/water as a reducing agent: Formation of ~ from selenium (SC) 308 [G.E. 317]
Water gas shift reaction with the aid of selenium/platinum catalyst (SC) 1007 [G.E. 1040]
Selenium-catalyzed reduction of aromatic nitro compounds to amines by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
Photoreduction of ketones and aldehydes to alcohols with ~ (SC) 1008 [G.E. 1041]
Selectivity, Outer sphere electron transfer reactions. Novel linear relationship between ~ and normal potential of reducing agents (SC) 558 [G.E. 580]
1,2,3-Selenadiazoles, Reactions of cycloalkeno-~ with transition metal carbonyls (SC) 632 [G.E. 650]
Selenium, Carbon monoxide/water as a reducing agent: Formation of selane from ~ (SC) 308 [G.E. 317]
Water gas shift reaction with the aid of ~/platinum catalyst (SC) 1007 [G.E. 1040]
~-catalyzed reduction of aromatic nitro compounds to amines by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
Selenium bromide, Molecular and crystal structure of β-~ (SC) 645 [G.E. 646]
Selenium compounds, 6-Fulveneselone (SC) 69 [G.E. 52]
Unusually bridged tungsten complexes with $W(ER)_2W(ER)_3W$ skeleton (E=S or Se; R=C_2H_5, n-C_4H_9 or C_6H_5) (SC) 397 [G.E. 403]
Selenoantimonate(III) anions, Novel ~ in $Na_4Sb_4Se_{11}$ (SC) 324 [G.E. 310]
Semibullvalenes, One-pot synthesis of substituted ~ (SC) 456 [G.E. 464]
Semiconductors, Liquid metals and liquid ~ (FP) 593 [G.E. 598]
Semiquinone, Photooxidation of the ligands of bis(o-~-diimine)nickel(II) and -platinum(II) (SC) 221 [G.E. 228]
Short-path pyrolysis: silabenzene (SC) 51 [G.E. 56]
Si_4 clusters, $Li_{12}Si_7$, a compound having trigonal planar Si_4 cluster and planar Si_5 rings (SC) 1033 [G.E. 1070]
Silabenzene, Short-path pyrolysis: ~ (SC) 51 [G.E. 56]
~ (SC) 52 [G.E. 58]
Silica, Chemistry of ~ (Book Review) 230
Silicates, Amorphous silver ~, storage elements with low switching field strength (SC) 386 [G.E. 386]
Silicon compounds, Matrix isolation of OSiS: IR spectroscopic evidence for the Si=S double bond (SC) 323 [G.E. 310]
Zintl phases with complex anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$ (SC) 490 [G.E. 480]
Unusually rapid cis-trans isomerization of a tetrasilylated ethylene: Generation of free radicals during rotation (SC) 620 [G.E. 632]
$Li_{12}Si_7$, a compound having trigonal planar Si_4 cluster and planar Si_5 rings (SC) 1033 [G.E. 1070]
Planar tetracoordinated silicon? (SC) 1033 [G.E. 1070]
Planar tetracoordinated silicon—A reply (SC) 1034 [G.E. 1071]
Silver catalyst, Acetaldehyde as main product of oxidation of ethylene oxide on a ~ (SC) 407 [G.E. 389]
Silver silicates, Amorphous ~, storage elements with low switching field strength (SC) 386 [G.E. 386]
Silyl derivatives, Synthesis and properties of the first organosilyl-gallium compounds (SC) 55 [G.E. 62]
Tetrakis(trimethylsilyl)borate and other trimethylsilylborates (SC) 58 [G.E. 65]
Singlet oxygen, Oxidation reactions of benzvalene: Ozonolysis, cis-hydroxylation, epoxidation, and ~ addition (SC) 458 [G.E. 466]
Size exclusion chromatography, Determination of morphological properties of swellable solids by ~ (FP) 24 [G.E. 25]
Slime mold, Indole pigments from the fruiting bodies of the ~ Arcyria denudata (SC) 459 [G.E. 463]
Solids, Reversible topotactic redox reactions of ~ by electron/ion transfer (FP) 983 [G.E. 1015]
Solid state chemistry, High-resolution transmission electron microscopy re-examined as a tool in ~ (FP) 505 [G.E. 531]
Solubility of nonvolatile biochemical substances in compressed carbon dioxide (SC) 623 [G.E. 633]
Solvolysis, Coupling of ~ and C—C linkage: A promising synthetic route to functionalized carboxylic acids, aldehydes, and ketones (FP) 171 [G.E. 169]
Spectroscopy, Polarized low-temperature crystal spectra of inorganic complexes (FP) 290 [G.E. 290]
Spirohydrocarbons, (+)-(2R)-5,5′-Dimethyl-2,2′-spirobi(2,3-dihydro-1H-cyclopenta[a]-naphthalene)—A chiral spirohydrocarbon containing orthogonal naphthalene units (SC) 308 [G.E. 318]
Spiropentene (SC) 928 [G.E. 969]
Squaramidine, Thermal rearrangement of tetrakis(phenylimino)cyclobutane and crystal structure of tetraphenyl-~ (SC) 1012 [G.E. 1045]
Stabilization, Cycloadditions with silver-ion stabilized (2RS,3RS)-3-methoxy-trans-cycloheptene (SC) 1032 [G.E. 1068]
Stereoselectivity, Highly stereoselective aldol condensation using an enantioselective chiral enolate (SC) 557 [G.E. 573]
"Synthetic enzymes". Highly stereoselective epoxidation of chalcone in a triphasic toluene-water-poly[(S)-alanine] system (SC) 929 [G.E. 968]
Steroid synthesis, Photochemical route to (±)-estrone (SC) 1027 [G.E. 1060]
Asymmetric total synthesis of (+)-estrone (SC) 1029 [G.E. 1062]
Stilbene, Photoreactions of ~ with caffeine. Known, and new types of reactions (SC) 714 [G.E. 735]
Strained hydrocarbons, Synthesis of unusual organic molecules from azoalkanes (FP) 762 [G.E. 815]
Strained organic molecules (Book Review) 75
Strontium compounds, Zintl phases with complex anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$ (SC) 490 [G.E. 480]
Structure-activity relationships, Chemische Struktur und biologische Aktivität von Wirkstoffen. Methoden der Quantitativen Struktur-Wirkung-Analyse (Book Review) 572
Styrene, (1,2,5,6-η-1,5-Cyclooctadiene)(1,2,7-η-7-methylbenzyl)(7,8-η-styrene)rhodium(I)—Antarafacial fluctuation of the benzyl ligand and temperature-dependent coordination of ~ (SC) 468 [G.E. 475]
Substituent effect, Base-catalyzed conversion of an equatorial into an axial methoxycarbonyl group due to a 1,5-long-range ~ (SC) 543 [G.E. 577]

Sulfinates, Direct synthesis of the perfluoroalkane-~ of iron(II), cobalt(II), and nickel(II): SO_2-assisted addition of alkyl halides to transition metals (SC) 128 [G.E. 124]
N-Sulfinylnonafluorobutanesulfonamide—A superenophile (SC) 732, 840 [G.E. 748]
3-Oxa-ene reactions of N-sulfinylnonafluorobutanesulfonamide with alkanones—General synthesis of 2-oxoalkanesulfinic acid derivatives (SC) 737 [G.E. 750]
Sulfonamides, Photochemistry of ~ and sulfonylureas: A contribution to the problem of light-induced dermatoses (SC) 648 [G.E. 647]
N-Sulfinylnonafluorobutanesulfonamide—A superenophile (SC) 732, 840 [G.E. 748]
3-Oxa-ene reactions of N-sulfinylnonafluorobutanesulfonamide with alkanones—General synthesis of 2-oxoalkanesulfinic acid derivatives (SC) 737 [G.E. 750]
4-Sulfobenzyl, a new carboxy protecting group (SC) 394 [G.E. 394]
Sulfonium salts, Synthesis and rearrangement of azulene-~ (SC) 621 [G.E. 635]
Sulfonylureas, Photochemistry of sulfonamides and ~: A contribution to the problem of light-induced dermatoses (SC) 648 [G.E. 647]
Sulfur-atom transfer, Activation and ~ of cluster-bonded S_2^{2-}-bridge ligands: synthesis of the new cluster $[Mo_3^{IV}S_4(CN)_9]^{5-}$ from $[Mo_3^{IV}S(S_2)_6]^{2-}$ and CN^- (SC) 72 [G.E. 69]
Sulfur compounds, Crystal structure of 2-lithio-2-methyl-1,3-dithiane tetramethylethylenediamine (SC) 53 [G.E. 59]
Tetrathiafulvalenoparacyclophanes (SC) 66 [G.E. 49]
[2.2]- and [3.3]-Tetrathiafulvalenophanes (SC) 67 [G.E. 51]
Activation and sulfur-atom transfer reaction of cluster-bonded S_2^{2-}-bridge ligands: synthesis of the new cluster $[Mo_3^{IV}S_4(CN)_9]^{5-}$ from $[Mo_3^{IV}S(S_2)_6]^{2-}$ and CN^- (SC) 72 [G.E. 69]
Synthesis and crystal structure analysis of decathia-cyclotetradecane-6,7,13,14-tetraone, $S_{10}(CO)_4$ (SC) 125 [G.E. 122]
Addition of alkanethiols to diketene (SC) 127 [G.E. 123]
α-Carbamoyloxymethyl-substituted lithium enethiolates from 1-(N,N-dimethylcarbamoylthio)-2-methyl-1-propenyllithium (SC) 303 [G.E. 305]
Unusually bridged tungsten complexes with $W(ER)_2W(ER)_3W$ skeleton (E = S or Se; R = C_2H_5, n-C_4H_9 or C_6H_5) (SC) 397 [G.E. 403]
New aspects of the reaction of difluorosulfur imides with fluorine (SC) 408 [G.E. 393]
B_8S_{16}—An "inorganic porphine" (SC) 481 [G.E. 479]
N-Fluoroiminosulfur tetrafluoride, F—N=SF_4 (SC) 643 [G.E. 659]
A novel SN-ligand: Structure of $PtCl(S_4N_3)$ (SC) 653 [G.E. 644]
Sulfur-fluorine compounds, Tris(fluorosulfonyl)methane, $HC(SO_2F)_3$ (SC) 942 [G.E. 954]
Sulfur monoxide, First fixation of the unstable species ~ in a cluster: Synthesis and structure of $Fe_3(CO)_9(S)SO$ (SC) 226 [G.E. 225]
Sulfur-nitrogen-fluorine compounds, Chemistry of thiazyl fluoride (NSF) and thiazyl trifluoride (NSF_3): A quarter century of (FP) 883 [G.E. 904]
Sulfur-nitrogen rings, (8→5)Contraction of the eight-membered ring of $S_4N_4O_2$ (SC) 943 [G.E. 959]
Sulfur oxides, Dimerization of S_6O to $S_{12}O_2$: Crystal structure analysis of $S_{12}O_2 \cdot 2SbCl_5 \cdot 3CS_2$ (SC) 325 [G.E. 313]
Supercritical fluid chromatography, Physicochemical principles and applications (SFC) (FP) 575 [G.E. 585]
Superenophile, N-Sulfinylnonafluorobutanesulfonamide—A superenophile (SC) 732, 840 [G.E. 748]
Swellable solids, Determination of morphological properties of ~ by size exclusion chromatography (FP) 24 [G.E. 25]
Symbolic language of the chemist (FP) 110 [G.E. 106]
Synthetic enzymes. Highly stereoselective epoxidation of chalcone in a triphasic toluene-water-poly[(S)-alanine] system (SC) 929 [G.E. 968]
Synthetic methods, Synthesis of unusual organic molecules from azoalkanes (FP) 762 [G.E. 815]

TACTICITY, Stereospecific polymerization of propylene: An outlook 25 years after its discovery (FP) 857 [G.E. 869]
Tellurium compounds, Bis(di-tert-butylphosphino)tellurium(II): A derivative of phosphinous anhydride exhibiting umpolung (SC) 554 [G.E. 562]
Template polymerization of rhodium(I) with rigid bent diisocyanide ligands (SC) 633 [G.E. 649]
Template synthesis of clusters using the tripod ligand $HC(PPh_2)_3$: $Ni_3(CO)_6$(tripod) (SC) 1025 [G.E. 1059]
Tetra-tert-butylcyclobutadiene, Structure (SC) 211 [G.E. 214]
Tetracyanoethylene, Nitrile function of ~ as dienophile in Diels-Alder reactions (SC) 810 [G.E. 836]
Tetracyclo[6.2.1.$1^{3,6}$.$0^{2,7}$]dodecane, Synthesis of the epimeric 4-methyl derivatives of endo-endo- and exo-endo-~ (SC) 318 [G.E. 306]
Tetradecker complexes, Bis(η-cyclopentadienyliron-μ,η-thiadiborolene)iron—Structure of a η-C_5H_5 tetradecker sandwich complex (SC) 746 [G.E. 758]
Tetrahedrane, Structural changes on oxidation: Flattening of the C_4-cluster of ~ (SC) 209 [G.E. 213]
Tetrakis(phenylimino)cyclobutane (tetrameric phenyl isocyanide) (SC) 136 [G.E. 134]
Thermal rearrangement of ~ and crystal structure of tetraphenylsquaramidine (SC) 1012 [G.E. 1045]
Tetrathiafulvalene, Synthesis of a homologous ~ with central bicyclo[4.4.1]undeca-1(10),3,5,8-tetraene-2,7-diylidene group (SC) 204 [G.E. 199]
Tetrathiafulvalenoparacyclophanes (SC) 66 [G.E. 49]
Tetrathiafulvalenophanes, [2.2]- and [3.3]-~ (SC) 67 [G.E. 51]
Tetrazolo[1,5-a]pyrimidine, ^{15}N-NMR Spectroscopic detection of the ~/2-azidopyrimidine equilibrium (SC) 924 [G.E. 957]
Thermodynamic properties, Influence of isomerism of alkanes on ~ of cyclohexane/alkane mixtures (SC) 223 [G.E. 209]
Thiadiborolene, Bis(η-cyclopentadienyliron-μ,η-~)iron—Structure of a η-C_5H_5 tetradecker sandwich complex (SC) 746 [G.E. 758]
Thiazyl fluoride, Chemistry of ~ (NSF) and thiazyl trifluoride (NSF_3): A quarter century of sulfur-nitrogen-fluorine chemistry (FP) 883 [G.E. 904]
Thiazyl trifluoride, Chemistry of thiazyl fluoride (NSF) and ~ (NSF_3): A quarter century of sulfur-nitrogen-fluorine chemistry (FP) 883 [G.E. 904]
Thiepin derivatives, Thermal additions of dimethyl acetylenedicarboxylate to cyclic thioenol ether 1-oxides with ring expansion (SC) 833 [G.E. 849]
2-Thietanimines from α-deprotonated β-lactones and phenyl isothiocyanate—A novel four-membered ring/four-membered ring recyclization (SC) 466 [G.E. 470]
Thioacetate, Double addition of a nucleophile to carbyne and carbonyl C-atom: S-Phenyl 2-phenyl-2-(phenylthio)-~ from trans-bromotetracarbonyl(phenylcarbyne)-chromium and thiophenolate (SC) 205 [G.E. 206]
Thiocin derivatives, Thermal additions of dimethyl acetylenedicarboxylate to cyclic thioenol ether 1-oxides with ring expansion (SC) 833 [G.E. 849]
Thioenol ethers, Thermal [2+2]-cycloadditions of tetracyanoethylene to cyclic ~ (SC) 831 [G.E. 848]
Thermal cycloadditions of dimethyl acetylenedicarboxylate to cyclic enol ethers and ~ (SC) 832 [G.E. 848]
Thioenol ether 1-oxides, Thermal additions of dimethyl acetylenedicarboxylate to cyclic ~ with ring expansion (SC) 833 [G.E. 849]
Thioketene, Direct detection of dicyano-~ in the gas phase (SC) 740 [G.E. 752]
Thioketones, ^{13}C-NMR study of protonated ~ in superacidic media: Significance of mercaptocarbenium ion contributions (SC) 811 [G.E. 837]
Thiols, Exceedingly mild desulfurization of ~ by sodium triethylhydroborate and transition metal chlorides (SC) 315 [G.E. 321]
Thiomolybdates, MoS_4^{2-} and $MoOS_3^{2-}$ as structurally versatile and biochemically interesting ligands in crystalline multinuclear Cu- and Fe-complexes (SC) 654 [G.E. 665]
Thionyl chloride, Are α-oxothioacyl chlorides formed in the reaction of methyl ketones with ~? (SC) 563 [G.E. 559]
Thiophene derivatives, Thermal [2+2]-cycloadditions of tetracyanoethylene to cyclic thioenol ethers (SC) 831 [G.E. 848]
Thermal cycloadditions of dimethyl acetylenedicarboxylate to cyclic enol ethers and thioenol ethers (SC) 832 [G.E. 848]
Thermal additions of dimethyl acetylenedicarboxylate to cyclic thioenol ether 1-oxides with ring expansion (SC) 833 [G.E. 849]
Thiophenol, Relation between orbital character and reaction product in the reaction of benzvalene and homobenzvalene with ~ (SC) 457 [G.E. 465]
Thiopyran derivatives, Thermal [2+2]-cycloadditions of tetracyanoethylene to cyclic thioenol ethers (SC) 831 [G.E. 848]
Tin complexes, X-Ray structure analysis of bis(O,O'-diphenyldithiophosphato)tin(II), a bicyclic dimer held together by η^6-C_6H_5/Sn^{II} interactions (SC) 309 [G.E. 326]
Tin compounds, Nucleophilic addition of triphenylstannyllithium to carbon disulfide (SC) 220 [G.E. 227]
^{195}Pt-NMR spectroscopy of catalytically active complexes. Extremely large spin-spin coupling between platinum and tin (SC) 316 [G.E. 323]
Cubane-type Sn_4N_3O cage (SC) 401 [G.E. 408]
Tin(II) hydroxide, New variant of the amphoterism of ~: $Sn(OH)_2$ as stannio complex ligand (SC) 553 [G.E. 561]
Titanium compounds, Geminal dialkylation of ketones with Grignard compounds and methyltitanium(IV) chlorides (SC) 900 [G.E. 931]
Chemoselective and position specific methylation of tert-alkyl halides with methyltitanium(IV) chlorides (SC) 901 [G.E. 933]
Chemo- and diastereoselective addition of alkyl- and aryl-titanium compounds to aldehydes and ketones (SC) 1011 [G.E. 1044]
Titanium sulfides, Nonstoichiometric alkali metal ~ with channel structure (SC) 492 [G.E. 477]
Topotactic redox reactions, Reversible ~ of solids by electron/ion transfer (FP) 983 [G.E. 1015]
Total synthesis, Photochemical route to (±)-estrone (SC) 1027 [G.E. 1060]
Trace analysis, Ultratrace analysis: Determination of Cr, Fe, and Co in the ppb and ppt range for checking the preparation of high-purity niobium (SC) 197 [G.E. 194]
Transmission electron microscopy, High-resolution ~ re-examined as a tool in solid state chemistry (FP) 505 [G.E. 531]
Transition elements, Trinuclear clusters of the early ~ (SC) 875 [G.E. 921]
Transition metal π-complexes, Alkali metal-~ (FP) 520 [G.E. 513]

Transylidation, Total reversibility of addition and ~ of trialkyl(alkylidene)phosphoranes to metal-coordinated carbon monoxide (SC) 1019 [G.E. 1063]
1,2,3-Triazolo[4,5-d][1,3]thiazine, a new heterocyclic system (SC) 310 [G.E. 319]
Tricyclo[4.1.0.0^{2,7}]heptane, New C_8H_{10} isomers: 2-Methylenebicyclo[3.2.0]hept-6-ene and 3-methylene-~—Thermal and metal-catalyzed rearrangements (SC) 634 [G.E. 651]
Trifluoromethane, Heterogeneously catalyzed gas-phase bromination of ~ (SC) 147 [G.E. 136]
(Trifluoromethyl)fluorogermanates (SC) 836 [G.E. 859]
Trimethylphosphane complexes of nickel, cobalt, and iron—Model compounds for homogeneous catalysis (FP) 362 [G.E. 362]
Trimethylsilyloxysulfonates, Fluoride-induced fragmentation of ~ to form cis-coupled hexahydroazulenones (SC) 830 [G.E. 832]
Trioxa-tris-σ-homotropone, "α,α,α"-, "α,β,α"-, and "α,α,β"-~ (SC) 214 [G.E. 216]
Triphenyl(phenyliminovinylidene)phosphorane, Synthesis of cyclic compounds from ~ carboxylic acids (SC) 822 [G.E. 856]
Triphenylstannyllithium, Nucleophilic addition to carbon disulfide (SC) 220 [G.E. 227]
Triple-decker sandwich complexes of 4d and 5d metals with cyclo-triphosphorus as μ,η^3-ligand: Structural and magnetic properties (SC) 405 [G.E. 412]
Tripod, Polymetal complexes: Complexation of cluster triangular faces by the ~ ligand, $HC(PPh_2)_3$ (SC) 1024 [G.E. 1059]
Template synthesis of clusters using the ~ ligand $HC(PPh_2)_3$: $Ni_3(CO)_6(\sim)$ (SC) 1025 [G.E. 1059]
Tripropylcarbazoyllithium (SC) 762 [G.E. 764]
Triptycenes, 1,4-Dihydro-1,4-bis(dicyanomethylene)-~. Synthesis and intramolecular charge-transfer interaction (SC) 543 [G.E. 565]
Tris(fluorosulfonyl)methane, $HC(SO_2F)_3$ (SC) 942 [G.E. 954]
Tris[2.1.1]-σ-homobenzenes, cis-/trans-~. Synthesis and stereochemistry of [„2+„2+„2]-cycloreversions (SC) 567 [G.E. 575]
Tris(triazolo]triazine, Trimerization of an Azomethine imine by three successive 1,3-dipolar cycloaddition reactions (SC) 906 [G.E. 936]
Tungsten complexes, $(AsPh_4)[W_2NCl_{10}]$, a μ-nitrido complex containing tungsten(V) and tungsten(VI) (SC) 220 [G.E. 211]
Unusually bridged tungsten complexes with $W(ER)_2W(ER)_3W$ skeleton (E=S or Se; R=C_2H_5, n-C_4H_9, or C_6H_5) (SC) 397 [G.E. 403]

ULLMANN's Encyclopedia of Industrial Chemistry, Ullmanns Encyklopädie der technischen Chemie (Book Review) 148
Ultratrace analysis: Determination of Cr, Fe, and Co in the ppb and ppt range for checking the preparation of high-purity niobium (SC) 197 [G.E. 194]
Umpolung, Bis(di-tert-butylphosphino)tellurium(II). A derivative of phosphinous anhydride exhibiting ~ (SC) 554 [G.E. 562]
Uranium hexafluoride, Direct photolysis of ~ as a preparatively utilizable endothermic reaction (SC) 227 [G.E. 226]
Urea, Carbonates and polycarbonates from ~ and alcohol (SC) 718 [G.E. 742]

VALIENAMINE, Synthesis of chiral ~ (SC) 904 [G.E. 930]
Verdazyls, 6-Oxo-~ (SC) 724 [G.E. 766]
Vesicles with a monolayer, redoxactive membrane (SC) 550 [G.E. 564]
Vinamidinium salts, 1,3-Bis(dialkylamino)-1,3-butadiene from 1-methyl-~ (SC) 216 [G.E. 207]
1,3-Bis(dimethylamino)-2-aza-1,3-butadienes from 1-alkyl-2-aza-~ (SC) 217 [G.E. 208]
Vinylcarbene, Tetrachloro-~ from tetrachlorocyclopropene; facile synthesis of vinylcyclopropanes (SC) 138 [G.E. 135]
Vinylcyclopropanes, Tetrachlorovinylcarbene from tetrachlorocyclopropene; facile synthesis of ~ (SC) 138 [G.E. 135]
2-Vinylidene-2H-indene (SC) 821 [G.E. 846]
Vinylidene phosphorane, Synthesis of cyclic compounds from triphenyl(phenyliminovinylidene)phosphorane and carboxylic acids (SC) 822 [G.E. 856]
Vinylsilanes, $Ru_3(CO)_{12}$-catalyzed synthesis of ~ from olefins and hydrosilanes (SC) 928 [G.E. 974]
Viroids: A class of subviral pathogens (FP) 231 [G.E. 233]
Vitamin B_{12} and a vitamin B_{12} model compound as catalyst of reductive removal of β-haloethyl protecting groups from acids (SC) 629 [G.E. 643]

WATER, Carbon monoxide/~ as a reducing agent: formation of selane from selenium (SC) 308 [G.E. 317]
Photolysis of ~ catalyzed by transition metal dithiolenes (SC) 645 [G.E. 664]
A novel proton-ordered, two-dimensional cross-linking of ~ molecules in pyridine trihydrate (SC) 552 [G.E. 559]
Water cleavage, Cyclic ~ by visible light: Drastic improvement of yield of H_2 and O_2 with bifunctional redox catalysts (SC) 646 [G.E. 663]
Water gas, Selenium-catalyzed reduction of aromatic nitro compounds to amines by CO/H_2O in the presence of triethylamine (SC) 1007 [G.E. 1040]
Water gas shift reaction with the aid of selenium/platinum catalyst (SC) 1007 [G.E. 1040]

XANTHENIDE anion, Generation and direct observation of the ~.—A stable 4nπ-system (SC) 43 [G.E. 53]

YLIDE carbene complexes, Phosphorus ~—Synthesis and structure (SC) 1020 [G.E. 1065]
Ylide complexes, Phosphorus ylide carbene complexes—Synthesis and structure (SC) 1020 [G.E. 1065]
Ylides, Intramolecular cycloadditions of carbonyl ~ (SC) 47 [G.E. 48]

ZEOLITES, Dehydroxylation of hydrogen ~: Conditions for the preparation of thermally stable catalysts (SC) 743 [G.E. 759]
Amorphous ~ (SC) 745 [G.E. 755]
Ziegler catalysts, "Living polymers" on polymerization with extremely productive ~ (SC) 390 [G.E. 396]
Zintl phases with complex anions: $Sr_3Si_2As_4$ and $Sr_3Ge_2As_4$ (SC) 490 [G.E. 480]
Zirconium complexes, "Living polymers" on polymerization with extremely productive Ziegler catalysts (SC) 390 [G.E. 396]